Training Modules for Medical Officers on HIV Care and Treatment (Including ART)

Participant's Guide

May 2007

National AIDS Control Organisation
Ministry of Health & Family Welfare
Government of India

Training Modules for Medical Officers on HIV Care and Treatment, Including ART

*P*artici*p*ant's *G*uide

May 2007

*N*ational A*IDS* Control Organisation
Ministry of Healt*h* & *F*amily *W*elfare
*Go*vernment of India
(*Wit*h su*pp*ort from *W*HO and C*DC*)

Acknowledgments

The roll out of free ART programme by NACO included training of different categories of health care providers. This component on building capacity of health providers is crucial to the success of the programme. A technical committee was constituted at NACO in Dec. 2005 to look into different aspects of ART programme and a sub group on training was constituted. The group looked into various issues like updating the training curriculum and materials, building a pool of master trainers, refresher training and strengthening of the training institutions in order to improve the quality of training. A series of meeting were conducted in Delhi, Chennai and Bangalore followed by extensive e-mail consultation and exchange of material. The modules of training of specialist doctors, medical officers, nurses, lab technicians and counselors have been developed.

This revision of Training modules for Medical Officers on HIV Care and Treatment (including ART) curriculum has been done on the initial version completed in May 2006. Revisions were made to reflect training participants' evaluation feedback, a twelve-day programme, updates in NACO guidelines, develop interactive sessions/case studies, and develop a companion Trainer's Guide. We are thankful to the support of WHO and CDC, I-Tech specially Dr. Dora Warren (CDC), Dr. G. Manoharan, Dr. Swapna, Dr. Vijay, and Ms. Sornaveni (I-Tech). The content review was conducted by the Health Communications and Clinical Team at I-TECH Headquarters. Select sessions were reviewed by the following experts: Dr. Thara Francis (GHTM), Dr. Jessie Lionel (CMC), Ms. Magdalene Jeyarathnam, Consultant, Counselling; Dr. Parthasarathy (Madurai), Dr. Rajasekaran (GHTM), Dr. S. Subramanian (CMC) and Dr. Valsen (CMC, Vellore). We are also thankful to the following in-charges of Training Centres and their training team : Dr. O.C. Abraham (CMC, Vellore) Dr. Richa Dewan, (MAMC, Delhi), Dr. Manisha Ghate (NARI, Pune), Dr. S.K. Guha (STM, Kolkata), Dr. A L Kakrani (BJMC, Pune), Dr. B.D. Mankad (BJMC, Ahmedabad), Dr. A.R. Pazare (KEM Mumbai), Dr. A.K. Tripathi (KGMU, Lucknow), Dr. Ajay Wanchu (PGI, Chandigarh), and the Director, RIMS, Manipur.

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Table of Contents

For Annexures, refer to Trainer's CD-Rom. Copies of the most up-to-date, finalized NACO Guidelines may need to be obtained by Training Centre. Copies of Annexures will need to be copied for all participants and distributed during Registration with the Participant's Guide.

Acronyms

ART: **Antiretro*v*iral T*h*era*p*y**
ARV: **Antiretro*v*iral**
ATT: **Anti-Tuberculosis T*h*era*p*y**
AB*G*: **Arterial Blood *G*as**
AI*DS*: **Acquired Immuno *D*eficiency *S*yndrome**
Ab: **Antibody**
Ag: **Antigen**
A*N*C: **Ante-*N*atal Care**
ALT: **Alanine Transaminase**
A*S*T: **As*p*artate Transaminase**
AZT: **Azidot*h*ymidine or Zido*v*udine**
A*P*V: **Am*p*rena*v*ir**
ABC: **Abaca*v*ir**
ATV: **Atazana*v*ir**
BMI: **Body Mass Index**
BM TRE*P*HI*N*E: **Bone Marrow Tre*ph*ine**
CT/CAT: **Com*p*uterised Tomogra*ph*y/Com*p*uterised Axial Tomogra*ph*y**
CMV: **Cytomegalo Virus**
C*SF*: **Cerebro *Sp*inal *F*luid**
CHO: **Carbo*h*ydrate**
CBHC: **Community Based Healt*h* Care**
C*D*: **Cluster *D*ifferentiation**
D*OT/*D*OT*S: ***D*irectly Obser*v*ed T*h*era*p*y/*Sh*ort course**
***DN*A**: ***D*eoxy Ribo *N*ucleic Acid**
d4T: ***St*a*v*udine**
ddI: ***D*idanosine**
ddC: **Zalcita*b*ine**
***D*LV**: ***D*ela*v*erdine**
DD: ***D*e*p*uty *D*irector**
DSPN: ***D*istal *S*ymmetric *P*oly *N*euro*p*at*h*y**
EBV: Eb**stein** B**arr Virus**
E/R: E**lisa Test/Ra*p*id Test**
E*FV*: E**fa*v*iranz**
ECV: Ex**ternal Ce*ph*alic Version**
ESI: E**m*p*loyees *S*tate Insurance**
***F*TC**: E**mtricita*b*ine**
***F*CM**: ***F*low Cytometry**
G*ER*D: ***G*astro Eso*ph*ageal Refle*x* *D*isease**
HCV: **He*p*atitis C Virus**
HBV: **He*p*atitis B Virus**
HBs Ag: **He*p*atitis B *S*urface Antigen**
HAART: **Hig*h*ly Acti*v*e Antiretro*v*iral T*h*era*p*y**
Hb: **Hemoglo*b*in**
HREZ: **Isoniz*i*d, Rifamycin,** E*th*am*b*u**tol, *P*yrazinamide**

HO*D*: **Head of *Dep*artment**
H*S*V: **Her*p*es *S*im*p*le**x **Virus**
I*D*U: **Injection *D*rug U**ser
IRI*S*: **Immune Reconstitution Inflammatory *S*yndrome**
IU*G*R: **Intra U**terine ***G*rowt*h* Retardation**
I*D*V: **Indina*v*ir**
ICMR: **Indian Council of Medical Researc*h***
ICT: **Integrated Counseling and Testing Center**
J*D*: **Joint *D*irector**
L***P*V**: L**o*p*ina*v*ir**
L***P*V/r**: L**o*p*ina*v*ir/Ritona*v*ir**
L*F*T: Li*v*er ***F*unction Tests**
L*N FN*AC/*FN*A: Lym***p****h*node ***F*ine needle As*p*iration Cytology**
L*N*E: Lym***p****h*node E**nlargement
MEMS*S*: **Medicated E*v*ent Monitoring *S*ystem**
MRI: **Magnetic Resonance Imaging**
Mod. Z*N*: **Modified Zie*h*l *N*eelson *S*taining**
MAC: **Myco*b*acterium A*v*ium Com*p*le**x
M&E: **Monitoring and E*v*aluation**
MSM: **Men w*h*o *h*a*v*e *S*ex wit*h* Men**
*N***AC*P***: *N*ational AI*DS* Control *P*rogramme**
*N***RTI**: *N*ucleoside Re*v*erse Transcri*p*tase In*h*i**b**itor**
*NN***RTI**: *N*on *N*ucleoside Re*v*erse Transcri*p*tase In*h*i**b**itor**
*N***tRTI**: *N*ucleotide Re*v*erse Transcri*p*tase In*h*i**b**itor**
*N***V*P***: *N*e*v*ira*p*ine**
*NF***V**: *N*elfina*v*ir**
*N***ACO**: *N*ational AI*DS* Control Organi**z**ation**
*N***GO**: *N*on ***G****o**v*ernmental Organi**z**ation**
*N***AT**: *N*ucleic Acid Am*p*lification Tec*h*nologies**
*NS***AI*D***: *N*on *S*teroidal Anti inflammatory *D*rugs**
OI: **O*pp*ortunistic Infections**
O*P*D: **Out *P*atient *Dep*artment**
***P*I**: ***P*rotease In*h*i**b**itors**
PCP: ***P*neumocystis Carinii *P*neumonia (*P*neumocystis Jero*v*ici *P*neumonia)**
P*E*P: ***P*ost-Ex*p*osure *P*ro*p*hylaxis**
***P*HC**: ***P*rimary Healt*h* Centre**
***PP*TCT**: ***P*re*v*ention of *P*arent-to-C*h*ild Transmission**
P*LHA/*P*LW HA**: ***P*erson(s) Li*v*ing *W*it*h* HIV/AI*DS
***PP*E**: ***P*ersonal *P*rotecti*v*e Equi*p*ments**
***P*aO2**: ***P*artial *p*ressure of O**xygen
QA/QC: **Quality assessment and Quality Control**
RTV: **Ritona*v*ir**
R*N*A: **Ri**bo ***N*ucleic Acid**
*S***AC*S***: ***S*tate AI*DS* Control *S*ocieties**
*S***TI**: ***S*exually Transmitted Infections**

*S***QV**: *S*aquina*v*ir
*S***QV/R**: *S*aquina*v*ir/Ritona*v*ir
*S***AT**: *S*elf Administered T*h*era*p*y
TM*P*-*S*MX: Trimet*h*o*p*rim and *S*ul*ph*amet*h*oxazole Combination
TLC: Total Lym*ph*ocyte Count
TB: Tuberculosis
T-20: Enfu*v*iritide
T*DF*: Tenofo*v*ir
T*P***V**: Ti*p*rana*v*ir
U***P***: Uni*v*ersal *P*recautions
U/*S* Abd: Ultra *S*ound of t*h*e Abdomen
V*D***RL**: Venereal *D*isease Researc*h* Laboratory
VCT: Voluntary Counseling and Testing
*W***HO**: *W*orld Healt*h* Organization

Background of the Global and Indian HIV Epidemic

Nearly six million people are estimated to be living with HIV/AIDS in South-East Asia Region and it is estimated that around 600,000 people are in need of HIV/AIDS care and antiretroviral therapy.

In India, the estimated number of HIV infections as of November 2006 is 5.2 million. The distribution of HIV infection and mode of transmission varies by state. Most HIV infections in India (more than 80% of reported AIDS cases) are due to unprotected heterosexual transmission (UNAIDS, 2006 Report on Global AIDS Epidemic). HIV prevalence tends to be higher in the industrialized, peninsular states. The six states with the highest HIV prevalence are: Maharashtra, Andhra Pradesh, Tamil Nadu, Karnataka, Manipur, and Nagaland.

In India, (30,000-35,000) people living with HIV/AIDS are accessing ART from public sector hospitals/ clinics. NACO proposes to deliver ARV therapy through effectively functioning health infrastructure and properly trained and motivated staff. Building capacity to train all cadres of health professionals in HIV/AIDS care and simplified, standardised ARV therapy is urgent in the Indian context. This Specialists Training is one part of the overall NACO training agenda and will hopefully contribute to the development of a knowledgeable medical team responsive to the HIV epidemic.

About This Training

Who this Training is For

This training is designed for Medical Officers working at NACO ART Centers.
The aim of this training is to provide a general overview of HIV care and treatment to enhance the skills of health care specialists in comprehensive diagnosis and management of HIV, including ART. This is an intensive, two-week training programme, including an extensive hands-on component, to address ART and HIV care, treatment and support.

Training Objectives

- Provide an overview of the HIV/AIDS epidemic and efforts to contain it
- Enhance skills of health care personnel in comprehensive diagnosis and management of HIV infection and associated diseases including opportunistic infections
- Provide detailed background information on the need for ART, rationale for use of ART and adherence
- Acquaint the participants with National Strategies for HIV/AIDS comprehensive care at different levels
- Focus on modalities of operationalising ART strategies at the state level
- Facilitate capacity building of institutions for training of health care workers in the context of providing ART and HIV/AIDS related care

How This Training is Organised

The design of this training reflects the assumption that the participants are junior Medical Doctors, mostly undergraduates and likely have some experience in providing care and treatment to persons with HIV. A variety of approaches to teaching and learning will be utilised, with the underlying assumption that participants are adult learners who will take considerable responsibility for their own learning. The focus will be on active learning and should emphasise the key knowledge and skills needed for Medical Officers caring for individuals living with HIV/AIDS.

This training consists of 36 classroom-based sessions and 12 hands-on learning sessions in the hospital/ clinic setting. Sessions are 30-120 minutes long and include the following teaching/learning methods:

- Lecture
- Case studies
- Role plays
- Large and small group discussions
- Individual work
- Videos
- Clinical site visits and bedside teaching

Each classroom session is structured in the following manner:

- Session Objectives
- Content interspersed with interactive aspects (e.g., case studies, discussion questions)
- Key Points

Each clinic-based session is structured in the following manner:

- Classroom session on previous day addresses content to be observed during clinic visits on following day. For example, Day 1 has a classroom session on Universal Precautions and Biomedical Waste Disposal. This is then observed during hospital rounds during the morning of Day 2.
- Use of Hands-On Training Checklists and Worksheets to document observations in clinic setting
- Debriefing session to discuss observations seen in the clinic

Summary of Training Materials

A. Slides

PowerPoint slides are provided for each module. These are replicated in a small version in the Participant's Guide and the Trainer's Guide.

B. Participant's Guide

Participants should receive a Participant's Guide, which serves as the primary textbook for this training. This Guide was developed to enhance learning and participation in the training and includes the objectives, steps, key points, slides, Reader's Notes, and Handouts. Encourage participants to take notes in their Guides during sessions.

C. **Trainer's Guide**

This Trainer's Guide was developed to enhance teaching and effective facilitation of the 12-day training. This Guide contains a sample training schedule, information about the training and how to prepare, trainer's steps for each session, Handouts, Trainer's and Reader's Notes, and copies of the slides. Note: the Trainer's Guide contains everything in the Participant's Guide, in addition to Trainer's Notes and Trainer's Versions of the Handouts with Answers.

D. **Annexures**

Annexures are included in the Trainer's CD-Rom and should be provided by the Training Centre to participants as part of the training materials. These include Training Schedule, Evaluation Forms, Hands-On Training Checklists, and NACO Guidelines. These are also listed in the Table of Contents.

How This Training is Evaluated

There are two methods used to assess and evaluate participant learning and the effectiveness of the training. Each of these evaluations is included here and a soft copy is available in the folder: "Evaluation Tools."

A. ***P*re- & *P*ost-Test**

A pre- and post-test will enable Training Coordinators to evaluate the transfer of knowledge. Provide participants 30 minutes at the beginning of Day 1 and at the end of Day 12 to complete these tests. Ideally, the Pre-Test responses will be aggregated by the end of Day 1. This will give the Trainers information on participant knowledge and gaps in knowledge. At the end of the Post-Test, review answers to the assessment together as a group and/or distribute to participants as take-home materials.

Training Centre staff shall give each participant a unique number (e.g., 1, 2, 3,) for the pre-test and write the number on the participant's folder. At the time of taking the pre-test, the participant should be asked to write the same number on the post-test. This will help to track change in knowledge across participants.

Training staff shall summarize pre-test data by Day 2 so the information can be shared with trainers. This way, trainers will know what to emphasize based on gaps in knowledge. Post-test data shall be tallied by the Training Centre staff within one week of the training.

B. **Daily Evaluation Form**

The anonymous Daily Evaluation Form should be completed at the end of each day as indicated in the schedule. This Form asks participants to describe what they liked and what questions they have. It also asks participants to rank their knowledge/skills in the training topic areas before and after the session. The last Daily Evaluation Form also asks participants to assess their overall training experience.

SESSION 1-5

DAY - ONE

SESSION

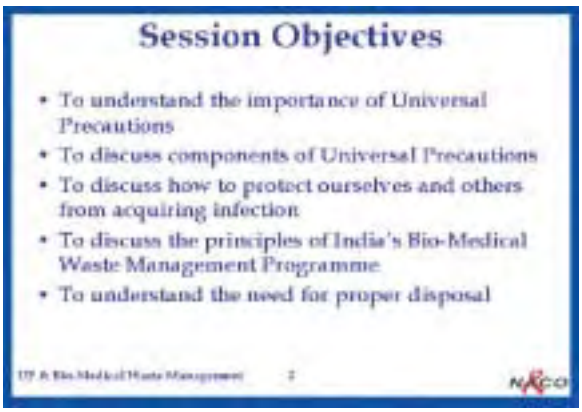
UNIVERSAL PRECAUTIONS AND BIO-MEDICAL WASTE MANAGEMENT

1

Total Session Time: 1 hour 15 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Understand the importance of Universal Precautions
- Discuss components of Universal Precautions
- Discuss how to protect from acquiring infection
- Discuss the principles of India's Bio-Medical Waste Management Programme
- Understand the need for proper disposal

Slide 1		
Slide 2		

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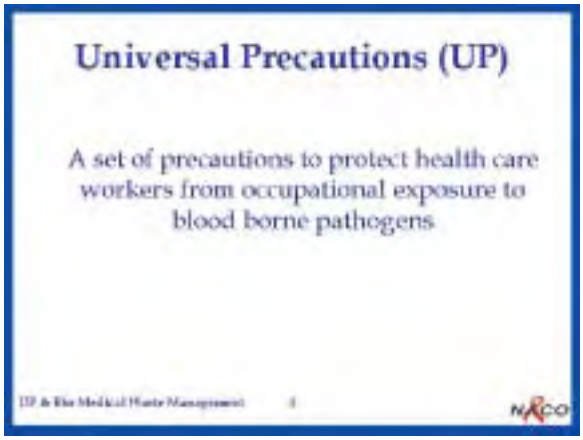
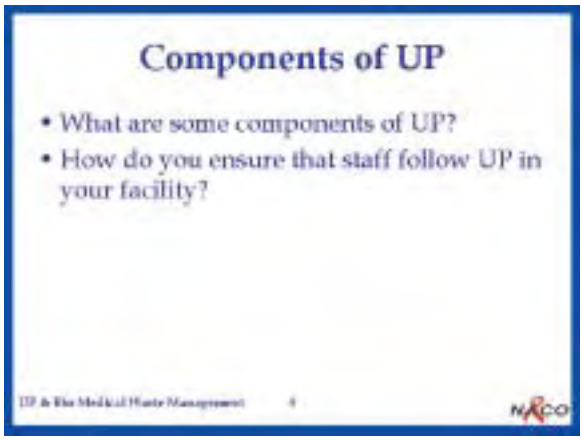
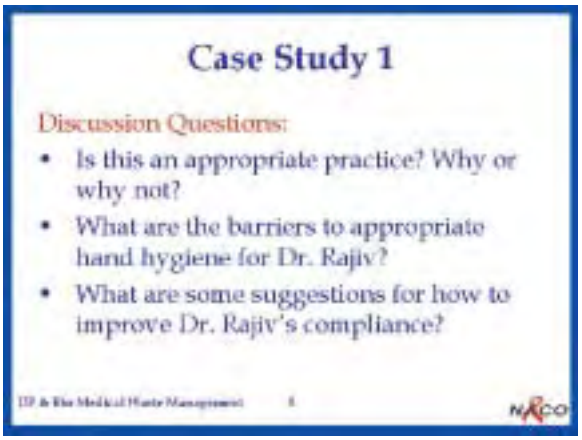


Reader's Notes:

- Universal precautions are methods of personal protection, barrier techniques and work practices that reduce the risk of transmission of microorganisms across cutaneous, mucous membrane and respiratory surfaces.
- Universal precautions are designed to reduce the risk of transmission of blood borne pathogens (blood and body fluids) and are applied to ALL patients regardless of their known or presumed status.
- An occupational exposure may place a health care provider at risk to HBV, HCV or HIV when a type of body fluid capable of transmitting the virus comes into contact through the following ways:
- **A percutaneous exposure**
  - Involves tissue under the skin (E.g. through a needle stick or a cut).
- **A mucocutaneous exposure**
  - Involves mucous membranes (E.g. through a splash to the eyes, nose or mouth)**.**
- **Non-intact skin**
  - (E.g. when the skin is chapped, scraped or afflicted with dermatitis).
- Injuries can occur through these various routes but can be prevented by making use of various components of Universal Precautions.

Slide 4



Slide 5		**Reader's Notes:** • Refer to **Handout 1: Case Studies on Universal Precautions**.

Handout 1: Case Studies on Universal Precautions

Instructions:

- The instructions for conducting this activity which appears on Slide number 5, 7 and 11.
- Refer participants to Handout 1: Case Studies on Universal Precautions.
- Ask participants to read through Case Study 1.
- Ask for volunteers to answer Case Study 1 questions.
- Be sure to facilitate an open discussion before reviewing any of the answers.
- Return to this Handout on Slide 7 and Slide 11 to conduct the same activity for Case Study 2 and Case Study 3.

Case 1

Dr. Rajiv works in a maternity clinic. The building is old and none of the sinks are located in or near the examination rooms. Though Dr. Rajiv examines many clients during the day, he does not routinely wash his hands before or after examining them. Dr. Rajiv finds washing his hands inconvenient and, besides, his hands don't look dirty.

Questions

Q. 1. Is this an appropriate practice? Why or why not?

Q. 2. What are the barriers to appropriate hand hygiene for Dr. Rajiv?

Q.3. What are some suggestions for how to improve Dr. Rajiv's compliance?

Case 2

At the Maternity Clinic, used surgical instruments are processed by placing them in a metal basin filled with an antiseptic solution. They are left in the solution until they are used in another procedure.

Q.1. Is this an appropriate practice? Why or why not?

Case 3

Ms. Ramachandran, as the new district supervisor, made her first visit to the Maternity Clinic. Upon visiting the waste disposal site, she found a large pit , half full with a layer of leaves and other garden debris. She saw a gardener dump a wheelbarrow full of debris into the pit. Then, against the outside of the fence, she found a pile of medical waste, complete with bloody dressings, waste from the labour room and exposed needles attached to IV tubing.

Q.1. What are the waste-disposal issues here?

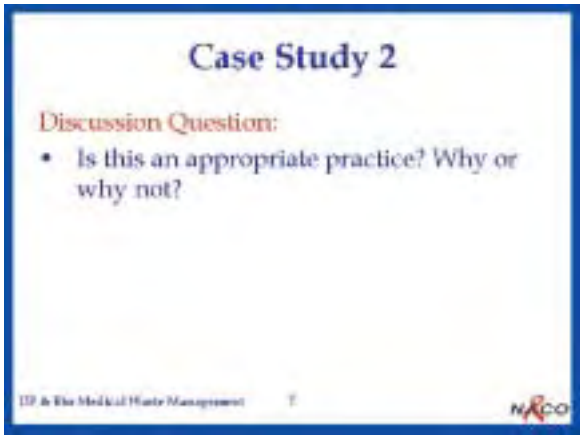
Q.2. What could be done about this situation?

Slide 6

Reader's Notes:

- Transmission of health-care related pathogens from one patient to another via the hands of a health-care staff is a **common**, but **preventable** problem.
- A common mistake is to use gloves rather than take the time to wash hands.
- Always wash and dry your hands after removing gloves because:
  - The germs on your hands will grow well in a hot moist environment (under the gloves) and the amount of germs will increase while you wear gloves.
  - Gloves often develop tears so germs enter and contaminate the hands.
- Used utility gloves should be considered heavily contaminated **inside and out**, and hands should be washed after wearing them.

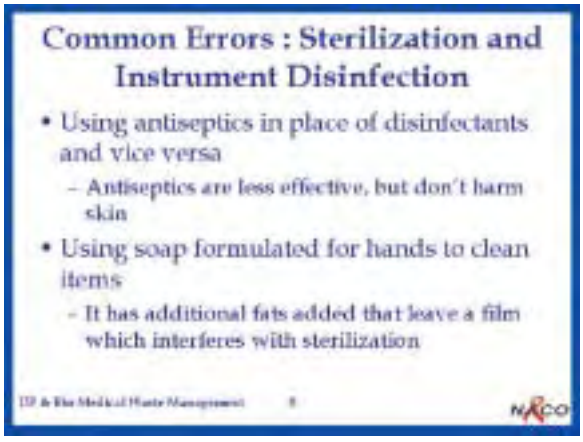
Slide 7



Reader's Notes:

- Refer to **Handout 1: Case Studies on Universal Precautions**.

Slide 8

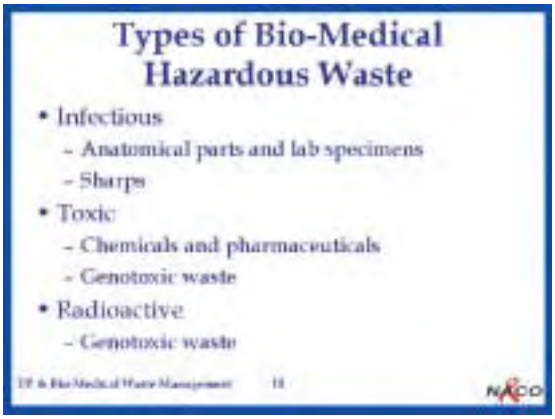


Reader's Notes:

- When cleaning instruments and using disinfectants, be sure to wash them in clean/sterile water to remove any remnants of the chemical which may harm the patient's mucosa or skin **before** using the instrument on a patient.
- The appropriate concentration of disinfectants applied for the appropriate duration kill germs.

Slide 9

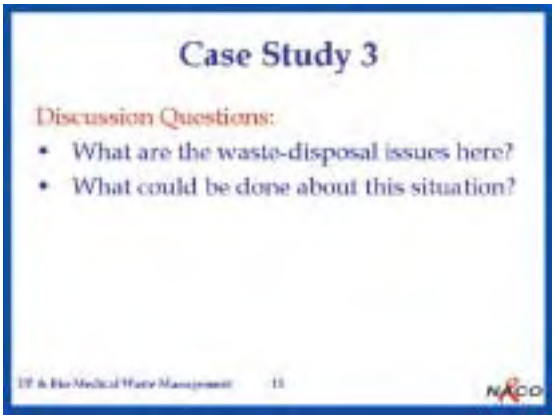
Slide 10



Reader's Notes:

- **Sharps:**
  - Sharps should ideally be stored in puncture proof containers. These containers are usually painted blue/ white and have a biohazard symbol on them.
  - Larger boxes may be kept in the nurse's station and treatment rooms, and smaller ones in injection trolleys, according to need.
  - Ideally these should be available at strategic points (near point of use), thereby avoiding the need for the health care workers to walk around with a sharp, posing a risk to oneself and others.
- **Genotoxic waste:**
  - Waste generated by Nuclear Medicine department, Radioimmunoassay (RIA), Tracer Applications, Calibration Sources, Bio-medical Research, Sources used in Teaching, etc. Information on how and where to apply for radioactive waste is available from the Govt of India Atomic Energy Regulatory Board website. A formal application needs to be sent to the **Govt of India Atomic Energy Regulatory Board — Application for Authorisation to Dispose of Radioactive Wastes under G.S.R.125 - Atomic Energy (Safe Disposal of Radioactive Wastes) Rules, 1987 - Rule 4.**

Slide 11



Reader's Notes:

- Refer to **Handout 1: Case Studies on Universal Precautions** .

Slide 12

Slide 13

Reader's Notes:

- Colour coded bins and bags (as per Indian govt. guidelines) are available through the Ministry of Forestry and Environment website. (Refer Annexure: **Bio-Medical Waste (Management and Handling) Rules, page 5-6**)
- The different colours are:
  1) Red or Pink — contaminated plastics.
  2) Yellow — anatomical and infectious but non-plastic waste. Segregation should take place under supervision.
  3) Blue or White puncture proof container for sharps. Should be placed near point of use.
  4) Black — for toxic and radioactive waste (hazardous non-infectious waste). No breakable items should go into this black bag or bin. Glass materials should go into cardboard boxes.
- All colour-coded bins and bags must have bio-hazard sign on them.
- Segregation helps reduce the bulk of infectious waste and contains spread of infection to general waste.
- This practice reduces the total treatment cost, the impact of waste in the community and workers' risk of becoming infected.
- Weighing the waste helps to keep stock of the amount of waste being collected in each category, to encourage the facility to minimize waste and to use the treatment facility to optimum.
- The quanta of waste from high income countries is up to 6 Kg/person/year while in low income countries is approximately 0.5 to 3.0 Kg/person/year.
- The Indian government may charge from Rs 2.50-5.00 per bed for the treatment of waste from a health care facility. Waste amount varies from state to state.

Slide 14

Reader's Notes:

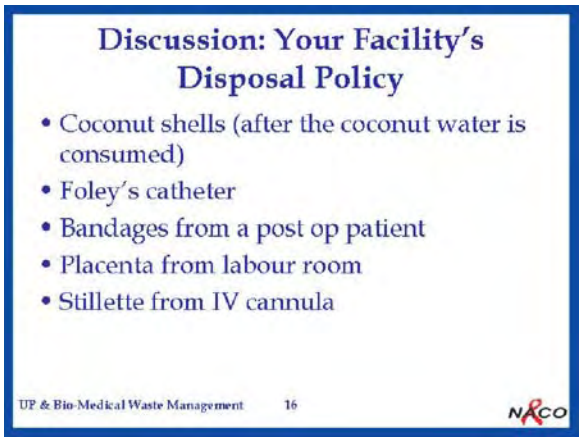
- Transportation should be done:
  - According to guidelines to ensure safety of the health workers and to avoid contamination of the environment.
  - At regular intervals. Proper containers should be used for filling in. All precautions should be taken to prevent spillage at the time of transfer and transport.
- The bags should be appropriately identified and labeled at the site of collection.
- Transportation should be done by trained personnel under supervision and through designated areas only, to minimize the chance of a mishap. The bags should be handled properly, preferably with claps to prevent injury to handler. The bags should never make contact with the body of the personnel, and mixing of the different categories should be prevented, and to this effect, custom made transportation trucks may be considered.

Slide 15

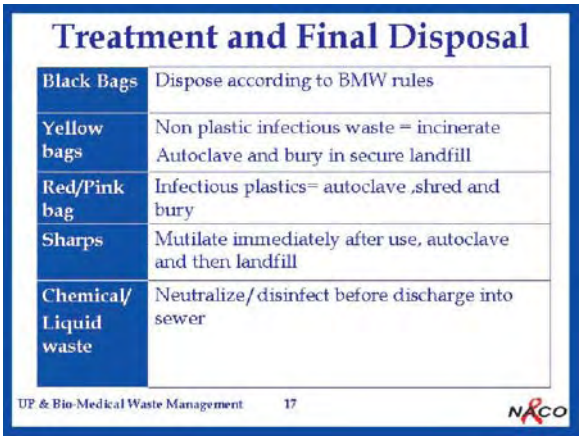
Reader's Notes:

- Bio-medical hazardous waste needs to be stored temporarily before disposal as it may not be feasible to discard all wastes on a daily basis.
- A designated yard should be used for storage of items and no segregation should occur at this point.
- No untreated bio-medical waste can be stored at the facility beyond a period of 48 hours (Bio-Medical Waste (Management and Handling) Rules, 1998 (amendment 2003) by the Ministry of Forestry and Environment **(Refer Annexure: Bio-Medical Waste (Management and Handling) Rules).**

Slide 16



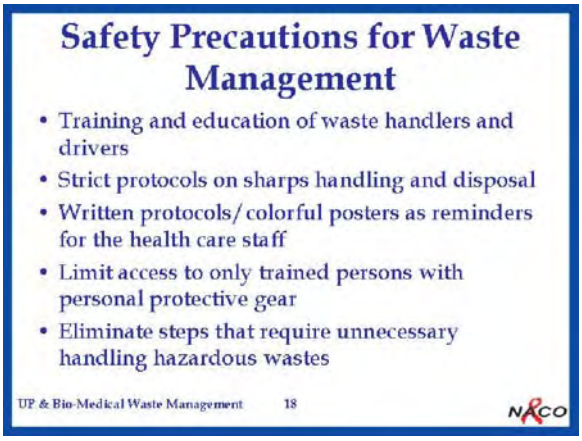
Slide 17



Reader's Notes:

- Waste in the black bag may vary, therefore it should be labeled with information on where the waste originated, along with its contents.
- According to Bio-Medical Waste (Management and Handling) Rules, 1998 (amendment 2003) by the Ministry of Forestry and Environment **(Refer Annexure: Bio-Medical Waste (Management and Handling) Rules).**
- Infectious non-plastic waste needs to be incinerated but since the Government of India has banned incineration, so the best option is to make them noninfectious before disposing them in a landfill.
- Standards for treatment and disposal of bio-medical waste and for waste autoclaving are available at the website.
- Liquid waste/effluents: The treatment could consist of:
- Chemical disinfection using pre-chlorination with a contact time of 15 to 45 minutes and dosing of 6-25 mg/L of chlorine.
- Followed by neutralization, coagulation and flocculation, skimming and filtration and post chlorination with 1-5 mg/L of chlorine. The resultant effluent can be let into the public sewers.

Slide 18



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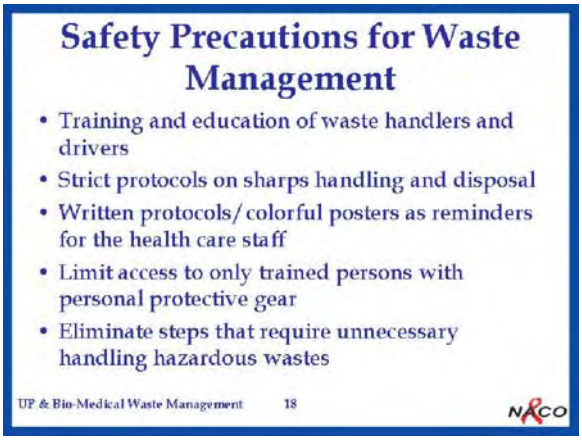
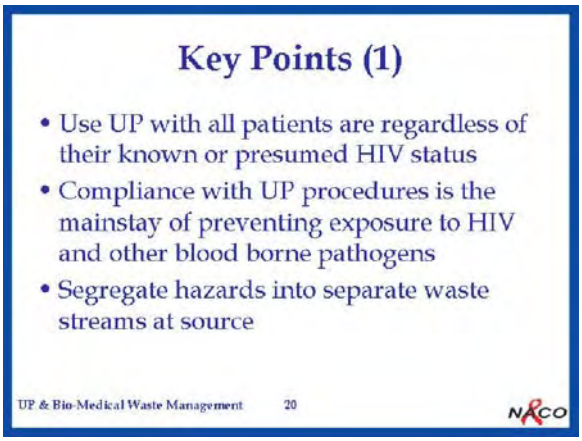
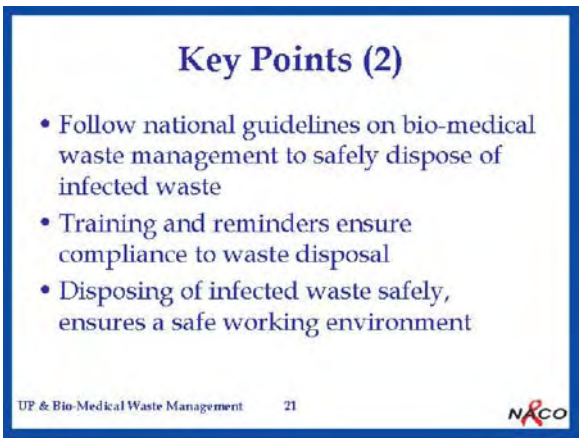


Slide 20		
Slide 21		

SESSION

MY HOSPITAL MY WORK

2

Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

- To describe HIV service delivery at the Training Centre's ART Centre
- To provide participants with the opportunity to reflect on their ART Centre service delivery
- To share information on HIV, ART, and supportive care services at the participants' different ART Centres

Handout 1: My Hospital, My Work Planning Worksheet

Instructions: If you are attending the training with a colleague from your Centre, work with your colleague to complete this worksheet. Describe your ART Centre's service delivery system as per the categories listed below. Prepare a 10-minute presentation for the other training participants summarizing your ART Centre during the training programme (see Schedule). You can develop using PowerPoint, flipchart paper, or whiteboard.

ART Centre Name: _____

1. **Infrastructure facilities at the ART OPD/Centre**

2. **Adults and Adolescents: HIV and ART care provided**

3. **Paediatric services: HIV and ART care provided**

4. **Voluntary Counselling and Testing Services and Integrated Counselling Services offered**

5. **PPTCT Services provided**

6. **Interdepartmental cooperation and administrative support**

7. **PEP protocol, notification, and treatment system**

8. **Hospital infection control policies and practices**

9. **Networking with CBOs, NGOs and PLHA networks**

10. **Methods of reducing stigma and discrimination among patients**

11. **Overall strengths and areas of improvement at Centre**

SESSION 3

SESSION

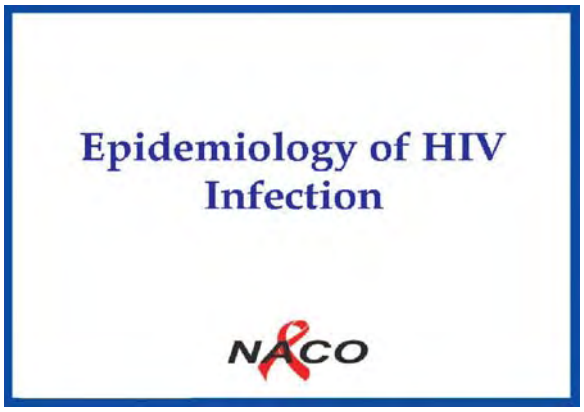
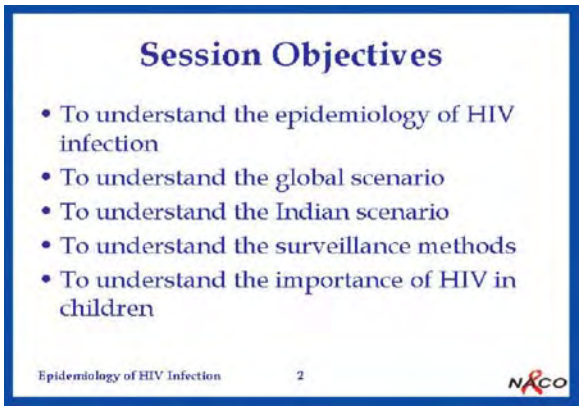
EPIDEMIOLOGY OF HIV INFECTION

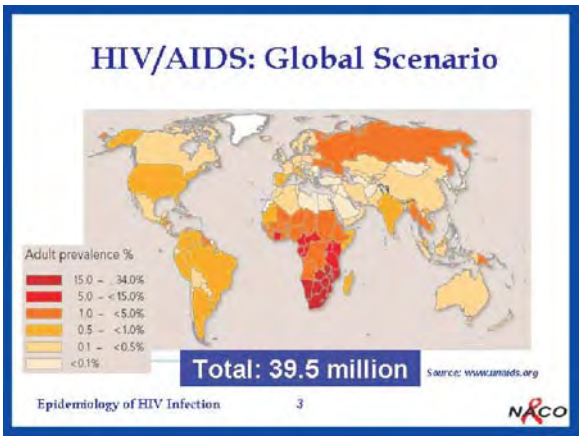
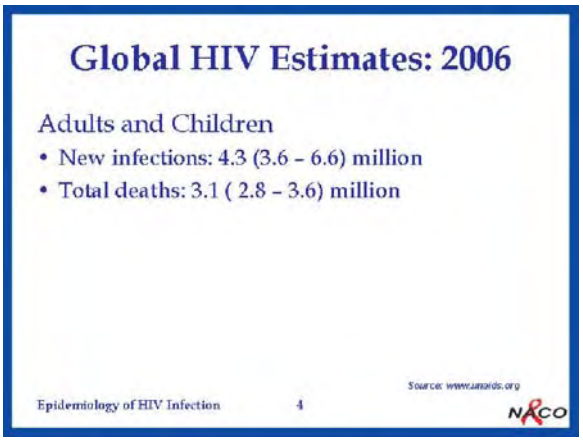
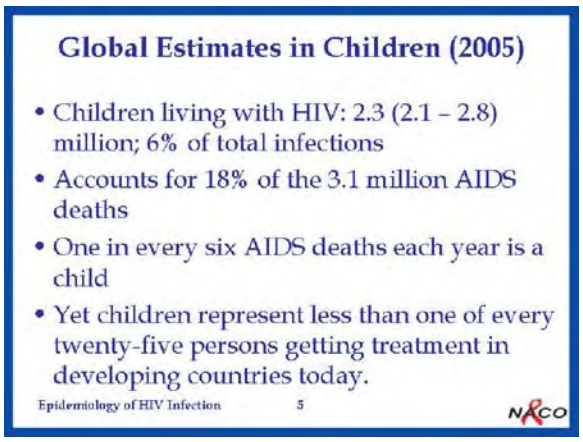
3

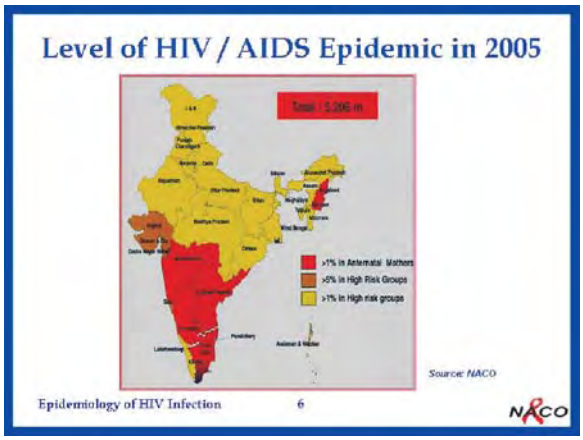
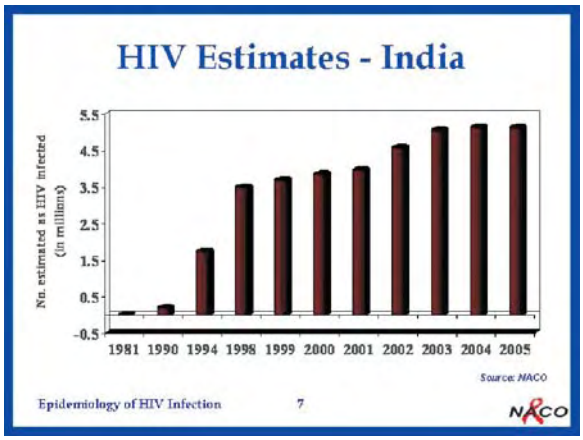
Total Session Time: 45 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Understand the epidemiology of HIV infection
- Understand the global scenario
- Understand the Indian scenario
- Understand the surveillance methods
- Understand the importance of HIV in children

Slide 1		
Slide 2		

Slide 3		
Slide 4		**Reader's Notes:** • Source:www.unaids.org
Slide 5		

Slide 6		
Slide 7		

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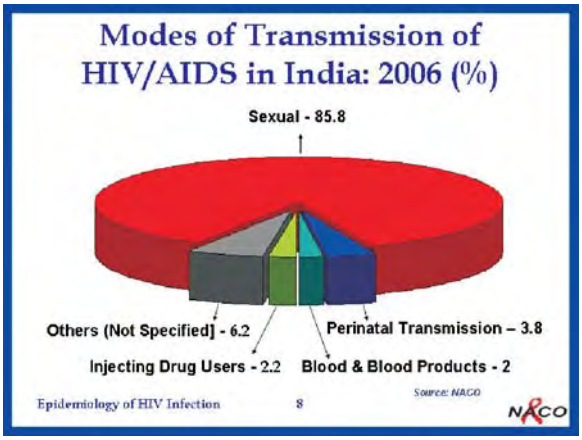
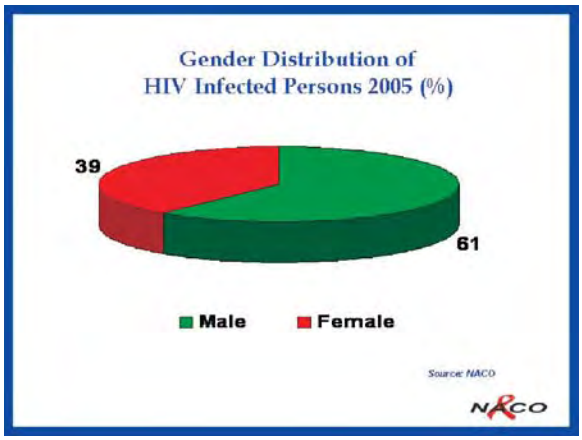


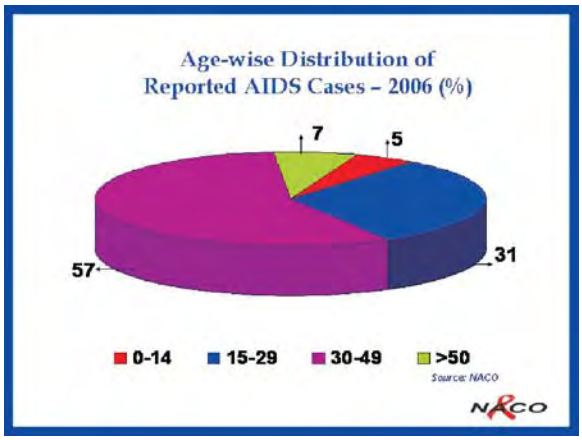
Reader's Notes:

- The most common mode of HIV transmission in India is the sexual route.
- The next common route of transmission is perinatal transmission.
- The "other" category in the pie chart denotes transmission mode is unknown.
- HIV can be transmitted to any individual (heterosexual or homosexual) through an act of unprotected sexual intercourse in which a condom is not used where one partner is infected with HIV. The risk of becoming infected through an act of unprotected sexual intercourse depends on four main factors:
  - **The likelihood that the sex partner is infected:** The probability that a person has become infected with HIV is in general proportionate to the number (frequency) of unprotected sex acts and the number of high risk partners with whom the person has had sexual contact in recent years.
  - **The type of sex act:** All unprotected acts of sexual penetration (anal, vaginal, oral) carry a risk of HIV transmission because they bring sexual secretions directly into contact with exposed mucous membrane. Injury to the mucous membrane of the rectum, the vagina or the mouth may help the virus to enter into the bloodstream. "Receptive" partners are thus at a greater risk than "Insertive" partners in acts of intercourse. However, HIV can be transmitted even through unbroken mucous membrane.
  - **The amount of virus present in the blood or sexual secretions (semen, vaginal or cervical secretions) of the infected partner:** Individuals with HIV infection become more infectious as they progress to HIV related diseases and AIDS. There is also an early period of high infectiousness around the time of seroconversion.
  - **The presence of other sexually-transmitted infections and/or genital lesions in either partner:** HIV can be transmitted sexually even when neither partner has any of the other sexually-transmitted infections. However, there is strong evidence that men and women with genital ulcer disease or urethral discharge are at increased risk of acquiring and transmitting HIV.

Slide 9



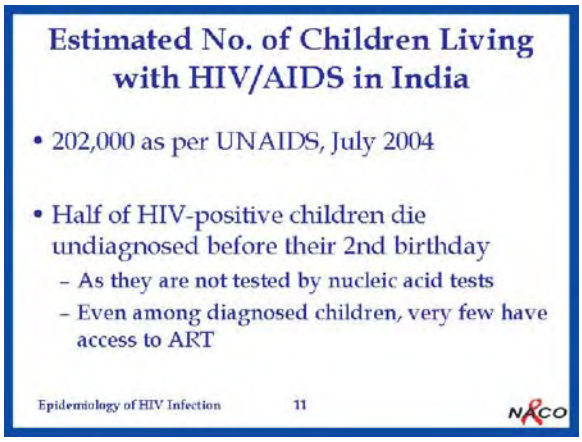
Slide 10

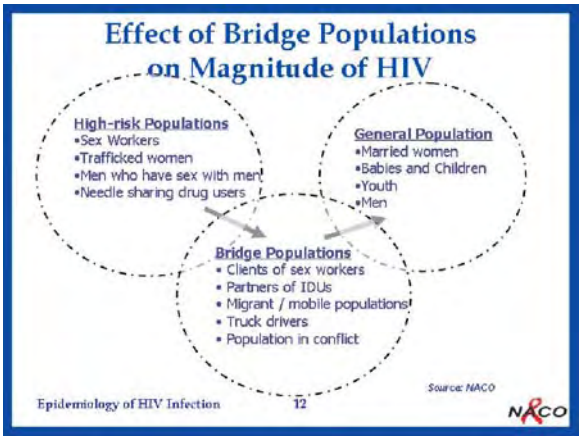
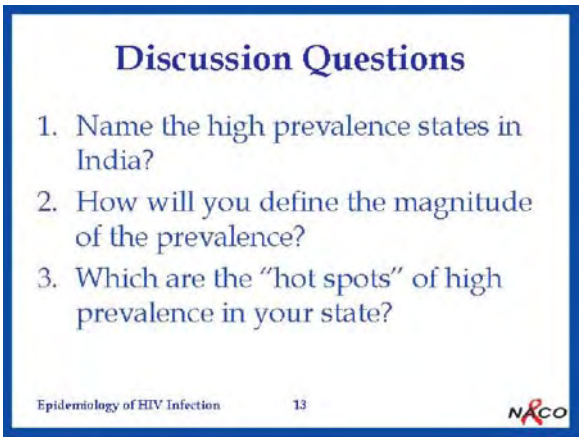


Reader's Notes:

AIDS Cases in India	Cumulative	August 2006
Males	88,245	90
Females	36,750	36
Total	1,24,995	126

Slide 11



Slide 12		
Slide 13		

Handout 1: NACO HIV Epidemic: Definitions

Classification of prevalence as:

1. High prevalence (Generalized): Where the prevalence of HIV is >1% in general population (like antenatal clinic data) and >5% in the high risk groups like sex workers.

- States thus affected are Maharashtra, Karnataka, Andhra Pradesh, Tamil Nadu, Manipur and Nagaland.

2. Moderate prevalence (Concentrated): Where the prevalence of HIV is <1% in the general population but >5% of the high risk population- like among commercial sex workers.

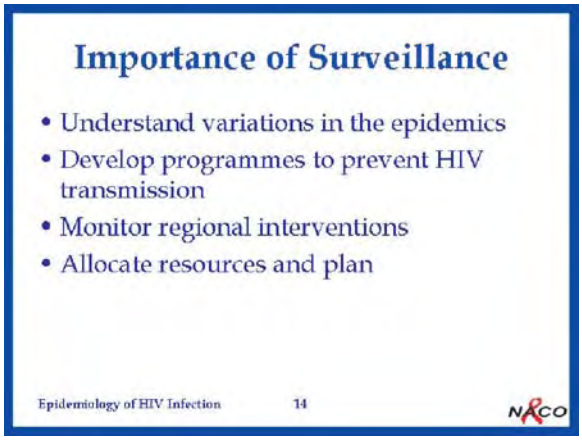
- States thus affected are Gujarat, Goa and Pondicherry.

3. Low level prevalence: Where the prevalence of HIV is <5% among the high risk population.

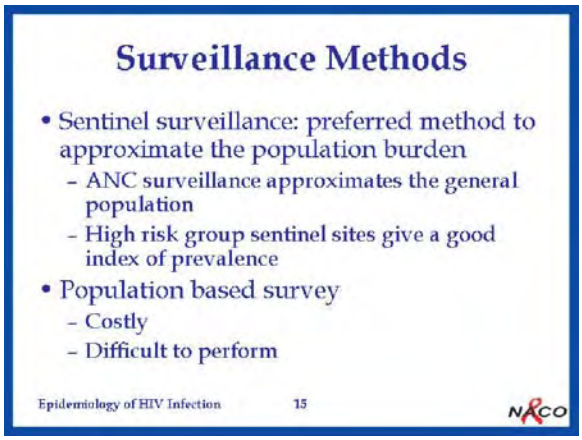
Some states are **classified as highly vulnerable** due to their low socio economic status, poor health status, high level of migrant population, significant presence of tribal population or limited health infrastructure/access.

- The **vulnerable states** are Arunachal Pradesh, Haryana, Jammu & Kashmir, Meghalaya, Mizoram, Sikkim, Tripura, Andaman & Nicobar Islands, Chandigarh, D&N Haveli, Daman & Diu, and Lakshadweep.The highly vulnerable states are Assam, Bihar, Delhi, Himachal Pradesh, Kerala, Punjab, Jharkand, West Bengal, Orissa, Madhya Pradesh, Chattisgarh, Rajasthan, Uttar Pradesh and Uttaranchal.

Slide 14



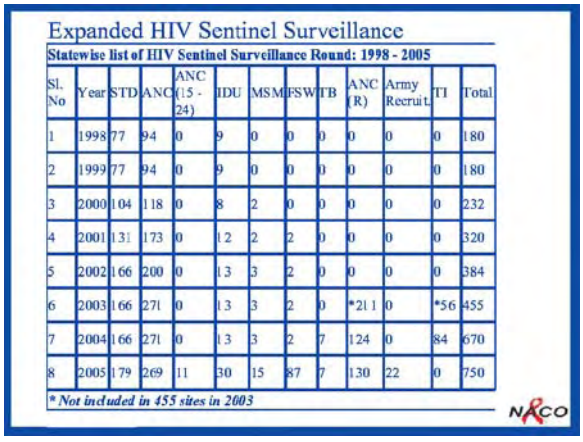
Slide 15



Reader's Notes:

- The most preferred method to estimate prevalence of HIV is by a population based survey. This is costly and difficult to perform. Sentinel surveillance remains the next preferred way of approximating the population burden. In a full fledged epidemic antenatal clinic data closely mirrors the data from the general population.
- In concentrated epidemics, data from high risk group sentinel sites give a good idea of the prevalence. NACO uses such markers in calculation of the burden of HIV in the country.

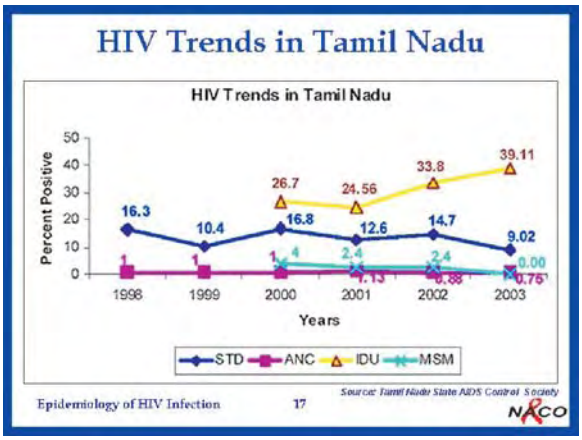
Slide 16



Reader's Notes:

- Sentinel surveillance is being done in the following areas 1. Antenatal clinics 2. STI clinics 3. IV drug users 4. Female sex workers 5. Men having sex with men.
- In 1998 there were only 180 sites, which is now expanded to 750 sites in India (the data is up to 2005 only).
- As per the executive summary of the NACP III report, there are 2815 ICTC (integrated counselling and testing centres-ICTC) all over India.
- The ICTC includes the following services; (1) VCTC, (2) PPTCT, (3) ART Counselling, and it includes access to the following services through linkages; IEC/BCC, condom promotion, STI treatment linkages, prophylaxis and early management of OI's, DOTS for TB, and ART services.

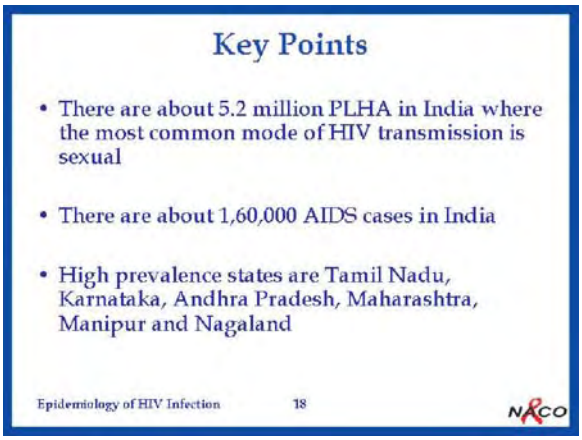
Slide 17



Reader's Notes:

- This slide shows sentinel surveillance data from Tamil Nadu, it shows reduction in antenatal surveillance rate from 1 (1998) to 0.75 (2003). This indirectly infers reduction of prevalence in the general population.

Slide 18



SESSION 4

SESSION

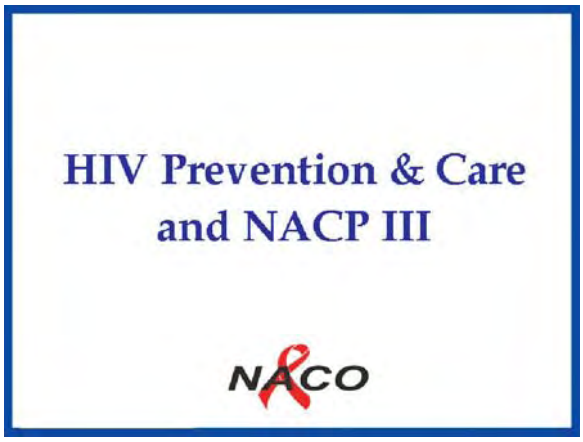
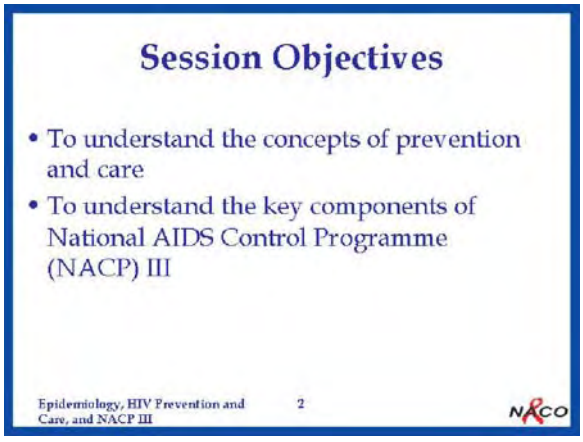
HIV PREVENTION, CARE AND NACP III

4

Total Session Time: 45 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Understand the concepts of prevention and care
- Understand the key components of National AIDS Control Programme (NACP) III

Slide 1		
Slide 2		

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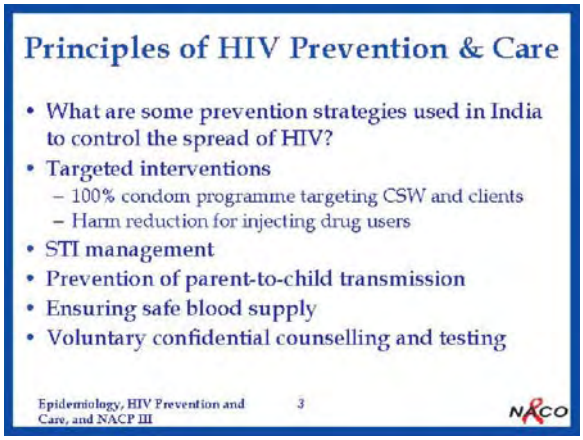
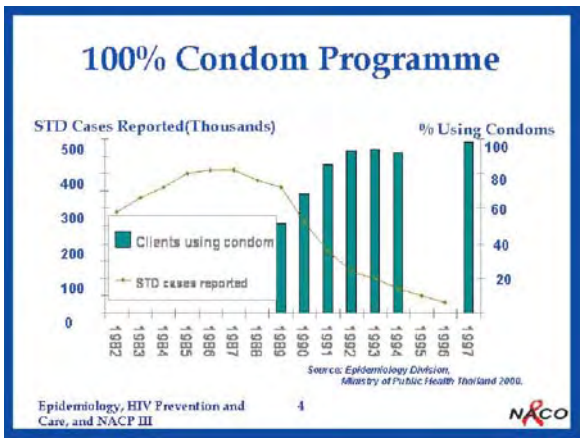


Reader's Notes:

- Intervention strategies to control HIV/AIDS may be aimed to target the high risk groups, the bridge population or the general population.Some interventions are classified as cross cutting interventions as they are effective for more than one group. Condom promotion remains important even after the roll out of ART and should be emphasized for patients on ART. Even after starting ART, patients can transmit HIV to others through high-risk behaviour.

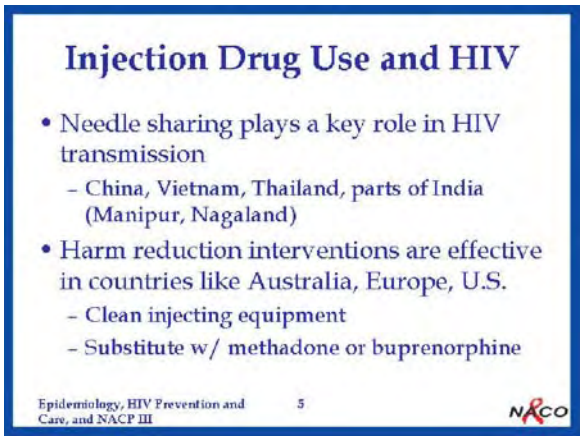
Slide 4



Reader's Notes:

- Considering that the main mode of transmission of HIV is the sexual route in India, condom promotion remains the mainstay of HIV prevention. Aggressive condom promotion campaigns are one of the best success stories in HIV prevention.
- In Thailand, over the course of a decade, the acceptance of use of condoms by clients was an indication of the sustained effort of the government's aggressive condom promotion campaigns.There was a noticeable reduction in the number of sexually transmitted diseases reported. This benefit has been sustained and its fall parallels the rise in condom acceptance.

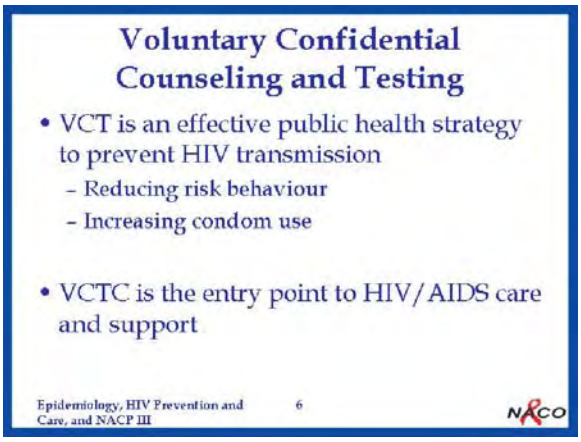
Slide 5



Reader's Notes:

- Recognizing that the HIV epidemic was also being fuelled by injection drug use and needle sharing, the Thai government embarked on an aggressive harm reduction campaign. This approach has also been tried in many South East Asian countries, but the response has not been as dramatic as seen with the condom promotion campaign.
- There are many barriers to this idea, especially for the concept of drug substitution. It is perceived that unless there is good control, the intervention may do more harm than good, as this could introduce buprenorphine into the streets.
- Needle exchange programs have enjoyed success and the data on drug substitution from Australia and Europe is very encouraging.

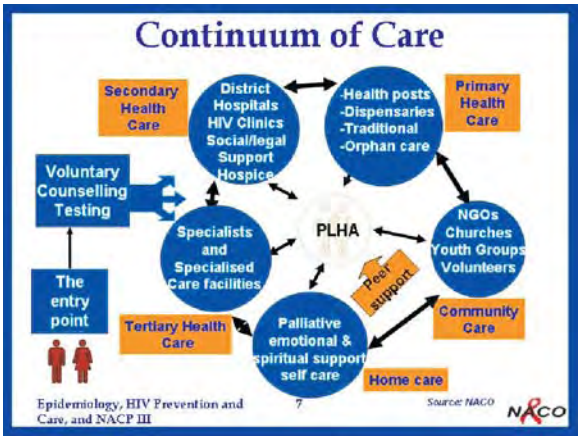
Slide 6



Reader's Notes:

- VCTC is an effective public health strategy in preventing the transmission of HIV.
- Studies from developing countries have shown it to be far more cost effective as a prevention tool as compared to the more developed countries. This reduction in transmission is achieved by reduction in risk behaviour and increase in the condom use.
- Bear in mind that the quality of services at a VCTC- accessibility, patient friendliness, networking and linkage to care and support- can enhance the efficacy of this intervention.
- VCTCs are also a good entry point into the ART programme, and for these reasons, it should be widely promoted.
- VCTCs are now a part of the ICTC (integrated counselling and testing centre).

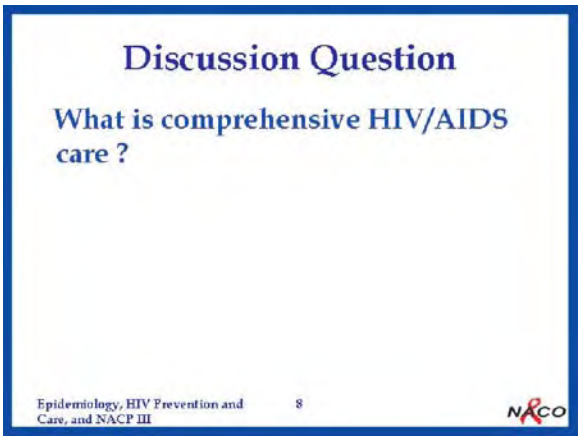
Slide 7



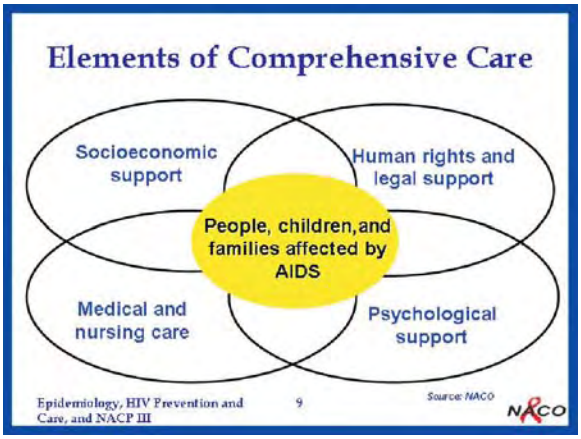
Reader's Notes:

- The graphic shows the VCTC as the entry point for HIV-infected persons at a secondary or tertiary care level, as they are available only at most district headquarters as of today.
- If a person is found to be HIV-positive at the VCTC, the person is subsequently referred to appropriate areas to facilitate care. Once the person's care issues are sorted out and a long term plan is made, the PLHA is referred to a lower level- to primary care, home care etc- for further follow up. They can be subsequently referred back if they develop new problems that require special intervention (e.g., need for starting ART).
- There is interaction with NGOs, CBOs and other support groups to facilitate the process. The PLHA network can offer assistance in the form of peer support. This ensures that good quality care can be accessed by all PLHA without having to approach tertiary institutions.

Slide 8



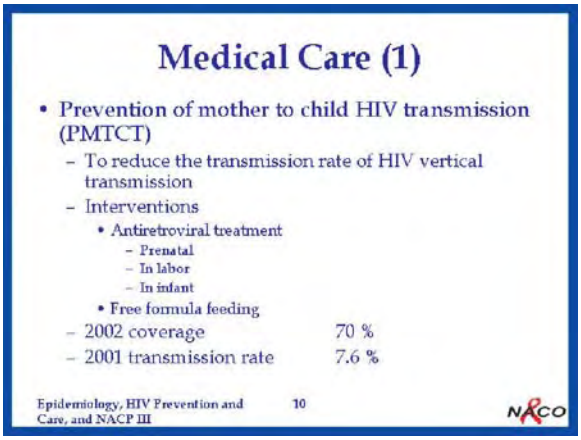
Slide 9



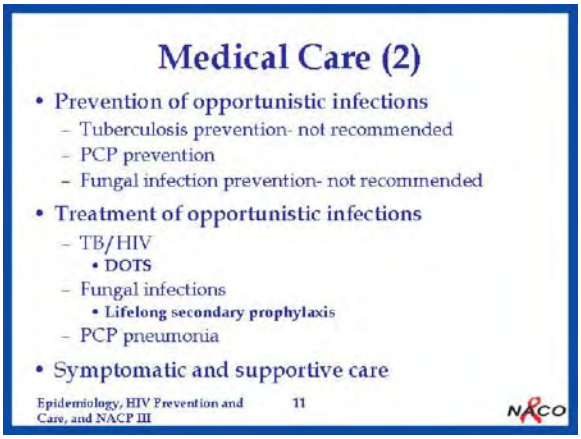
Reader's Notes:

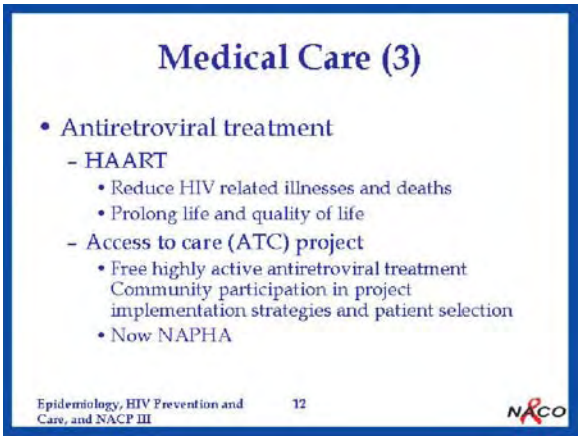
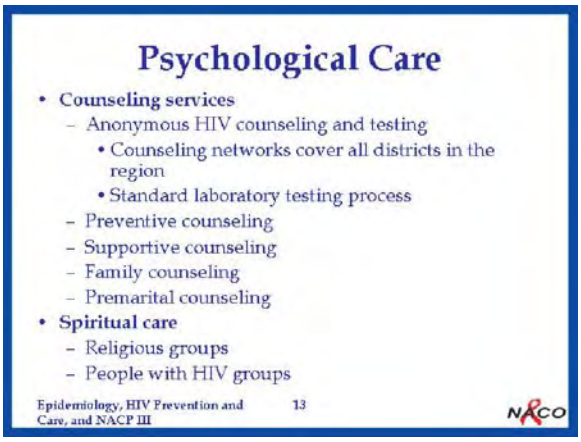
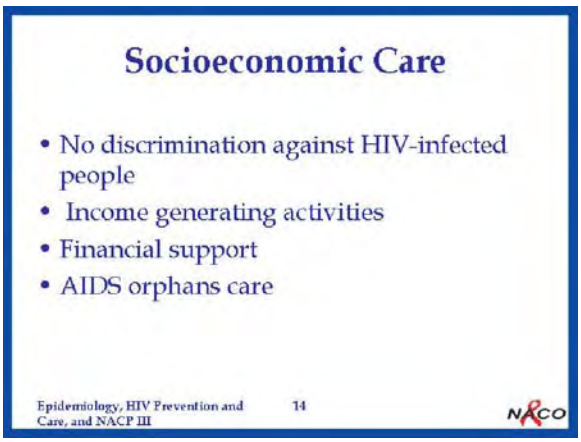
- Comprehensive HIV/AIDS care of PLHA **extends beyond medical** care.
- In asymptomatic PLHA, the major need is for **psychosocial support** and counselling, and the need for this is likely to increase with advancement of the disease.
- Given the current environment of stigma and discrimination in the workplace, many PLHA will require **economic and employment support** and help with housing.
- Advocacy, including **legal assistance** will help mitigating the stigma and discrimination. As there is a large burden of financially destitute orphans and widows of PLHA, interventions are needed for their long term **rehabilitation**. On going training on care and support for **care givers** is also important to ensure a good quality of care.

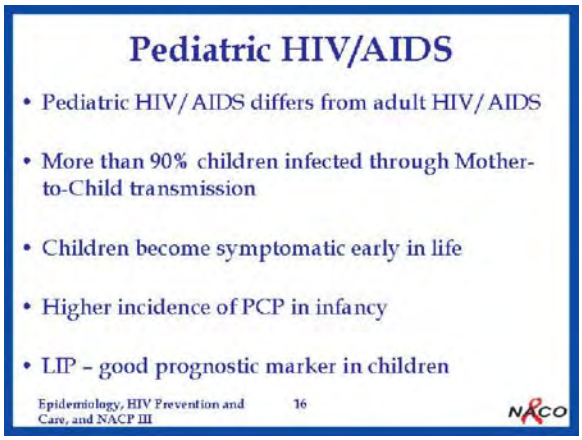
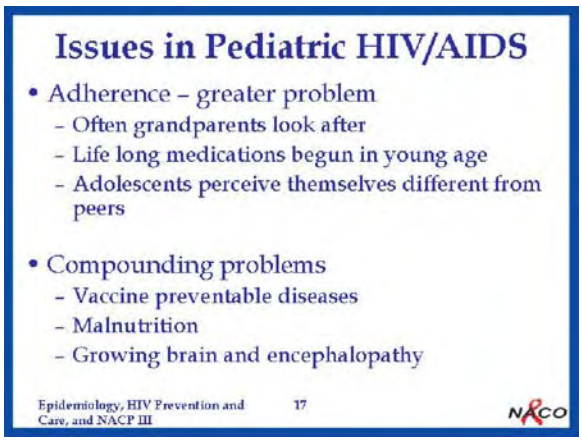
Slide 10



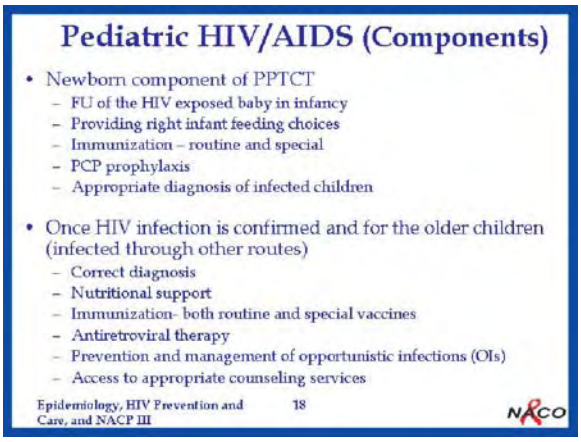
Slide 11



Slide 12		
Slide 13		
Slide 14		

Slide 15		
Slide 16		**Reader's Notes:** • Peadiatric HIV is different from adult HIV in many ways including the modes of transmission, the duration of asymptomatic period and the commonest OIs etc.
Slide 17		**Reader's Notes:** • Peadiatric HIV also differs from adult HIV on the following ways. • If the children are started on ART, Adherence becomes a greater issue as depicted in this slide. • Most of the children are orphans and they have only the grandparents to take care of them. • The children need to take medications life-long and this process needs to be started at a very young age. • Other problems like malnutrition, mental and physical development are also becoming an issue in Peadiatric HIV.

Slide 18

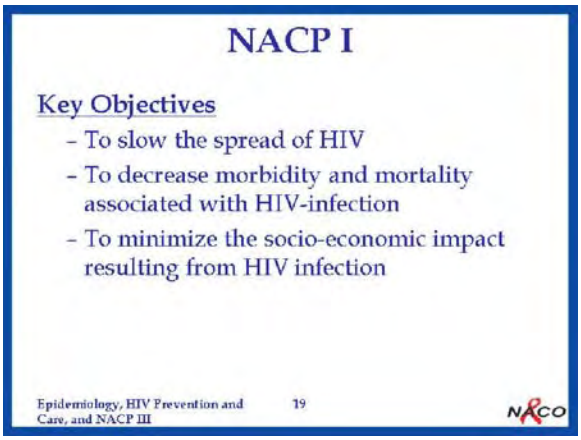


Reader's Notes:

The care components of peadiatric HIV are as follows.

- The new born babies exposed to HIV are to be followed up regularly.
- They should be provided with correct infant feeding choices.
- Appropriate Prophylaxis for OIs need to be given and the diagnosis of OIs have to be correct and appropriate.
- Among the older children, diagnosis of HIV status is very important apart from the above mentioned care and support activities

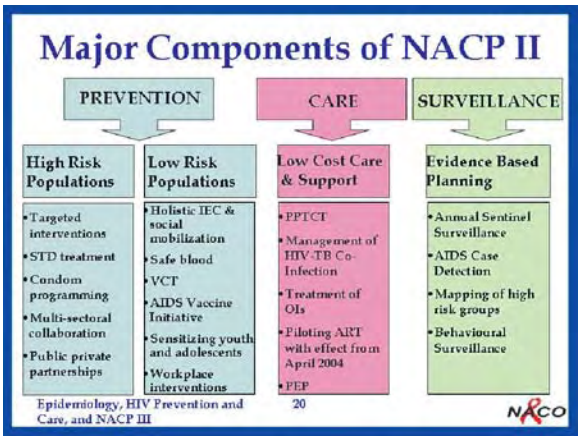
Slide 19



Reader's Notes:

- Source - Draft NACP III Strategy and Implementation Plan July 2006.

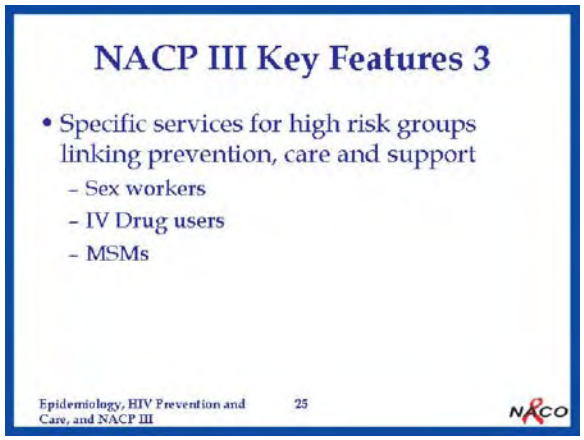
Slide 20



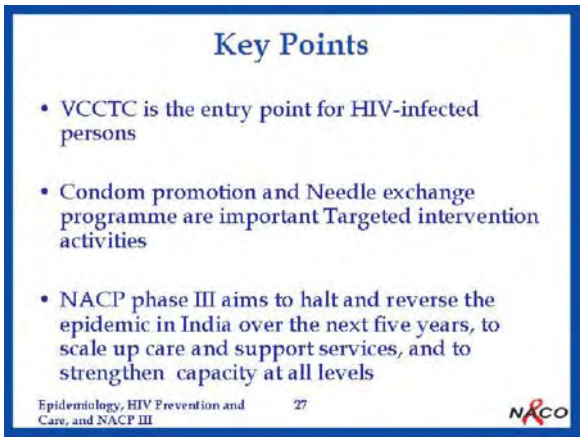
Reader's Notes:

- The major components of the National AIDS Control Program are prevention, care and surveillance.
- Prevention is appropriately targeted both at high risk and low risk populations, and with the ART initiative, has been further strengthened.
- Low cost care and support and evidence based surveillance are also integral to the success of the initiative.

Slide 21	**National AIDS Control Programme Phase III (NACP III) 2006 - 2011: Goal** • Halt and reverse the epidemic in India over the next five years • Reduce new infections by – 60% in high prevalence states – 40% in vulnerable states Epidemiology, HIV Prevention and Care, and NACP III 21 NACO	
Slide 22	**NACP III 2006 - 2011: Goal (2)** • Prevent new infections • Increase proportion of PLHA receiving care, support and treatment • Strengthen capacity at district, state and national levels • Build strategic information management systems Epidemiology, HIV Prevention and Care, and NACP III 22 NACO	**Reader's Notes:** • Prevention of new infections (saturation of high risk group coverage and scale up of interventions for general population).
Slide 23	**NACP III Key Features 1** • Prevention Services – Integrated counselling and testing (ICT) – Creating awareness about symptoms, spread, prevention and treatment – PPTCT – Blood safety – Access to STD and reproductive tract infections (RTI) services – Condom promotion – Promotion of safe practices and infection control Epidemiology, HIV Prevention and Care, and NACP III 23 NACO	

Slide 24		
Slide 25		
Slide 26		**Reader's Notes:** **NACP III: Targets** • Saturation of HRG (1 million sex workers, 1.15 million MSM and 0.19 million IDUs) through Targeted Interventions. • Focus on bridge population (truckers, migrants): 3 million. • Reach out to cover rural population (15-49 yrs): 280 million. • PPTCT: 10.8 million and ICTC: 22 million tests. • Blood Units: 8.5 million. • STI: 30 million (50% to be covered). • Condom: 3.5 billion per year. • Provision of ART (3,00,000) and community care centers (350) and their effective linkages with TIs. • Expansion of HIV Sentinel surveillance (1200 sites). • M&E at district, state and national levels to be established.

Slide 27		


Key Points
• VCCTC is the entry point for HIV-infected persons
• Condom promotion and Needle exchange programme are important Targeted intervention activities
• NACP phase III aims to halt and reverse the epidemic in India over the next five years, to scale up care and support services, and to strengthen capacity at all levels
Epidemiology, HIV Prevention and Care, and NACP III
27
NACO

SESSION 5

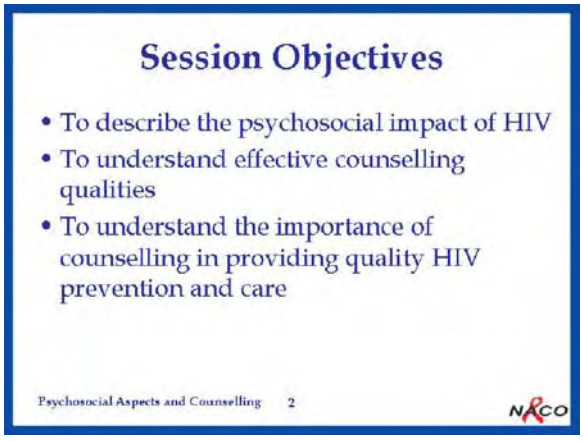
SESSION 5

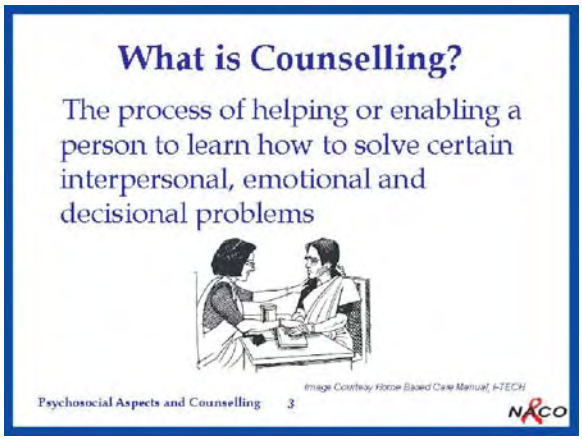
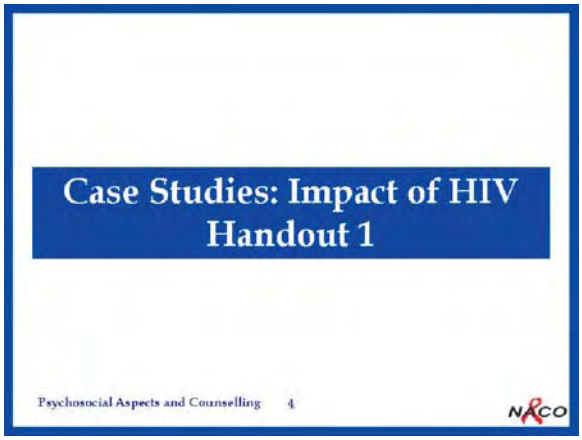
PSYCHOSOCIAL ASPECTS AND COUNSELLING

Total Session Time: 1 hour 15 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Describe the psychosocial impact of HIV
- Understand effective counselling qualities
- Understand the importance of counselling in providing quality HIV prevention and care

Slide 1		
Slide 2		

Slide 3		**Reader's Notes:** • HIV/AIDS counselling is an essential and integral component of HIV prevention, treatment, care and support programmes. • Counselling can involve an individuals, couples or families. • The Specialist has an important role in counselling patients. People take the words of their doctors very seriously. Doctors should have effective communication skills not only to deliver basic medical information to patients but also to provide psycho-social support. • In order to better serve the patients, physicians must understand basic principles and skills involved in counselling patients.
Slide 4		

Handout 1: Case Study 1: *Impact of HIV- On Individuals*

Instructions: Read out the case study and then discuss the possible answers to the questions in a group and present it to the large group.

Sandhya, a 12 year-old girl studying in 6th standard, was diagnosed with HIV 6 months ago. She belongs to a middle class family. Her father is a businessman and her mother is a housewife. Her parents who were quite healthy were shocked. Her parents both took HIV tests as suggested by the care team and were found to be positive. The father of the child confided to the counsellor that he had indulged in high-risk behaviour before marriage. Sandhya also has a younger sibling, a 7-year-old girl, who is found to be HIV- negative. Sandhya is started on ART, but she develops complications and dies two months later.

Group Discussion

1. What are the possible psychosocial effects of HIV/AIDS on the different individuals of the family described in the case study:

a) Father who engaged in high-risk behaviour in the past

b) Mother who finds herself HIV positive

c) Sandhya who is dying of AIDS

d) HIV negative sibling

Handout 1: Case Study 2: *Impact of HIV — On Families/Communities*

Rajeshwari, a housewife, was happily married with one 3 year-old son and lived in a small village along with her parents and in-laws. Her husband worked for a company in a near-by small town. Over the past few years he had not been well and eventually he died. After his death, Rajeshwari was told that she had AIDS and later tests revealed that both she and her son are HIV- positive as well. The in-laws blamed her for the misfortune, threw her out of their house, and told everyone in the village. Her parents who lived in the same village took her in, but the villagers are so enraged and that they sent Rajeshwari out of the village. One year later, her son also died.

Group Discussion

1. Explain the behaviour of the husband's family. What are some reasons why they reacted this way?

2. What are the likely effects of their behaviour on Rajeshwari

Handout 1: Case Study 3: *Impact of HIV— On the Health* Care Workers

Ms. Ravina is a staff nurse working in a medical ward caring for seriously ill patients including PLHAs. She joined this profession with the noble intention of serving those who were suffering. She has worked in the hospital for the past 3 years. Of late, she has been feeling exhausted, been having multiple somatic problems and her attendance at work has been irregular.

At home, her family notices that she is quite irritable and moody, at times crying and not sleeping adequately. At work, her colleagues notice that she is not as involved in her work as she once was. She is also behaving as if she was the only one who is working and has made some harsh comments about the lack of involvement of her juniors. She is pulled aside by her superiors and reprimanded for the harsh comments. The nurse feels that hospital does not deserve any of her services. She makes the decision to put an end to her suffering and quits being a nurse.

Group Discussion

1. Identify the syndrome.

2. What are the various manifestations of this syndrome?

3. What are the interventions that can be used to prevent this?

Slide 5	**Case Study 1:** **Impact of HIV on Individuals** What are the possible psychosocial effects of HIV/AIDS on… 1. Father 2. Mother 3. Sandhya 4. HIV-negative sibling Psychosocial Aspects and Counselling 5 NACO	
Slide 6	**Case Study 2:** **Impact of HIV on Families** 1. Explain the behaviour of the husband's family. What are some reasons why they reacted this way? 2. What are the effects of their behaviour on Rajeshwari? Psychosocial Aspects and Counselling 6 NACO	
Slide 7	**Case Study 3:** **Impact of HIV on HCWs** 1. Identify the syndrome 2. What are the various manifestations of this syndrome? 3. What are the interventions that can be used to prevent this?  Psychosocial Aspects and Counselling 7 Image Courtesy Home Based Care Manual, I-TECH NACO	**Reader's Notes:** • For further study, Refer to **Handout 2: Possible Interventions for Some of the Psychosocial Issues Identified.**

Handout 2 : Possible Interventions for Some of the Psychosocial Issues Identified

Psychosocial Issues — One-to-one counselling, family counselling and group counselling sessions could be some of the interventions used here to handle such issues

Fear:

Fear can arise in the infected person from the unpredictable nature of the disease. Fear can aggravate depression symptoms and lead to feelings of hopelessness, frustration and being overwhelmed. Fear can also arise in others, with repercussions for the person with HIV/AIDS. Friends and co-workers may pull away because of irrational fears of infection or fears of a person's death, therefore leaving the person with HIV with a deep sense of isolation and loss.

Loss:

HIV has been called a disease of losses. Sadness is one outcome of experiencing repeated losses. People living with HIV/AIDS may have to grieve the loss of deceased lovers, children and friends while at the same time mourning the loss of their own future. With many successive losses, it can take the form of "chronic, unrelenting loss". Other losses can include loss of partner, family, friends, co-workers, mobility, strength, weight, appetite, and physical attractiveness, locus of control, social role, income, employment, housing to name a few.

Grief:

Three stages of grieving can be identified: 1) How did the person die? What caused the death? Was the death sudden, gradual, painful, and easy, etc.? 2) What did the person mean to you? Were they a friend, partner, co-worker, parent, child? 3) How will you learn to live without the person? What do you need to do to go on living? Anticipatory grief (i.e., grief about possible future losses) and bereavement often result in anger and depression.

Anger:

Anger may be directed at several targets at the same time. The person with HIV disease may blame the following: themselves for getting infected and the resulting physical and mental loss; at family not being able to do anything; at one's support system for lack of understanding, empathy or compassion; at society for their rejection; and the medical establishment, for failing to find a cure. The need to stay in control can sometimes produce behavior such as quarrelling, arguing, complaining, or being demanding.

Depression:

Feelings of depression can be expected and surface as feelings of discouragement, dejection, or helplessness. Signals that depression is being experienced include disturbance in sleep, appetite changes, withdrawal from all activity, failure to find pleasure in favourite activities, or difficulty in concentration. If depression is unresolved, a maladaptive coping strategy is substance abuse or attempted suicide. Psychological causes can include the

anticipation of dying and death; the loss of friends, lovers, parents, or children; the possibility of becoming disabled; and the discomfort of becoming increasingly dependent on others.

Feelings of Dependency:

People can experience feelings of dependency with disabilities arising from a loss of functional capacity in both physical and emotional areas. Being dependent on others brings on threats to self-sufficiency, privacy, control, and independence and feelings of helplessness and vulnerability that are often intolerable. This can have the effect of being unwilling to ask for accommodation because of change in identity, feelings of shame, not wanting to feel different or pitied.

Hope:

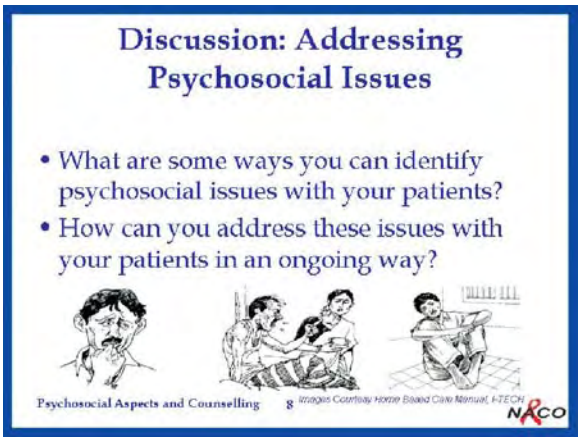
Not all emotional responses to HIV/AIDS are negative. For people with HIV/AIDS, maintaining hope is not merely a virtue, but a primary task. It appears that people actually live longer when they can hope for and plan future activities, achievements and relationships. Hope sustains them through the inevitable "bad days" and increases the capacity to appreciate periods of good health. The most important factor in maintaining hope is active participation in decision-making. Any intervention that enables a person with HIV/AIDS to feel in greater control of their health care and activities strengthens their feelings of hope.

Social Issues - Programmes like community awareness programmes could be done in villages which help support PLHA. Support group meetings held by networks are also places where PLHA could receive some help.

Social Stigma and Discrimination:

The consequences of HIV/AIDS related stigma and discrimination are serious and wide-ranging. Stigma and discrimination impact on individual behaviour, employment, and the delivery of services and on treatment and prevention strategies. The impact of stigma on the individual can be experienced in two distinct ways, felt and enacted. 'Felt' stigma is the impact on individual feelings such as shame, guilt, withdrawal, and self-stigmatization. 'Enacted' stigma relates to experiences. Individuals can be denied access to information, health services, company and the support they need. They can also face loss of job, compulsory testing, even violence and quarantine.

Slide 8

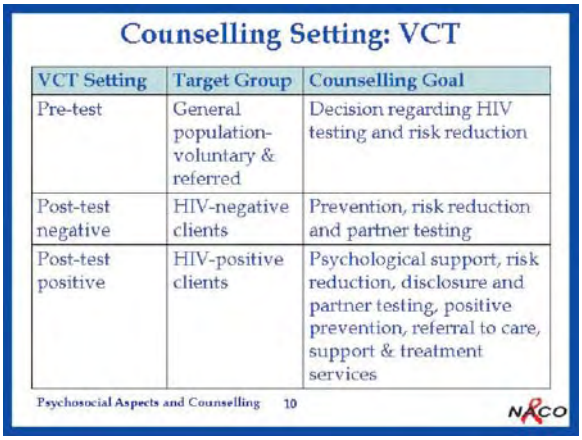


Slide 9

Reader's Notes:

- The type of counselling conducted by the counsellor is dependent on the needs of each individual client.
- Each type of counselling requires a certain set of skills and has different goals.
- Risk assessment and risk reduction counselling are important parts of HIV Prevention counselling (preventing HIV transmission). Risk reduction and behaviour change counselling are methods of working with HIV-infected patients to reduce further risks that can compromise their health and prevent infection to others. The most critical component of risk reduction counselling is to be non-judgmental.
- ART readiness counselling takes place when the patient is registered for ART, but is not yet eligible as their CD4 count is above 300.
- Adherence counselling begins before starting medications and continues at every patient follow up appointment.
- Crisis intervention counselling usually takes place immediately after a crisis. An example is a person finding out that their partner or themselves are infected.
- Grief counselling may take place when someone is very ill, for example at the end stage of AIDS. It often includes the infected person and their family.
- Refer to the "NACO Counselling Guidelines" for guidance on the latest national recommendations. Source: http://www.nacoonline.org /guidelines/ vct_guidelines.pdf.

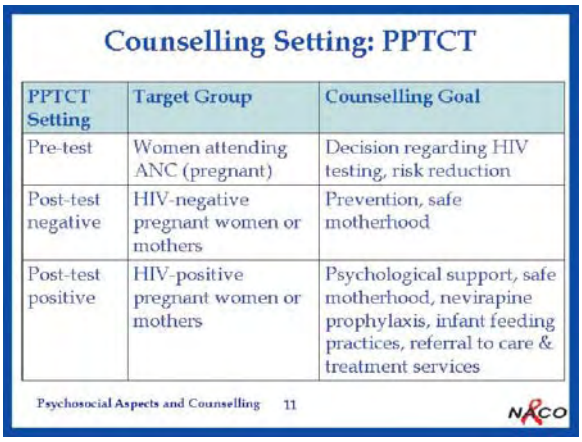
Slide 10



Reader's Notes:

- This slide illustrates types of VCT counselling along with the target patients and the main counselling goal. Note that partner notification, disclosure of HIV status to partner(s), is often discussed with clients in the pre-test session. One important aspect to stress with clients in the post test negative session is the window period. Antibodies generally appear within three months after infection with HIV, but may take up to six months in some persons.

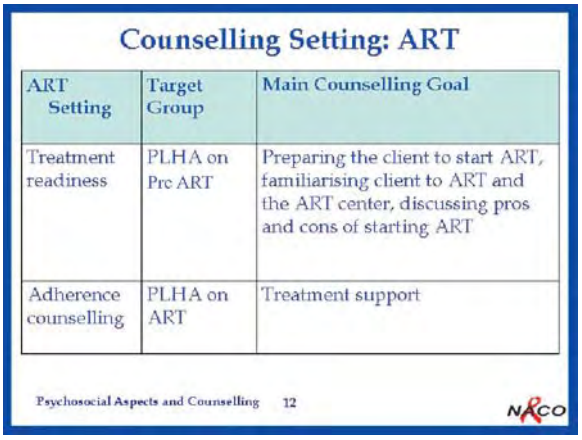
Slide 11



Reader's Notes:

- This slide illustrates types of PPTCT counselling along with the target patients and the main counselling goal.
- In a PPTCT setting, the types of counselling are similar to VCT settings. Some ANC clients may not have an accurate perception of their risk or vulnerability to HIV. The counselling session needs to be delivered differently than in a VCT setting where clients may perceive themselves to be at risk.
- **Safe motherhood**—To ensure that all pregnant women receive the care they need to be safe and healthy throughout pregnancy and childbirth.
- Safe motherhood care begins before pregnancy with proper nutrition, healthy lifestyle and finally appropriate prenatal care. Prevention of complications whenever possible and early effective treatment for complications. The ideal result is the pregnancy at term without unnecessary interventions, the delivery of a healthy infant, and a healthy postpartum period in a positive environment that supports the physical and emotional needs of the woman, infant, and family.

Slide 12



Reader's Notes:

- This slide illustrates types of ART counselling along with the target patients (PLHA not yet on ART) and the main counselling goal.
- Counsellors in the ART centres should give information to every client who attends the center about ART drug information, CD4 count tests, resistance tests, disclosure, and eligibility criteria for ART.
- After it is determined that the patient is eligible and ready for the ART drugs, patients must attend adherence counselling. The goals of adherence counselling are:
  - Education is very important when a patient begins ART. Adherence counselling should include discussion of: risks and benefits, side effects, drug interactions and lifelong commitment to therapy. Patients should understand that intermittent treatment is not effective and can lead to a drug resistant virus and treatment failure.
  - It is very important to note that majority of our patients continue with the ART drugs mainly because of the good relationship they share with the health care professionals.
- Refer to **Handout 3: Criteria to Assess Eligibility for ART.**

Handout 3: Criteria to Assess Eligibility for ART

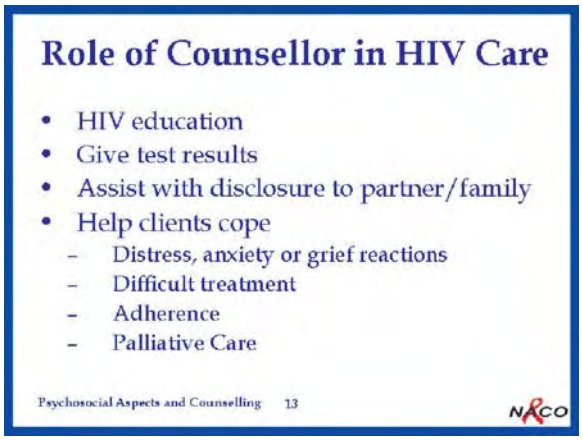
Clinical criteria that determines whether someone is ready for ART:

- As per the NACO guidelines, the accepted protocol for consideration of PLHA for ART is either WHO Stage IV, illnesses (where a CD4 count is unnecessary) or based on CD4 count.
- Viral load estimation is not required for decision making on need for treatment. There is data that shows that the response to therapy is similar irrespective of the viral loads at the time of starting.
- In the event that a patient does not have an AIDS defining illness, CD4 testing should guide the need for therapy. All patients with a CD4 less than 200, as discussed earlier, should be offered therapy.
- In addition, therapy may be offered to patients with a CD4 less than 350, especially if the patient is symptomatic. It is advised that patients be started on therapy when the CD4 is between 200-250 itself. If the CD4 is more than 350 cells, then therapy can be deferred for later.
- Refer to NACO ART and WHO Guidelines.

Para-clinical criteria include:

- The situation at home for the PLHA should be supportive, stable and comfortable.
- Ideally, PLHA to have jobs that give regular income, so that they are not struggling financially for daily food etc.
- In order to take ART, PLHA should not abuse alcohol as this could interfere with the ART medicines. Abusing alcohol as well as taking ART drugs could lead to serious repercussions in terms of serious damage to the liver, pancreas, etc.
- ART centers must be accessible to the patients. They should be close enough to come to the treatment center whenever they become ill or sick because of the ART drugs or opportunistic infections.
- All ART doctors must refer patients who have psychiatric problems to the necessary unit.

Slide 13



Reader's Notes:

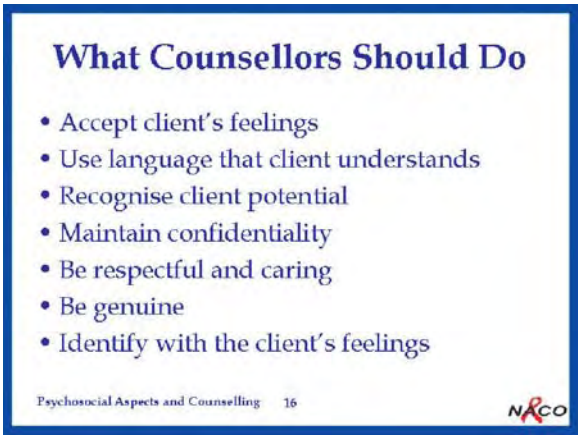
- As HIV progresses, the counsellor needs to support the clients according to his/her need at each stage of the illness. This involves every stage from giving HIV test results to supporting the client and his/her family up to the time of death.

Slide 14

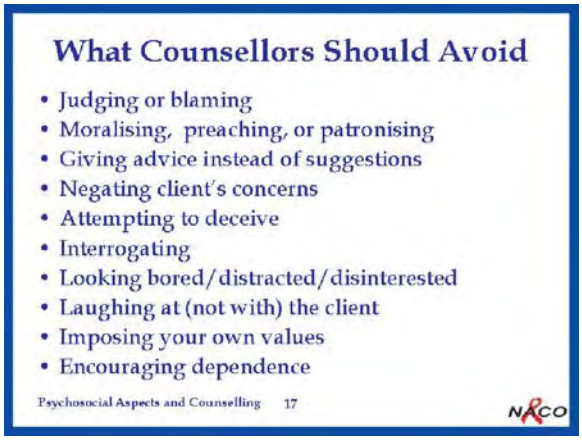
Slide 15

Reader's Notes:

- It is important that clinicians demonstrate these same qualities with patients in order to improve care.
- To review the distinctiveness between client-centered and family-centered counselling.
- **Client-centered counselling:**
- Client-centered counselling refers to counselling conducted in an interactive manner approachable to client needs.
- The focus is on developing prevention objectives and strategies with the client rather than simply providing information. An understanding of the unique circumstances of the client is required - behaviors, sexual identity, race/ethnicity, culture, knowledge, and social and economic status.

		• The counsellor's role is not to assess or evaluate the client, but to feed this natural capacity for change through empathy and unconditional acceptance. • The primary technique of client-centered counselling is to actively listen and reflect the client's statements in a nondirective, nonjudgmental manner, so providing a safe environment for the client's self-exploration. This relationship enables the counselor to clarify the client's feelings without imposing external assessments or values. • **Family-centered counselling:** • Family counseling - Counselling the family as a whole rather than singling out specific individuals for independent counselling. • HIV/AIDS affects the whole family it can sometimes help if you all see a counsellor together. Family members may be too scared to express how to express their feelings about one family members HIV positive status.Talking to children about HIV/AIDS can be very difficult and upsetting. • Having the support of a family counsellor may help make these thing easier. Seeing a counsellor together with family members will allow the family members to set time to listen to each other's worries. • It can really help give everyone in the family a better understanding of what is happening. • It can also bring the family members much closer together and encourage to give each other more support.
Slide 16		**Reader's Notes:** • A counsellor always believes in the potential of each client to make decisions for himself or herself. • A counsellor also maintains confidentiality of the client at all costs.

Slide 17



Reader's Notes:

- It is critical for doctors to conduct effective counselling for clients who present for HIV testing. Clients who present for HIV testing are dealing with a heightened sense of fear, stigma, and shame. They may also fear: reactions of significant others, pain death and disfigurement. The counsellor must focus on the client's concerns and feelings.
- Never be judgmental or blame the client for their current situation. Moralizing, preaching or patronizing will only alienate the client, and is unlikely to help establish a rapport.
- It is always very tempting to categorize clients into diagnostic labels, rather than look at their practical worries for the future. The counsellor must focus on the client's concerns and feelings.
- Never give false hopes or reassurances like "don't cry everything will be alright" or "don't cry you will live for a long time."
- It is important to accept the patient's feelings without interrogating the client in a disdainful manner. Use of medical jargon can be very confusing for some clients. It is acceptable to laugh with the client, but never at the client. The client has not approached the system to get a new set of values; therefore imposing them on him/her is counter productive. Very importantly, a good counsellor is one who promotes the independence of his/her client, not his/her dependence.

Slide 18

Reader's Notes:

- The objectives of pre-test counselling:
- Assess a client's risk of HIV infection after exploring the risk behaviours of the client.
- Understand the implications of taking the test.
- Understand what it means to get a positive/negative result to facilitate a client's informed decision regarding HIV testing.
- Develop specific risk reduction strategies.
- Provide psychosocial and emotional support for behaviour change.
- Support the process of treatment preparedness, adherence treatment and follow-up.
- It is important to note that the pre-test counselling sessions don't necessarily have to be one session. In order to thoroughly discuss all issues before the client takes the HIV test, the pre-test sessions could be conducted over a period of time. Covering a wide range of issues in the pre-test session, ensuring that client's understand testing implications may mean that clients are better prepared for the post test session. Refer to the **Handout 4: Simple Steps of Pre/Post-test Counselling.**

Handout 4: Simple Steps of Pre-and Post-test Counselling

Pre-test Counselling:

- Explain about confidentiality.
- Knowledge on HIV.
- Risk Assessment.
- Implication of testing on individual/ spouse/ partner/community.
- Testing process.
- Types of test results.
- Risk reduction strategies.
- Obtained consent for HIV testing.

Post-test Counselling:

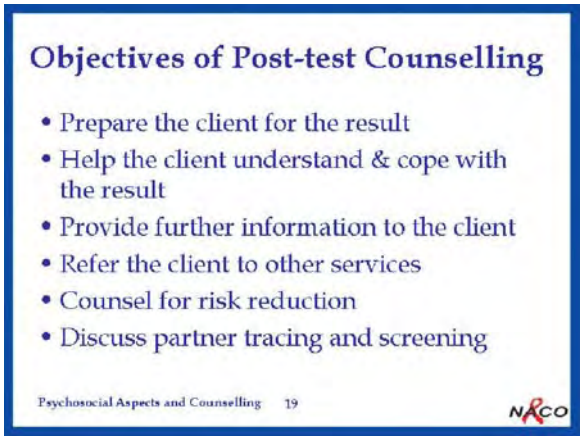
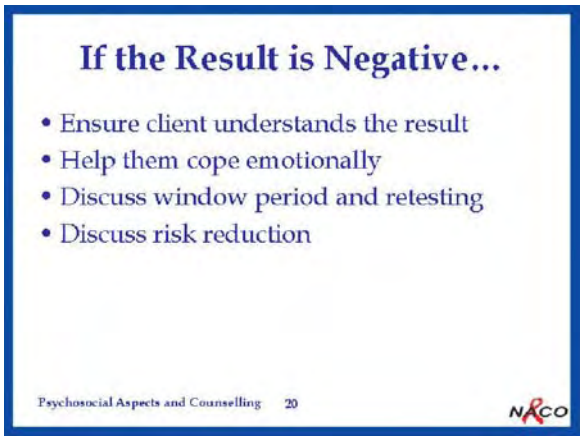
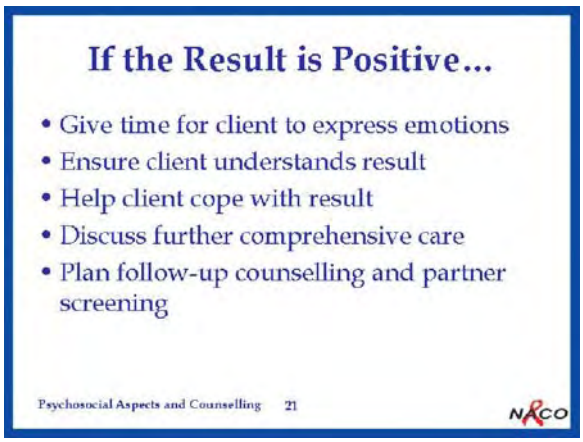
The counsellor should disclose the status only in person, not by telephone, message or mail.

HIV-Negative:

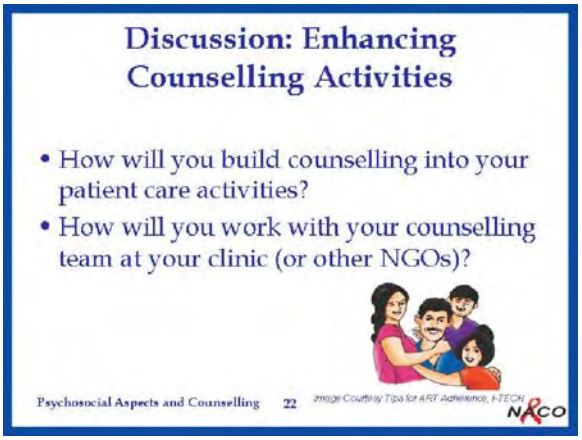
- Discuss possible significance of 'window period' if recent high risk behaviour and need for repeat test for final confirmation.
- Reinforce behavioural changes needed to prevent HIV infection in future e.g., condom use, and information on needle exchange outlets/services.

HIV-Positive:

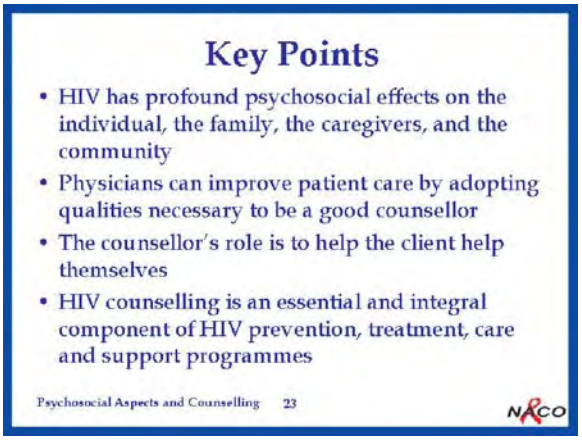
- Schedule adequate time to give positive results.
- Schedule clinical appointments early care is vital.
- Arrange initial psychological support arrangements and follow-up appointment.
- Discuss need for further testing (repeat/confirmatory test, viral load, CD4 count).
- Provide information on HIV and community resources.
- Referral for specialist counselling and support.
- Reinforce safe sex and needle-using behaviours.
- Explain partner notification and other implications of positive diagnosis.
- Follow-up counselling and support as required.

Slide 19		**Reader's Notes:** • The counsellor must give the result as soon as possible. It is important not delay giving the result when the client comes in to receive the result. Post-test counselling helps the client cope with the emotions based on the result.
Slide 20		**Reader's Notes:** • The client may be very relieved about receiving a negative result. The counsellor must remind the client about the window period and discuss the importance of returning for a repeat test if the client has engaged in risk behaviour in the past 3-6 months.
Slide 21		**Reader's Notes:** • The counsellor must spend time to emotionally support the client who has just received a positive result. Sometimes the client is too overwhelmed to speak and the counsellor must give the client time to express his/her feelings when he/she is ready.

Slide 22



Slide 23



Reader's Notes:

- **For further study refer to website references:**
- http://bmj.bmjjournals.com/cgi/content/full/322/7301/1533.
- http://synkronweb.aidsalliance.org/graphics/secretariat/publications/ppr0703_positive_prevention.pdf.
- www.nbcounseling.com/benefit.html.
- http://en.wikipedia.org/wiki/Personal_development.
- http://www.unfpa.org/publications.
- NAIDS. HIV/AIDS prevention in the context of new therapies. March 1999.
- Summerside J and Davis M, ed Cooper A. Keeping it to ourselves: strategic directions in sexual health promotion and HIV prevention for people with HIV. 2002.
- Counselling materials & NACO guidelines website reference: http://www.nacoonline.org/guidelines/vct_guidelines.pdf.

SESSION 6-7

DAY - TWO

SESSION 6

SESSION

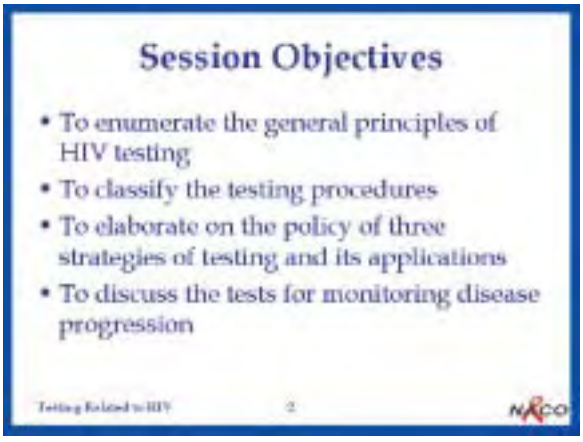
TESTING RELATED TO HIV

6

Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Enumerate the general principles of testing
- Classify the testing procedures
- Elaborate on the policy of three strategies of testing and its applications
- Discuss the tests for monitoring disease progression

Slide 1		
Slide 2		

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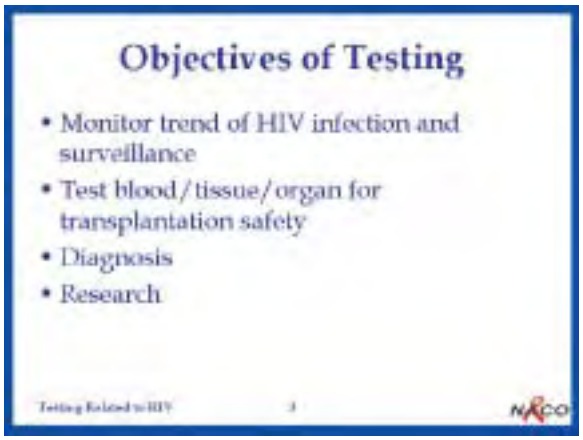
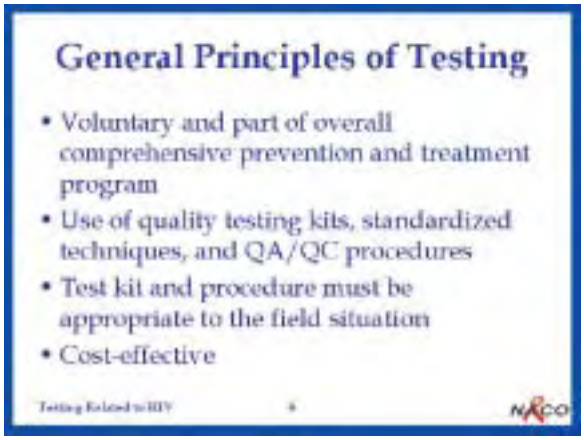


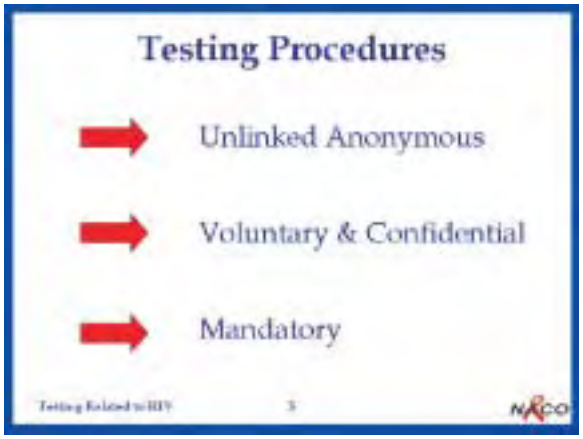
Slide 4



Reader's Notes:

- The concept of **voluntary** testing for HIV is very important. Mandatory testing performed in certain private sector institutions should be condemned. These services include pre-employment checks and health check profiles, without pre-test counselling or consent of the individual.
- Quality assurance (QA) and Quality Control (QC) procedures are very important in lab testing protocols to avoid erroneous test results. NACO and SACS have procedures built-in to ensure procurement and use of kits of acceptable quality. However the importance of external and internal quality assurance must be stressed for ideal standardization of the techniques and accuracy of the results.
- Appropriate to the field takes into account the situation where testing is offered and the type of testing offered. For example, for a woman in advanced labour, it would be inappropriate to test with a procedure that may take 3 hours to generate the result. Instead, a rapid test which offers a result in 15 minutes or less would be more appropriate.
- Cost effectiveness must be an important consideration in resource limited or constrained areas. In the governmental sector, resources are not generated from the patient population. It is important to maintain a balance through use of the most appropriate tests without compromising quality.

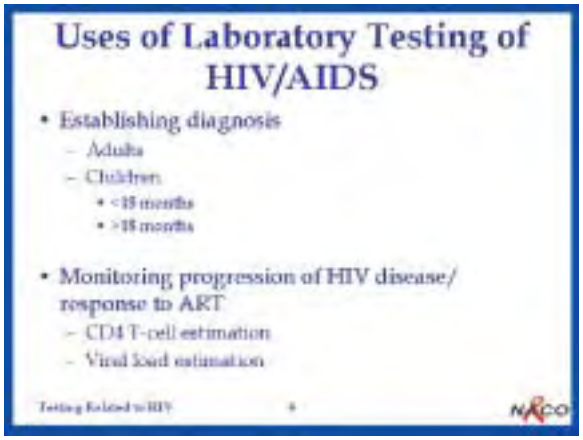
Slide 5



Reader's Notes:

- Three methods to label blood samples to ensure confidentiality:
- **Unlinked anonymous** - all identifiers are removed from blood and it is HIV antibody tested- as in ***sentinel surveillance.***
- **Linked testing** —the blood sample sent has an identifier on it, such as a name, PID or a centre number, which links the sample to the individual client. Ideally samples sent for HIV testing should not be identified with a name, but with some other identifier.
- **Linked-anonymous testing** - no names or other identifiers from the client are recorded. The client receives a unique number (in no way linked to any medical records) that matches the number placed on the blood sample sent to the laboratory.

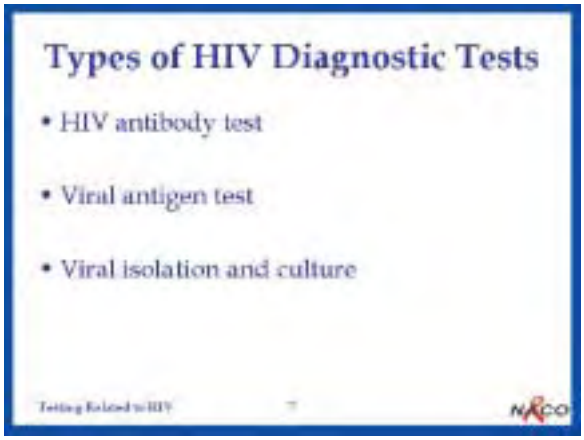
Slide 6



Reader's Notes:

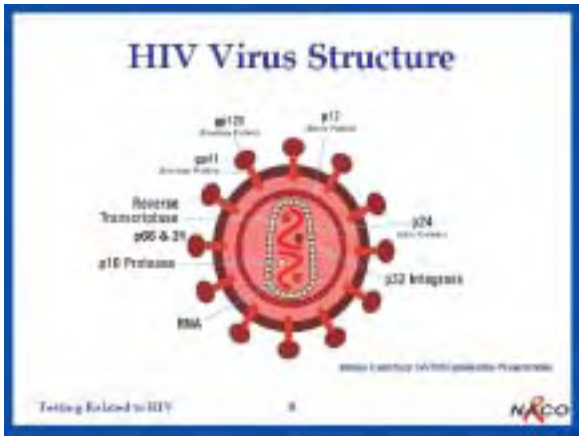
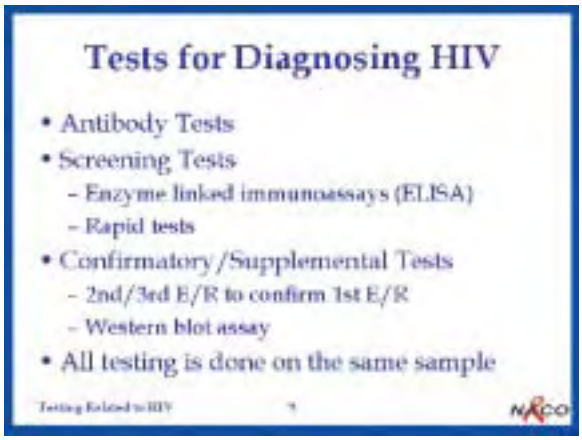
- Laboratory testing of HIV/AIDS is an organized process that involves first establishing the HIV status of an individual. Tests for diagnosing HIV differ between adolescents and adults as compared to infants <18 months of age. Infant testing will be discussed briefly in subsequent slides.
- Tests for monitoring HIV involve studying the progress of the disease in 2 groups:
  1. Progress of disease in ART naïve patients.
  2. Response to therapy in patients on ART.

Slide 7



Reader's Notes:

- HIV antibody tests are the most commonly used test for the diagnosis of HIV infection. These tests are economical, rapid, and can be performed easily in most laboratories. HIV antibody assays are now commercially available in various formats.
- With improvement in the quality of kits, antibody tests have become the back-bone of HIV testing in diagnosis.
- Viral antigen tests are more specific for monitoring disease/response to ARV therapy and in infants <18 months. Being very expensive, requiring expertise and expensive infrastructure, they are not easily available.
- Viral culture is done in a reference lab due to the cumbersome nature of the tests.

Slide 8		
Slide 9		

Reader's Notes:

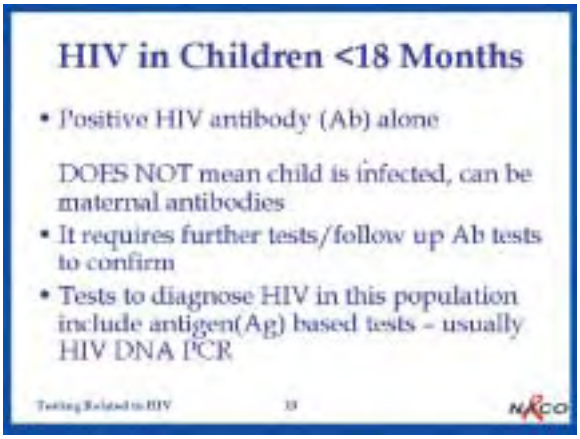
- The Microwell ELISA test can take up to 3 hours to complete, while rapid test readings should be available in less than 30 minutes from start of test (per NACO requirement).
- ELISA / Rapid - both have the possibility of false positives (as in any serological test). The result of HIV has a serious impact , hence all of the tests that result in a positive result, must be re-checked or confirmed by use of a 2nd/3rd set of tests. Currently the confirmation can be done by 2nd/3rd E/R (ELISA/Rapid) tests which narrows down the chance of a false positive. In the past, the western blot was used as the confirmation test, but due to the high cost per test, this is no longer the main stay of confirmation. It is now available only for isolated cases in reference labs.
- All such re-tests using 2nd/3rd tests should use the same serum/plasma sample as the 1st test.

Window period denotes the time lag between actual infection with HIV and the appearance of detectable antibody in serum/plasma using the currently available test kits.

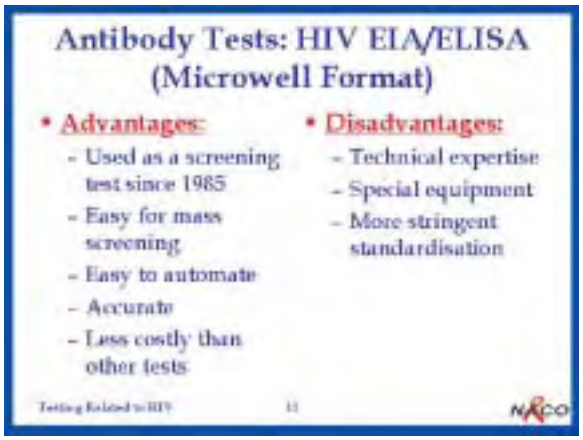
Interpretation of NEGATIVE TEST (For Ab)

Not infected (True —ve)	**Infected- but Antibody not measurable** (False —ve)

Slide 10



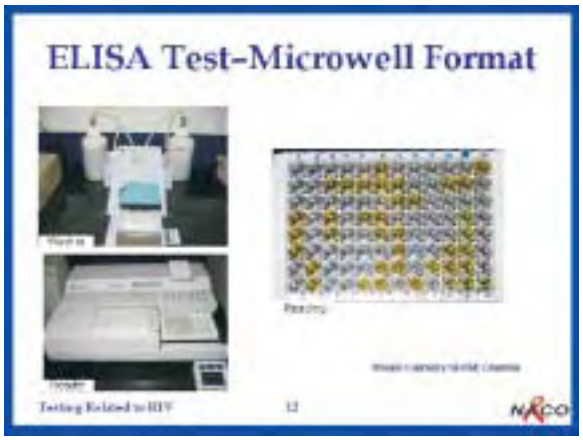
Slide 11



Reader's Notes:

- ELISA Test is the screening test used when >30 samples are tested in a batch.
- Cost per test is much less than rapid tests but requires expensive infrastructure as well as trained technicians.
- The QA/QC is more stringent.
- These tests also require a 2nd/3rd test for confirmation.
- The test reading is based on colour development in the positive samples. It is objective as it uses a reader for measuring the colour development.

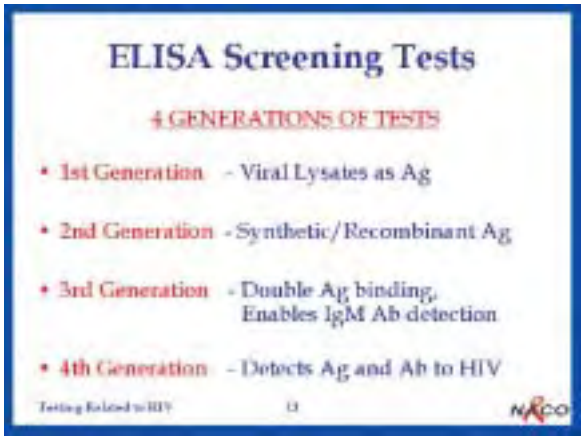
Slide 12



Reader's Notes:

- The ELISA Washer — is a 'multi-channel' automated washer, to assist in washing out the contents of the microwells between the various steps.
- The end result is a colour development which is quantified using an ELISA reader.
- The ELISA reader measures the colour developed in the wells as the 'absorbance ' or optical density (OD). This measurable result is then compared with the cut-off value set for that test run. The wells showing a reading above the cut-off value (COV) are reported as reactive (positive) and those below the COV are reported as non-reactive (negative). The readings by a Microwell ELISA test are thus objective and not subjective.

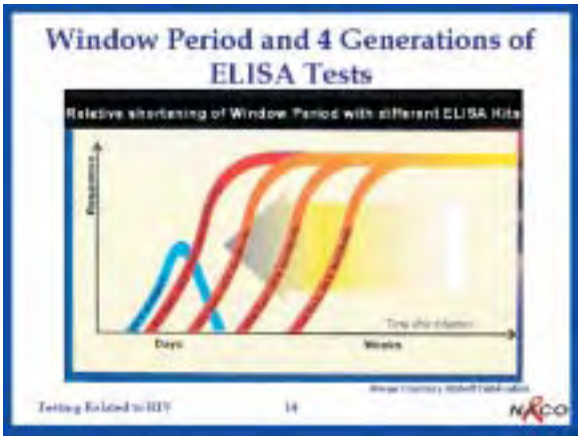
Slide 13



Reader's Notes:

- The first generation tests used viral lysates as antigens and false positives were a major concern.
- The second generation tests use recombinant HIV proteins and/or synthetic peptides as antigens.
- The third generation tests use double antigen binding and enable IgM detection also.
- The fourth generation tests are based on simultaneous detection of HIV antibodies, P24 antigen and immune complexes and have very high sensitivity and specificity. Their use narrows the window period to as close as the NAT, but the cost prevents its availability in the national program.

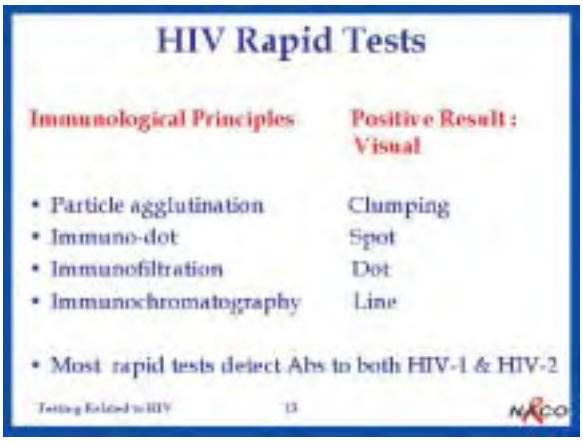
Slide 14



Reader's Notes:

- A graphic representation of the narrowing 'Window Period'.

Slide 15



Reader's Notes:

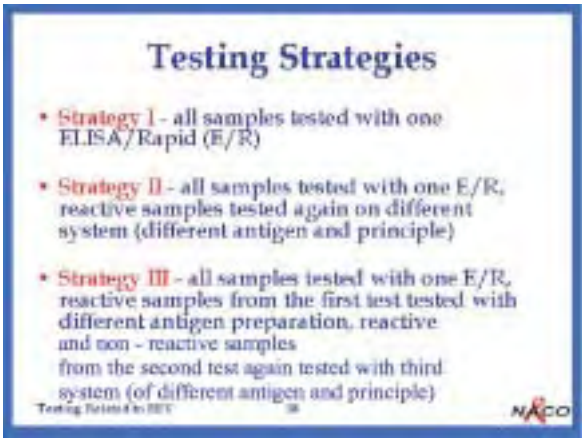
Advantages of Rapid HIV Antibody Tests:

- More flexible (1 - multiple tests at a time).
- Requires minimal equipment and reagents.
- Does not require highly skilled staff.
- On-site clinic or field testing possible.
- Very easy to interpret test results (naked eye).
- Samples can obtained less invasively (finger-prick) - safer for lab technician.
- Same-day screening and confirmation of results.(available <30 min.

Slide 16

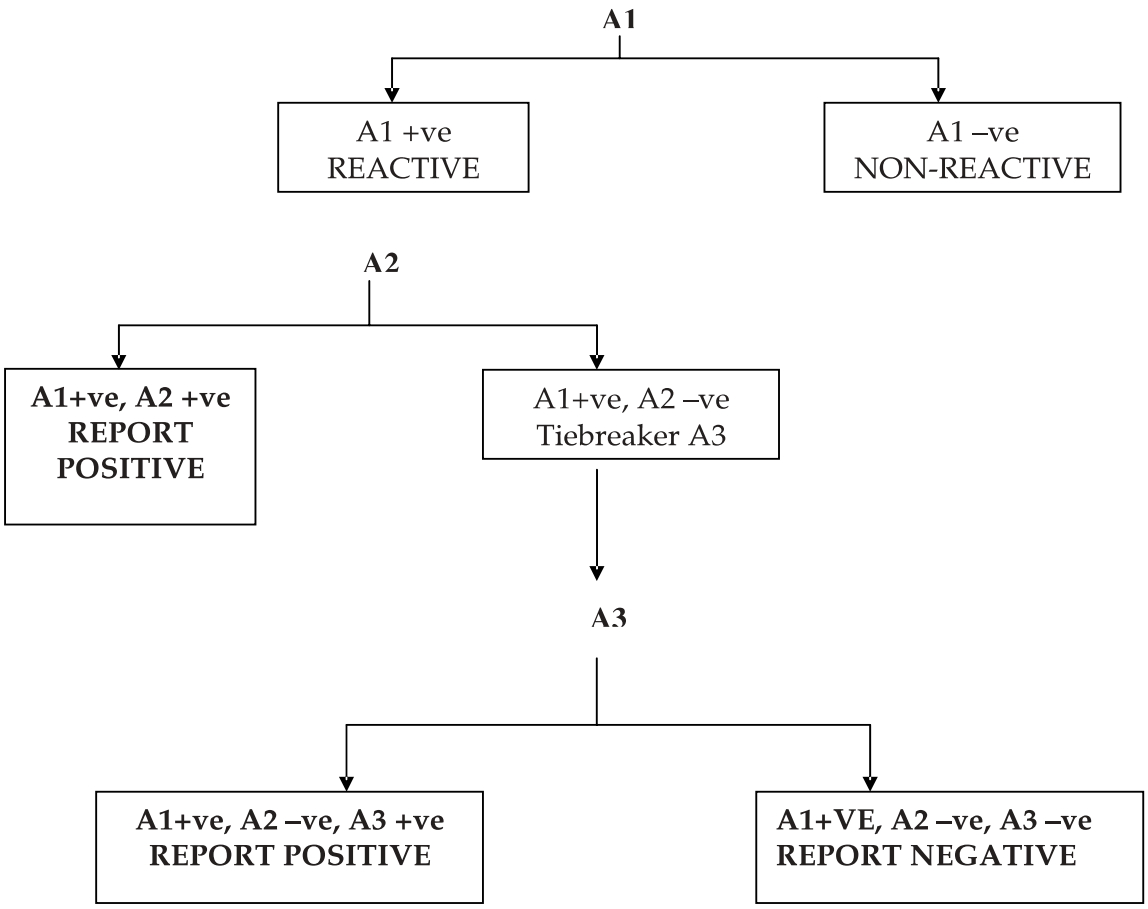
Reader's Notes:

- There are many causes of false positives. This is considerably reduced if quality kits are available.
- 2nd/3rd tests for confirmation of the 1st positive test are performed to overcome the possibility of a false positive.
- Other clinical causes of false positive are similar to those in other serological tests and are rare in practice.

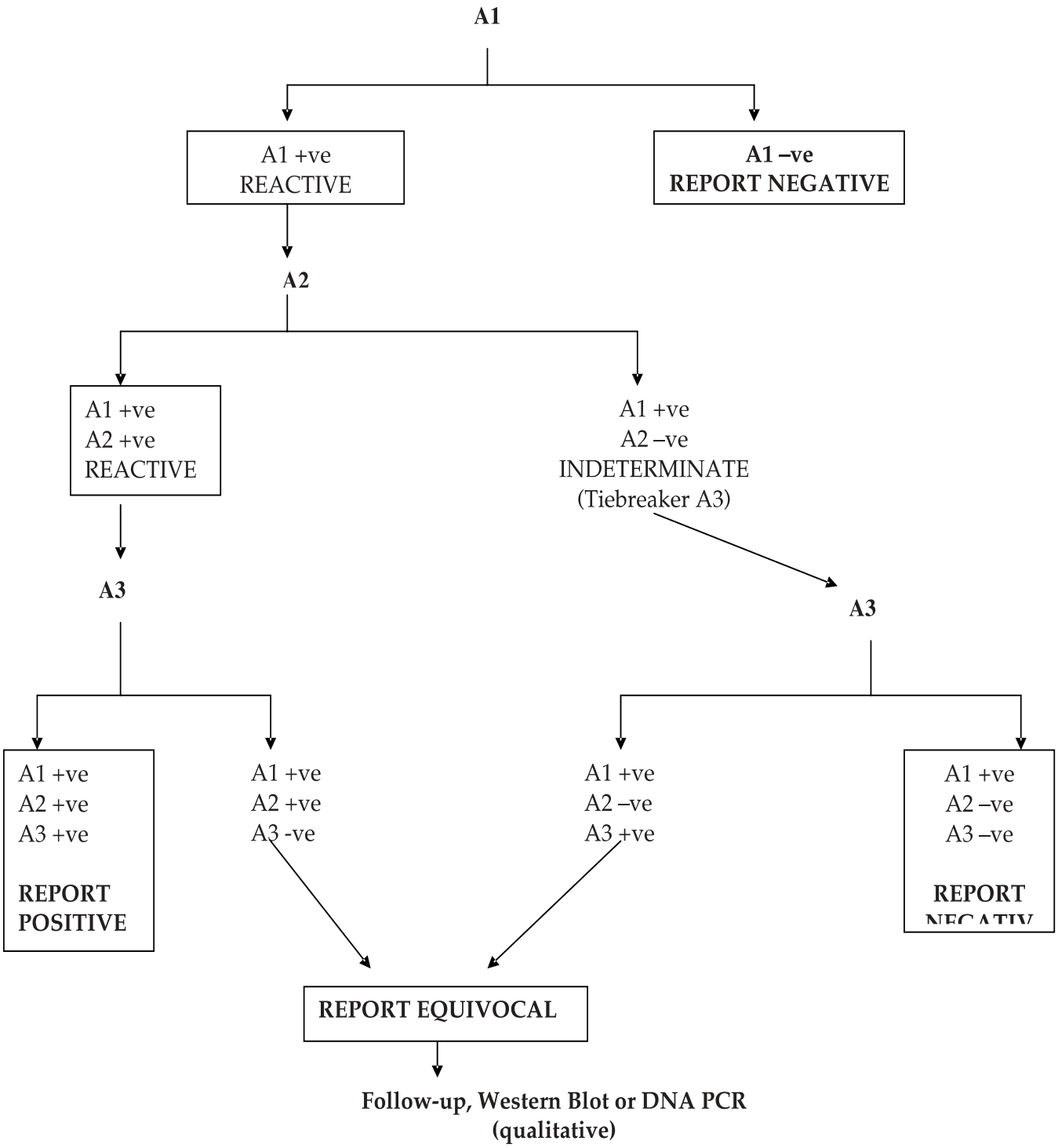
Slide 17		
Slide 18		

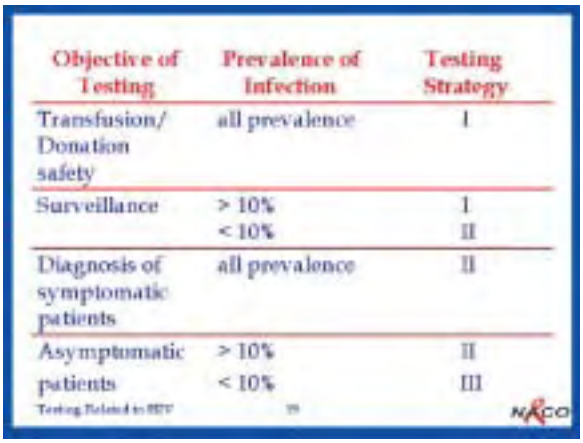
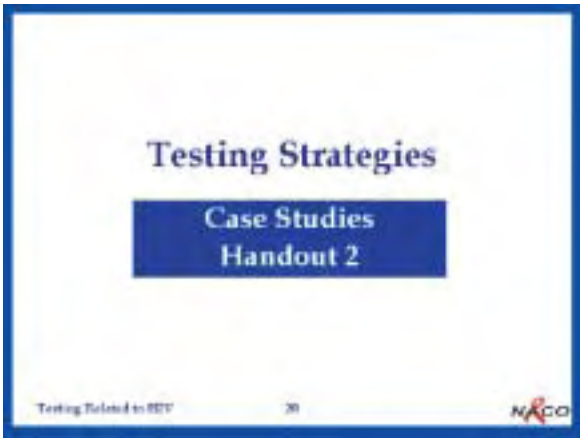
Handout 1: HIV Testing Strategies as per NACO Guidelines (March 2007)

HIV TESTING STRATEGY II B (BLOOD/ PLASMA/SERUM):
(for symptomatic cases)



HIV TESTING STRATEGY III:
(for asymptomatic cases)



Slide 19		
Slide 20		

Handout 2: Case Studies on HIV Testing Strategies

Case Study 1

28/M attends Outpatient Department with H/O of a painless ulcer on his penis for 1 week. He has been healthy prior to this problem. He denies risky sexual behaviours. He has never used a condom.

Questions / Answers with explanation:

Q. 1. Will you recommend HIV testing in this patient?

Q.2. What strategy will you use in this patient?

Case Study 2

30/F married woman with 3 children attends the hospital with H/O general fatigue and tiredness. She states that she received a blood transfusion during labour in the district hospital 2 years ago. The patient has no other symptoms or medical history. The patient has had no sexual partners other than her husband. Her husband is a local farmer without known risk behaviours.

Questions / Answers with explanation:

Q.1. Will you recommend HIV testing in this patient?

Q.2. What strategy will you use in this patient?

Q.3. What strategy should they have used for testing the blood prior to blood transfusion?

Case Study 3

40/M policeman comes to the doctor with H/O of back pain, cough with expectoration for 4 weeks and fever for 2 months. He gives history of drastic weight loss. He had been ill over the past few months and hospitalized twice for diarrhoea. His wife and 3 children are healthy. The patient said that he had a long history of multiple sexual encounters with sex workers. He consumed alcohol heavily on most weekends. He does not use condoms with his wife or other sexual partners.

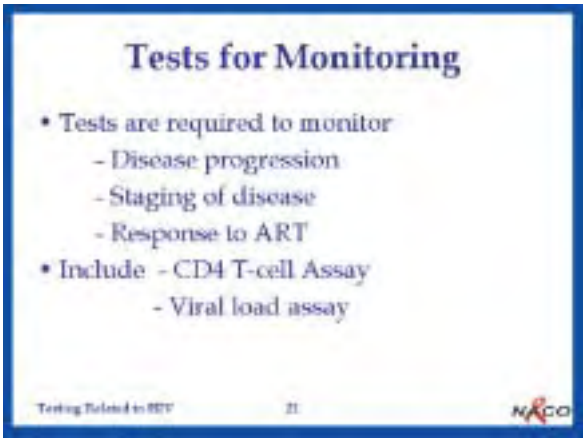
Questions / Answers with explanation:

Q.1. Will you recommend HIV testing in this patient?

Q.2. What strategy will you use in this patient?

Q.3. What strategy will you prefer for his wife?

Slide 21



Slide 22

Reader's Notes:

- Immunofluorescence assays by Flow Cytometry is the gold standard for CD4 cell measurements.
- CD4 — Methods of enumeration:
- The following two concepts are used to obtain the absolute CD4 cell count:

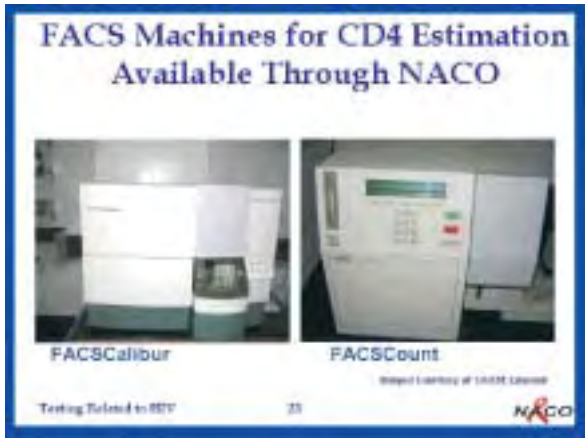
1. Dual platform approach:

- Uses two instruments to generate absolute CD4 cell counts: a FCM for generating a % of CD4 cells among lymphocytes and a hematology analyzer to enumerate the absolute lymphocyte count. An absolute CD4 count is then derived by multiplying the %CD4 by the absolute lymphocyte count.
- Instruments include BD FACSCalibur/ FASCScan/ FACSort or Beckman-Coulter Epics XL. Some of these combine the concept of a dual platform into one machine —e.g. a FACSCalibur. The results directly obtained include an absolute CD4 count and CD4%. The process involves 'gating' of CD45 bright cells (Lymphocytes).

2. Single platform approach:

- Enables absolute CD4 cell counts to be derived directly without the need for a hematological analyzer, e.g., the use of volumetric counting (Partec CyFlow), microfluorometry (Guava) and most commonly, the addition of a known density of reference flourescent beads to the sample (FACSCount).

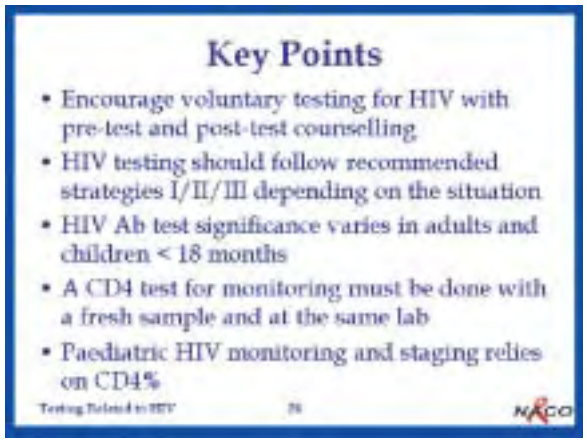
Slide 23



Reader's Notes:

- Keep in mind the following when requesting CD4 assays:
  - Repeat in same lab and by same method.
  - Blood should processed within 48 hours of collection for FACS Count.
  - Freezing blood - false low counts.
  - Ensure no clots (micro-clots) in sample.
  - False values- inter-current illness, acute infections, steroids, major surgery.
  - Normal variation up to 30%.
  - Children < 6 years have high CD4 counts.
  - Diurnal variation.
  - FACS Count gives results of absolute CD4, CD8, CD3 as well as CD4/CD8 ratio. It does not give CD4 percentage. One can do maximum of 30 tests per working day. It is easier to use and requires less training than the FACS Calibur.
  - FACS Calibur is a much more expensive equipment, has many more functions other than CD4 assay. This machine gives absolute and percentage of CD4 hence useful in Peadiatric HIV monitoring. Large number of CD4 estimations per day can be done (More than 100). However it requires much more training and equipment maintenance than the FACS Count.
  - Source: Guidelines for HIV Diagnosis and Monitoring of ART- Dec, 2005, WHO.

Slide 24



Reader's Notes:

- Further reading:
  1. NACO Guidelines on HIV testing.
  2. WHO Antiretroviral Therapy of HIV infection in Adults and Adolescents in resource-limited settings: Towards universal access — 2006.
  3. WHO Antiretroviral Therapy of HIV infection in infants and children in resource-limited settings: Towards universal access — 2006.

SESSION 7

SESSION

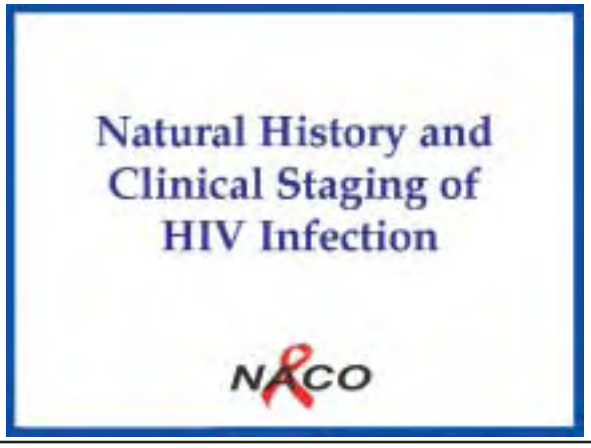
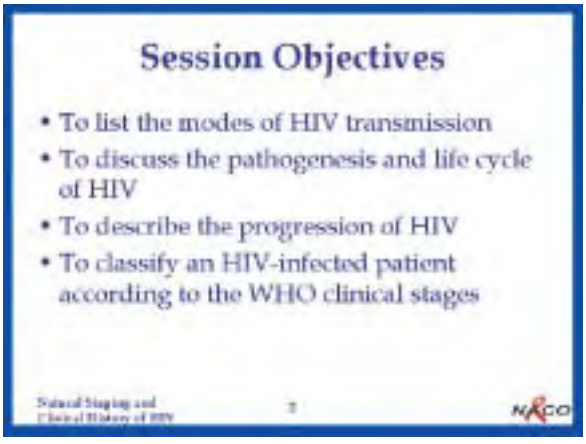
NATURAL HISTORY AND CLINICAL STAGING OF HIV INFECTION

7

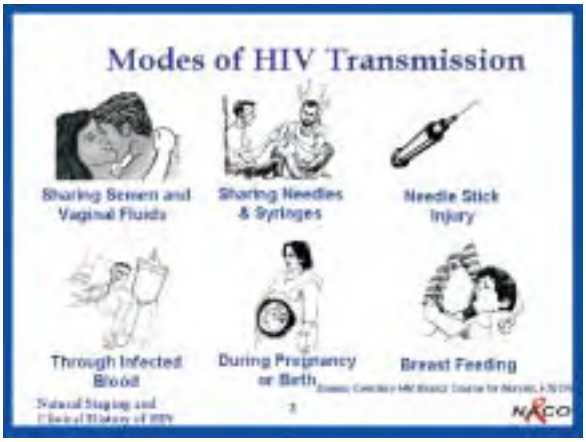
Total Session Time: 45 minutes

Session Objectives: At the end of the session, the participant should be able to:

- List the common modes of HIV Transmission
- Discuss the life cycle and pathogenesis of HIV
- Describe the progression of HIV
- Classify an HIV infected patient according to the WHO clinical stages

Slide 1		
Slide 2		

Slide 3

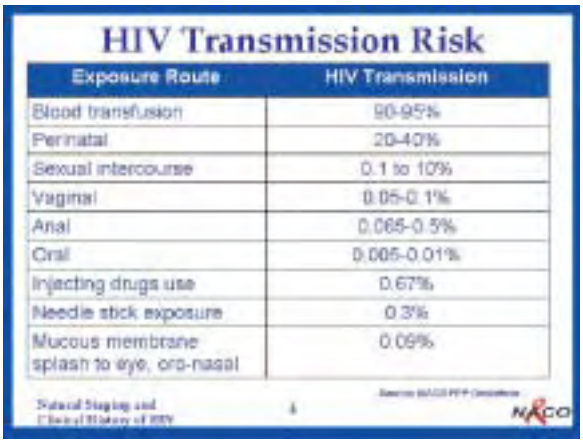


Reader's Notes:

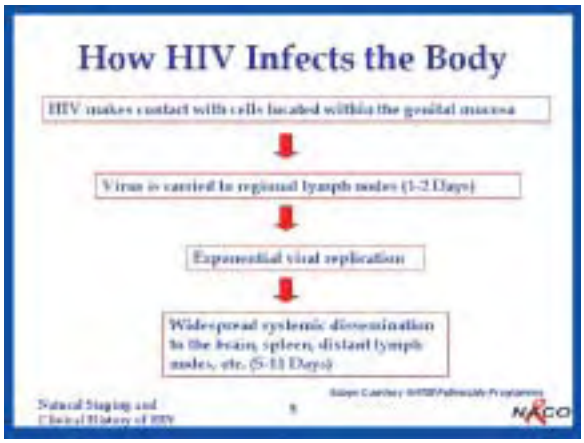
How HIV is transmitted:

- HIV is transmitted from one person to another through the exchange of blood and certain bodily fluids during sexual activity. Vaginal secretions and semen contain HIV. Sexual intercourse (vaginal and anal) is one way in which HIV is transmitted.
- Sharing needles, syringes and other paraphernalia receiving a blood transfusion, or getting a deep needle stick from a person infected by HIV during an occupational exposure, are ways transmission occurs when blood from an infected person is transmitted to another.
- Mothers can transmit the virus to their babies during pregnancy, delivery, or during breast feeding. This does not happen all the time - approximately 30-48% of the time as reported in India, but abroad it is less than 30%.

Slide 4



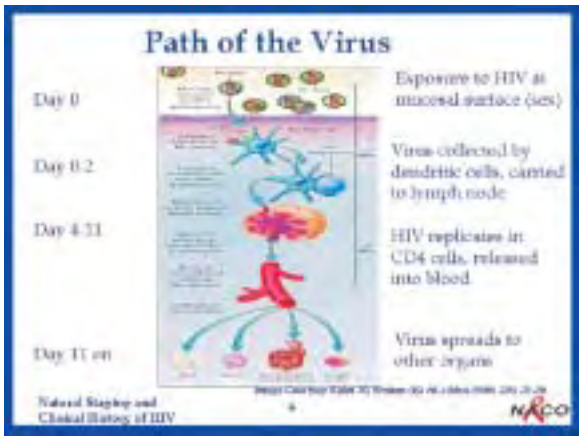
Slide 5



Reader's Notes:

- HIV transmitted through sexual activity enters the bloodstream via mucous membranes lining the vagina, rectum and mouth. Macrophages and dendritic cells on the surface of mucous membranes bind virus and shuttle it into the lymph nodes, which contain high concentrations of Helper T cells (CD4+ T cells).
- Once HIV has entered the body, the immune system initiates anti-HIV antibody and cytotoxic T cell production. However, it can take one to six months for an individual exposed to HIV to produce measurable quantities of antibody. The immune response is weakened as memory T cells (CD4+ CCR5+) are destroyed.
- HIV enters the body and binds to dendritic cells (orange cells with projections) which carry the virus to CD4+ T cells in lymphoid tissue establishing the infection.
- Virus replication accelerates producing massive viremia and wide dissemination of virus throughout the body's lymphoid tissues.
- An immune response against virus causes some protection but a chronic persistent infection is established. The production of cytokines and cell divisions that regulate the immune response for protection also cause HIV replication.
- There is a rapid turnover of CD4+ T cells that ultimately leads to their destruction and to a change in lymphoid tissues that prevent immune responses.

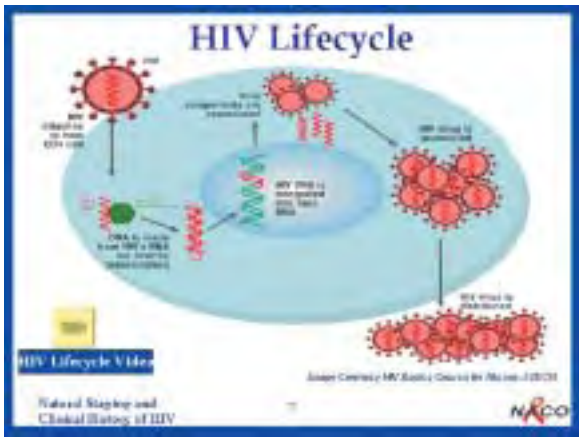
Slide 6



Reader's Notes:

- Cytotoxic lymphocyte production follows the rise of HIV in the blood.
- HIV specific CD4+ T cells may be especially susceptible to attack and destruction by HIV. HIV binds to CD-SIGN, a glycoprotein expressed on dendritic cells. Migration of HIV bearing activated dendritic cells to helper T cell areas of lymph nodes may specifically infect helper T cells specific for HIV peptides.
- Reductions in HIV specific helper T cell numbers may lead to decreased activation and survival of cytotoxic CD8 T cells.
- Reduced CD4 T cells may also result in an incomplete activation of CD8 T cells that can remove HIV infected cells, resulting in a decreased ability to destroy virally infected cells.
- The rapid loss of memory helper T cells, and the inability to replace these cells leads to increasing immunodeficiency.
- High mutation rates of HIV also allow the virus to escape adaptive immune responses.

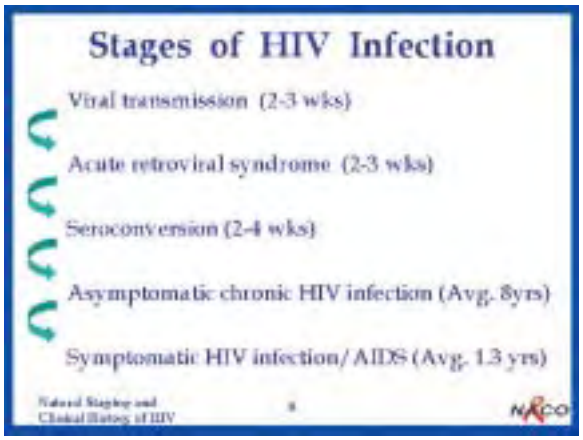
Slide 7



Reader's Notes:

- The 6 stages of the HIV life cycle are essential to understand the site of action of ARVs on HIV. HIV uses the CD4 cell like a factory to reproduce itself:
- HIV attaches to the CD4 cell & releases RNA & enzyme on entry.
- The enzyme 'Reverse Transcriptase' makes a DNA copy of the viral RNA.
- New viral DNA is then integrated into the CD4 cell nucleus using 'Integrase.'
- New viral components are then produced, using the cell's machinery. These are assembled together using the enzyme 'Protease' & then released as new viruses.
- The host CD4 cell gets destroyed during this process.
- Source video: http://www.jhu.edu/Johns Hopkins' video on HIV viral replication: duration 2 minutes.

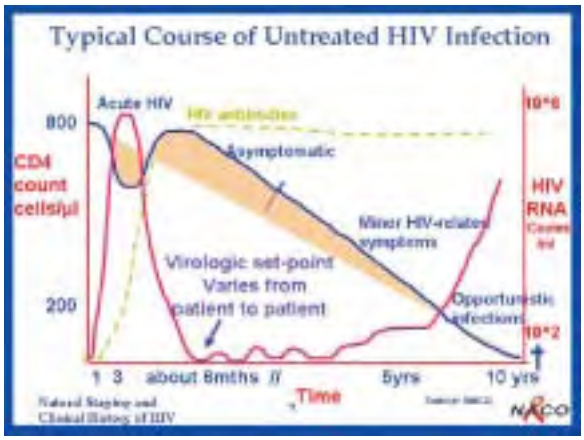
Slide 8



Reader's Notes:

- Acute retroviral syndrome occurs when the virus is disseminated. It is characterized by fever, rash, lymphadenopathy and sore throat (like other viral infections).
- On recovery, the patient will have antibodies to HIV that can be detected by tests like ELISA.
- The patient remains without symptoms for many years until he or she develops symptomatic HIV or AIDS about 8 years down from the time of infection. This period, as also the time period between development of AIDS to death is highly variable.

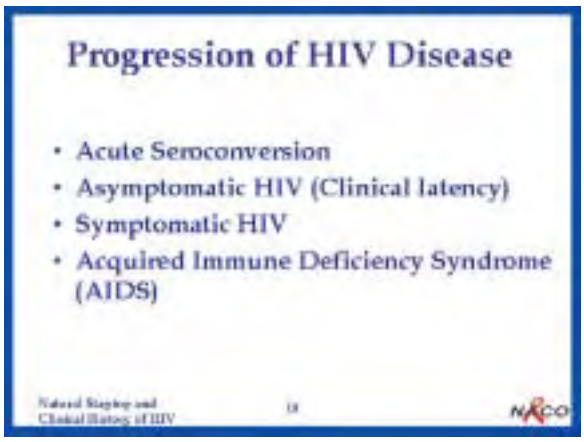
Slide 9



Reader's Notes:

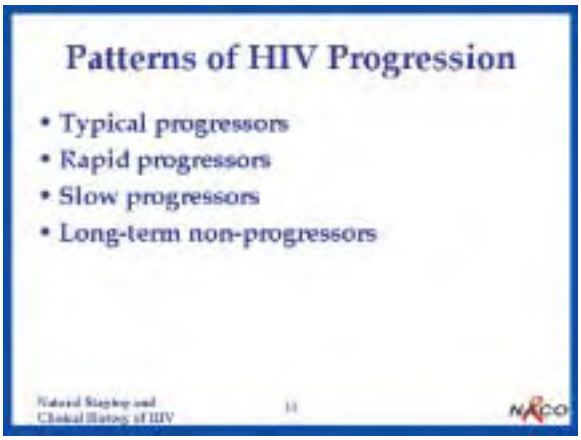
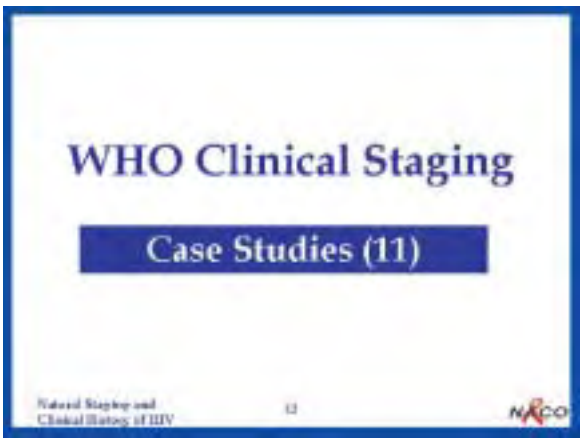
- Pink color depicts the viral load. It reaches the maximum level during acute retroviral syndrome, then it settles down to a "viral set point" and this set point is maintained over a period of years. After 5-8 years the viral load starts increasing again and the patient progresses to the stage of AIDS.
- The blue line depicts the CD4 count. The CD4 count is depleted initially and then reaches a set point which is maintained over a period of 5-8 years. When the patient reaches the stage of AIDS, CD4 count starts declining very fast.

Slide 10



Reader's Notes:

- **Acute seroconversion:**
  - Fever, rash and adenopathy
  - Usually 3-6 weeks after exposure
- **Asymptomatic HIV (clinical latency):**
  - Patient often unaware of infection, antibodies detectable.
  - Immune system able to control virus to limited extent and CD4 > 350/cu.mm
  - Able to transmit HIV to others
- **Symptomatic HIV:**
  - Minor to moderately severe symptoms
  - Recurrent symptoms
- **AIDS:**
  - Severe immunosuppression associated with opportunistic infections or cancers.

Slide 11		**Reader's Notes:** • Typical progressors have a drop of 35-50 CD4 cells/ year. • Rapid progressors ("CD4 crash") have a drop of 50 CD4cells per month after seroconversion. • Slow Progressors have a CD4 decline that is very slow compared to the typical progressors. • Long term non-progressors have CD4 counts that are stable at a baseline for many years.
Slide 12		

Handout 1: WHO Clinical Staging for HIV-infected Adults and Adolescents

Clinical Stage 1

- Asymptomatic
- Persistent generalized lymphadenopathy

Clinical Stage 2

- Unexplained moderate weight loss (<10% of presumed or measured body weight)[1]
- Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)
- Herpes zoster
- Angular cheilitis
- Recurrent oral ulceration
- Papular pruritic eruptions
- Seborrhoeic dermatitis
- Fungal nail infections

Clinical Stage 3

- Unexplained[2] severe weight loss (>10% of presumed or measured body weight)
- Unexplained chronic diarrhoea for longer than one month
- Unexplained persistent fever (above 37.5°C intermittent or constant for longer than one month)
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis
- Severe bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia,)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained anaemia (<8 g/dl), neutropenia (<0.5 x 10^9 /L) and or chronic thrombocytopenia (<50 X 10^9 /L^3)

Clinical Stage 4[3]

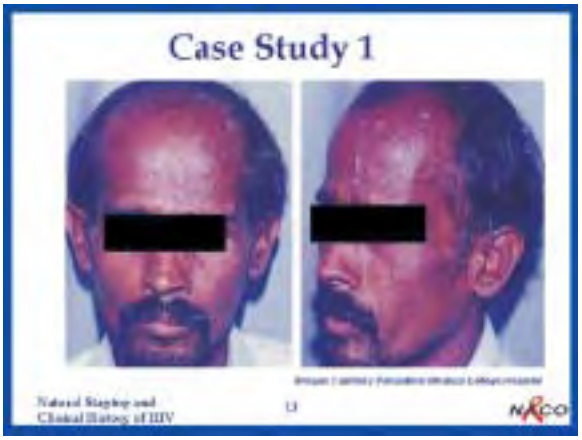
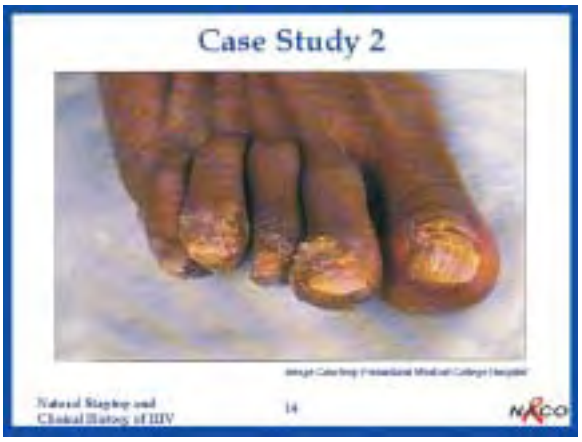
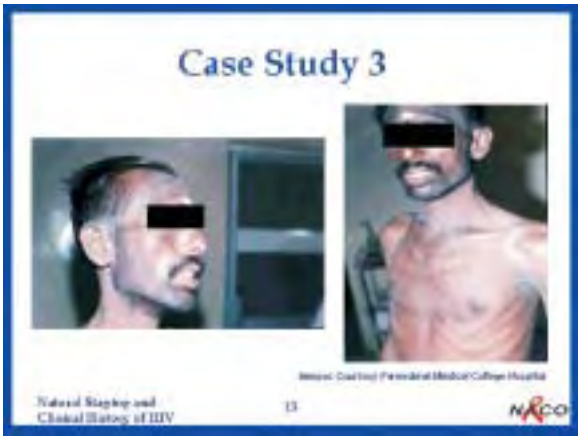
- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site)
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi's sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs)
- Central nervous system toxoplasmosis
- HIV encephalopathy

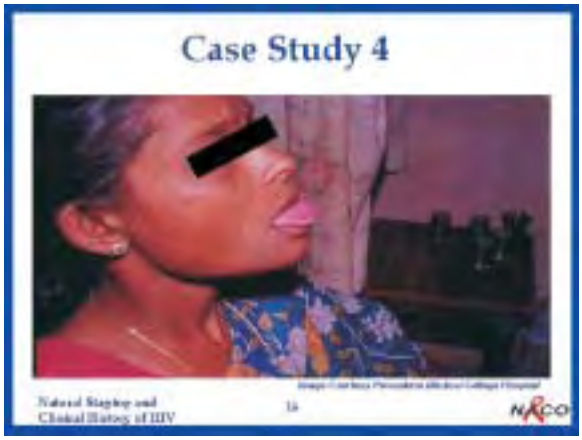
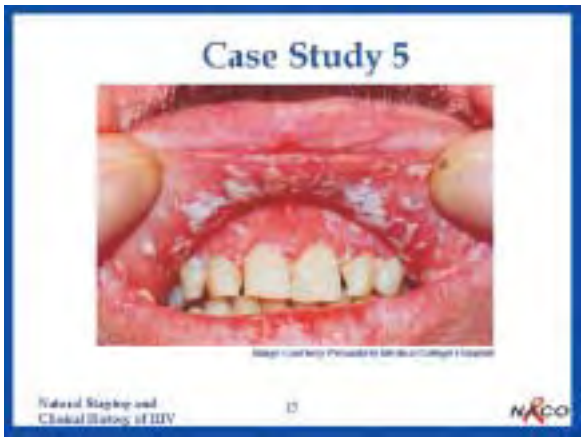
- Extrapulmonary cryptococcosis including meningitis
- Disseminated non-tuberculous mycobacteria infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated mycosis (extrapulmonary histoplasmosis, coccidiomycosis)
- Recurrent septicaemia (including non-typhoidal salmonella)
- Lymphoma (cerebral or B cell non-Hodgkin)
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis
- Symptomatic HIV associated nephropathy or Symptomatic HIV associated cardiomyopathy.

[1] Assessment of body weight in pregnant woman needs to consider expected weight gain of pregnancy.

[2] Unexplained refers to where the condition is not explained by other conditions.

[3] Some additional specific conditions can also be included in regional classifications [e.g. reactivation of American trypanosomiasis (meningoencephalitis and/or myocarditis) in Americas region, Penicilliosis in Asia].

Slide 13		
Slide 14		
Slide 15		

Slide 16		
Slide 17		
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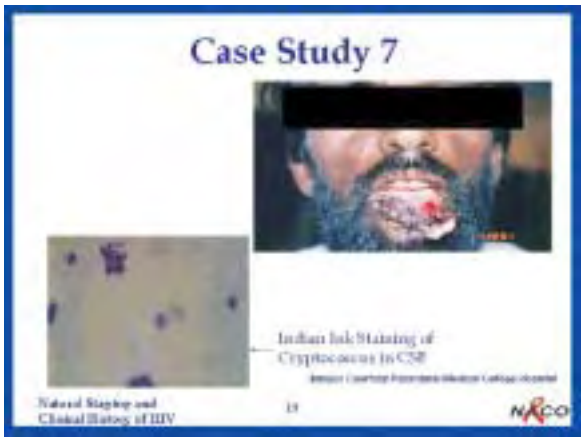
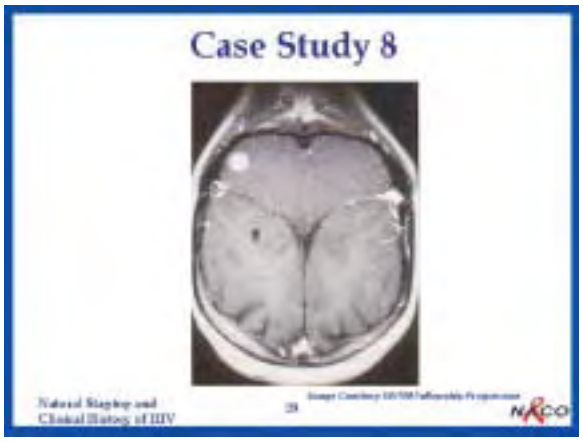
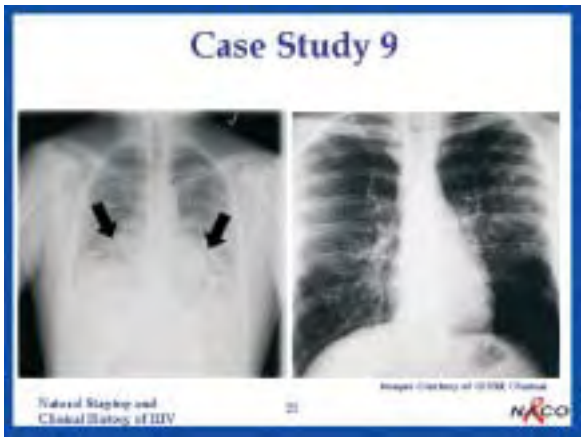
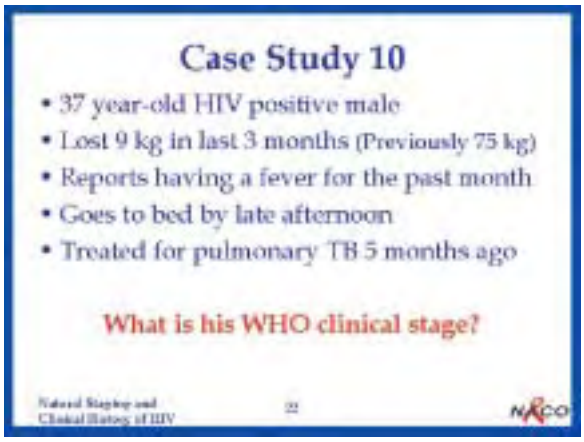
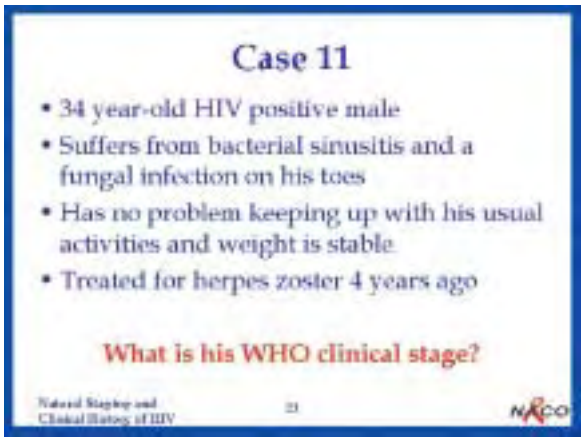
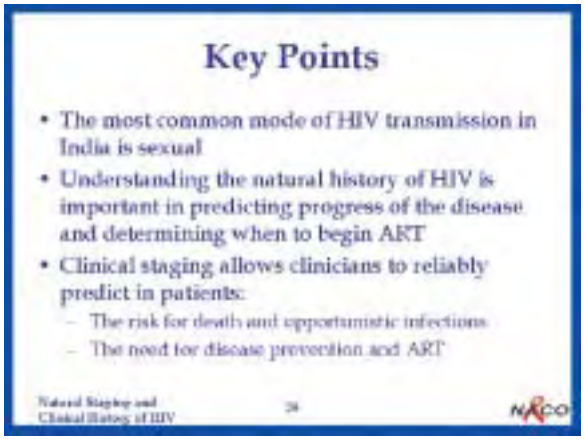
Slide 19		
Slide 20		
Slide 21		

Slide 22		
Slide 23		
Slide 24		

SESSION 8-11

DAY - THREE

SESSION 8

SESSION

CLINICAL PHARMACOLOGY OF ARV DRUGS

8

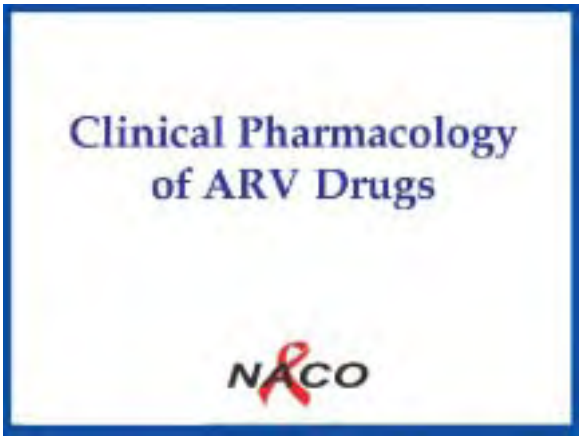
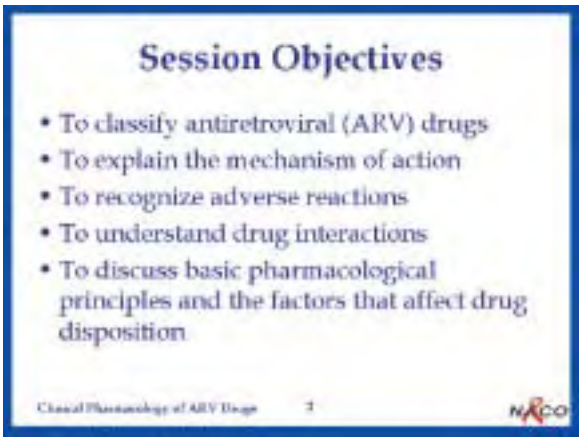
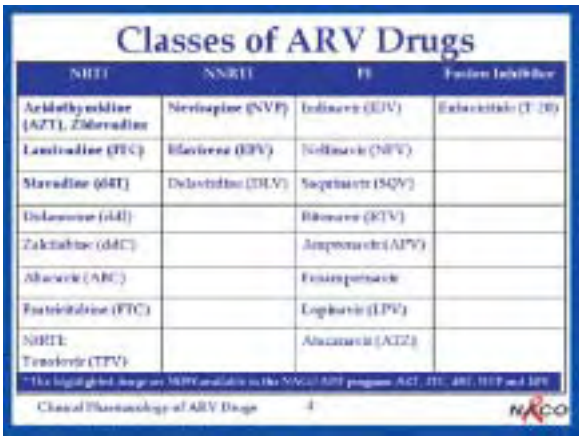
Total Session Time: 45 minutes

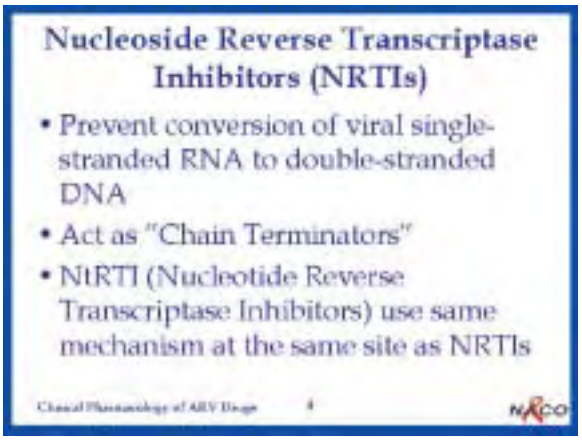
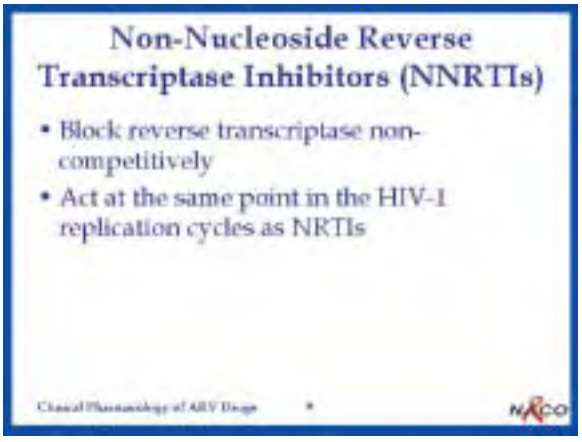
Session Objectives: At the end of the session, the participant should be able to:

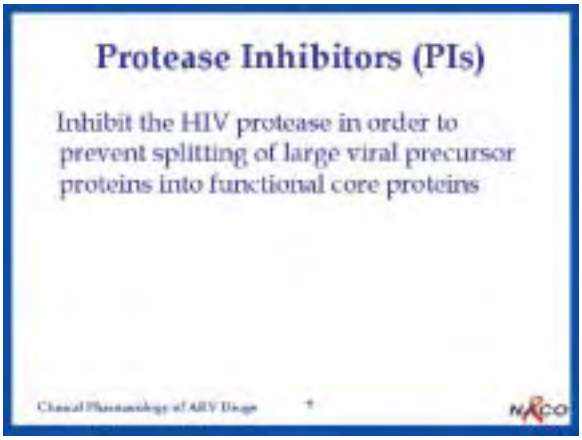
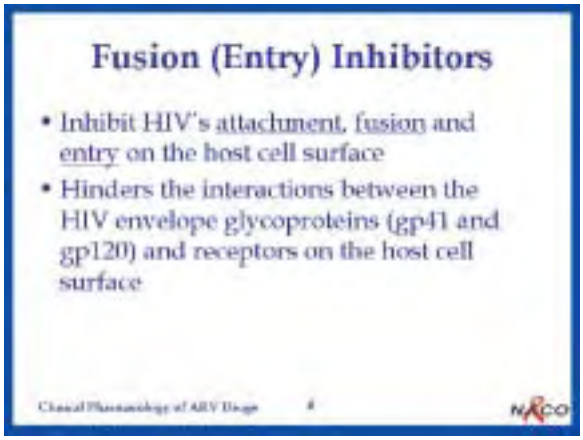
- Classify antiretroviral (ARV) drugs
- Explain the mechanism of action
- Recognize adverse reactions
- Understand drug interactions
- Discuss basic pharmacological principles and the factors that affect drug disposition

Session Overview:

Step	Time	Activity/Method	Content	Resources Needed
1	3 minutes	Trainer Presentation	Introduction and Classes of Antiretrovirals (Slides 1-3)	LCD or Overhead Projector Handout 1
2	10 minutes	Play video, Trainer Presentation	Life Cycle and Action of Different Classes of ARV Drugs (Slide 4)	LCD or Overhead Projector, Video 1
3	5 minutes	Trainer Presentation	Mechanism of Action (Slides 5-8)	LCD or Overhead Projector
4	7 minutes	Trainer Presentation	Adverse Side Effects (Slides 9-17)	LCD or Overhead Projector
5	8 minutes	Case Study	Case Study 1 (Slides 18-21)	LCD or Overhead Projector
6	8 minutes	Trainer Presentation	Pharmacodynamics (Slides 22-26)	LCD or Overhead Projector
7	4 minutes	Trainer Presentation	Summary (Slides 27-28)	LCD or Overhead Projector

Slide 1		
Slide 2		
Slide 3		

Slide 4		**Reader's Notes:** • Video o: Boehringer Ingelheim's video on mechanism of action of different classes of ARV drugs: duration 5 minutes.
Slide 5		**Reader's Notes:** • NRTIs exert their action in the cytoplasm of the host cells by inhibiting the viral encoded reverse transcriptase enzyme. • This prevents the conversion of viral single stranded RNA into double stranded DNA and thus prevents HIV from incorporating its genetic material into the genome of the host cell.
Slide 6		**Reader's Notes:** • The NNRTIs bind to the reverse transcriptase enzyme at its active site and prevent it from adding any new nucleoside to the growing DNA chain. • Because of this different mechanism of action, the viral mutations that encode for resistance to NRTIs are different from those that encode for resistance to NNRTIs.

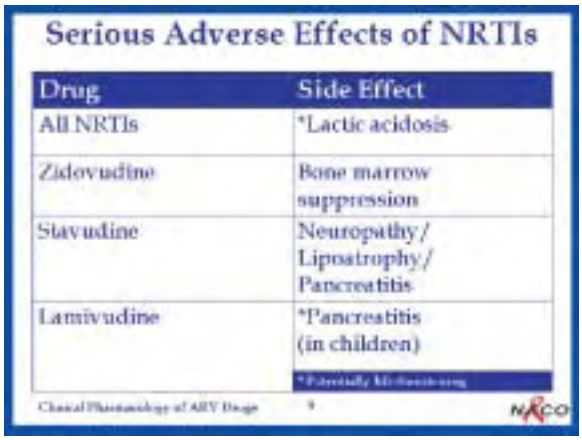
Slide 7		
Slide 8		**Reader's Notes:** • Refer to the following information at: http://www.who.int/hiv/pub/guidelines/arvguidelines2006.pdf. 1. Dosages of Retroviral Drugs for Adults and Adolescents. 2. Storage of Antiretrovirals. 3. Drugs that Interact with Antiretrovirals. • Refer to the following information in the NACO: ART Guidelines for Adults and Adolescents. 1. Table 2 (Signs and Symptoms: Response - page 12). 2. Table 3 (Clinical Signs and Symptoms, Monitoring and management of Serious Adverse Effects of ART Which Require Drug Discontinuation - Page 13-14). 3. Annex D (Long Term Toxicities of ARV Drugs).

Handout 1: Classes of Antiretrovirals (2006)

NRTI	NNRTI	PI	Fusion Inhibitor
Azidothymidine (AZT)	**Nevirapine (NVP)**	Indinavir (IDV)	Enfuviritide (T-20)
Lamivudine (3TC)	**Efavirenz (EFV)**	Nelfinavir (NFV)	
Stavudine (d4T)	Delavirdine (DLV)	Saquinavir (SQV)	
Didanosine (ddI)		Ritonavir (RTV)	
Zalcitabine (ddC)		Amprenavir (APV)	
Abacavir (ABC)		Fosamprenavir	
Tenofovir (TFV)		Lopinavir (LPV)	
Emtricitabine (FTC)		Atazanavir (ATZ)	

* The highlighted drugs are NOW available in the NACO ART program: AZT, 3TC, d4T, NVP and EFV.

Slide 9



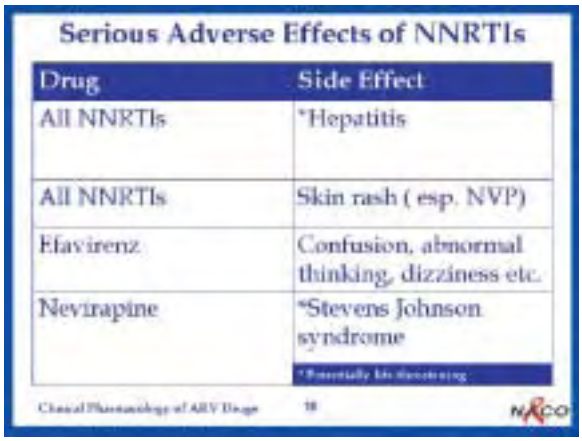
Serious Adverse Effects of NRTIs

Drug	Side Effect
All NRTIs	*Lactic acidosis
Zidovudine	Bone marrow suppression
Stavudine	Neuropathy / Lipoatrophy / Pancreatitis
Lamivudine	*Pancreatitis (in children)

*Potentially life-threatening

Clinical Pharmacology of ARV Drugs 9 NACO

Slide 10



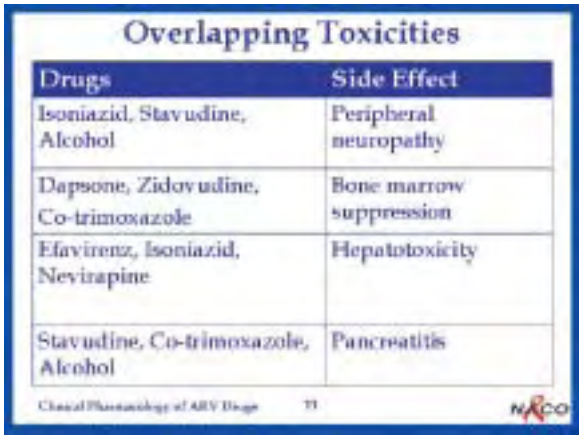
Serious Adverse Effects of NNRTIs

Drug	Side Effect
All NNRTIs	*Hepatitis
All NNRTIs	Skin rash (esp. NVP)
Efavirenz	Confusion, abnormal thinking, dizziness etc.
Nevirapine	*Stevens Johnson syndrome

*Potentially life-threatening

Clinical Pharmacology of ARV Drugs 10 NACO

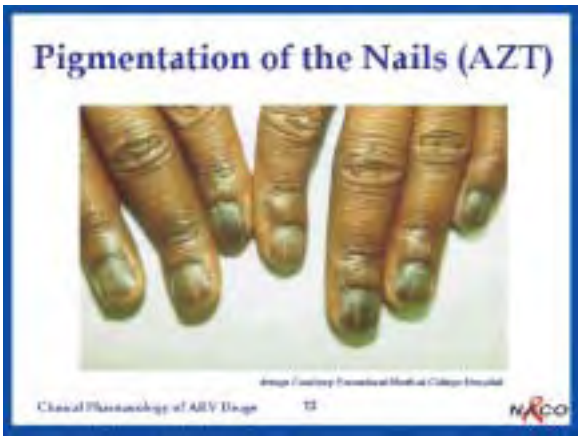
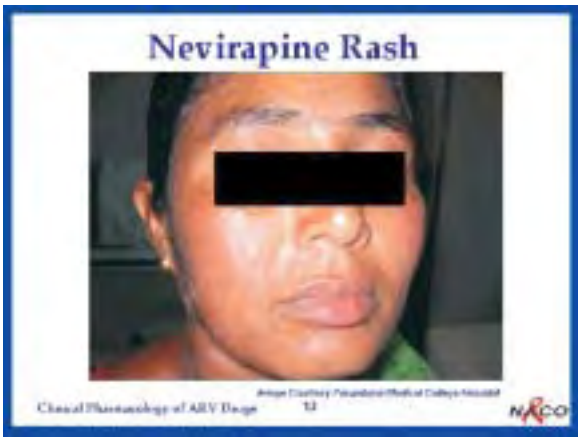
Slide 11

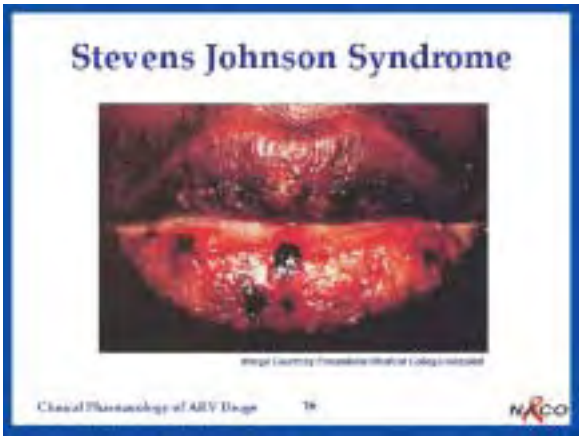


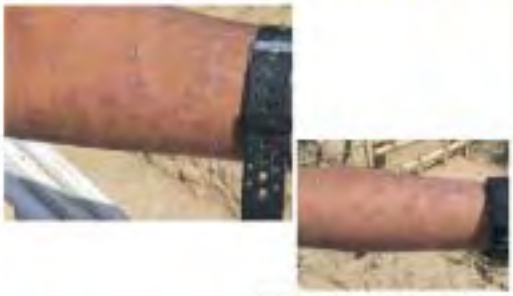
Overlapping Toxicities

Drugs	Side Effect
Isoniazid, Stavudine, Alcohol	Peripheral neuropathy
Dapsone, Zidovudine, Co-trimoxazole	Bone marrow suppression
Efavirenz, Isoniazid, Nevirapine	Hepatotoxicity
Stavudine, Co-trimoxazole, Alcohol	Pancreatitis

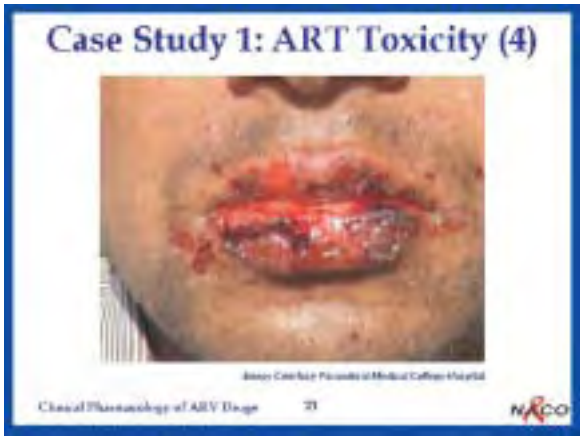
Clinical Pharmacology of ARV Drugs 11 NACO

Slide 12		
Slide 13		
Slide 14		

Slide 15		
Slide 16		
Slide 17		

Slide 18	**Case Study 1: ART Toxicity** • 24 year-old HIV-positive man started on: AZT, 3TC and NVP • CD4 count = 120cells/cu.mm • Other lab tests were normal • He was already on cotrimoxazole proplylaxis • 1st Follow-up (after 1 month): Good adherence, but complained of itching in his forearms	
Slide 19	**Case Study 1: ART Toxicity (2)** 	**Reader's Notes:** • What is your diagnosis? • How will you manage the patient?
Slide 20	**Case Study 1: ART Toxicity (3)** • After one week, the patient returns for a follow-up: – The patient developed fever and redness of the eyes – The rash spread to his lips, aspect of the cheeks, mouth, palms and soles – His ALT is normal	

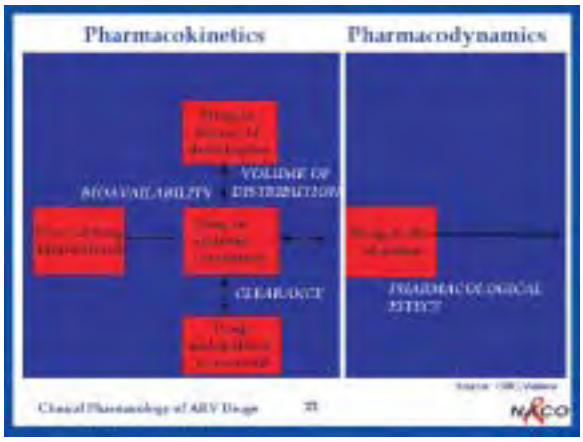
Slide 21



Reader's Notes:

- What is your diagnosis?
- How will you treat this patient?

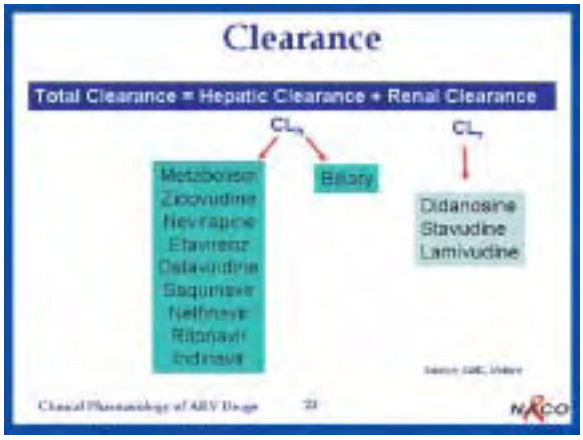
Slide 22



Reader's Notes:

- A simple way to describe pharmacokinetics and pharmacodynamics is this:
  - **Pharmacokinetics** is what the body is doing to the drug.
  - **Pharmacodynamics** is what the drug is doing to the body.
- Pharmacokinetics is the process by which a drug is absorbed, distributed, metabolized and eliminated by the body.
- When a drug is administered, it enters into systemic circulation in the body; it may also move into the tissue spaces. It also continuously undergoes degradation and excretion.
- The active component at the site of action is determined by the level of the drug in the systemic circulation.
- This exerts the desired effect- pharmacodynamics- or what the drug is doing to the body.

Slide 23

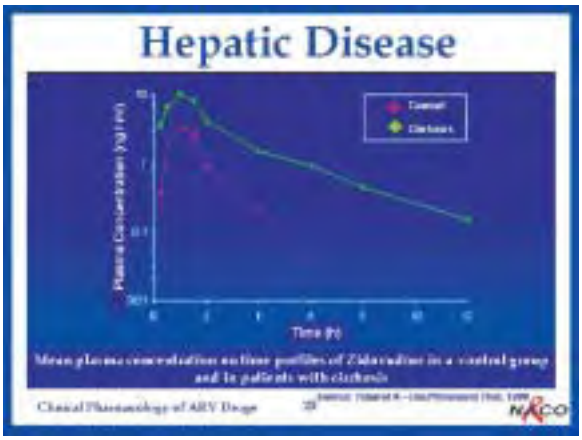


Reader's Notes:

- Clearance: Most of the metabolic load of toxins and drugs are cleared by the liver or the kidney.
- Hepatic clearance is achieved either by metabolic clearance or by biliary clearance.
- All the important ARV drugs are cleared metabolically in the liver with the exception of Didanosine, Stavudine and Lamivudine (that are cleared by the kidney).

Slide 24

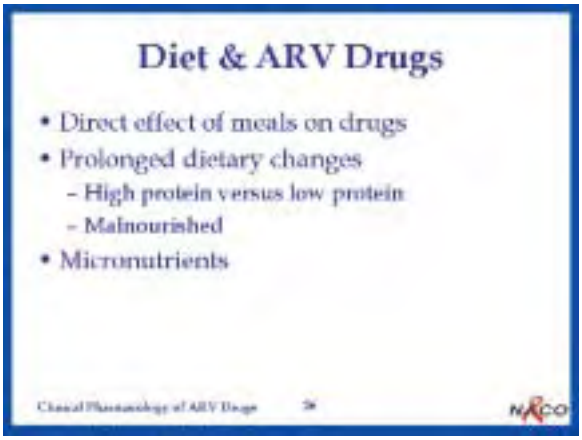
Slide 25



Reader's Notes:

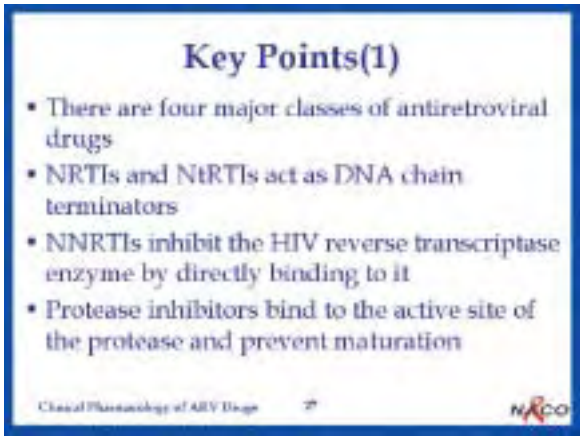
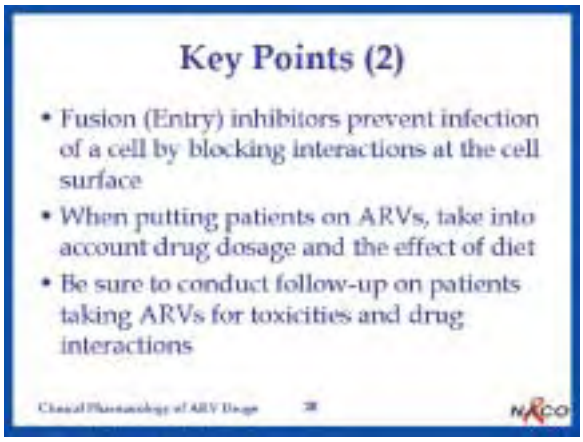
- A patient with significant hepatic disease would have higher levels of drugs metabolized in the liver (like Zidovudine) for a longer period of time when compared to a normal person.
- This may increase the risk of developing toxicity. This should be considered especially in patients where:
- The route of HIV transmission is intravenous.
  - Where there is a significantly higher risk of hepatitis B and hepatitis C induced liver damage.
  - This should also be considered in chronic alcohol abusers.
  - Source: Taburet A, Naveau S, Zorza G, et al: Pharmacokinetics of zidovudine in patients with liver cirrhosis. Clin Pharmacol Ther 47:731-739, 1990.

Slide 26



Reader's Notes:

- In some situations, the direct effect of food itself is quite clear.
- In the case of saquinavir (a protease inhibitor), taking the drug with meals results in better levels being achieved as compared when taken on an empty stomach. This is however not true of all the drugs of its class. It is important to keep this in mind when prescribing ARV drugs. As a rule of thumb, for drugs in the national program, all drugs except efavirenz may be taken after meals.

Slide 27		
Slide 28		

SESSION 9

SESSION

THE IMPACT OF HAART

9

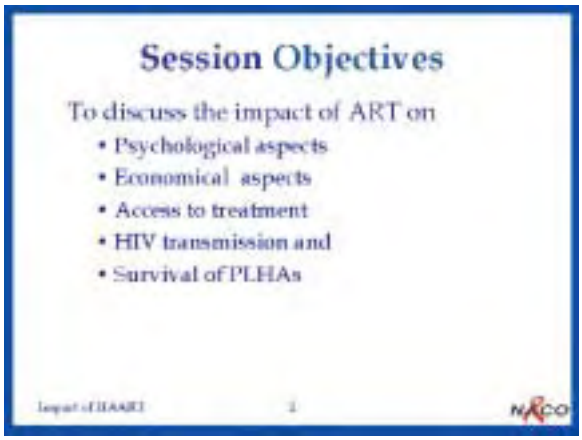
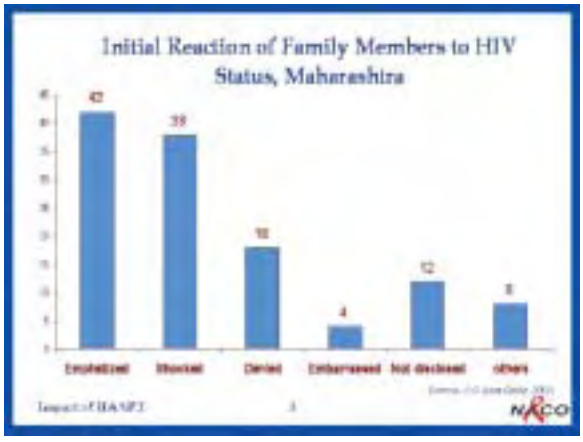
Total Session Time: 45 minutes

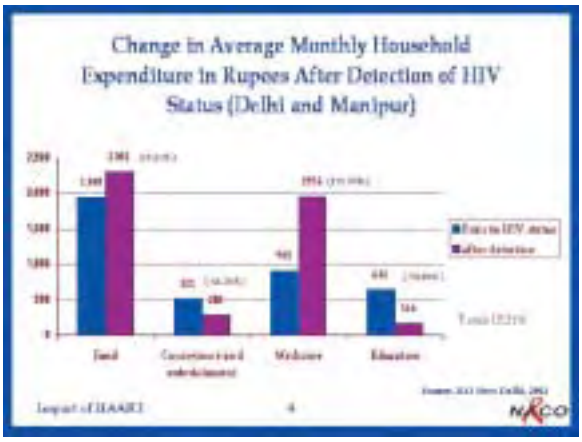
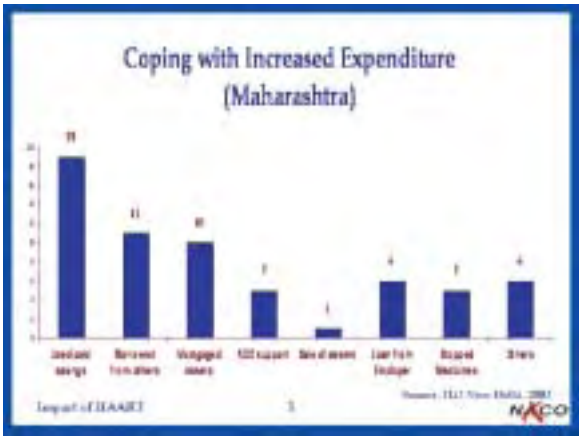
Session Objectives: At the end of the session, the participant should be able to:

- Discuss the impact of ART on
  - Psychological aspects
  - Economical aspects
  - Access to treatment
  - HIV transmission and
  - Survival of PLHAs

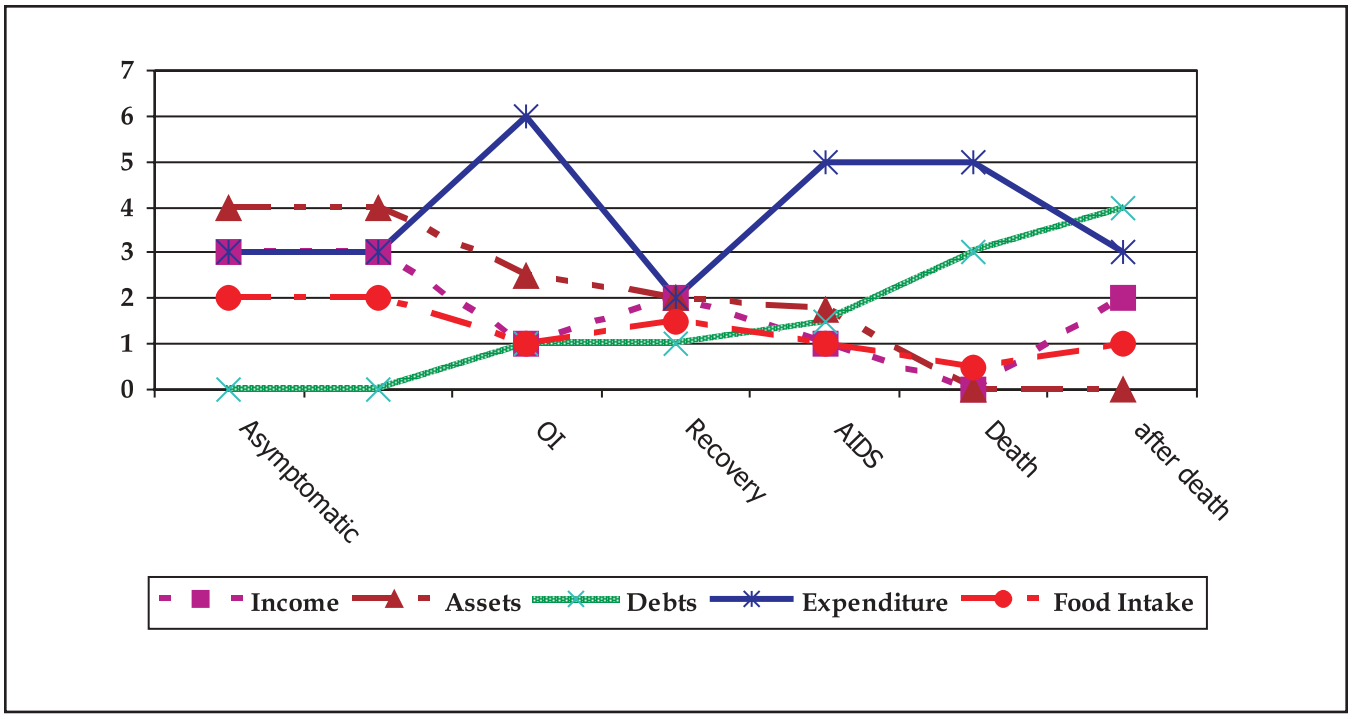
Session Overview:

Step	Time	Activity/Method	Content	Resources Needed
1	2 minutes	Trainer Presentation	Introduction,Session Objectives (Slides 1-2)	LCD or Overhead Projector
2	4 minutes	Trainer presentation	Impact on fam ily and expenditure after HIV detection in Indian scenario, Challenges (Slides 3 to 6)	LCD or Overhead Projector, Handout 1
3	10 minutes	Trainer presentation	Brazilian ART access program (Slides 7-13)	LCD or Overhead Projector,
4	8 minutes	Trainer presentation	Impact of advocacy, corporate responsiveness and market forces, ART on access to treatment and survival benefit (Slides 11-16)	LCD or Overhead Projector
5	4 minutes	Trainer presentation	GHTM study on survival function based on age and gender (Slides 17-20)	LCD or Overhead Projector Handout 2
6	15 minutes	Screening Video	Jyothi's Hope Video	LCD or Overhead Projector, Video 1
7	2 minutes	Trainer presentation	Lessons learned, Review and Clarification of Key Points (Slide 21-22)	LCD or Overhead Projector

Slide 1		
Slide 2		
Slide 3		**Reader's Notes:** • When a person is detected to be HIV infected, most family members tend to be either shocked or feel empathy, but a significant number of people go into a denial phase; some are embarrassed. • Some patients do not disclose the result of the test to their family, and this can make early and timely testing of the partner difficult.

Slide 4		**Reader's Notes:** • Food and medication related expenditure increases and this is coupled with a decrease in spending on education and entertainment. • Overall expenses rise above the level when compare to the expenditure before the diagnosis of HIV status.
Slide 5		**Reader's Notes:** • Most patients cope with the increased expenditure by using their savings in the past and assets or borrowing from others. Some patients receive assistance from non governmental organizations

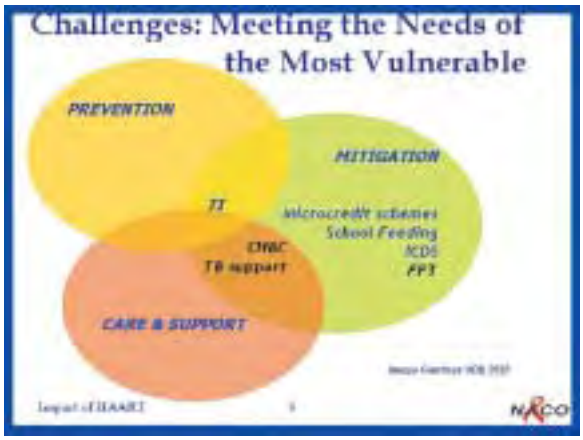
Handout 1: Impact of HIV/AIDS/TB on a Household's Assets, Income & Expenditures



Notes:

- The shift in expenditure leads to a vicious downward spiral and a debt trap.
- Initially, when the patient is asymptomatic, the ends are met with difficulty; with the onset of infections like tuberculosis or when the stage of AIDS sets in, the financial burden forces most patients to sell assets and take loans.
- With recovery, some of these problems may be offset, but this improvement is only temporary.
- The patient will develop another problem (infection) and this time, treatment is costly, and sometimes ineffective.
- The debts tend to soar to very high levels, beyond the capability of the family and these tend to be a source of burden even after the death of the index patient.

Slide 6



Reader's Notes:

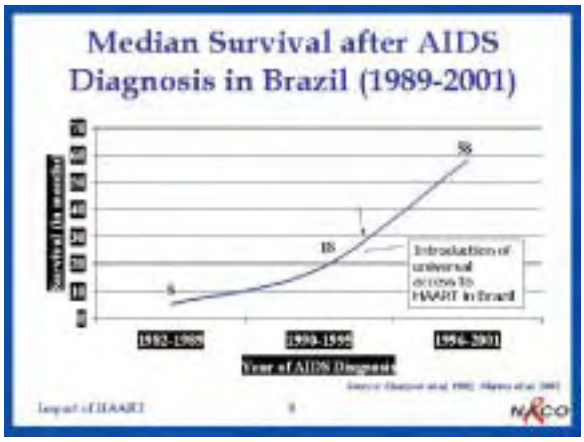
- The challenges caused by HIV/AIDS is met by a three pronged strategy.
- Prevention of infection remains the most important and effective strategy to date.
- Some of the financial problems could be mitigated through micro credit schemes, supplemental nutrition (to defray some of the food related expenditure) and other support systems.
- Care and support remains the most visible area that will be the thrust of the "3-by-5" initiative.
- Abbreviations:
  - TI: Targeted Intervention
  - CHBC: Community Home Based Care
  - ICDS: Integrated Credit Deposit Scheme

Slide 7

Reader's Notes:

- Since November 1996, by Presidential decree, ART has been freely available in Brazil for all those who require it. It has been implemented after development of national guidelines for its use in adults, children and pregnant women.
- Guidelines for other related problems- tuberculosis and hepatitis- that is seen commonly in this population have also been written. These guidelines are updated on a yearly basis. This effort had shown positive effect in psychological, financial and social life of PLHAs in Brazil.
- By the end of 2001, approximately 113,000 patients received ARV through the public health system, and this represents roughly US$ 235 million in expenditures.
- By the end of 2004, 160,000 individuals will be treated with HAART in the Brazilian Public Health System.
- Simultaneously, a network of more than 1000 public alternative care and laboratory facilities was built up on regional administrative basis in accordance with complexity of particular care needs, with improving the monitoring of HIV infection and for diagnosis and medical observation of AIDS related opportunistic diseases.
- Also worthy to say that these expenditures with Antiretrovirals represents only 1.6 % of the total budget of Ministry of Health and less than 0.05% of Brazilian GDP in 2001.

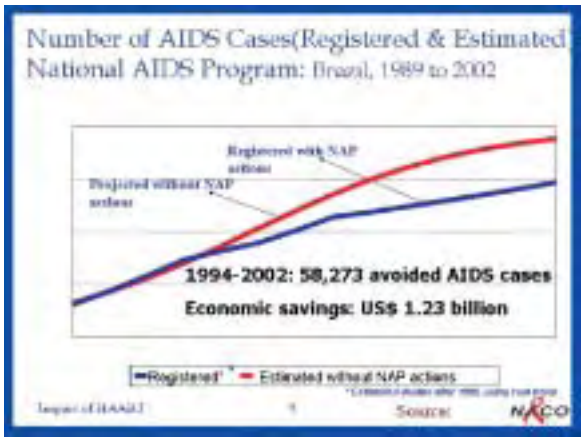
Slide 8



Reader's Notes:

- After five years, the results of the prevention and care strategies were impressive. Since 1996 there has been a striking reduction on mortality, morbidity and hospitalization needs of HIV+ patients.
- A recent evaluation have shown that the survival of AIDS survival have increased substantially, particularly after the introduction the universal access to HAART in mid nineties.

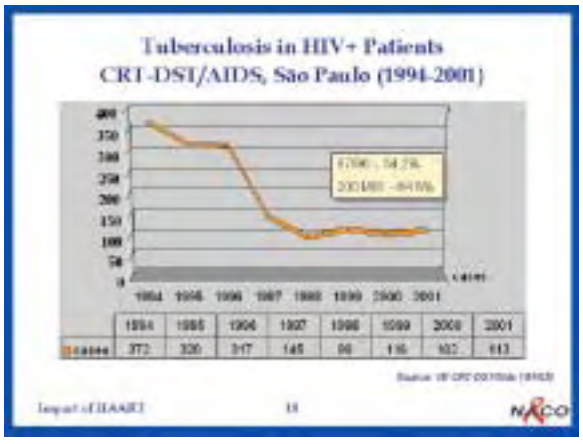
Slide 9



Reader's Notes:

- Another striking event related to universal access to HAART in Brazil was the reduction in AIDS related deaths Since the mid nineties, it is estimated that more than 90.000 deaths were avoided, as we can see in this slide.
- This phenomena was more evident in big cities like São Paulo and Rio de Janeiro, where a 70% reduction in AIDS related deaths has been observed in the last few years.
- Around the country the mean reduction rate was 50%. However we should note that the curve started to flatten even before 1996, probably due to improve in care of HIV+ patients and use of chemoprophylaxis, but become more evident in Post-HAART Era.
- In the last decade, the actions of Brazilian STD/AIDS Program have prevented close to 60.000 new AIDS cases with an estimate of economic savings of more than 1.2 billion in ambulatory care.
- These numbers are quite significant, particularly in developing countries like Brazil. We also estimate that approximately 360.000 AIDS-related hospital admissions were avoided in the last five years, with an extra savings of 1.1 billion.

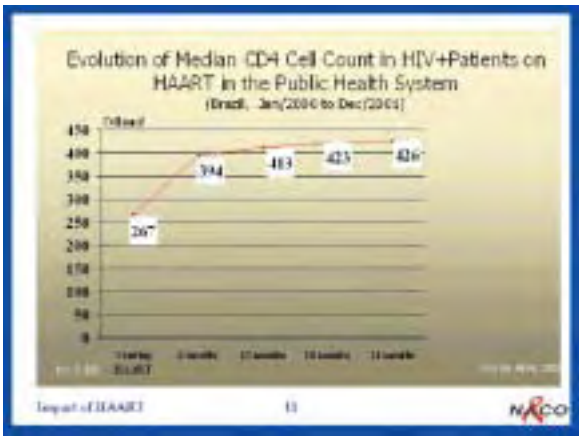
Slide 10



Reader's Notes:

- As an additional and important example of morbidity reduction, the number of tuberculosis cases among HIV+, dropped by 65% in the last five years, in the State of Sao Paulo, which carries roughly fifty per cent of all AIDS cases reported in Brazil.

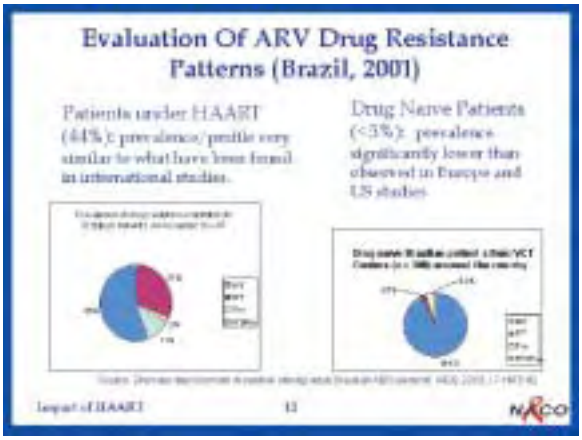
Slide 11



Reader's Notes:

- Another figure reflecting the impact of the Brazilian policy of universal access to Antiretrovirals is the phenomenon of immune reconstitution promoted by the treatment.
- In a study conducted by MOH in 2002, the mean CD4 cell counts rose progressively from 276 cells/mm3 to 426 cells/mm3 after 24 months of treatment with combined ARV regimens.
- This improvement seems to contribute significantly to the reduction in the frequency and severity of opportunistic diseases associated with HIV and a good indicator of the better quality of life of treated patients in the public health network.

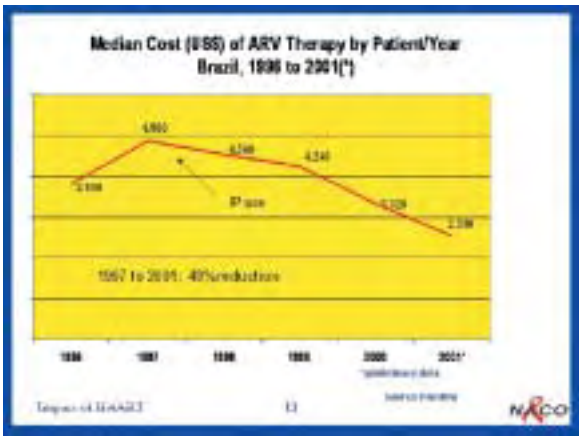
Slide 12



Reader's Notes:

- An old concern about widespread use of ARV in poor resource countries was related to a theoretical risk of multi-drug resistance development.
- Until this moment, the prevalence and profile of drug resistance mutations in Brazilian patients under HAART has been very similar to what have been found in other international studies.
- However, the prevalence of primary resistance in drug naive patients is less than 5 %, which is significantly lower than we have seen in Western Europe and US.
- Together with striking reduction on mortality, morbidity and hospitalization rates of HIV+ patients, it reinforces the quality, safety and efficacy of generic antiretroviral drugs and the policy of universal access to ARV therapy adopted by the Brazilian Ministry of Health in the last decade.
- Source: Dramatic improvement in survival among adult Brazilian AIDS patients. Marins JR, Jamal LF, Chen SY, Barros MB, Hudes ES, Barbosa AA, Chequer P, Teixeira PR, Hearst N,*AIDS 2003; 17:1675-82.*

Slide 13



Reader's Notes:

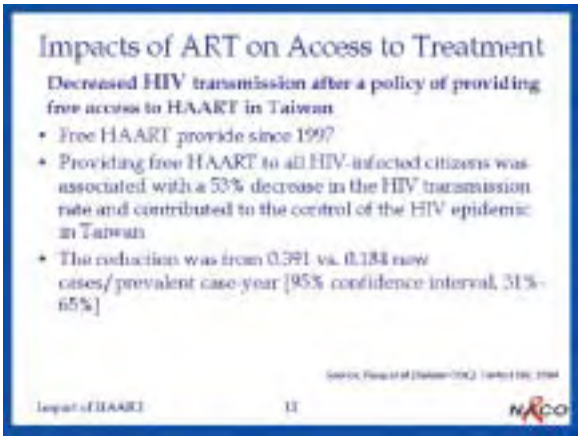
- Thanks to generic Antiretrovirals, the average cost for patient/year in antiretroviral therapy decreased by half in later years, in spite of the proportional increase in the number of patients needing more expensive and complex treatments.

Slide 14

Reader's Notes:

- Advocacy, corporate responsiveness, & market forces have reduced ARV prices by 95% in 3 years
- Finally, the situation is still changing- the prices have been continuously falling.
- The UN drug access initiative, domestic production, and accelerated access initiative have contributed to this.
- The production of generic drugs has brought down costs to an all time low and it is hoped that this trend would continue.

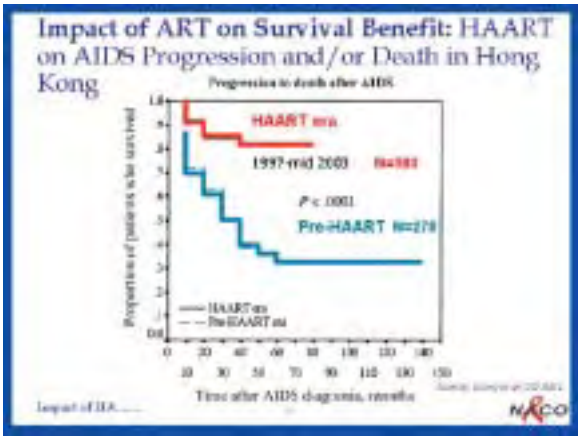
Slide 15



Reader's Notes:

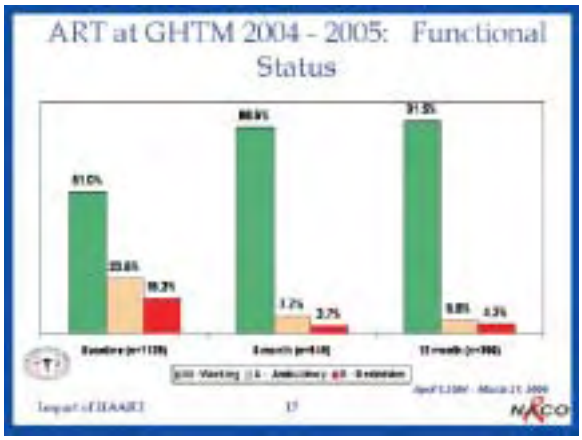
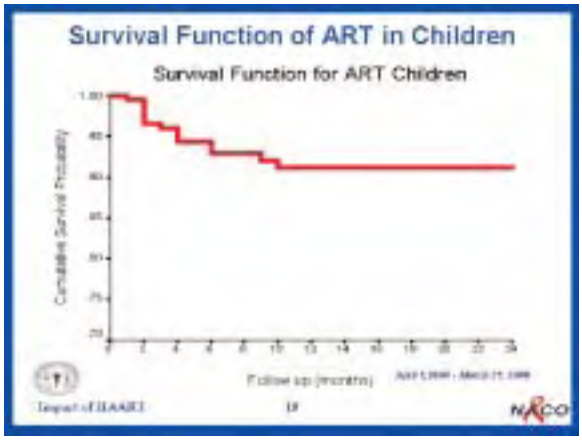
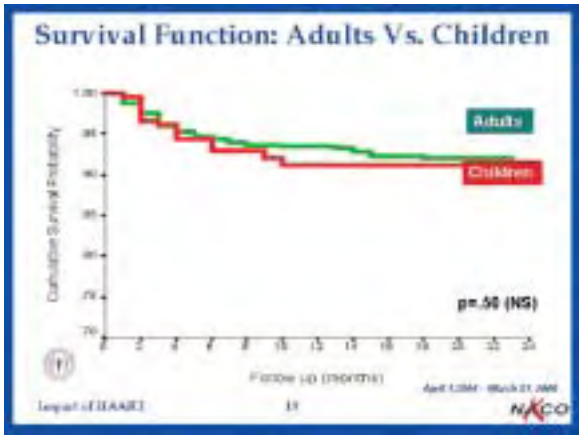
- The ART program reduces the transmission of HIV among the population.
- Provides widespread access to treatment ! Leading to positive consequence on the HIV-prevention
- More widespread access to treatment has the potential to attract millions of people into health-care settings, in which HIV-prevention messages can be delivered and reinforced
- Reference: www.thelancet.com Vol 364 July 3, 2004

Slide 16



Reader's Notes:

- Hong Kong Study : Median survival after AIDS increased from 29.8 months during the pre-HAART era to 170 months during the HAART era ($p<0.001$).
- CID:Clinical infectious diseases.
- Taiwan Study : In a 5-Year Prospective Study, there was an approximately 75% reduction on the mortality.
- Patients with an initial CD4+ <100 and follow-up
- For mortality in patients who received HAART compared with those who did not
- Risk ratio (RR) was 0.25 (95% CI, 0.13-0.49; p = .0001)
- Reference:Hung et al. JAIDS 2004

Slide 17		
Slide 18		
Slide 19		

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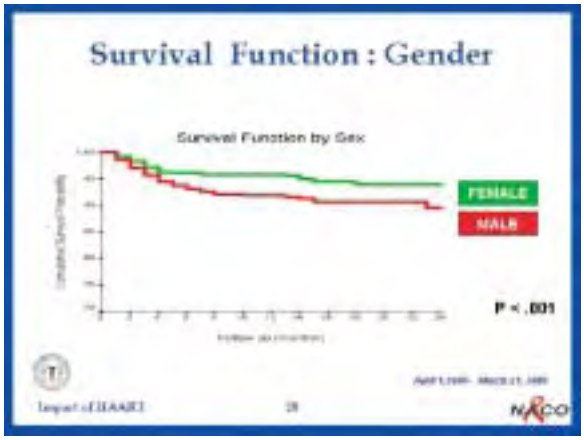


Reader's Notes:

- Refer to **Handout 2: Impact of ART on Patients: A Mother's Happiness (GHTM story).**

Handout 2: Impact of ART on Patients: A Mother's Happiness (GHTM story)

"When I brought my son for ART screening, he was too sick. He was too thin and so was very delicate to handle. He was not able to open his eyes and used to cry as and when somebody touches him. I used to carry him even to the toilet. But after he was put on ART, within a week he started going to the toilet on his own. Today he is as good as a normal child. Now he is healthy, happy and energetic. I am very happy."

"I am very thankful to God for giving me a negative child. I was afraid that I would leave my daughter as an orphan because I was too sick then.
But now after being started on ART I could feel the difference myself. Now I feel healthier and able to go to work and earn money for my daughter and me.
I am happy and confident that I can live longer and be with my daughter for at least 10 more years."

"I was working as a manager in a company. As my health started deteriorating, my physical appearance changed too. All my friends and colleagues started questioning me, so I withdrew from them and quit the job. I was roaming about doing nothing.
But now, after ART I got back my appearance and personality as before. Now I am going to work in the same executive line. I am very much confident that I can do this."

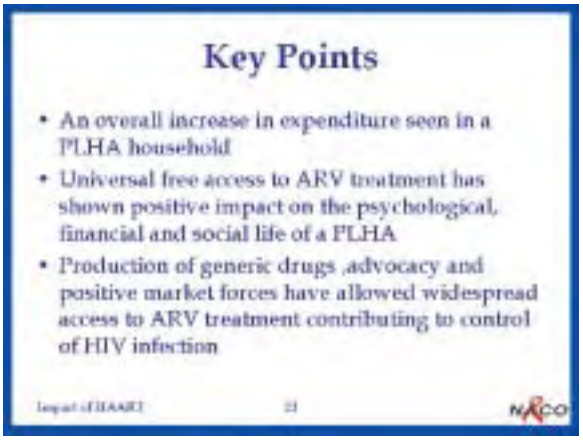
"All my family members thought that I would die. My brother carried me and put me in this hospital. I never expected that I will live. CD4 testing was done for me and ARV drugs were given.
If it had not been for ART, ants and mud would have eaten my body. Now I am doing so well with ARV drugs. This is actually my rebirth."

"My uncle gave me Rs. 5000 as the last instalment and sent me out of the home. I came to Tambaram Hospital. After taking ARVs, I have become more energetic. Now I have the confidence of working as a normal person. I will earn and return back the money to my uncle."

"After taking ARV, my appetite has increased. I do not have money and I am not eating anything. Please get me a job or else, you stop the ART."

"For the past month I was not able to eat anything because of oral ulcers; I was totally bedridden and I thought I would be dying soon. But luckily after taking ARV I have increased appetite. I am eating very well and I have put on weight.
Now I spend Rs 200 to come to Tambaram from Namakkal to collect the medicines, and if the medicines are made available in Namakkal GH itself, then I have to spend Rs. 11 only."

"Even if they are going to give free ARV in the District Headquarters Hospital, I prefer to come to Tambaram only, because other people in my locality will come to know of my HIV status."

Slide 21		**Reader's Notes:** • Source video: Jyothi's Hope, duration 12 minutes.
Slide 22		
Slide 23		

SESSION 10

SESSION

ANTIRETROVIRAL THERAPY: INITIATION

10

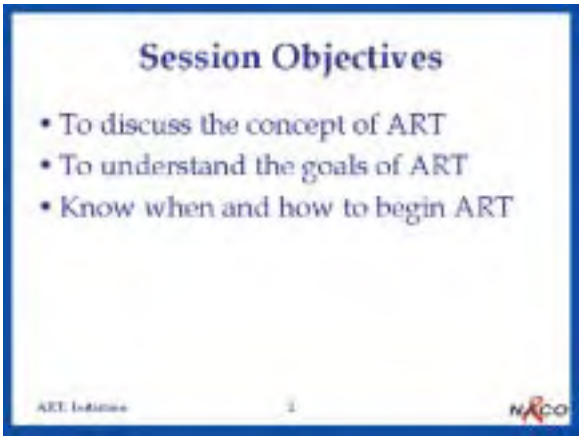
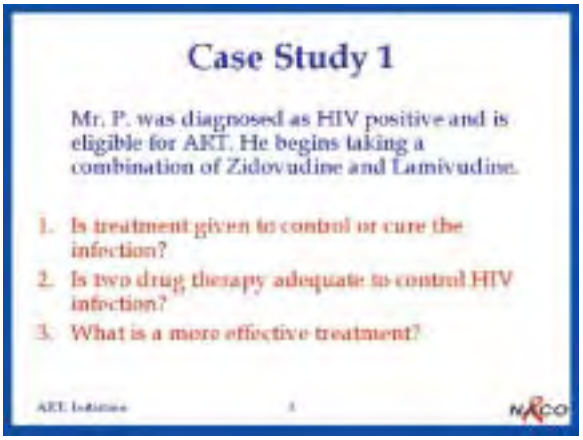
Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Discuss the concept of ART
- Understand the goals of ART
- Know when and how to begin ART

Session Overview:

Step	Time	Activity/Method	Content	Resources Needed
1	2 minutes	Trainer Presentation	Session Objectives (Slides 1-2)	LCD or Overhead Projector
2	4 minutes	Trainer Presentation	Methods of ARV Therapy (Slides 3-5)	LCD or Overhead Projector
3	15 minutes	Trainer Presentation Case Study (Part 1 and 2) Small Group Activity	Toxicities, IRIS, Therapy Management (Slides 6-10)	LCD or Overhead Projector
4	5 minutes	Trainer Presentation	Drug Interactions(Slides 11 to 13)	LCD or Overhead Projector
5	12 minutes	Trainer Presentation Case Study (Part 3)	Substitution of ARVs (Slides 14-20)	LCD or Overhead Projector
6	4 minutes	Case Study (Part 4)	Treatment Failure, Second Line Drugs (Slides 21-23)	LCD or Overhead Projector
7	3 minutes	Trainer Presentation	Summary (Slides 24-25)	LCD or Overhead Projector

Slide 1		
Slide 2		**Reader's Notes:** • Please refer to the Annexure: **NACO Guidelines in menagement of Antiretroviral therapy in Adults and Adoloscents, March 2007**
Slide 3		

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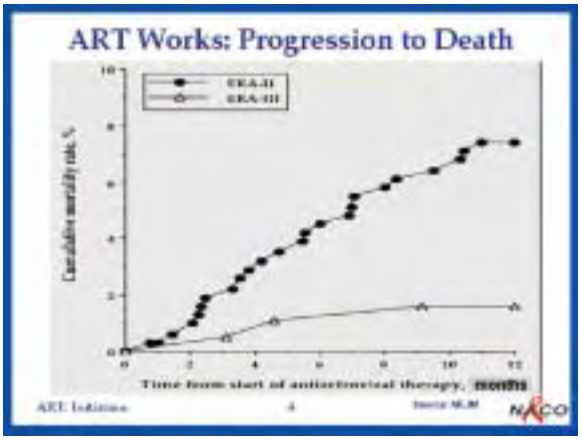


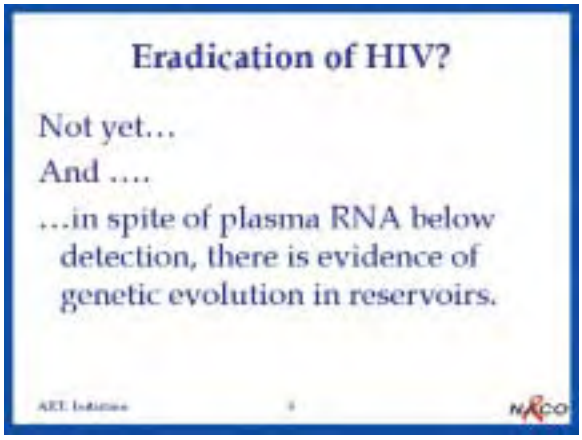
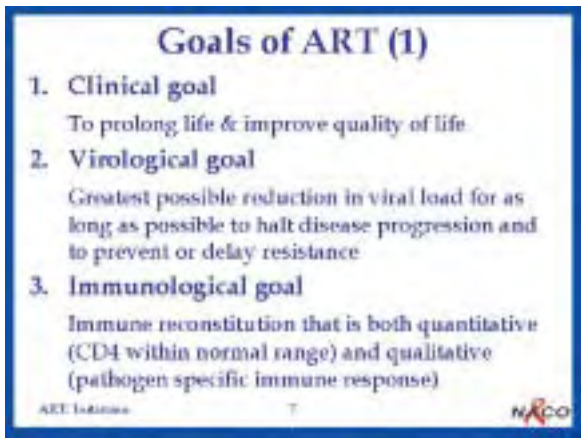
Reader's Notes:

- The inferiority of the two drug therapy is clearly seen in this graph. This data was obtained by comparing Canadian patients in whom treatment was started in different time periods- era II, which was the time of two drug therapy and era III, the time of triple combination treatment. As can be seen quite clearly, in spite of treatment, patients taking the two drug therapy had a 7% chance of dying within 1 year, as compared to less than 1.5% mortality in the triple drug therapy group.
- Further follow-up would reveal that this effect becomes progressively more profound as time goes on. This is because 2 drug therapy could never hope to achieve the kind of virological control that is required during treatment of this infection. Only the three drug combination therapy can achieve complete suppression of viral replication and stabilize the infection.

Slide 5

Reader's Notes:

- ART anti retroviral therapy, is a combination of at least three drugs, with representation from at least 2 classes of the drugs.
- This is required for achieving the end point of maximal and durable viral suppression.
- It is important to remember that the suppression should be maximal, preferably below the level of detection of current testing kits, and also durable, meaning the suppression should be long lasting. By achieving this, we can prevent the emergence of drug resistant strains.
- Once viral suppression is achieved, the body's immune system improves, as reflected by an improved survival and quality of life.

Slide 6		**Reader's Notes:** • Could ART ultimately result in eradication of the virus completely and therefore, a cure? There is evidence that in spite of complete viral suppression in the blood (which is measurable), the virus can continue replicating in other parts of the body like lymph nodes (reservoirs). This is important, because it establishes that treatment is essentially life long. • There is data that shows there can be replication in the genital tract that is independent of viral suppression in the blood. Patients on ART can still spread the virus therefore PLHA on ART should also be encouraged to use barrier contraceptives.
Slide 7		
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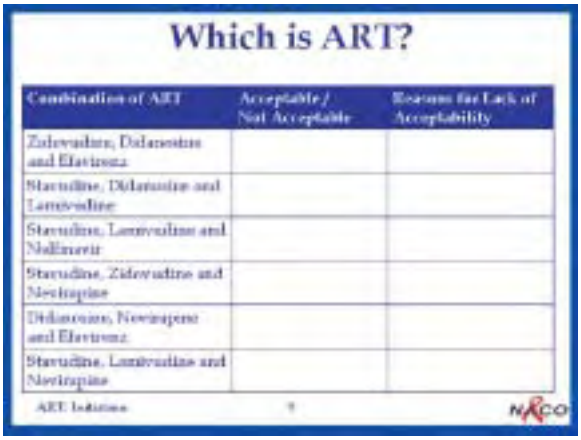
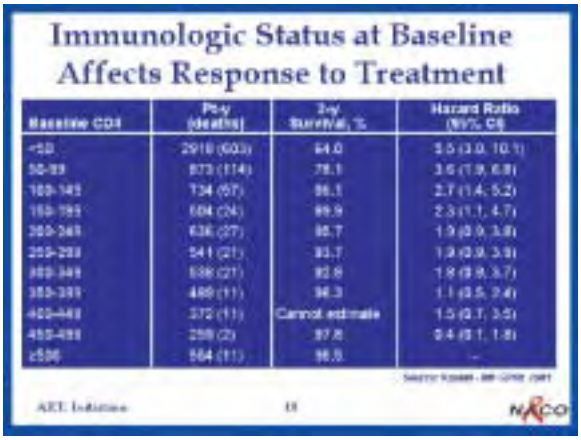
Slide 9



Reader's Notes:

- Which combinations of medications are acceptable or unacceptable combinations?

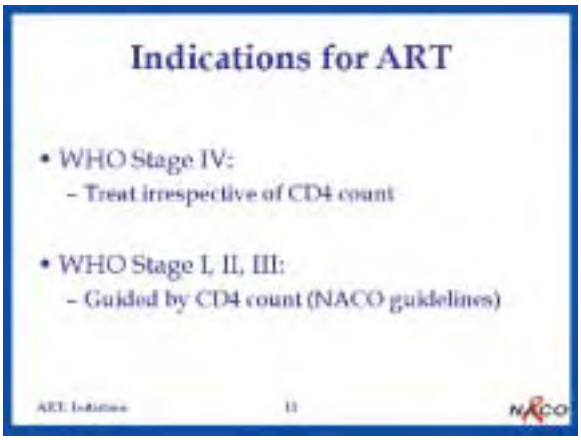
Slide 10



Reader's Notes:

- This data reviews the two year survival of PLHA based on whether they were started on ART or not.
- The patients were stratified according to their baseline CD4 count, to see if the relationship was linear.
- It stands to reason that a PLHA with a high CD4 count, say more than 500, is unlikely to benefit by ART. In fact, there is evidence that some toxicities, like Nevirapine induced hepatitis, are higher in PLHA with better CD4 counts.
- By the same token, a person with very poor immune status, say CD4 less than 50, is unlikely to survive very long without ART.
- Therefore, somewhere in between, there is a breakeven point, below which therapy is beneficial and above which therapy does not provide benefits.
- From this table it is evident that above the CD4 count of 200, survival is statistically the same, irrespective of use of ART, but below a count of 200, the survival advantage of ART is marked. This data, and others like this, form the backbone of the criteria in use for selecting patients for ART under the Indian National treatment program.

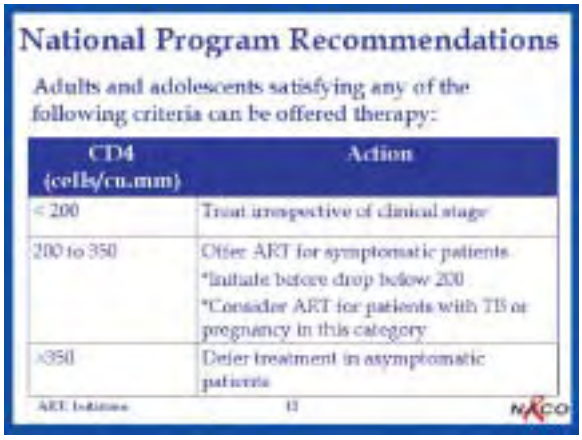
Slide 11



Reader's Notes:

- Currently, only clinical staging and/or CD4 levels are markers for the need for ART.
- As per the NACO guidelines, the accepted protocol for consideration of PLHA for ART is either WHO Stage IV, illnesses (where a CD4 count is unnecessary) or based on CD4 count.
- Viral load estimation is not required for decision making on need for treatment. There is data that shows that the response to therapy is similar irrespective of the viral loads at the time of starting.

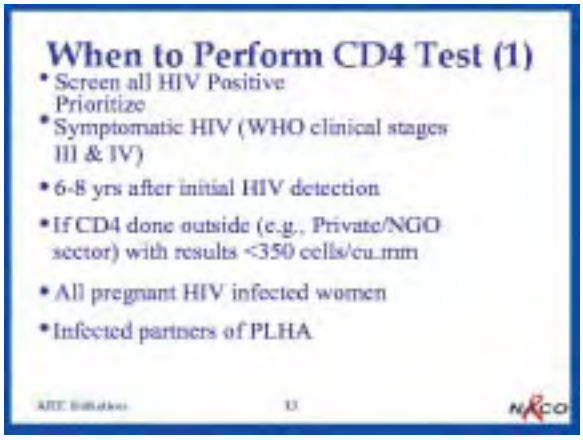
Slide 12



Reader's Notes:

- In the event that a patient does not have an AIDS defining illness, CD4 testing should guide the need for therapy. All patients with a CD4 less than 200, as discussed earlier, should be offered therapy.
- In addition, therapy may be offered to patients with a CD4 less than 350, especially if the patient is symptomatic. It is advised that patients be started on therapy when the CD4 is between 200-250 itself. If the CD4 is more than 350 cells, then therapy can be deferred for later.
- Refer to NACO ART and WHO Guidelines.

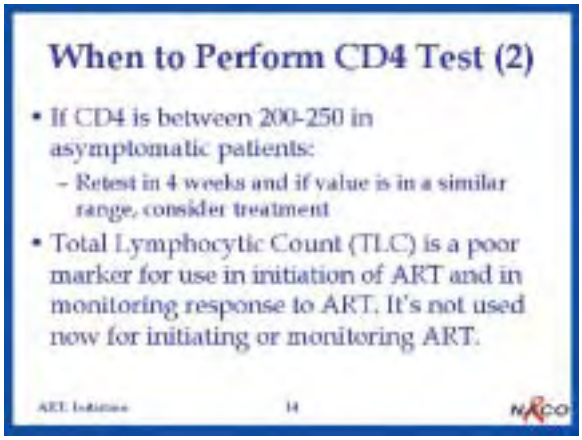
Slide 13



Reader's Notes:

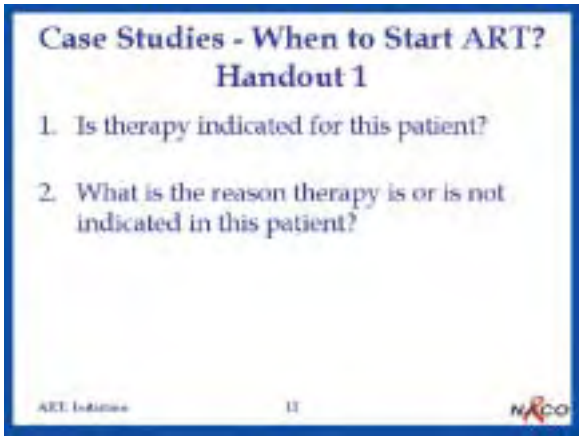
- All ART centers have access to CD4 testing. This may be done either within the campus, or the sample may need to be transported to a nearby location for testing.
- The choice for patients for CD4 testing is crucial to ensure that the kits are properly utilized.

Slide 14



Reader's Notes:

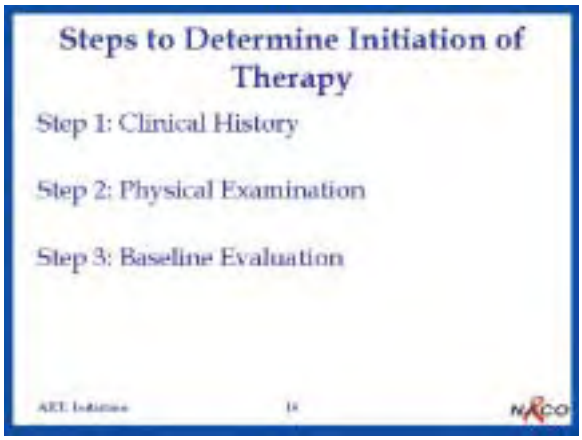
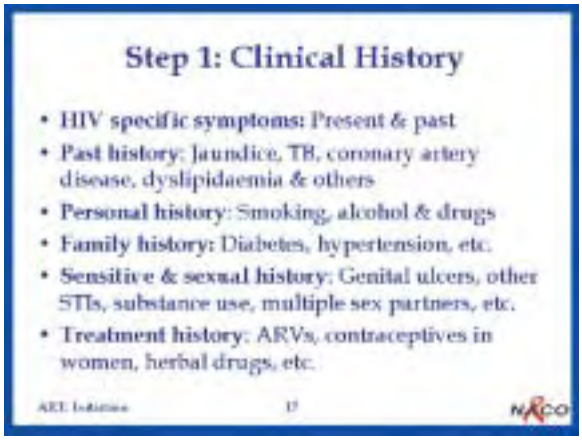
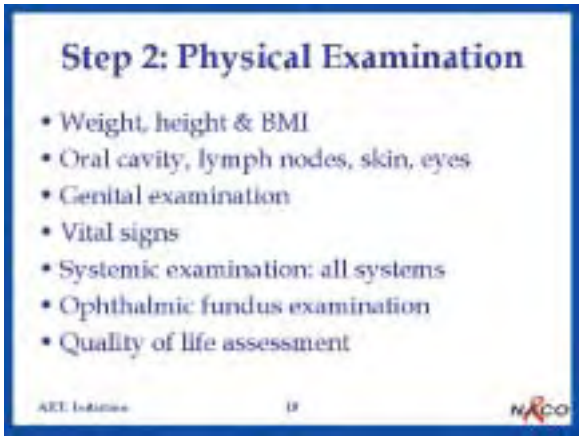
- If the CD4 in an asymptomatic individual is between 200-250, then the person should be retested in 4 weeks time, and treatment should be strongly considered if the repeat value is also in a similar range.
- Total lymphocyte count (TLC) is very inaccurate and is not as reliable as a tool for initiation of therapy or for monitoring response to therapy. TLC should not be used in the Indian National treatment program as global evidence showed that TLC is a poor marker for use in initiation of ART and monitoring response to ART. It is no longer considered for baseline work up patients towards ART.

Slide 15		

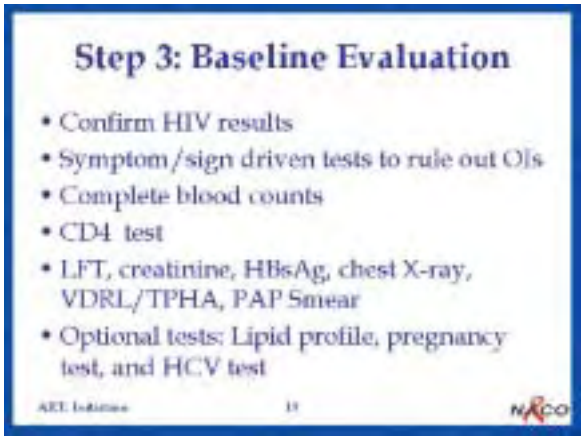
Case Studies - When to Start ART?
Handout 1
1. Is therapy indicated for this patient?
2. What is the reason therapy is or is not indicated in this patient?

Handout 1: Case Studies: Initiation of ART

Case	Scenario	Therapy Indicated Yes/ No
1	35 year-old HIV infected man, admitted and treated for PCP. After 3 months CD4-190 cells/mm^3.	Yes
2	27 year-old HIV infected woman, diagnosed to have Cryptococcal Meningitis 2 months ago and is now on fluconazole.	Yes
3	38 year-old HIV infected housewife, with Herpes zoster of T6 and T7 dermatomes, improving with therapy. CD4 count is 270 cells/mm^3.	Yes
4	40 year-old HIV infected woman with white discharge per vagina. Vaginal exam is normal. Her CD4 count is 350 cells/mm^3.	No
5	28 year-old HIV infected businessman, with fatigue and sleeplessness. CD4- 300 cells/mm^3.	No
6	25 year-old STD clinic attendee on treatment for genital ulcer presents with pneumonia. CD4 count is 280 cells/mm^3	Yes

Slide 16		
Slide 17		
Slide 18		

Slide 19



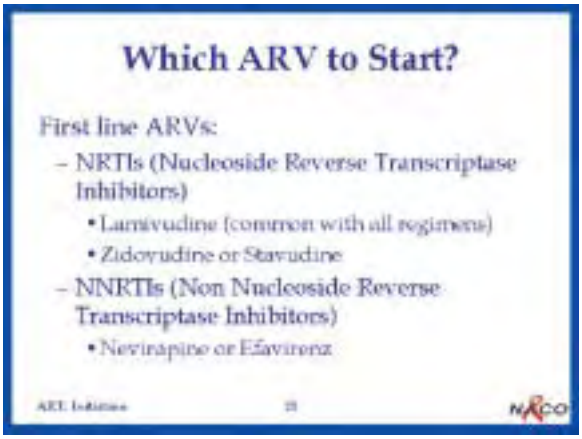
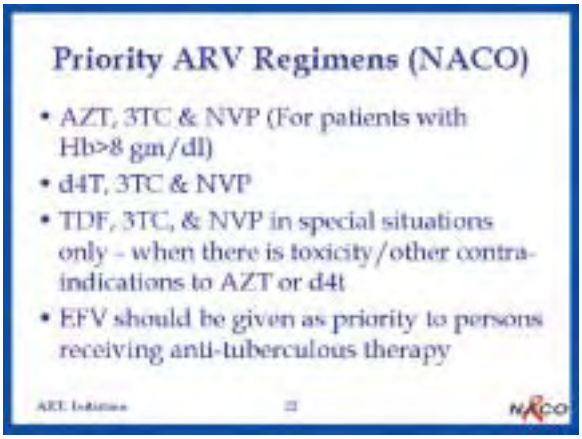
Reader's Notes:

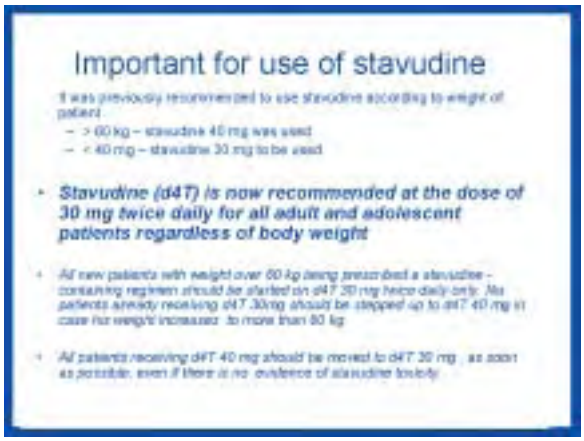
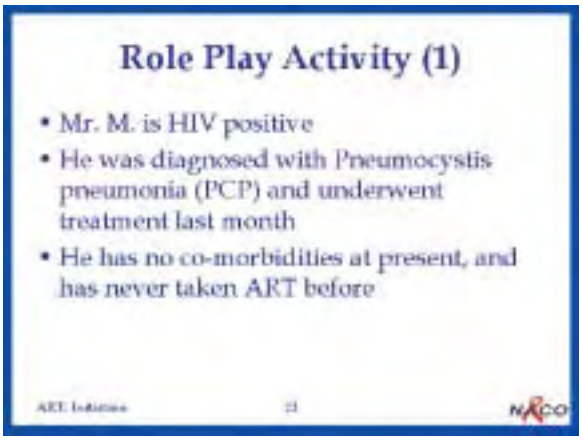
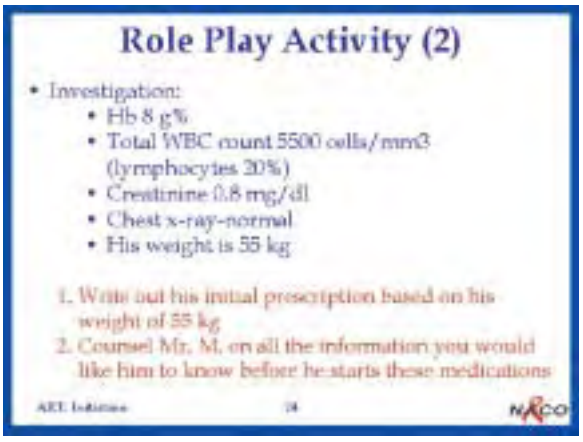
- The purpose of baseline laboratory evaluation is to (1) Stage the HIV disease, (2) Rule out concomitant infections, (3) Determine baseline safety parameters.
- The next important step in starting a patient on therapy is to ascertain that the patient is truly HIV infected. Details on date, place and method of testing should be carefully documented.
- Blood tests are done as an adjunct to the clinical evaluation, and in all patients, some tests are mandatory.
- The mandatory tests include HIV testing as per NACO protocol and a haemogram (hemoglobin and white cell counts).
- Other tests that can be done include liver functions (especially in IV drug users, where hepatitis virus co-infection induced liver disease is common), renal functions in patients with renal disease, chest X ray (to rule out tuberculosis) and screening for other sexually transmitted infections, notably syphilis.
- Refer participants to Annexure: **NACO National Guidelines for Implementation of Antiretroviral Therapy (ART), Draft, July 2006, page no 55 - "NACO Comprehensive Clinical Evaluation of the HIV/AIDS Patient."**

Slide 20

Reader's Notes:

- Counselling is very important to ensure that the patient is ready for therapy - not just medically. It is important to ensure that all relevant information is given to the patient so that the PLHA is able to gain maximal benefit from treatment. It is also important to discuss issues related to adherence before starting therapy.
- ART is not an emergency treatment.
- **READINESS** - If the patient has understood the following points. We can say that the patient is ready for therapy. Only important points are given. This is not the exhaustive list.
- The therapy achieves control but not cure.
- You need to take it regularly for indefinite period of time, probably lifelong.
- You cannot afford to miss even one tablet as this may lead to drug resistance.
- Nevirapine dose has to be increased after 14 days.
- There are no special food requirements.
- If you have any rash, skin reaction, yellow coloring of the eye, excessive vomiting or new problem, tingling or numbness of the feet come back immediately.

		• Do not alter your medications without consulting. Do not take any new medications without confirming if these will create a problem for the HIV medicines. • You will need regular check up and you need to come back after 14 days for the first check up. • You can still transmit the virus to your sex partner(s) so continue using condoms. Do not donate blood. • You will need monthly check-ups for clinical assessment and blood tests.
Slide 21		**Reader's Notes:** • As per the Government program, the decision on the choice of antiretroviral is listed in this slide. • Lamivudine is common for all regimens; the other NRTIs could be either Zidovudine or Stavudine. • The NNRTIs available include Nevirapine or Efavirenz.
Slide 22		**Reader's Notes:** • The ART regimens have been indicated in order of priority as per the NACO guidelines. • EFV is contraindicated in pregnant HIV-infected woman during the first trimester of pregnancy because of concerns of teratogenecity. • NVP hepatotoxicity is increased in women with CD4 more than 250 and in men with CD4 more than 400. and in those with baseline liver disease; may avoid NVP in these persons if possible. • EFV should be used cautiously in women of child bearing age unless contraception is assured. • Zidovidin based regimen is recommended for the patients with hemoglobin more the 8 gms %, if it is less than 8 gms%, the Stavudine based regimen is recommended. • **Necessity of Dose Titration Period of NVP:** • You would need a dose titration period of NVP because of its enzyme induction (self induction) that reduces the NVP levels after two weeks. Therefore, the NVP levels are therapeutic even though you are dosing once daily. Dosing needs to be increased to twice daily to account for self induction. NVP should be dosed once daily before increasing to twice daily after two weeks to avoid added toxicity.

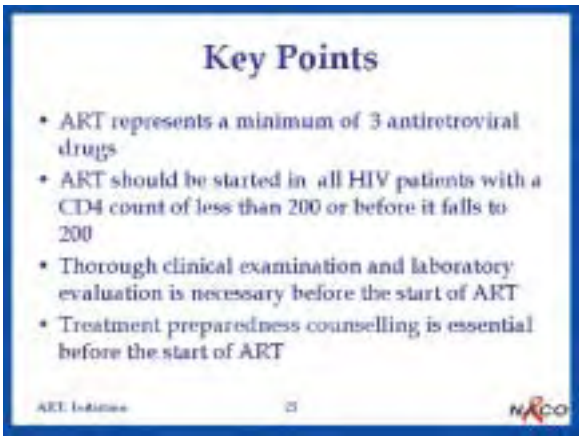
Slide 23		
Slide 24		
Slide 25		

Handout 2: Antiretroviral Therapy Initiation

The following instructions should be given to Mr. M. before he starts ART:

1. The therapy achieves control but not cure.
2. You need to take it regularly for indefinite period, probably lifelong.
3. You cannot afford to miss even one tablet as this may lead to drug resistance.
4. Nevirapine dose has to be increased after 14 days.
5. There are no special food requirements.
6. If you have any rash, skin reaction, yellow coloring of the eye, excessive vomiting or new problem, tingling or numbness of the feet come back immediately.
7. Do not alter your medications without consulting. Do not take any new medications without confirming if these will create a problem for the HIV medicines.
8. You will need regular check up and you need to come back after 14 days for the first check up.
9. There is a still a chance that you can spread the virus, so it would be advisable to continue using condoms. You should not donate blood.
10. You will need monthly check ups for clinical assessment and blood tests.

Slide 25


Key Points
• ART represents a minimum of 3 antiretroviral drugs
• ART should be started in all HIV patients with a CD4 count of less than 200 or before it falls to 200
• Thorough clinical examination and laboratory evaluation is necessary before the start of ART
• Treatment preparedness counselling is essential before the start of ART

SESSION 11

SESSION

ART THERAPY: SWITCHING THERAPY AND FOLLOW-UP

11

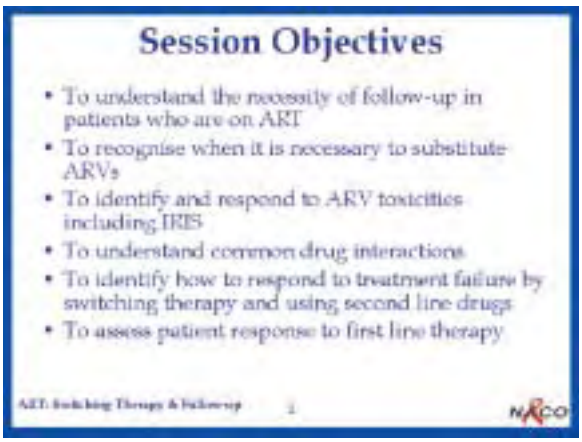
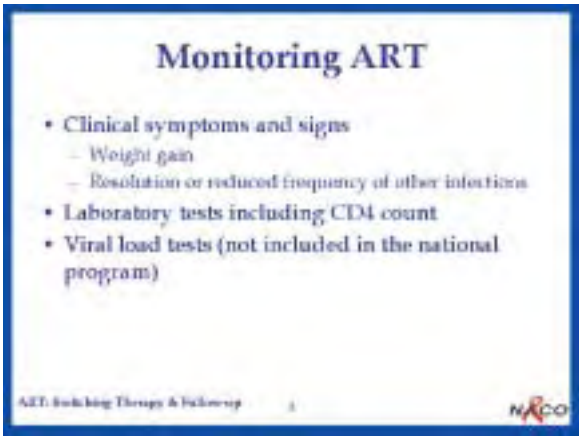
Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Understand the necessity of follow-up in patients who are on ART
- Recognise when it is necessary to substitute ARVs
- Identify and respond to ARV toxicities including IRIS
- Understand common drug interactions
- Identify how to respond to treatment failure by switching therapy and using second line drugs
- Assess patient response to first line therapy

Session Overview:

Step	Time	Activity/Method	Content	Resources Needed
1	2 minutes	Trainer Presentation	Session Objectives (Slides 1-2)	LCD or Overhead Projector
2	4 minutes	Trainer Presentation	Methods of ARV Therapy (Slides 3-5)	LCD or Overhead Projector
3	15 minutes	Trainer Presentation Case Study (Part 1 and 2) Small Group Activity	Toxicities, IRIS, Therapy Management (Slides 6-10)	LCD or Overhead Projector
4	5 minutes	Trainer Presentation	Drug Interactions (Slides 11 to 13)	LCD or Overhead Projector
5	12 minutes	Trainer Presentation Case Study (Part 3)	Substitution of ARVs (Slides 14-19)	LCD or Overhead Projector
6	4 minutes	Case Study (Part 4)	Treatment Failure, Second Line Drugs (Slides 20-22)	LCD or Overhead Projector
7	3 minutes	Trainer Presentation	Summary (Slides 23-24)	LCD or Overhead Projector

Slide 1		
Slide 2		
Slide 3		

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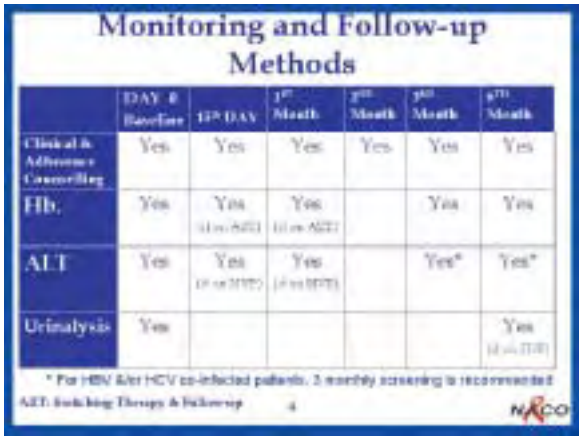

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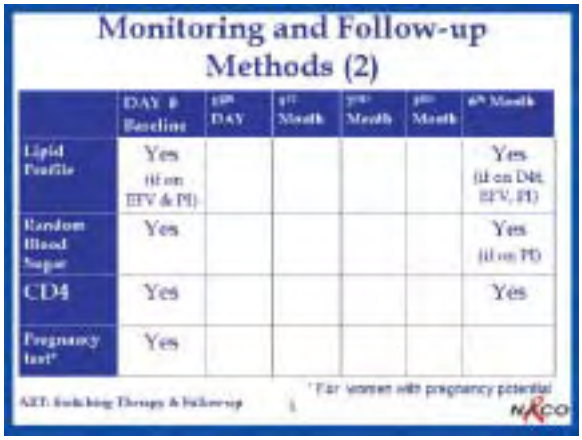

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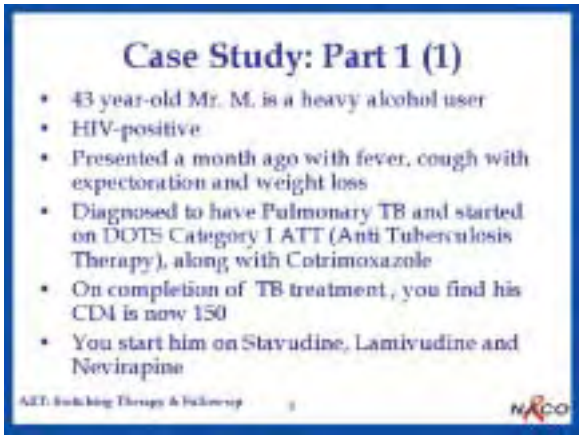
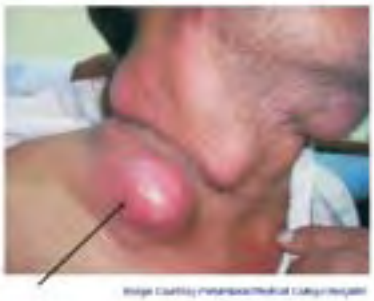


Slide 7	**Case Study: Part 1 (2)** 1. Considering this patient's heavy alcohol use: a. What are some important adherence issues to consider? b. What are some important nutritional issues to consider? 2. What are some of the toxicities due to drugs (including alcohol) that may occur in this patient? 3. Can IRIS occur in this patient?	
Slide 8	**Case Study: Part 2** • 2 months after starting therapy, Mr. M. presented to the ART clinic with mild fever and swelling in the neck • He is adherent to ARV drugs • He denies drinking alcohol in the past one month	
Slide 9		

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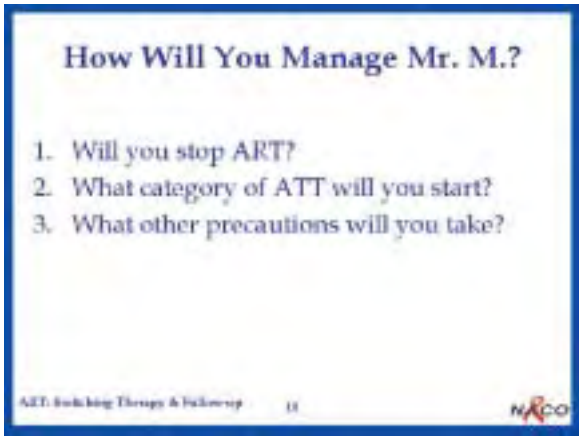

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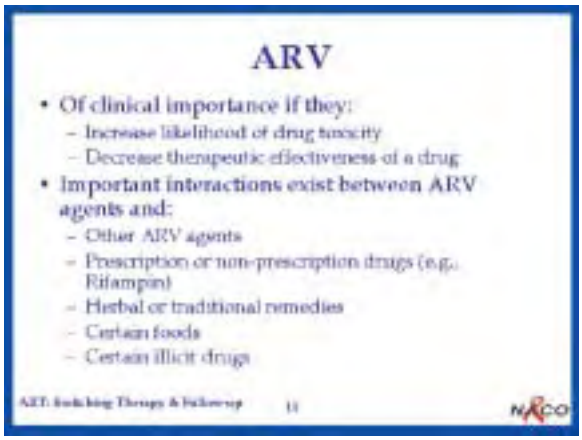
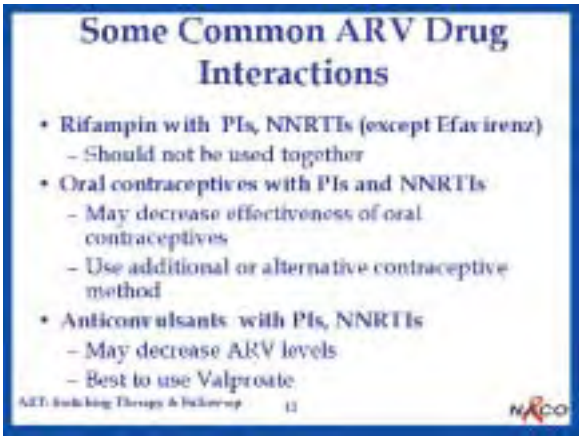


Reader's Notes:

- Many antiretroviral agents interact with other drugs. These drug interactions are of clinical importance if they increase the likelihood of drug toxicity or if they decrease the therapeutic effectiveness of an administered drug.
- Significant drug interactions may be seen between different antiretroviral agents, with other prescribed or non-prescribed drugs, or with herbal or traditional treatments.
- There can also be interactions between antiretroviral agents and certain foods and with certain illicit drugs. It is a common misconception that all herbal remedies are "safe". A classic example of this error is St John's Wort, an herbal remedy used in the U.S. St John's Wort has hepatic enzyme inducing ability, and this interaction has resulted in treatment failure in many patients.
- It is not known if any of the alternative medications commonly used in India have such properties, as they have not been well studied. They do not have any role, as of today, in the routine management of PLHA until more data is available.

Slide 12



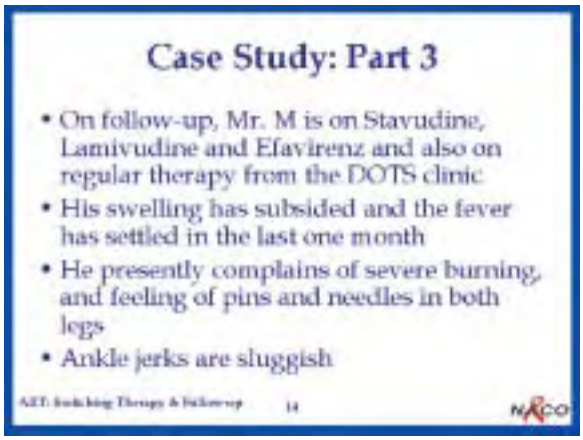
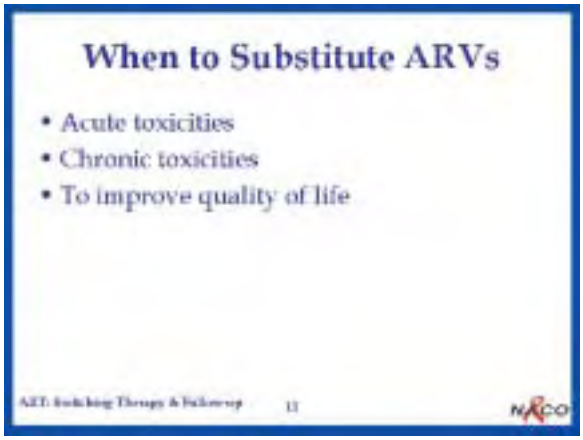
Reader's Notes:

- In resource restricted settings where ART is being rolled out, there are some interactions that are important and frequently encountered:
- Rifampicin, used in treating tuberculosis, should not be used in combination with protease inhibitors or with NNRTIs except Efavirenz. Therefore, in a PLHA co-infected with Tuberculosis and requiring ART, the most appropriate course of action would be a referral to DOTS for Rifampicin based regimen and ART with an Efavirenz based regimen.
- Several of the protease inhibitors and NNRTIs also decrease the concentration of ethinyl Estradiol in oral contraceptive pills and therefore may decrease the effectiveness of oral contraceptives. **It is recommended that women on antiretroviral regimens containing these specific drugs should use an additional or alternative method of contraception, ideally a barrier method.**
- PLHA who are taking anticonvulsants may have a decrease in the levels of protease inhibitors or NNRTIs. This may increase their risk of treatment failure and may promote the development of resistance. **These drugs should be avoided and keep in mind that they are used for other reasons as well- for psychiatric diseases and peripheral neuropathy.**

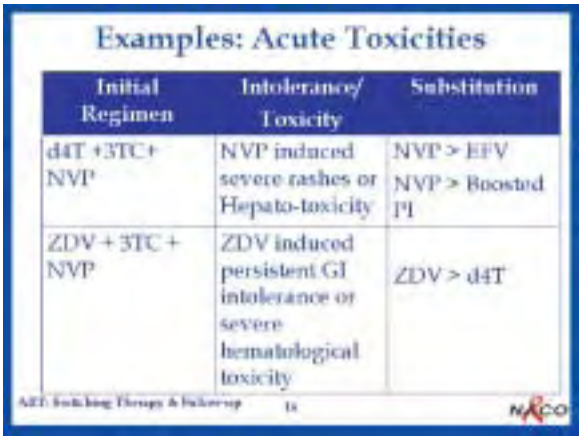
Slide 13

Reader's Notes:

- Some of the other common interactions are listed here.
- The levels of lipid lowering agents of the class HMG CoA reductase inhibitors (statins) increase to dangerous levels in the presence of protease inhibitors, especially Simvastatin, Lovastatin, and Atorvastatin. This interaction is important, as one of the common side effects of PI based therapy is dyslipidaemia and statins, in general, are preferred for therapy. Best statin to use if needed is Pravastatin.
- As mentioned earlier, Rifampicin is contraindicated when the patient is taking PIs and/or Nevirapine, but is probably acceptable with Efavirenz.
- Opioids like Methadone have significant interactions with NNRTI and PI class of drugs and this interaction causes a significant fall in levels of the ART drugs. This interaction is of great significance in IV drug users. There may be a rationale in drug substitution or de-addiction in PLHA who are methadone dependent prior to initiation of ART. Methadone can also cause prolonged QT interval that can lead to torsade de pointe.
- Psychotropics like Midazolam and Triazolam, ergot alkaloids like Dihydorergotamine and non sedating

		antihistamines like Astemizole are contraindicated when taken with PIs. As a rule of thumb, if antihistamines are deemed necessary, it may be better to use sedating drugs like Chlorpheniramine (Avil) and Hydroxyzine (Atarax). • Sildenfil (Viagra) is best avoided in patients on ART. • The herbal remedy, St John's Wort is known to decrease the potency of PI and NNRTI class of drugs and should be avoided. There is no data on the interactions due to herbal preparations with the ART drugs to date and given the propensity for interactions, the concomitant use of herbal remedies is best avoided.
Slide 14		
Slide 15		

Slide 16



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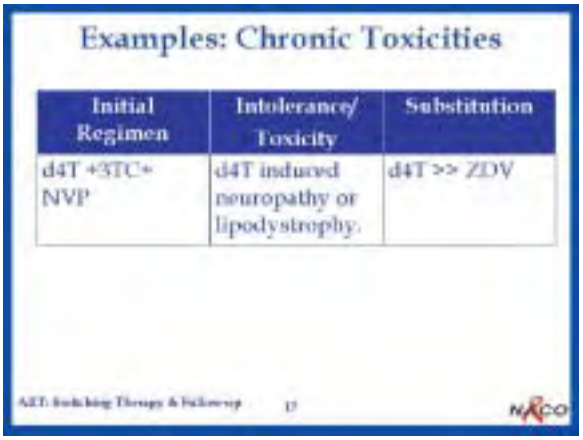
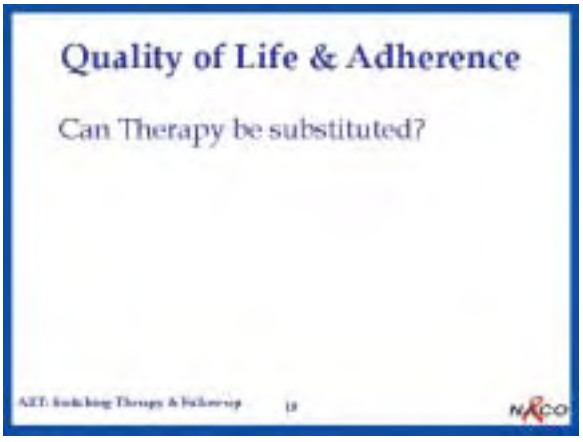
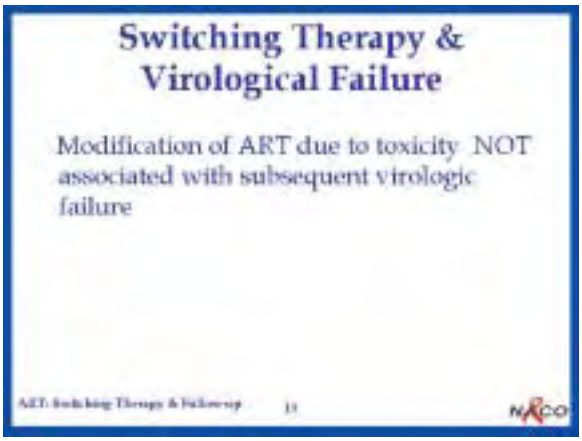


Slide 18

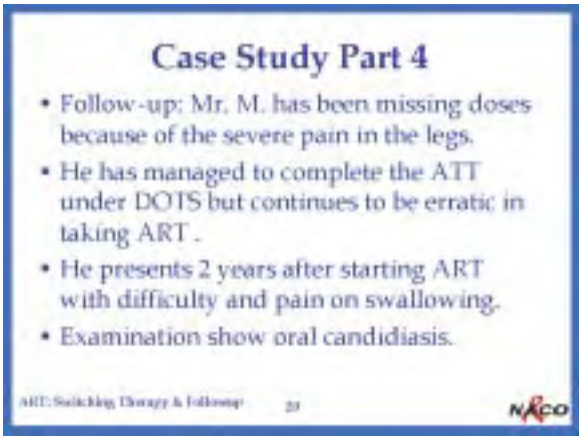


Reader's Notes:

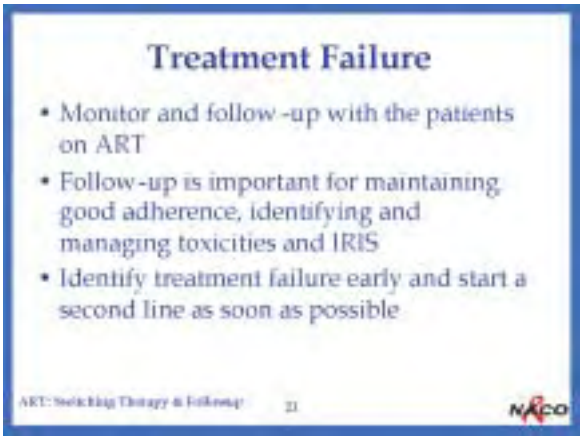
- **Answer: Simplifying complex ARV regimens (by substituting a PI with NNRTI in patients with full virological suppression on a PI based regimen) improves adherence and Quality of life.**
- In the late 90's anti retroviral therapy involved in taking medications at least three times a day, often with food and water restrictions and high number of pills. But now a days we have fixed dose combination drugs, once daily drug therapy etc. which will make the life of the patients easy. So if the difficult regimens are changes to newer simpler, but still effective regimens that will not only ease adherence but also enhance their quality of life.
- **Sources:**
- Becker S, Rachlis A, Gill J, DeJesus E, Pierone G, Kirkland L, et al. Successful substitution of Protease inhibitors with efaviranz in patients with undetectable plasma HIV-1 RNA levels: results of prospective,randomised, multicenter, open label study (DMP 266-049) Fifth International Congress on Drug

		Therapy in HIV infection; October 22-26, 2002; Glasgow, Scotland. Abstract P 21. • Clumeck N, Goebel F, Rozenbaum W, Gerstoof J, Staszewski S, Johnson M, Gazzard B, Stone C, Athisegaran R, Moore S. Simplification with Abacavir-based triple nucleoside therapy versus continued protease inhibitor-based antiretro viral therapy in HIV-1 infected patients with undetectable plasma HIV-1 RNA. Aids 2001; 15:1517-26. • Opravil M, Hirschel B, Lazzarin A, Furrer H, Chave JP, Yerly S, Bisset LR, Fischer M, Vernazza P, Bernasconi E, Battegay M, Ledergerber B, Gunthard H, Howe C, Weber R, Perrin L. A randomized trial of simplified maintenance therapy with abacavir, lamivudine, and zidovudine in human immunodeficiency virus infection. J Infect Dis 2002; 185:1251-60. • Ruiz L, Negredo E, Domingo P, Paredes R, Francia E, Balague M, Gel S, Bonjoch A, Fumaz CR, Johnston S, Romeu J, Lange J, Clotet B. Antiretroviral treatment simplification with nevirapine in protease inhibitor-experienced patients with hiv-associated lipodystrophy: 1-year prospective follow-up of a multicenter, randomized, controlled study. J Acquir Immune Defic Syndr 2001; 27:229-36.
Slide 19		**Reader's Notes:** • Toxicities from ART are common and may necessitate changes in medications. • The majority of these toxicities are not life threatening but can affect quality of life and negatively impact patients' willingness to adhere to their regimens. • In fact, several cohort studies suggest that toxicities are a more common reason for changing ART. Review of published cohort studies that examined modification of initial antiretroviral regimens found that antiretroviral intolerance and toxicity was the most common reason • **Source:** Le Moing V, Chene G, Leport C, Lewden C, Duran S, Garre M, Masquelier B, DuponM, Raffi F. Impact of discontinuation of initial protease inhibitor therapy on further virological response in a cohort of human immunodeficiency virus-infected patients. Clin Infect Dis 2002; 34:239-47.

Slide 20



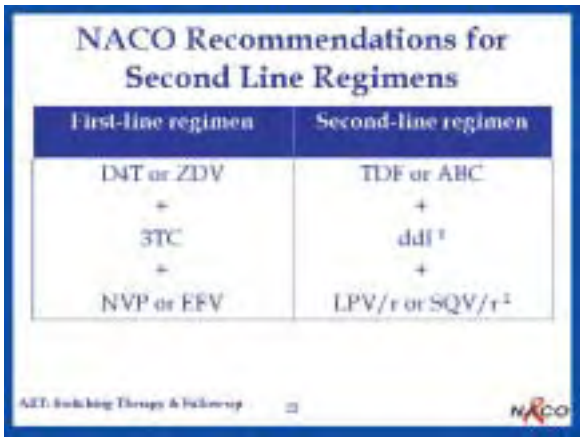
Slide 21



Reader's Notes:

- **Clinical failure:** Certain WHO clinical stage 3 conditions (e.g. Pulmonary TB, severe bacterial infections) may be an indication of treatment failure and thus requires consideration of second line therapy. Some WHO clinical stage 4 conditions (Lymphnode TB, uncomplicated TB pleural disease, Oesophageal candidiasis, recurrent bacterial pneumonia) may not be indicators of treatment failure and thus do not require consideration of second line therapy.
- **Immunological failure:** Some experts consider that patients with persistent CD4 cell count below 50cells/cu.mm. after 12 months on ART may be more appropriate.
- **Virological failure:** The optimal viral load value at which ART should be switched has not been defined. However, values of more than 10,000 copies/ml have been associated with subsequent clinical progression and appreciable CD4 cell count decline.
- **Source:** WHO Antiretroviral Therapy for HIV Infected Adults and Adolescents in Resource Limited Settings: Towards Universal Access. Recommendations for a Public Health Approach. 2006 Revision. Pages ages 1-4.

Slide 22



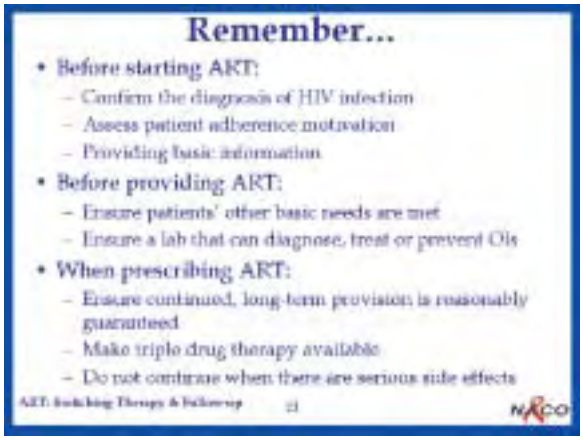
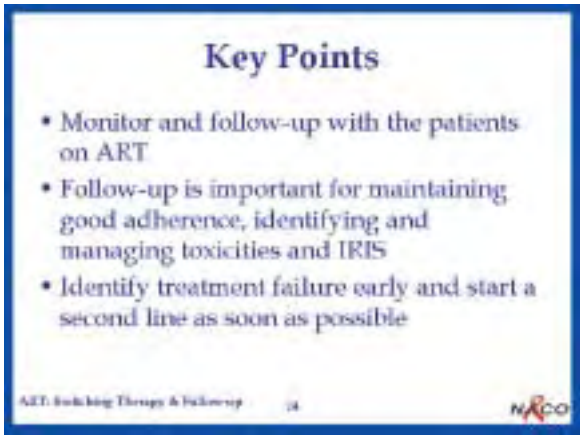
Reader's Notes:

- Superscripted numbers in the table denote:

  1. Dose of ddI should be reduced from 400 mg to 250 mg when administered with TDF.

  2. LPV/r and SQV/r require secure cold chain. NFV can be considered as an alternative in resource settings without cold chain.

- **Source: NACO Guidelines in management of Antiretroviral therapy in Adults and Adoloscents, Draft March 2007**

Slide 23		**Reader's Notes:** • Basic information that should be provided to a patient **before starting** ARVs includes: • how/when to take the drugs. • potential side effect. • interactions with other drug. • Do not provide ART without addressing a patient's **basic needs** such as sufficient nutritional support and adequate home care. • Do not prescribe ART where only **mono-/dual therapy** is available (unless in PPTCT or PEP program).
Slide 24		

SESSION 12-16

DAY - FOUR

SESSION 12

SESSION

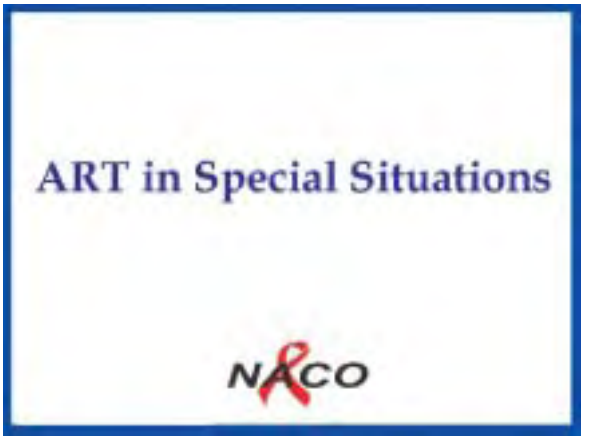
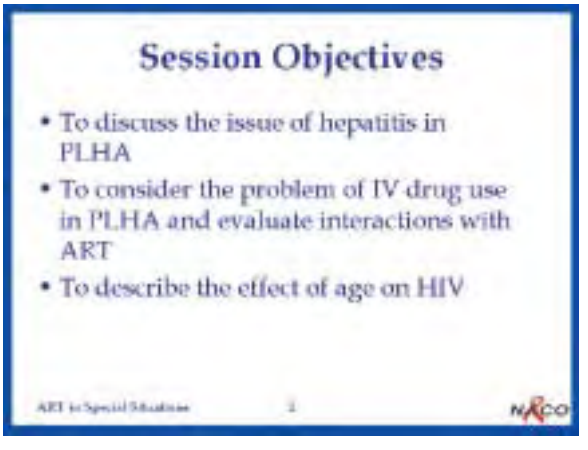
ART IN SPECIAL SITUATIONS

12

Total Session Time: 30 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Discuss the issue of hepatitis in PLHA
- Consider the problem of IV drug use in PLHA and evaluate interactions with ART
- Describe the effect of age on HIV

Slide 1		
Slide 2		

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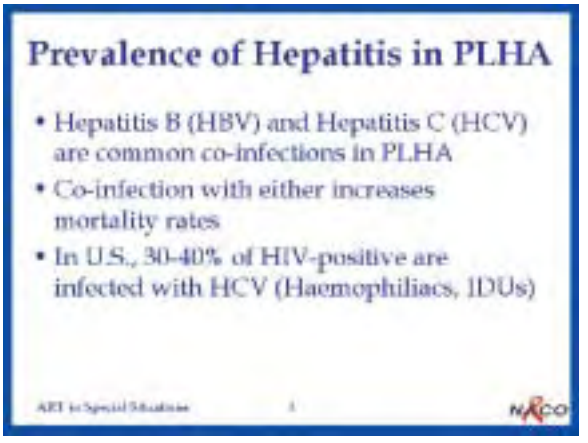

Reader's Notes:

- Hepatitis B and hepatitis C are common co-infections in PLHA. In fact, the commonest cause of death in PLHA in the United States is hepatitis virus related.
- In a data review from a tertiary institution from India (Christian Medical college, Vellore-unpublished date), over a two month period, more than 7000 serum samples were submitted for screening, 3% of the sample had antibodies to HIV. Hepatitis B co-infection was found in a significant number of the patients, and Hepatitis C was quite uncommon. This is the usual pattern across south east Asia, where Hepatitis B is endemic and Hepatitis C is unusual outside of certain high risk groups like IV drug users, haemophiliacs, and patients on dialysis.
- Other studies found that the presence of a co-infection increases mortality.
- Prevalence and incidence of Hepatitis B Virus infection in STD clinic attendees in Pune, India. A Risbud, S Mehendale, S. Basu, S Kulkarni, A Walimbe, V Arankalle et al Sex Transm Infect 2002;78:169-173.
- In the US, about 30-40% of injecting drug users and haemophiliacs are infected with Hepatitis C virus.
- IDUs: Intravenous drug users.

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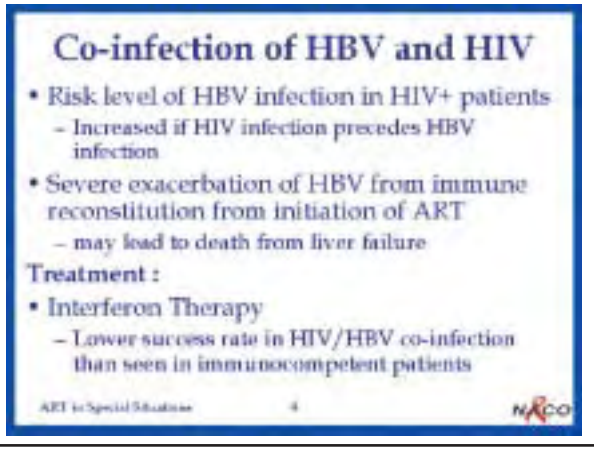

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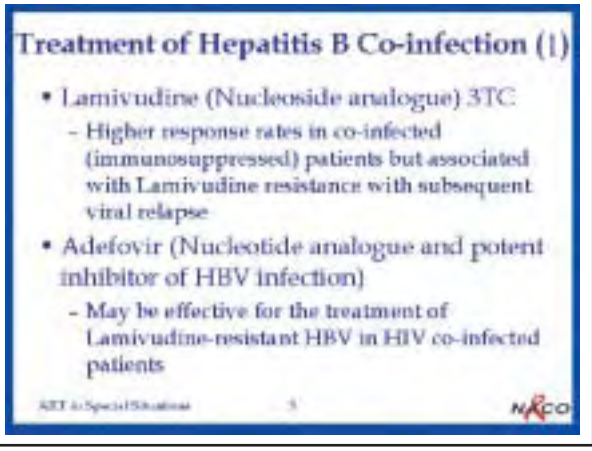

Reader's Notes:

- Adefovir (nucleotide analogue and potent inhibitor of HBV infection) has possible side affects which include renal failure and acute worsening of hepatitis B after discontinuation of therapy.
- **Source:** Antiretroviral therapy for HIV infection in adults and adolescents in resource-limited settings: Towards universal access WHO 2006, website: www.who.int/hiv.

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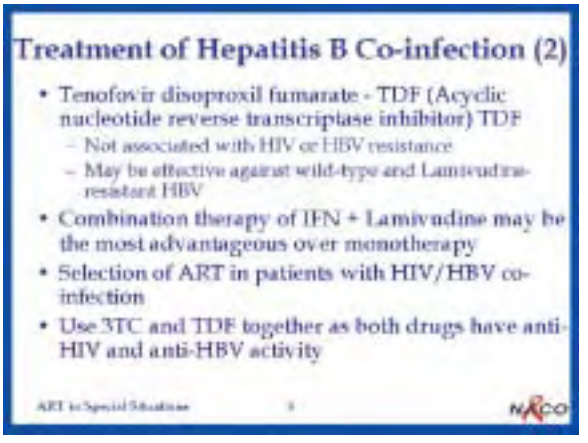

Reader's Notes:

- **Source:** Antiretroviral therapy for HIV infection in adults and adolescents in resource-limited settings: Towards universal access WHO 2006, Website: www.who.int/hiv.

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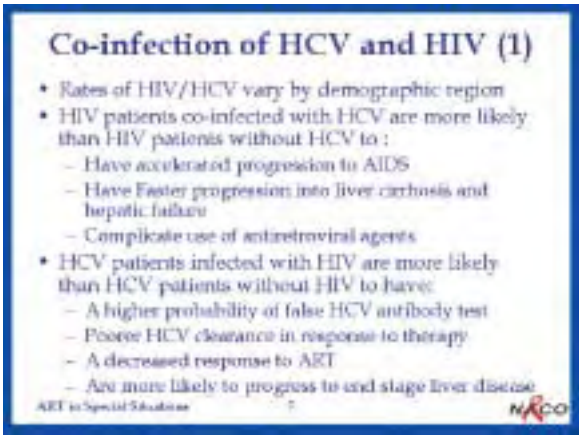
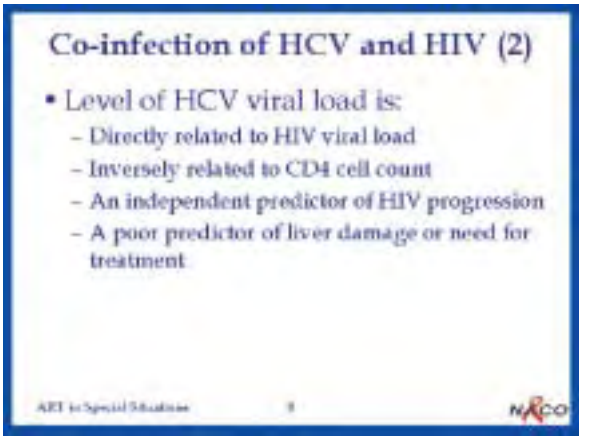
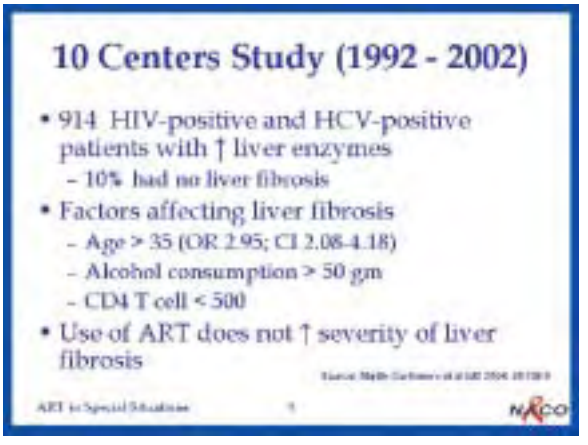


Reader's Notes:

- **Co-infection with HIV**
- HIV infected patients are more likely to progress to end stage liver disease as compared to those not dually infected.
- One study demonstrated end-stage liver disease in 13.5% of HIV-infected patients versus 6.5% of HIV-negative patients over 20 years ($p<0.01$). (Source: Impact of HIV on Progression to End-Stage Liver Disease in HCV Co-infected Hemophiliacs).
- M. RAGNI*. Univ. of Pittsburgh Med. Ctr. and Hemophilia Ctr., PA 7th Conference on Retroviruses and Opportunistic infections, San Francisco, 2000. Abstract 281).
- Progression of HIV appears to be accelerated (1-2) /or unchanged (3-4) in patients who are dually infected with HIV and HCV.
- **Sources:** 8th Conference on Retroviruses and Opportunistic Infections.
  (1) Abstract 35 Hepatitis C Virus (HCV) Clearance, Viral Load (vl) and Alanine Aminotransferase (ALT) Levels in HIV-Infected and Uninfected Hemophiliacs.
  E. S. Daar*1, H. Lynn2, S. Donfield2, E. D. Gomperts3, M. W. Hilgartner4, W. K. Hoots5, D. Chernoff6, S. Arkin7, W.-Y. Wong3, and C. Winkler8.8th CROI, San Francisco, 2001.

		(2) Abstract 572 Impact of Hepatitis C in HIV-Infected Individuals in an Urban Center in Madrid, Spain. J. Martín*, M. López, R. Arranz, M. Pérez-Olmeda, P. Martínez, J. González-Lahoz, and V. Soriano. Inst. de Salud Carlos III, Madrid, Spain. 8th CROI, Chicago, 2001. (3) Abstract 34 Effect of HCV Coinfection on HIV Disease Progression and Survival in HIV-Infected Adults. M. Sulkowski*, R. Moore, S. Mehta, and D. Thomas. Johns Hopkins Univ. Sch. of Med., Baltimore, MD. 8th CROI, Chicago, 2001. (4) Abstract 570 Does Hepatitis C Virus (HCV) Coinfection Modify Survival in HIV Patients on Combinations of Antiretrovirals? C. Rancinan*1, D. Neau2, M. Saves1, S. Lawson-Ayayi1, F. (5) Bonnet3, P. Mercie4, M. Dupon2, P. Couzigou4, F. Dabis1, G. Chene1, and The Groupe d'Epidemiologie Clin. du Sida en Aquitaine (GECSA). 8th CROI, Chicago, 2001.
Slide 8		**Reader's Notes:** • An HIV infected patient's response to HCV is dependent on the viral load. • In the presence of HIV infection, there is a higher probability of false negatives for HCV antibody tests, probably as a result of the waning of the antibody response in advanced infection. • 1st study demonstrated a <5% higher probability : Sources: 8th CROI, Chicago, 2001: 1.Sherman K. State of the Art Lecture. • 2nd study showed a 12% higher probability of false negative HCV antibody. Sources: 8th CROI, Chicago, 2001: Busch MP # 235. • Hepatitis C clearance has been shown to be poorer in some studies while other studies did not show any difference in response to therapy in studies of co-infected people, as compared to those with only hepatitis C infection and not HIV. • A study demonstrated a poor response to therapy in co-infected people (HIV and HCV) when compared to people with only hepatitis C and not HIV. (Source: Abstract 35 Hepatitis C Virus (HCV) Clearance, Viral Load (vl) and Alanine Aminotransferase (ALT) Levels in HIV-Infected and Uninfected Hemophiliacs. E. S. Daar*1, H. Lynn2, S. Donfield2, E. D. Gomperts3,

		• M. W. Hilgartner4, W. K. Hoots5, D. Chernoff6, S. Arkin7, W.-Y. Wong3, and C. Winkler8. 8th CROI, San Francisco, 2001). • Response to antiretroviral therapy also appears to be poorer. (Sources: Clinical progression, survival and immune recovery during antiretroviral therapy in patients with HIV-1 and Hepatitis-C virus co-infection : the Swiss HIV cohort study Greub G, Ledergerber B, et al Lancet 2000; 356: issue 9244 25 Nov,1800—1805.
Slide 9		**Reader's Notes:** • OR=Odds Ratio. • CI= Confidence Interval. • A larger subsequent study, found that advancing age, use of alcohol and lower CD4 levels were independent predictors of liver fibrosis in HIV infected patients co-infected with HCV. Use of ART has been considered dangerous in view of its hepatotoxicity, but in this study there was no increase in severity of liver fibrosis associated with the use of the drugs. • **Sources:** • Incidence and Predictors of Severe Liver Fibrosis in Human Immunodeficiency Virus Infected Patients with Chronic Hepatitis C: A European Collaborative Study, Author(s) Luz Martín-Carbonero, Yves Benhamou, Massimo Puoti, Juan Berenguer, José Mallolas, Carmen Quereda, Ana Arizcorreta, Antonio Gonzalez, Jurgen Rockstroh, Victor Asensi, Pilar Miralles, Montse Laguno, Leonor Moreno, José Antonio Girón, Martin Vogel, Javier García-Samaniego, Marina Nuñez, Miriam Romero, Santiago Moreno, Juan José de la Cruz, and Vincent Soriano. • **Journal** Clinical Infectious Diseases, volume 38 (2004), pages 128—133.

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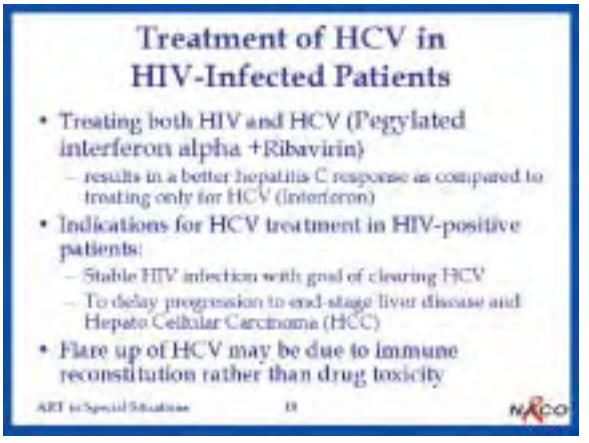
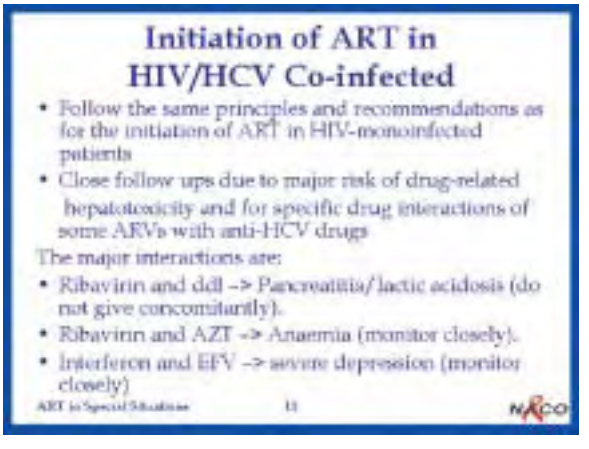


Reader's Notes:

- Treatment modalities in co-infected patients are still a source of controversy, but the consensus is that therapy given for both.
- The drugs for Hep C and HIV coinfection are complex to deliver and costly. They are not available through the public sector in resource limited settings. Guidelines on the use of the above drugs can be viewed in the following article.
- **Source;** Alberti A, Clumack N, et al: Short statement on the First European Consensus Conference on the treatment of Chronic Hepatitis B and C in HIV Coinfected patients. Journal of Hepatology 2005;42:615-24.
- In a study concomitant therapy for both HIV and HCV resulted in a better hepatitis C response as compared to therapy targeted at hepatitis C only. **Therefore, therapy for hepatitis C should be considered in patients towards the goal of clearing the virus, and also towards prevention of fibrosis and liver cancer.**
- 37 consecutive co-infected patients with a median CD4 cell count at 343 cells/µl were treated with Interferon or Ribavirin+Interferon. Sustained Hepatitis C virus response in 35% treated with combination versus 7% with monotherapy. (Source: Abstract S11 The Treatment of Chronic HCV Infection in HIV-Infected Persons. M. SULKOWSKI*. Johns Hopkins Univ., Baltimore, MD. 7th Conference of ReROI, San Francisco, 2000).
- Anecdotal case(s) support that the flare up of HCV may be due to immune reconstitution syndrome (IRIS) rather than drug toxicity.

Slide 11



Reader's Notes:

- In patients with high CD4 cell counts it is preferable to treat HCV infection before HIV. While concurrent treatment of both infections is feasible , it may be complicated by Pill burden (RBV+ARV drugs), drug toxicities and drug interactions. In patients who need ART it may be preferable to initiate ART and delay HCV therapy in order to obtain better anti-HCV response rates after immune recovery.
- **Source:** Antiretroviral Therapy for HIV infection in adults and adolescents in resource limited settings: towards universal access: recommendations for a public health approach 2006 revision.
- Website: www.who.int/hiv.

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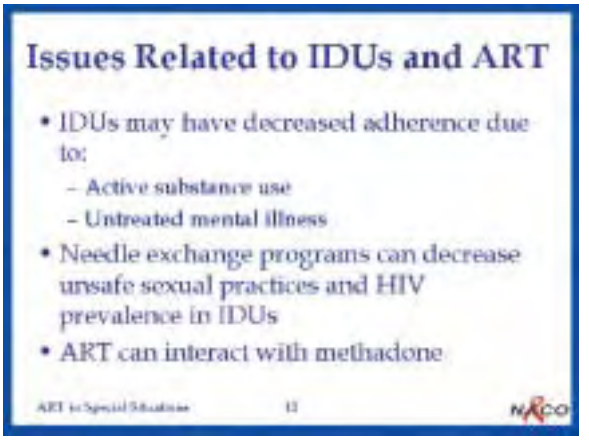

Reader's Notes:

- Intravenous drug use is a major problem in the north east and the interiors of some metropolitan areas. The prevalence of HIV in IDU (injection drug user) populations is a source of concern.
- Data from Canada shows that IDUs are likely to have other problems, including homelessness, imprisonment, mental illness, co-infections and participation in commercial sex. 70% of patients on ART had treatment interruption.
- **Sources:**
  1. Tyndall M, Yip B, Hogg R, et al. Coverage, adherence, and sustainability of antiretroviral therapy among injection drug users in Vancouver, Canada. 13th International AIDS Conference. Durban, South Africa, 2000. (Abstract ThPeB4990).
  2. Adherence and plasma HIV RNA responses to antiretroviral therapy among HIV-1 infected injection drug users Evan Wood , Julio S.G. Montaner , Benita Yip, Mark W. Tyndall et al. CMAJ, September 30, 2003; 169 (7) © 2003 Canadian Medical Association.
- Aggressive needle exchange programs benefit IDUs. A study of IDUs in New York demonstrated that as the rate of exchange of needles increased, there was a decrease in unsafe sexual practices and HIV prevalence. Methadone is a rigorously well-tested medication that is safe and efficacious for the treatment of narcotic (e.g., heroin) withdrawal and dependence. It is associated with reductions in opiate use. There are multiple possible drug interactions between methadone and ARVs. New York City Needle Exchange Program 1990—97.
- Needle exchange increased from 20 to 50% among participants and Unsafe sex fell from 18% to 11%. HIV incidence decreased from 4.4 to 0.8 per person-years at risk[2] The roles of syringe exchange and HIV counseling and testing in the declining HIV epidemic among IDUs in New York City. Des Jarlais, D., Perlis, T., Friedman, S. R., Marmor, M., Torian, L., Friedmann, P., Glebatis, D. Rockwell, R. and Paone, D. (2000b) Poster Presentation at the 13th International Conference on AIDS, Durban, abstract, MoP pD1124.

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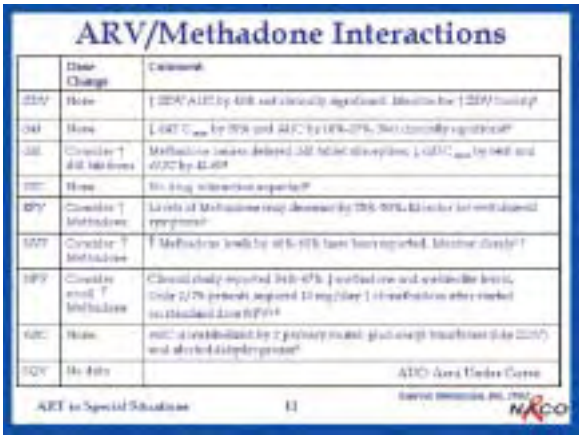

Reader's Notes:

1. Case reports/abstracted data;
2. Pharmacokinetic study;
3. Clinical study;
4. Manufacturer's information;
5. Expert opinion.

- **Sources:** http://www.law.duke.edu/aidsProject/400_01/GuideAntriRetros.pdf : Quick Reference Guide to Antiretrovirals.
- Methadone is a rigorously well-tested medication that is safe and efficacious for the treatment of narcotic (e.g., heroin) withdrawal and dependence.
- Methadone treatment causes significant interactions with NNRTIs and PIs. Co-administration increases the risk of failure of therapy.
- AUC: Area under curve: indicates the therapeutic level of a drug in the blood. This area for a particular drug will decrease when the other drug is co-administered.

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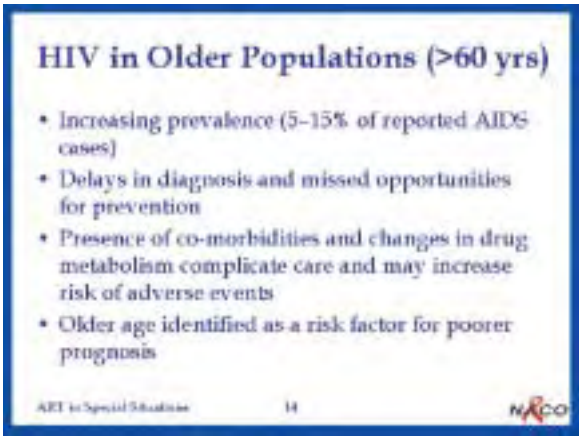

Reader's Notes:

- **Source:** Older People and HIV, AIDS Info Net, Fact Sheet Number 616, April 30 2005.
- Further information can be obtained from Volume 16, Number 6 The Hopkins HIV report November 2004: HIV in Patients Over 50: An Increasing Problem By Kelly A. Gebo, M.D., M.P.H.
- Website: http://hopkins- aids.edu/publications/report/nl_04_nov.pdf.

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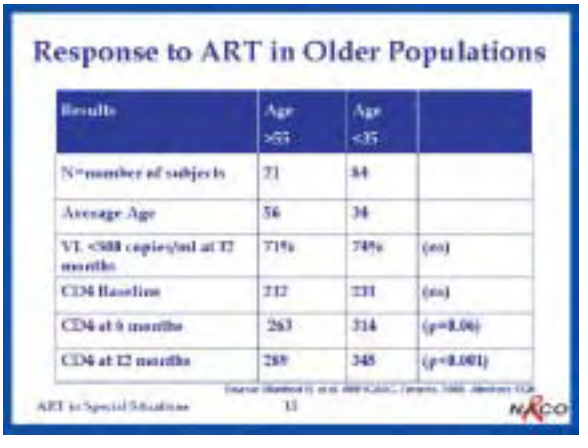
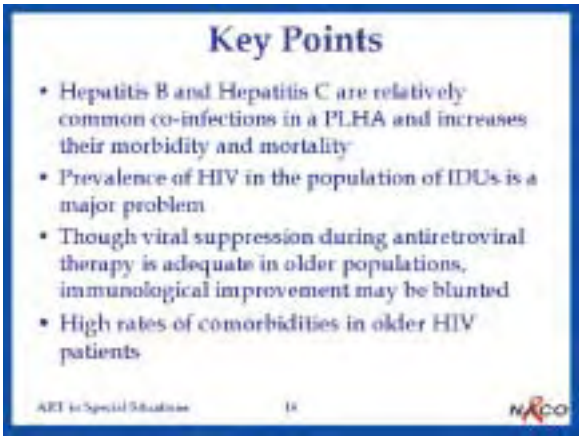


Reader's Notes:

- Data from the early ART era suggested that the speed of immune recovery after initiation of ART is inversely proportional to age and that older patients did not respond as well as younger patients. Further information can be obtained from the following sources:
  - Manfredi R and Chiodo F, AIDS 2000;14:1475-77.
  - Viard JP, et al. J Infect Dis 2001;183: 1290-1294.
  - Yamashita TE, et al. AIDS 2001;15:735-46.
- A consistent finding across studies, however, has been a smaller CD4 cell count increase in older patients compared to younger patients treated with ART. All of these trials were relatively small, however, with fewer than 400 patients over the age of 50 years. Further information can be obtained from the following source:
- Knobel H, et al. AIDS 2001:15:1591-93.

Slide 16		

Key Points
• Hepatitis B and Hepatitis C are relatively common co-infections in a PLHA and increases their morbidity and mortality
• Prevalence of HIV in the population of IDUs is a major problem
• Though viral suppression during antiretroviral therapy is adequate in older populations, immunological improvement may be blunted
• High rates of comorbidities in older HIV patients

SESSION 13

SESSION 13

ART TEAM

Total Session Time: 30 minutes

Session Objectives: At the end of the session, the participant should be able to:

- To list members of ART team
- To describe their roles and responsibilities

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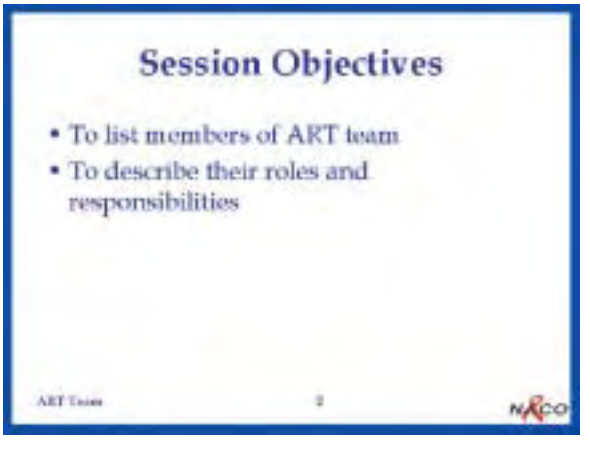
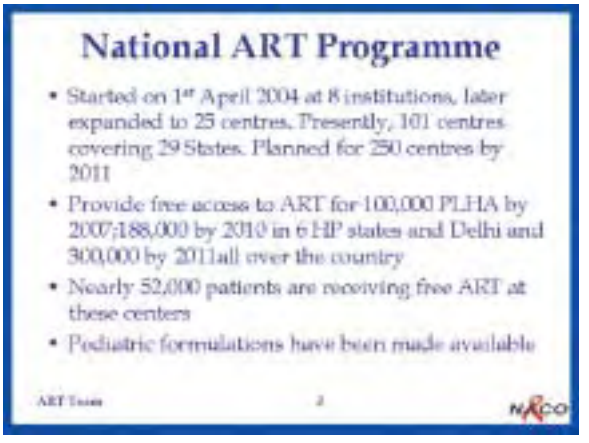
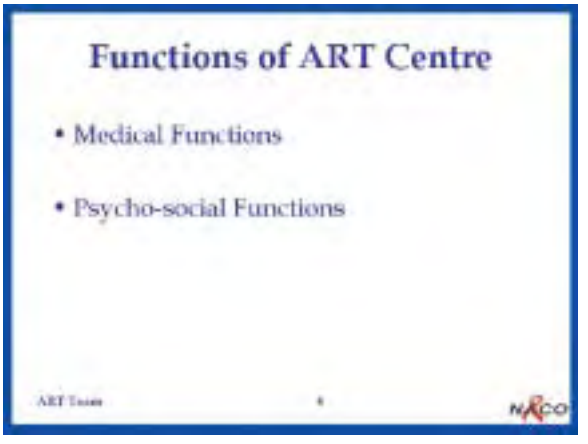
Slide 2		

Slide 3		
Slide 4		**Reader's Notes:** • **Medical Functions; they are (1)** To diagnose and treat Opportunistic Infections, (2) To screen HIV+ persons for eligibility to initiate ART, (3) To monitor patients on ART and manage side-effects, if any • To provide in-patient care as and when required, (4) To facilitate linkages between other service providers and (5) To facilitate easy access to specialist's care as necessary • **Psycho-social Functions are as follows: (1)** To provide psychological support to PLHA accessing the ART centre, (2) To provide counselling for adherence to ARV drugs, (3) To advise for risk reduction behaviour, (4) To educate PLHAs on proper nutrition, (5) To provide psychological support to PLHA accessing the ART centre, To provide counselling for adherence to ARV drugs, (6) To advise for risk reduction behaviour including usage of condoms, and (7) To educate PLHAs on proper nutrition.
Slide 5		

Handout 1 : ART Team Stakeholders and Job Responsibilities

ART Team Members:

*All the members of the ART team must have undergone ART training.

- Physician (4)
- Paediatrician (2)
- Obstetrician/ Gynaecologist (2)
- Microbiologist
- Dermatologist/ STD (2)

As per NACO guidelines, each ART centre will have the following staffing pattern:

1. Doctor
2. Counsellor
3. Lab Technician
4. Data Manager
6. Pharmacist (when the number of patients exceeds 500).
7. Nurse
8. Care Co-ordinator

The strength of each stage will depends on the number of pasents on ART at the Center.

Roles and Responsibilities:

Role of ART Medical Officers (MOs):

- Clinical service: OI care, ART management & monitoring
- Preparing monthly/quarterly analysis on ART
- Training the staff (medical, paramedical and other hospital staff such as clerical staffs)
- Overall supervision — counselling, pharmacy, M&E records
- Networking

Requirements for the 'ART Medical Officer':

- MBBS degree

Requirements for the 'Senior ART Medical Officer':

- Post graduate in medicine, paediatrics, obstetrics or STD back ground
- Experience in analysis and interpretation of data , Adequate knowledge of computer usage
- Along with the faculty, he or she will deliver ART service (which is his primary responsibility)

Role of an ART Counsellor:

- Vital in the treatment preparation for HAART and on going support
- Handles issues related to stigma and discrimination, and helps clients positively cope with psychological defense mechanisms.
- Educates clients on the risk of the disease progression and the changes in the body that can occur with

progression of disease and with the medications.

- Assists in managing occupational and financial issues (e.g., vocational training) in coordination with NGOs, self help groups and government sectors (e.g., Department of Social Defense).
- Plays a key role in ensuring adherence through 'identifying' the guardian,
- Links clients to appropriate support systems, periodically reviews clients' support systems.
- Develops individual adherence strategies especially for clients with a record of poor adherence.
- Gives guidance on concepts of palliative and home based care, nutrition issues and links clients to local service providers and NGOs serving in palliative care/nutrition support.
- May conduct group counselling (in appropriate areas like adherence counselling, treatment preparation counselling, counselling on CD4, ART eligibility criteria). Group counselling may be used as a strategy of time management in crowded centres and to infuse peer support.

Role of ART Lab Technician:

- Conducts blood sampling for CD4 cell count which determines ART eligibility.
- Maintains records related to CD4 tests/count.
- Monitors clients for repeat CD4 cell counts (in conjunction with medical officer and counsellor).
- Participation in performance CD4 testing (at centres with CD4 machine).
- Transportation of blood samples (if not provided with a machine) to linked centre for CD4 testing.

Role of ART Pharmacist:

- Dispenses ART medicines.
- Maintains drug stock and dispenses register.
- Monitors stock position so as to maintain buffer stock of three months.
- Counsels and demonstrates the ART and OI drug schedule to clients
- Counsels/monitors ART toxicity
- Provides ongoing counselling

Role of Record Keeper:

- Maintains individual patients' master cards
- Fills in appropriate columns in ART Registers
- Prepares monthly report and quarterly cohort analysis
- Prepares reports for local level meetings and maintains minutes
- Maintains all correspondence related to ARV treatment clinic in the hospital (inward, outward letters)
- Networks

Handout 2 : Hospital Based Stakeholders

1. Medical Stakeholders:

- **Primary level:** (Essential in delivering ART services)
  - ART centre staff: implementing, delivering, monitoring ART (program)
  - Physician: OI management, toxicity monitoring, IRIS.
  - Paediatrician: OI management, toxicity monitoring, IRIS, general medical care of children and helping ART Medical Officers in special circumstances (e.g., difficulty in clinical staging).
  - Chest/ TB Physician: Ruling out PT before initiation of ART, ART-ATT (co-infection) management, IRIS (TB)
  - Microbiologist: VCTC to identify and confirm test results
  - Obstetrician/Gynaecologist: PPTCT services and referral to ART, ART management in pregnant women, OI care
- **Secondary level:** (Provide need-based services)
  - Psychologist/Psychiatrist
  - Community Medicine specialist
  - Surgeon
  - ENT surgeon
  - Ophthalmologist
  - These stakeholders need active (established/strengthened) linkages with community medicine departments. In practice, at most of the medical colleges, community medicine departments are not adequately linked with clinical programmes operating in the medical college hospital. Through appropriate linkage strategies, the infrastructure and human resource of community medicine departments can be utilised in training, field visits and other related activities of ART centre.
  - Active linkage and expertise of the above departments is necessary to provide comprehensive care to clients.

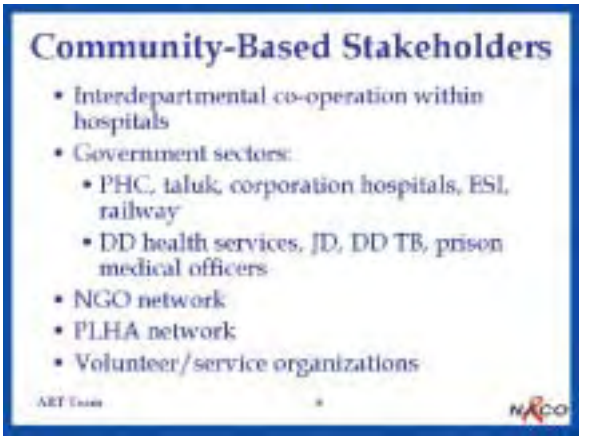
2. Paramedical Stakeholders:

- ***Counsellor***
  - Plays a key role in ART counselling including issues related to disease progression, WHO staging, CD4 count and ART eligibility criteria, toxicity, support systems, adherence, OI care and follow up.
- ***Pharmacist***
  - If there are less than 500 ART clients, a pharmacist will not be provided by NACO and hence there needs to be assurance that local chief pharmacist and pharmacy staff are involved in the programme.
- ***Lab Technician***
  - Need service of hospital lab technician to do tests in various specialties, e.g., biochemistry and also to relieve NACO lab technician on special occasions.
  - Nursing Superintendent and Staff
  - Current NACO policy states that nursing faculty for ART service should be allotted by local hospital)
  - Nutritionist

3. Administrative Stakeholders:

- Supervise and guide quality and policies of HIV related services (especially ART in the hospital).

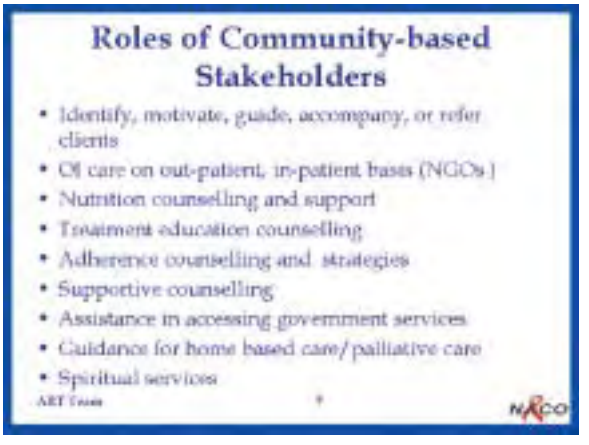
Slide 6



Reader's Notes:

- For better client care, networking with specialty service centres, charity organizations (e.g., Aravind eye hospital), ICMR clinics, ESI-if eligible, and railways- if eligible, is recommended when facilities are not available in local settings.
- All HIV related services (VCTC, PPTCT, OI care, STD care, ART, blood safety, PEP) should be linked adequately so that clients can avail maximum benefit of the service.
- Participation in monthly district level HIV committee meetings conducted by collectors and discussions with govt. health sector officials will enhance ART outreach and quality.
- Meetings of PHC Medical Officers at block PHC (also attended by NGOs working in that PHC area). Here they report their HIV/ART data to DD health - DD health reports at monthly district level HIV meeting collector office (participated by all stakeholders performing HIV service in the whole district along with JD, DD TB and other higher officials of health sector–active discussing on program implementation and monitoring and evaluation of activities
- Mapping NGOs (e.g., NGOs providing OI care, NGOs targeting preventive care) and services in localities (e.g., district, service area).
- Conduct regular meetings with NGOs and networks at ART centres to creatively solve issues and problems. Find ways to provide nutritional, educational and travel support for ART Centre patients.

Slide 7



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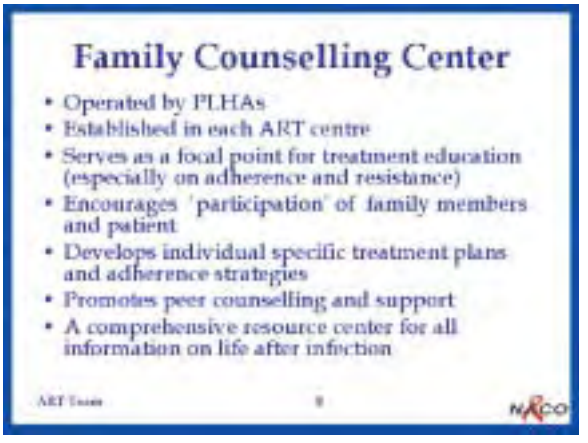

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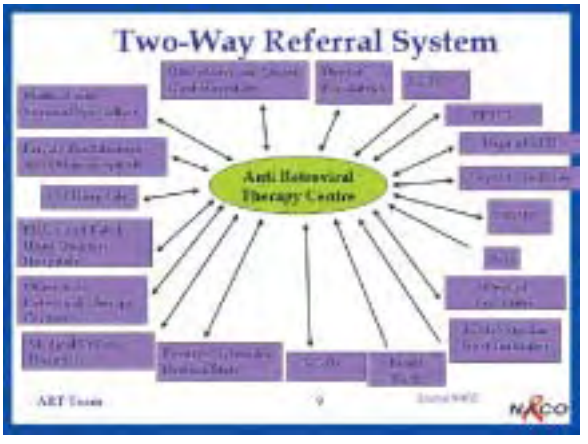
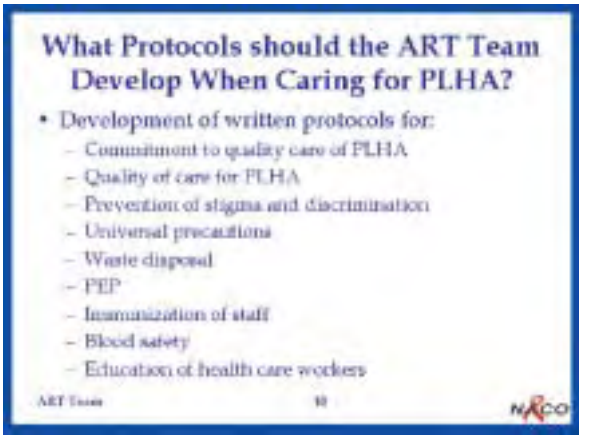
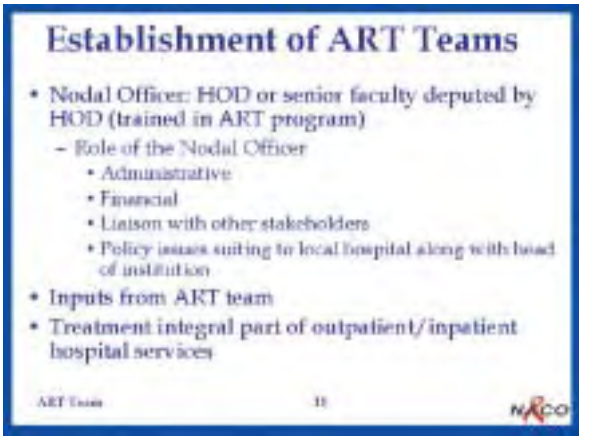


Reader's Notes:

- The ART centre should network with various partners to facilitate two way referrals of PLHA in order to ensure comprehensive care. The networking should be with organizations within the institution, (such as the PPTCT programme, the VCTC, the DOTS programme, the various departments and blood back), other institutions (both government and non government) and finally with home based, faith based and community based organizations, including the positive peoples' network.
- Example of a two-way referral system:
- Identification and referral to ART from ESI ART initiation under NACO guidelines-> referral back to ESI for OI care-> monthly review at ART centre (for ART delivery, adherence & toxicity monitoring) & reporting the remarks to ESI Medical Officer.
- Make sure that the linkage is two way: Each ART centre attendee should be referred to at least one referral point so that he or she can get OI care and other available service at that designated referral point.

  For each client, make note of the entry point (where the referral is from) and exit point (where is the referral to). On each visit to the ART centre, make sure that the client is under the care of a particular exit point (e.g., an NGO or private practitioner). This minimizes chances of patient drop out from the ART programme and makes monitoring adherence easier.

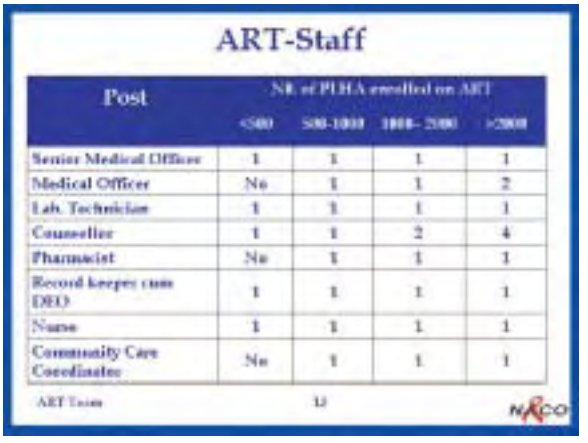
Slide 10		
Slide 11		

Slide 12

Reader's Notes:

- A minimum of 800 sq. ft. area is required for an ART centre having on an average 500 patients (i.e. 20/ day) on roll. It should have adequate rooms each measuring at least ten feet by ten feet (10' x 10') for the following staff/services listed below;
  1) Examination Room: for Medical Officers to examine the patients,
  2) Counselling Room: For individual, group and family counselling,
  3) Pharmacy: For distribution and stocking ARV & OI drugs with window for dispensing ,
  4) facility for stocking medicines without direct exposure to sunlight and separate storage facility for paediatric medicines,
  5) Laboratory: For collection and storage of samples and laboratory tests by Laboratory Technician,
  6) Office Space: for registration, record keeping and data entry by Record keeper cum data Entry Operator,
  7) Waiting Area: For patients and accompanying persons, where group therapy, counselling could also be conducted (20 x 10 feet). Television and other audio-visual facilities may be installed for educational purposes,
  8) Adequate space should be individually identified and provided taking into consideration the need of the particular centre. As NGO and peer support at the centre itself has proved to be an asset to patients and to the hospital, space should also be provided for volunteers from these organisations. The ART Centre should be clean and maintain the highest standards of cleanliness and hygiene, have proper ventilation, lighting, electric supply and water supply for effectively carrying out xamination, counselling, laboratory tests and record keeping.

Slide 13



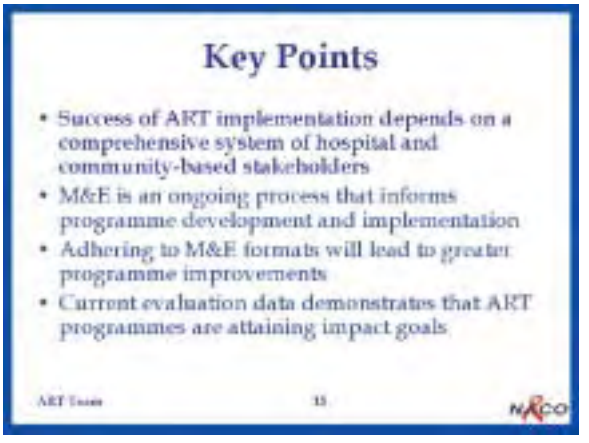
Reader's Notes:

1) The selection of staff shall be made by a panel consisting of SACS officials, representatives of the institution concerned and the in-charge of ART centre.
2) In case of contractual appointments, an open advertisement followed by interview of eligible applicants should be undertaken to select the most suitable candidates.
3) Attitude of candidates should be given due weightage in the selection process. Experienced, retired persons can also be re-appointed up to the age of 62 years.
4) Contractual appointments should preferably be made for a period of 3 years to ensure continuity. There should be an annual appraisal system for consultants/ contract staff based on which continuation and increments should be decided.

- The staff strength is included in the table;
- The faculty team in the institution:The ART Centre is an integral part of the Department of Medicine. Therefore the ART team at the centre should be headed by the Head of the Department (HoD) of Medicine. The HoD may nominate a senior faculty of Medicine as the nodal officer of the ART centre. In addition, two to four physicians, two paediatricians, two obstetrician-gynaecologists, one microbiologist and one or two dermatologists (or venereologists) should be part of the team. NACO will train all the members of the team for continuous supervision and optimal utilization of the Centre. The Department of Medicine should own up this Centre as an integral part.

Slide 14

Slide 15		


Key Points
• Success of ART implementation depends on a comprehensive system of hospital and community-based stakeholders
• M&E is an ongoing process that informs programme development and implementation
• Adhering to M&E formats will lead to greater programme improvements
• Current evaluation data demonstrates that ART programmes are attaining impact goals

SESSION 14

SESSION 14

ADHERENCE ISSUES

Total Session Time: 45 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Discuss the importance of patient adherence to ART
- Understand patient barriers to adherence
- Discuss ways of promoting patient adherence
- List methods of assessing adherence

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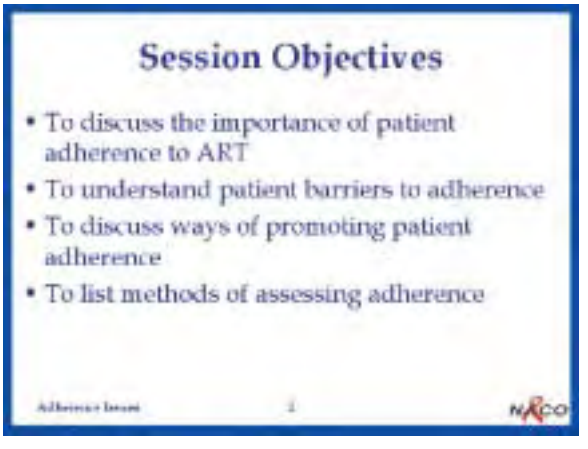
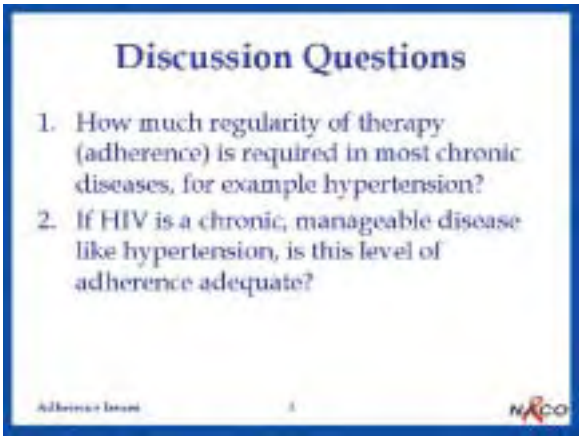
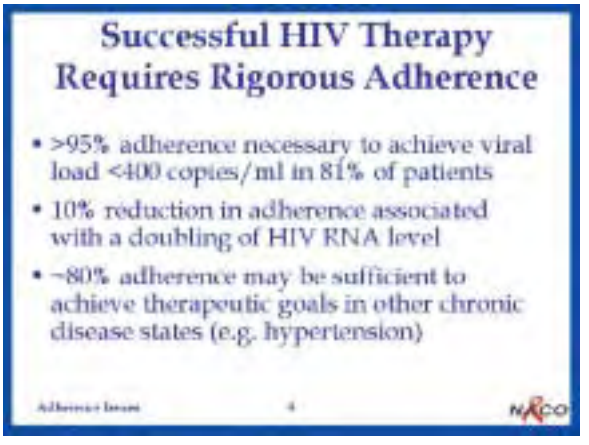
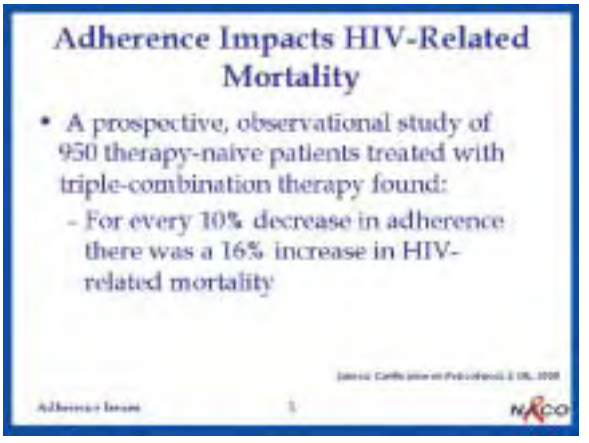
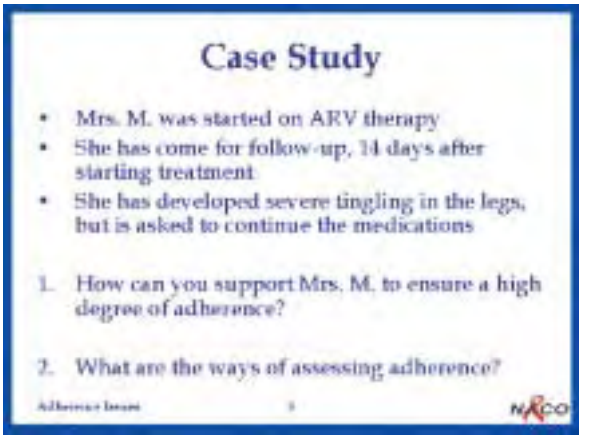
Slide 2		

Slide 3		

Slide 4		**Reader's Notes:**
		• It is important to remember that although there is enthusiasm in categorizing HIV as a chronic manageable disease, it is not as simple as managing other chronic illnesses like hypertension. Long-term success can only be achieved with complete virological suppression (as discussed in the session on ART), and this requires very high rates of medication compliance.
		• A small reduction in the regularity of taking medications can have disastrous long-term effects. Reflect for a minute on whether you have ever completed a full course of antibiotics as prescribed by a doctor.
		• **Sources:**
		  • 1st bullet: Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Paterson D et al. Ann Intern Med.2000; 133: 21-30.
		  • 2nd bullet: Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population Bangsberg DR et al. AIDS. 2000;14: 357-366.
		  • 3rd bullet: Compliance in hypertension: facts and concepts Luscher TF et al. J Hypertens. 1985; 3(suppl 1): S3-S9.

Slide 5		**Reader's Notes:** • The fall in virological suppression is not the only problem that is of concern. It has been shown that a decrease in medication compliance is associated with steeply rising mortality. • This will be observable even to physicians without access to testing techniques like CD4 and viral load estimation.
Slide 6		

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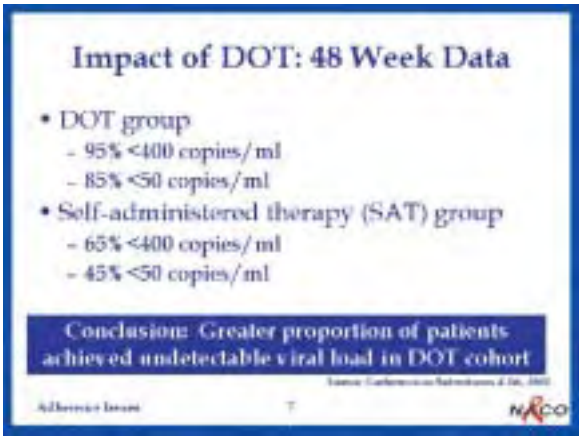
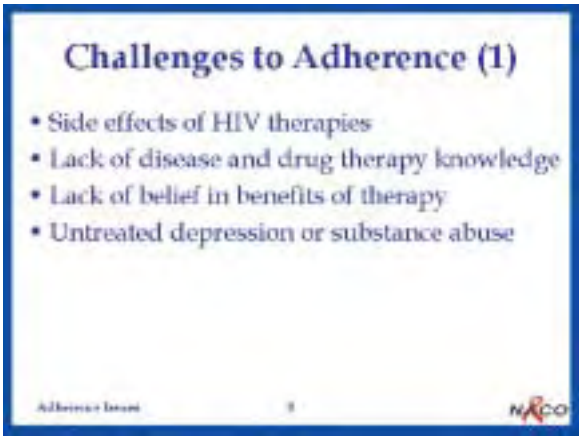


Reader's Notes:

- There were tremendous gains made by the DOTS initiative for TB. This idea has been successfully applied to the treatment of HIV.
- An interesting study was carried out in a prison in the US, in which HIV-infected inmates needing treatment were divided into two groups- one to take treatment by themselves after counseling (self administered group) and the second where a person was identified to supervise DOTS administration.
- At the end of nearly a year, the DOTS group had much better treatment outcomes as compared to the self administering group - both in terms of virus suppression and CD4 rise.
- The impact of the intervention can be gauged from the fact that the group on DOTS had more severe problems to start with - lower CD4 count, higher viral load, greater IV drug use- and in spite of this, this group had far fewer severe drug-related, adverse effects.
- This study gives us an important message- that patients having supervised therapy (DOTS) have better outcomes than self administered therapy, which works even in populations that have adverse risk factors.
- Source: Fischl M, et al. 7th Conference on Retroviruses & Opportunistic Infections (CROI), San Francisco, 2000. Abstract 71.

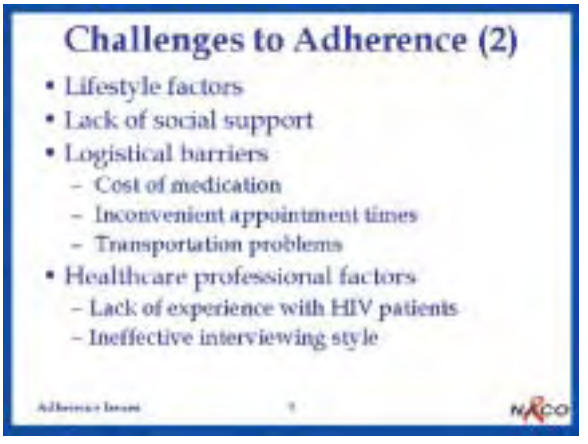
Slide 8



Reader's Notes:

- There are numerous reasons why patients do not take their medications regularly.
- Side effects of ART were reviewed in a previous module. Some of these are very acute, but most of them, like neuropathy of stavudine are long term and persistent. Some such as lipoatrophy have little remedy; and these can be a cause for concern. If side effects are not addressed, the patient may try to tailor therapy him or herself with disastrous long term consequences.
- The importance of educating the patient relevant to his or her level of understanding is very often overlooked. A patient who understands the disease, the therapy and the long term issues involved in taking ARVs usually has better compliance and better outcomes. In caring for HIV patients, often problems like drug/alcohol use and psychiatric issues are not addressed. These issues need to be dealt with before starting a patient on ART. Earlier ARV therapies were characterized by unrealistic dosing schedules, making them impossible to follow. The current regimen involves one pill twice daily. There are many studies that support this information (see below).

Slide 9



Reader's Notes:

- Studies demonstrate some reasons patients miss doses, these include forgetting, being too busy, being out of town, being asleep, being depressed, having adverse side effects, and being too ill.
- **Sources:**
  1. Deeks, SC, Loftus, R, Beatty, G, et al, "Incidence and predictors of virological failure of indinavir or ritonavir in an urban AIDS clinic." [abstract] International Conference on Anti-microbial Agents and Chemotherapy. Toronto. October, 1997.
  2. Website:http://ari.ucsf.edu/science/s2c/adherence.pdf : Adherence to HIV Therapies: Critical Issues.

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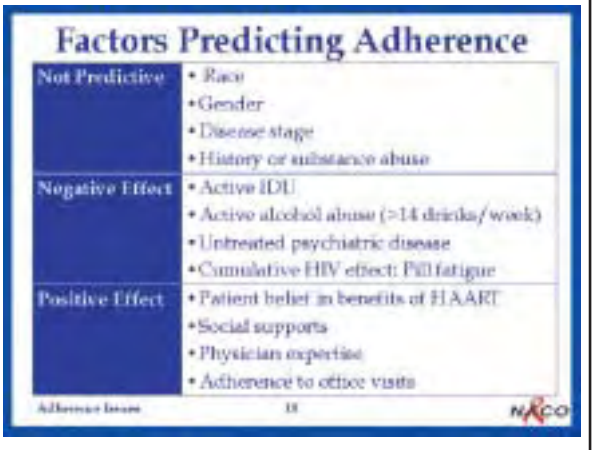

Reader's Notes:

- Race, gender, and severity of disease do not impact adherence.
- Alcohol, drug use and psychiatric illnesses have a negative impact on adherence.
- In contrast, if the patient believes in the effectiveness of the treatment, has good social support, and follows up regularly under an experienced physician, the chance of good adherence is enhanced.
- **Source:**http://www.retroconference.org/2001/abstracts. Is IIIicit Drug Use a Risk Factor for Non-Adherence to Antiretroviral Therapy? Gebo. 8th Conference on Retroviruses and Opportunistic Infections (CROI); 2001; Chicago. Abstract 477.
- Psychosocial Correlates of Incomplete Adherence to HIV Antiretroviral Therapy (HAART): Mental Health Matters, Ostrow. 8th Conference on Retroviruses and Opportunistic Infections (CROI); 2001; Chicago. Abstract 484.

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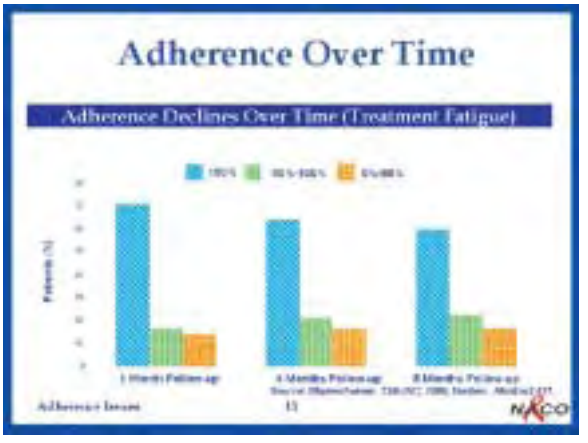


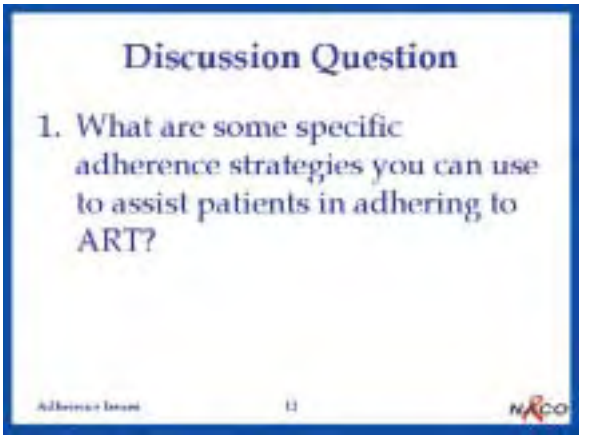
Reader's Notes:

- With time, even the most motivated patient tends to fatigue and the compliance to therapy steadily decreases. This can be prevented to some extent with continued counselling and use of supervision (DOTS). The value of reinforcement of adherence at every visit cannot be over emphasized.
- Regarding ART - taking behaviour, surveys have shown that one-third of patients missed doses within three days of the survey.

		• **Sources:** 1. Mannerheimer S, Friedland G, Matts J, Chen L, Child C, MacArthur R, et al . Self-reported antiretroviral adherence correlates with HIV viral load and declines over time. 13th International AIDS Conference. Durban: South Africa 2000 . Abstract No. Tu Or B 421.**Mannerheimer** et al. reported that in two ongoing randomized clinical trials in which 96 patients completed 8 months of follow-up, 70% of patients reported 100% adherence to their antiretroviral regimens at 1 month into **treatment**. By the 8-month time point, however, only 58% of patients were reporting 100% adherence. Graph source: Figure 2 from addressing the challenges of adherence. JAIDS Journal of Acquired Immune Deficiency Syndromes. 29 Supplement 1:S2-S10, February 1, 2002.Bartlett, John A. 2. Lckovics JR, Meisler AW. Adherence in AIDS clinical trials: A framework for clinical research and clinical care J Clin Epidemiol 1997. 50: 4 385-391. 3. Nischal KC, Khopkar U, Saple DG. Improving adherence to antiretroviral therapy. Indian J Dermatol Venereol Leprol 2005;71:316-20. 4. AIDS Patient Care and STDs Volume 19, Number 8, 2005 © Mary Ann Liebert, Inc.Barriers and Facilitators to Antiretroviral Medication Adherence Among Patients with HIV in Chennai, India: A Qualitative Study: N Kumarasamy et al.
Slide 12		**Reader's Notes:** • The practical strategies which have been shown to improve adherence are varied, with a few consistent themes. Adherence is achieved only when there is a negotiation of the treatment plan, where the patient feels that he/she is involved in the decision making process. • Currently, the national program supplies the triple combination as a single tablet to be taken twice daily. It may not be possible or necessary to simplify the regimen further. There is no interaction with food, and ideally adherence is relatively easy, if the patient is motivated. Assessing the **patient's substance use** Paging System (MediMom) to increase Adherence to ARV, Safren. 8th CROI; 2001; Chicago. Abstract 480. **and psychiatric issues** prior to therapy helps to improve adherence. **Patient education:** Discussing with patients the need for treatment, the expected side

		effects and management of common problems also helps improve adherence. **Simplification of the regimen**, i.e., with reduced pill numbers and frequencies, is associated with better adherence, as is the reduction and treatment of adverse events. • **Reminders:** Periodic reinforcement is important to ensure that the patient does not forget to take the medications. In resource limited settings involving other players like NGOs, Community Based Organizations, other organizations related to supporting PLHA and some form of supervision by family/ friend through DOTS could also help. • Recruitment of **family and friends** to support the therapeutic plan and its implementation is associated with improved outcomes. Family and friends can also be employed to supervise DOTS. • **Sources:** http://www.retroconference.org/ 2001/ abstracts. 1. Psychosocial Correlates of Incomplete Adherence to HIV Antiretroviral Therapy (HAART): Mental Health Matters, 2.Ostrow. 8th Conference on Retroviruses and Opportunistic Infections (CROI); 2001; Chicago. Abstract 484, 3. Effects of Group HIV Patient Education on Adherence to ARV: A Randomized Controlled Trail,Gifford. Abstract 479. 4. Intervention Trail Using a Novel Electronic Device in HAART Initiators: Impact of Cognitive Dysfunction, Andrade. Abstract 602. 8th Conference on Retroviruses & OIs (CROI); 2001; Chicago. 5. Initial Outcome of an On-Line

Slide 13



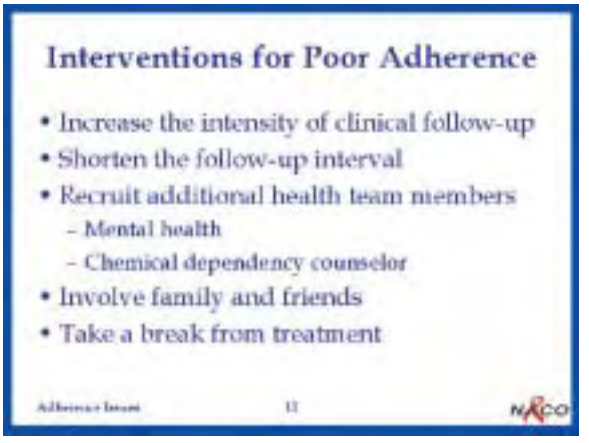
Slide 14

Reader's Notes:

- The instability of homelessness may lead to poor adherence, but not without exception; one recent program achieved a 70% adherence rate among the homeless utilizing flexible clinic hours, accessible clinical staff, and incentives.
- Obviously, not all patients or special populations are alike; physicians should employ an individualized case-by-case assessment of their patients and act accordingly to ensure and improve adherence.
- The response to the problem of adherence in special populations has not been well-studied. In the absence of data, a reasonable response is to address and monitor adherence in all HIV primary care encounters and incorporate adherence goals in all patient treatment plans and interventions.
- **Sources:**

1. Bangsberg D et al. Protease inhibitors in the HIV+ homeless and marginally housed: Good adherence but rarely prescribed. 12th World AIDS Conference. Geneva, June, 1998 [Abstract # 389/32406].
2. Adherence to Highly Active Antiretroviral Therapy in the Homeless Population in San Francisco: A Prospective Study Andrew R. Moss et al. Clinical Infectious Diseases, volume 39 (2004), pages 1190—1198.
3. Patrizia M et al. Compliance to multiple combination therapy with protease inhibitors among HIV-infected IDUs in France (cohort Manif 2000). 12th World AIDS Conference. Geneva, June, 1998 [Abstract #32359].
4. Adherence to Highly Active Antiretroviral Therapy (HAART) Among Individuals with HIV/AIDS: A Compendium of HAART Adherence Research, November 1997-November 1999 Website: http://www.hivforum.org/publications/adherence_haartresearch.pdf.

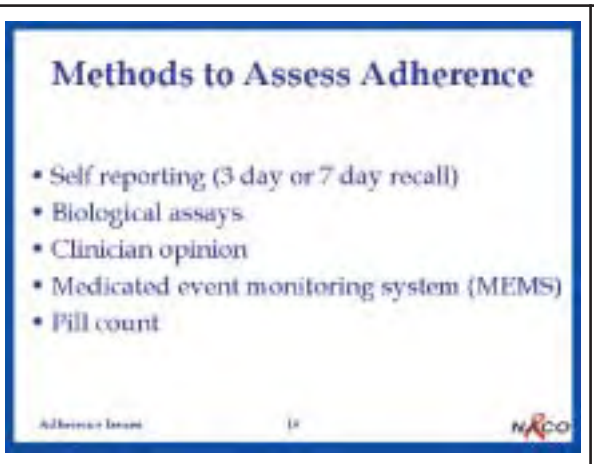
Slide 15



Reader's Notes:

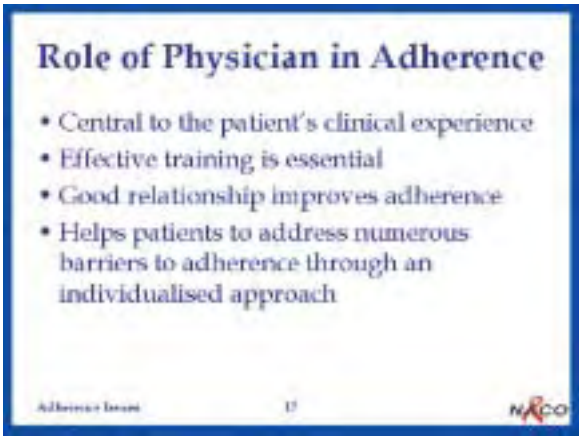
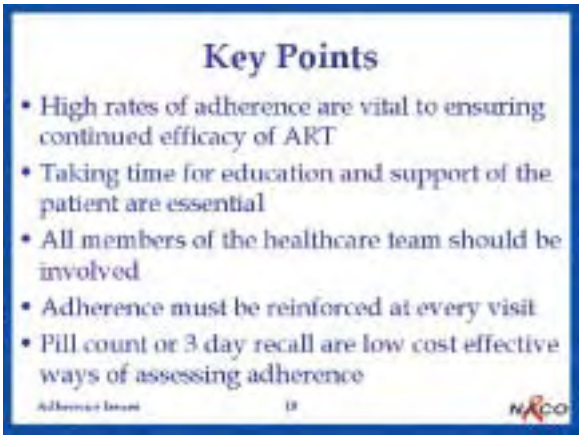
- With better monitoring, more patients with adherence issues can be identified early.
- Some patients may require ongoing assistance from support team members from the outset, such as chemically dependent patients, mentally impaired patients in the care of another, children and adolescents, or patients in crisis.
- New diagnoses or symptoms may influence adherence. For example, depression may require referral, management, and consideration of the short and long-term impact on adherence. Cessation of all medications at the same time may be more desirable than uncertain adherence during a two month exacerbation of chronic depression.

Slide 16



Reader's Notes:

- The issue of assessing adherence is very complicated. No method is fool proof, but some are more promising than others.
- **Self reporting** of adherence is flawed, especially when there is high expectation on the part of health care providers for patients to be adherent. However, data has shown that the use of a self reporting questionnaire for two week recall and one month recall are reasonably accurate. **Source:** Mannheimer S et al. The consistency of adherence to antiretroviral therapy predicts biologic outcomes for human immunodeficiency virus-infected persons in clinical trials. Clinical Infectious Diseases 34(8): 1115-21, 2002.
- When estimating adherence to any treatment, **biological assay** for drugs is considered the best method. However, this approach is very expensive and not possible at the periphery. **Source:** Eraker SA et al. Understanding and improving patient compliance. Annals of Internal Medicine (100): 258-268, 1984.
- **Clinician opinion** is also considered an alternative for the assessment of adherence. This is very error prone and studies have shown that clinicians consistently over estimate adherence. In fact, one study showed that patients with poor adherence were identified only about 24-66% of the time. Therefore this can only be used as an adjunct with some other form of assessment of adherence. **Source:** Bangsberg DR, Hecht FM, Clague H. Provider assessment of adherence to HIV antiretroviral therapy. J Acquir Immune Defic Syndr 2001;26(5):435-42.
- The medicated event monitoring system (**MEMS**) assesses the number of times the container cap is opened, presumably for taking out a tablet for consumption. This is very expensive and is still not completely accurate therefore can be used now only as a study tool. **Source:** Paterson DL, Swindells S, Mohr J. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Ann Intern Med. 2000;133:21-30.
- The **pill count** is the low cost alternative for assessment of adherence. It is more effective when unscheduled pill counts are performed and this correlates very well with success of therapy.
  Pill counting is recommended by the national program. At every visit for a prescription refill, the

		number of pills remaining in the medication box is counted (care should be taken to ensure that there is no judgemental or threatening atmosphere) and the number of pills consumed is estimated. This is compared against the number of pills expected to be consumed; this is expressed as a percentage equalling adherence. This can then be used to decide if the patient needs help with therapy. (The adherence estimate should be considered in context of other predictors like regularity for review visits.) **Source:** Liu H, Golin CE, Miller LG. A comparison study of multiple measures of adherence to HIV protease inhibitors. Ann Intern Med 2001;134(10):968-77.
Slide 17		
Slide 18		**Reader's Notes:** • It is important to discuss all issues with the patient before starting therapy- a check list has already been discussed at the end of the session on starting ART. • A team approach is required- a comprehensive effort by the physician, nurse, counsellor and pharmacist. Interventions focusing on the other personnel in the team have also shown major impacts on the adherence to ART in patients. Experience from many centers has shown that adherence wanes over time. Reinforce adherence at every visit.

SESSION 15

SESSION

POST-EXPOSURE PROPHYLAXIS

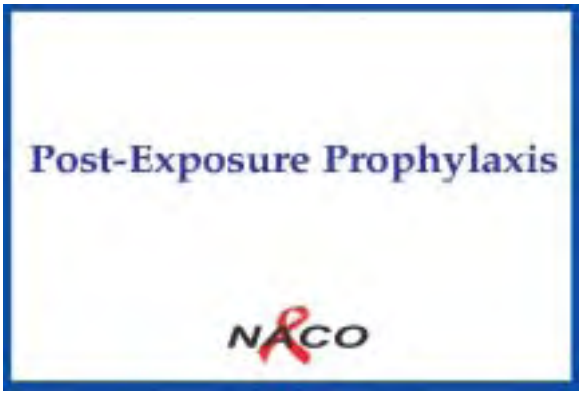
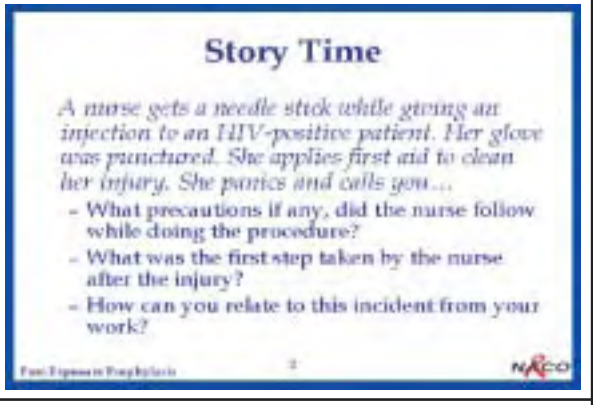
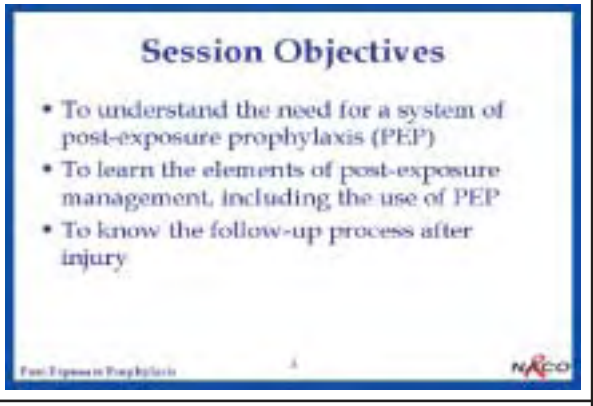
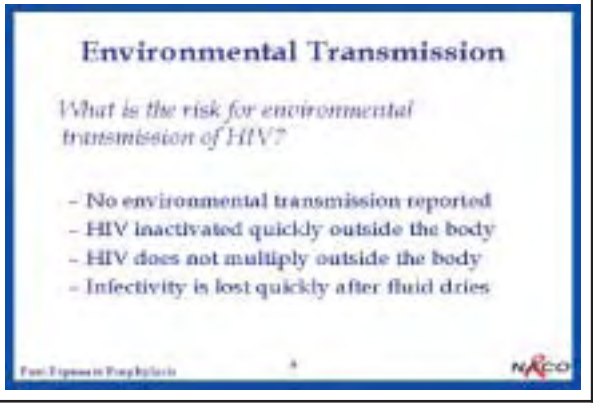
15

Total Session Time: 45 minutes

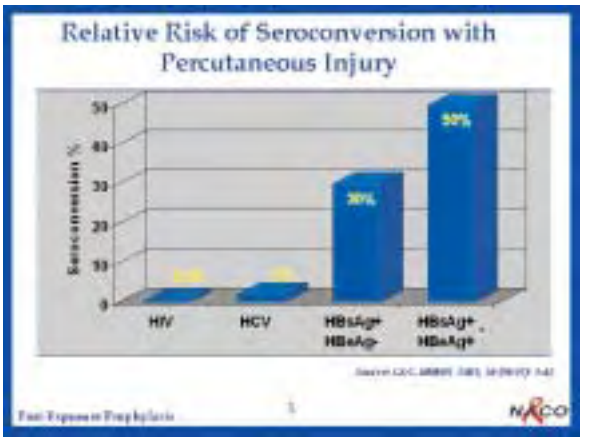
Session Objectives: At the end of the session, the participant should be able to:

- Understand the need for a system of post-exposure prophylaxis (PEP)
- Learn the elements of post-exposure management, including the use of PEP
- Know the follow-up process after injury

Step	Time	Activity/ Method	Content	Resources Needed
1	8 minutes	Trainer Presentation Group Discussion	Exercise 1: Story Time (Slides 1-2)	LCD or Overhead Projector
2	15 minutes	Trainer Presentation, Brainstorming	Presentation of Session Objectives, Introduction to Post-Exposure Prophylaxis, Environmental Transmission, Rationale for PEP (Slides 3-7)	LCD or Overhead Projector Flip chart Marker
3	4 minutes	Trainer Presentation, Group Discussion	Presentation of Elements of Post-Exposure Management Exercise 2: Assessing Exposure Code (Slides 8-9)	LCD or Overhead Projector
4	4 minutes	Group Discussion	Exercise 2 : Assessing Exposure Code (Slides 10)	Flip chart, Marker, Handout 1
5	12 minutes	Trainer Presentation Group Discussion	PEP and Health Care Workers and Exercise 3: Story Time Revisited (Slides 11-16)	LCD or Overhead Projector
6	2 minutes	Trainer Presentation	Summary (Slide 17)	LCD or Overhead Projector

Slide 1		
Slide 2		
Slide 3		**Reader's Notes:** • For further study refer to **Summary of Published Reports, Occupational transmission of HIV, March 2005, Health Protection Agency.**
Slide 4		**Reader's Notes:** • HIV is a very delicate virus. It cannot survive outside live human being for a long time unless under lab conditions. Hepatitis B is more dangerous than HIV as it can survive in dried blood for about 7 days. • Environmental transmission means the transmission of any infection/disease via physical contact with fomites, dust, air, water etc.

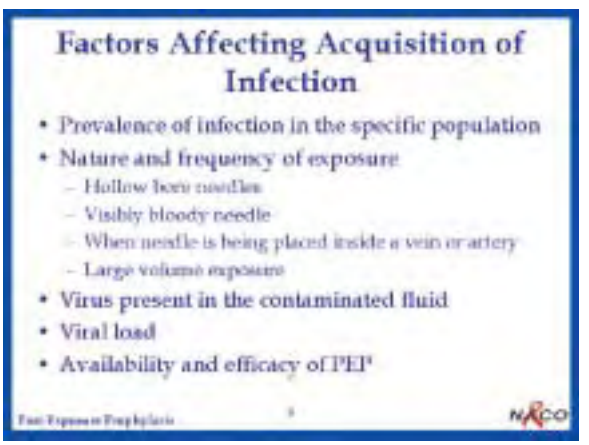
Slide 5



Reader's Notes:

- Although the number of HIV infections acquired occupationally remains low, it is the pathogen of greatest interest. The risk of transmission of HIV occupationally is negligible.
- In prospective studies of healthcare personnel, the average risk after a percutaneous exposure is about 3 per 1000; and less than 1 in a 1000 with mucus membrane exposure.
- Although transmission through non intact skin and by fluids has been reported, they are highly unusual.
- Even in the absence of any intervention, most exposures do not result in infection.
- In contrast, the risk of transmission of hepatitis B is far higher. The risk of transmission of hepatitis B is related to the status of the source patient. A source patient who is hepatitis B e antigen positive (active replicator), the risk of transmission is 40-60%; in the patient who is hepatitis B e antigen negative, the risk of transmission is 20-40%. Transmission of hepatitis C is intermediate, at about 2%.
- For further study refer to Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Post-Exposure Prophylaxis, CDC. MMWR 2001;50 (RR11):1-42.

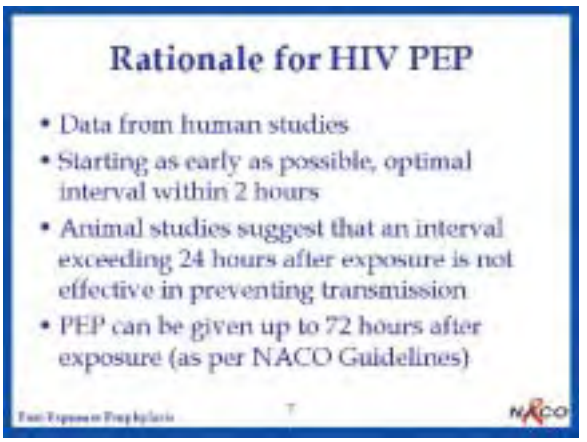
Slide 6



Reader's Notes:

- A retrospective review done in 1997 identified some important risk factors for transmission . The depth of the injury correlated strongly with the risk of transmission of the infection. If visible blood is noted on the instrument causing the injury, it increases the risk of transmission, and was made worse if the instrument was retrieved from a vein or artery of a patient. An increased risk is associated with exposure to blood from source persons with terminal illness, possibly reflecting either a higher titer of HIV in blood late in the course of AIDS or other factors. The only protective factor noted was the administration of PEP with zidovudine (as was the norm at that time), which decreased the risk five fold.
- **Source:** Cardo DM, Culver DH, Ciesielski CA, Srivastava PU,Marcus R, Abiteboul D. Casecontrol study of HIV seroconversion in health care workers after percutaneous exposure. N Engl J Med 1997;337:148590.

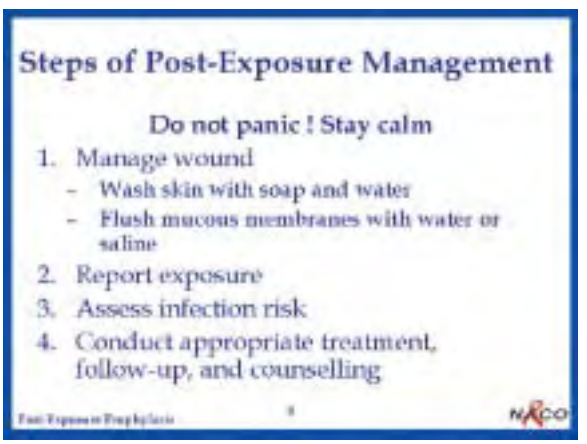
Slide 7



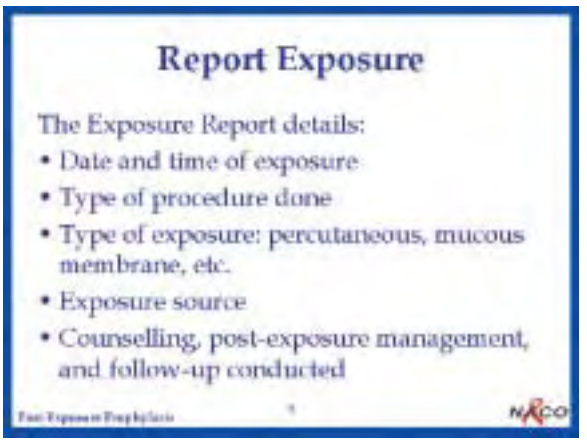
Reader's Notes:

- Data on human studies:
- ZDV PEP was associated with reduction in risk of HIV infection in HCW by 81%.
- **Source:** Cardo DM, Culver DH, Ciesielski CA, Srivastava PU,Marcus R, Abiteboul D. Casecontrol study of HIV seroconversion in health care workers after percutaneous exposure. N Engl J Med 1997;337:148590.
- ZDV administered to HIV-infected pregnant women during labor, delivery, and to their infants reduced HIV transmission by 67% (NEJM 1994;331:1173-80).
- One source of data on PEP efficacy in humans comes from the CDC case-control study, described earlier . Healthcare personnel from the U.S., France, the UK, and Italy who sustained percutaneous exposures to HIV were compared to healthcare personnel with similar exposures but who did not seroconvert. Use of zidovudine, or ZDV, was associated with an 81% decrease in the risk for HIV transmission. However, this study was limited by the small number of cases, and the fact that cases and controls came from different cohorts.
- For further study refer to Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Post-Exposure Prophylaxis. CDC. MMWR 2001;50 (RR11):1-42.

Slide 8



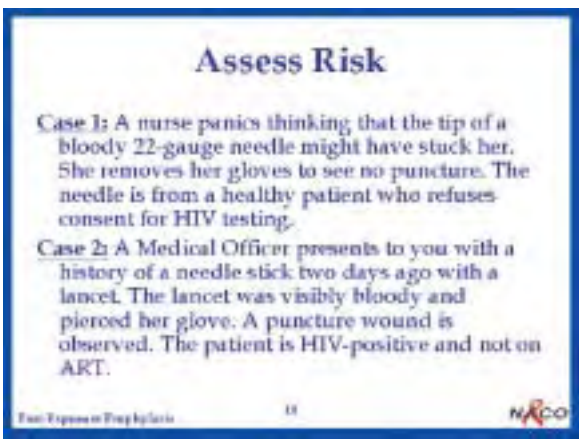
Slide 9



Reader's Notes:

- It is important to collect and record information about the exposure on an exposure report, and to maintain the confidentiality of both the worker and the source patient.
- An exposure report should include the date and time that the exposure occurred, as well as details of what procedure was being performed, where, how, and what device (if any) was involved.
- Details such as the route of exposure, body substance involved, and volume or duration of contact also should be included.
- Additionally, information about the source person and exposed person, if known, is critical, along with exposure management details, which will be discussed later.
- On the NACO site: www.nacoonline.org, reader can find a template for the exposure report in a publication titled: Specialists' Training Manual.

Slide 10



Handout 1: Post-Exposure Prophylaxis Code Determination

Figure One – Determination of the Exposure Code (EC)

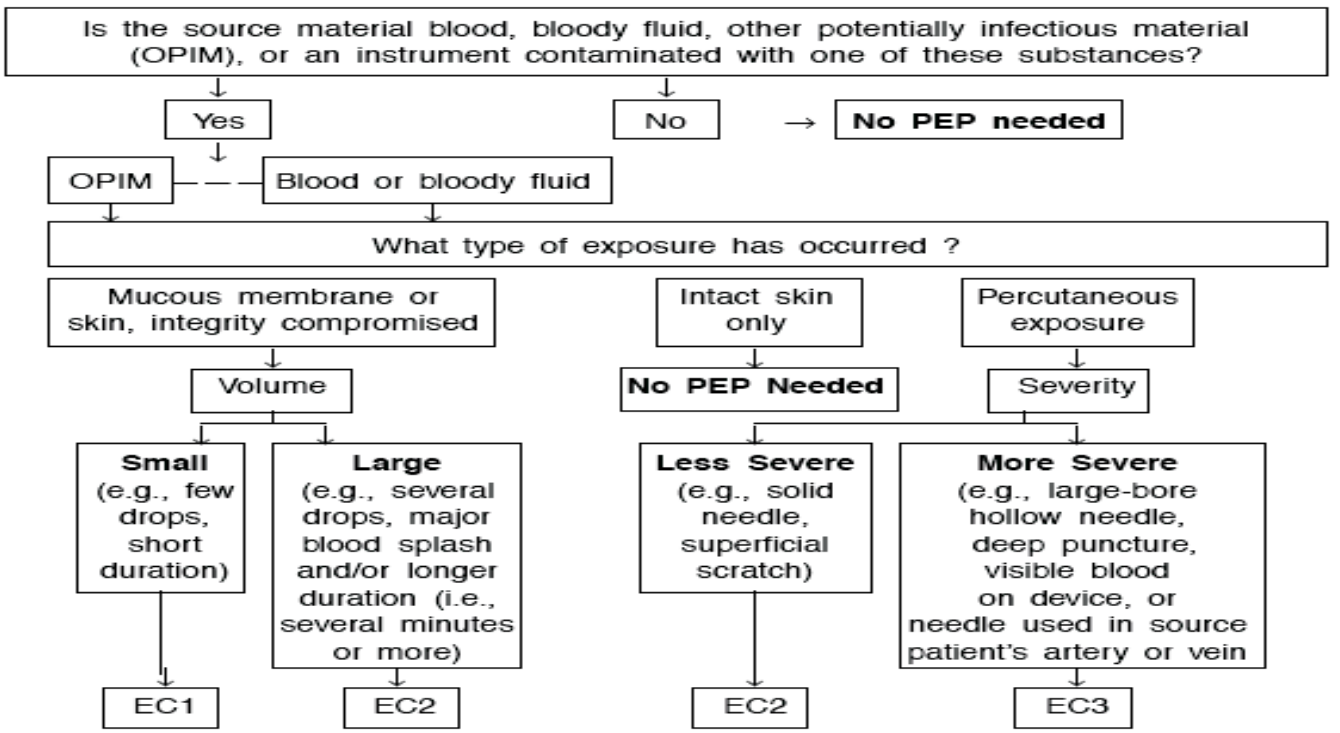


Figure Two – Determination of the HIV Status Code (HIV SC)

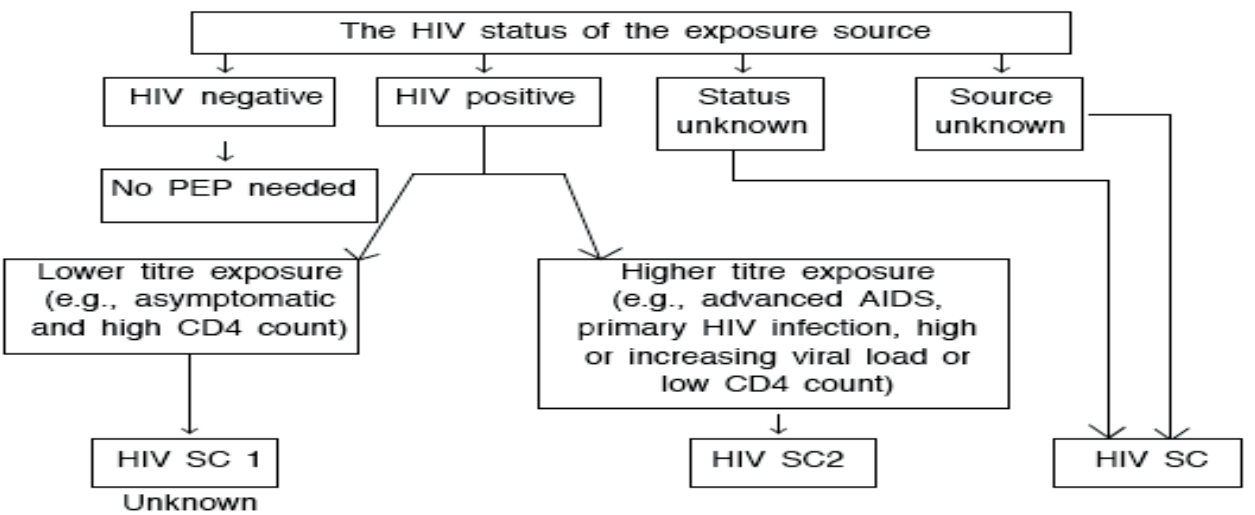
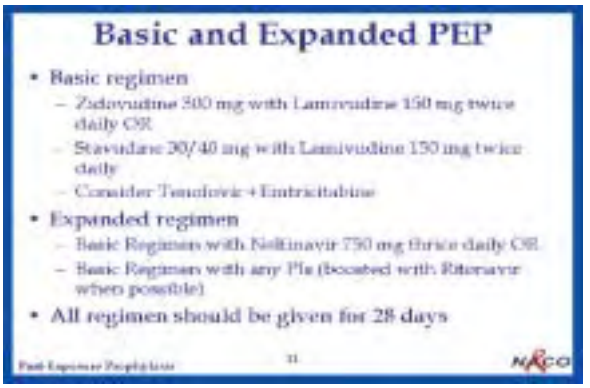
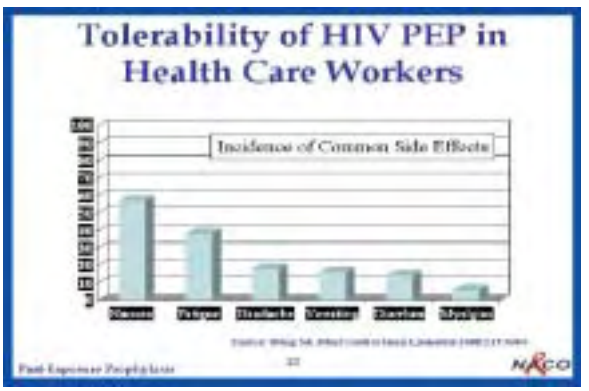
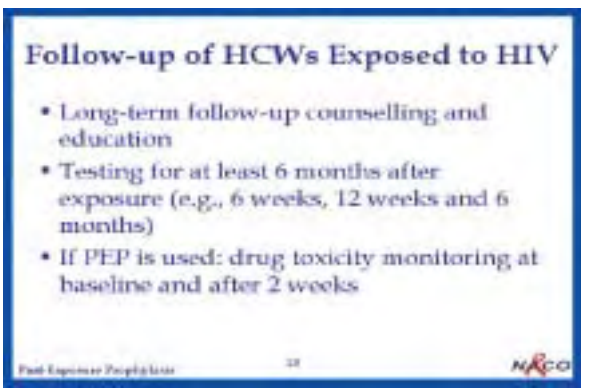
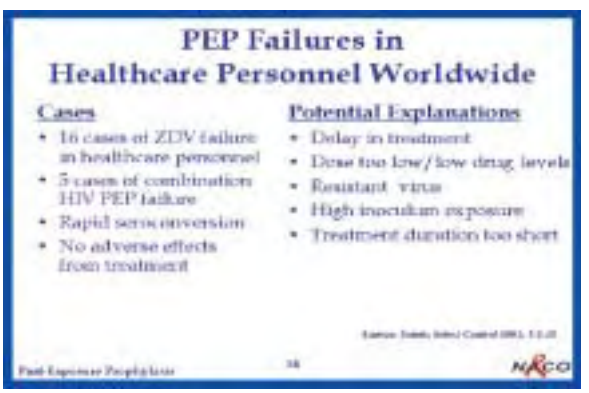
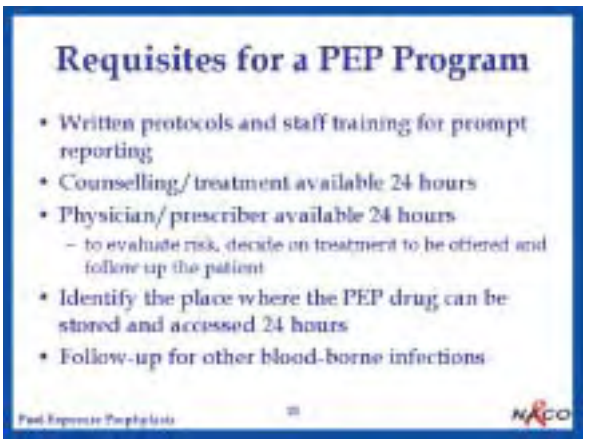
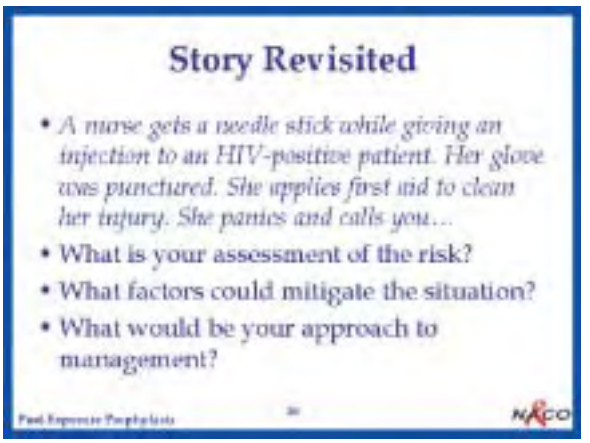
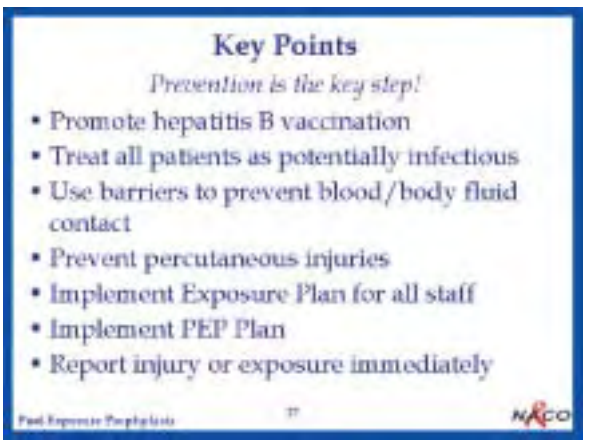


Figure Three. Determine the PEP recommendation

EC	HIV SC	PEP recommendation
1	1	PEP may not be warranted. Exposure type does not pose a known risk for HIV transmission. Whether the risk for drug toxicity outweighs the benefit of PEP should be decided by the exposed HCW and treating clinician.
1	2	Consider basic regimen. Exposure type poses a negligible risk for HIV transmission. A high HIV titre in the source may justify consideration of PEP should be decided by the exposed HCW and treating clinician.
2	1	Recommend basic regimen. Most HIV exposures are in this category; no increased risk for HIV transmission has been observed but use of PEP is appropriate.
2	2	Recommend expanded regimen. Exposure type represents an increased HIV transmission risk.
2/3	UNKNOWN	If the source, (in the case of an unknown source), the setting where the exposure occurred suggests a possible risk for HIV exposure and the EC is 2 or 3, consider PEP basic regimen.

Slide 11		
Slide 12		**Reader's Notes:** • The antiretroviral drugs will cause the following common side effects: • Nausea — 55% • Malaise/fatigue- 48% • Headache- 18% • Vomiting- 15% • Diarrhoea/ Myalgia /arthralgia /Abdominal pain/Rash —few% • Source: Wang et al. (2000) Experience of Healthcare Workers Taking Post-Exposure Prophylaxis After Occupational HIV Exposures. Infect Control Hosp Epidemiol 21:780-785.
Slide 13		**Reader's Notes:** • Counsellor/Doctor should cover the following points with the injured staff to allay fear or doubts: • PEP can fail. • Adherence problems. • Immediate concerns such as: • Fear for one's own personal health and mortality. • Concern about the reaction of family members and sexual partners. • Anxiety about job, especially if the HCW performs invasive procedures. • Concerns of breach of confidentiality.
Slide 14		**Reader's Notes:** • Refer to these studies for further information: • Source: Summary of Published Reports, Occupational transmission of HIV, March 2005, Health Protection Agency.

Slide 15		**Reader's Notes:** • Other elements requisite for a PEP program are: • Universal Precautions in place with adequate supplies. • Vaccination of health care staff at risk for hepatitis B. • Development of National Guidelines for PEP. • Keeping a list of centers that have PEP stocked in the vicinity. Hospital and national PEP registry to audit our practice and assess risk behavior.
Slide 16		**Reader's Notes:** • Using the **Handout 1: Post-Exposure Prophylaxis Code Determination**, source code and PEP recommendation chart, give your opinion on the risk assessment of the injured staff. • Specify what PEP regimen will you recommend and for how long.
Slide 17		

SESSION 16

SESSION

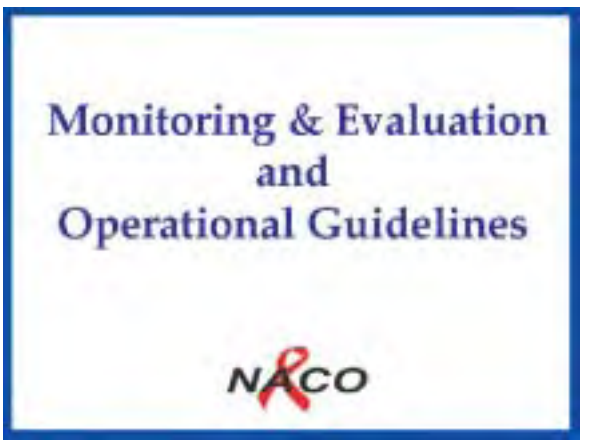
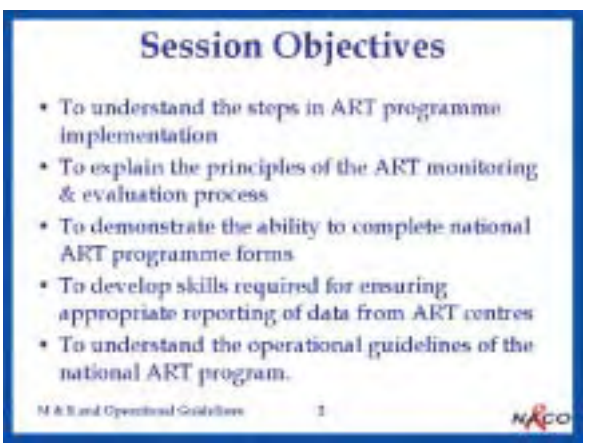
MONITORING & EVALUATION AND OPERATIONAL GUIDELINES

16

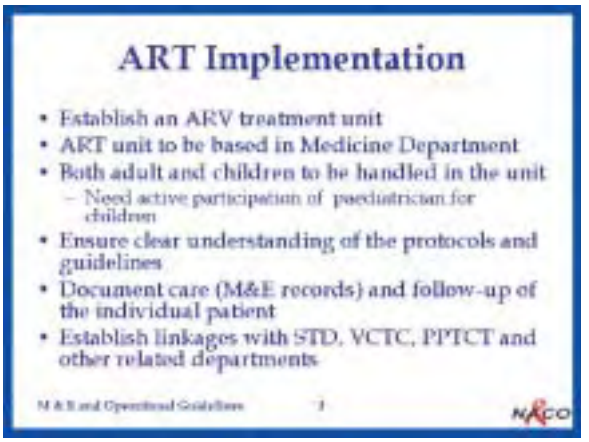
Total Session Time: 45 minutes

Session Objectives: At the end of the session, the participant should be able to:

- To understand the steps in ART programme implementation
- To explain the principles of the ART monitoring & evaluation process
- To demonstrate the ability to complete national ART programme forms
- To develop skills required for ensuring appropriate reporting of data from ART centres
- To understand the operational guidelines of the national ART program.

Slide 1		
Slide 2		

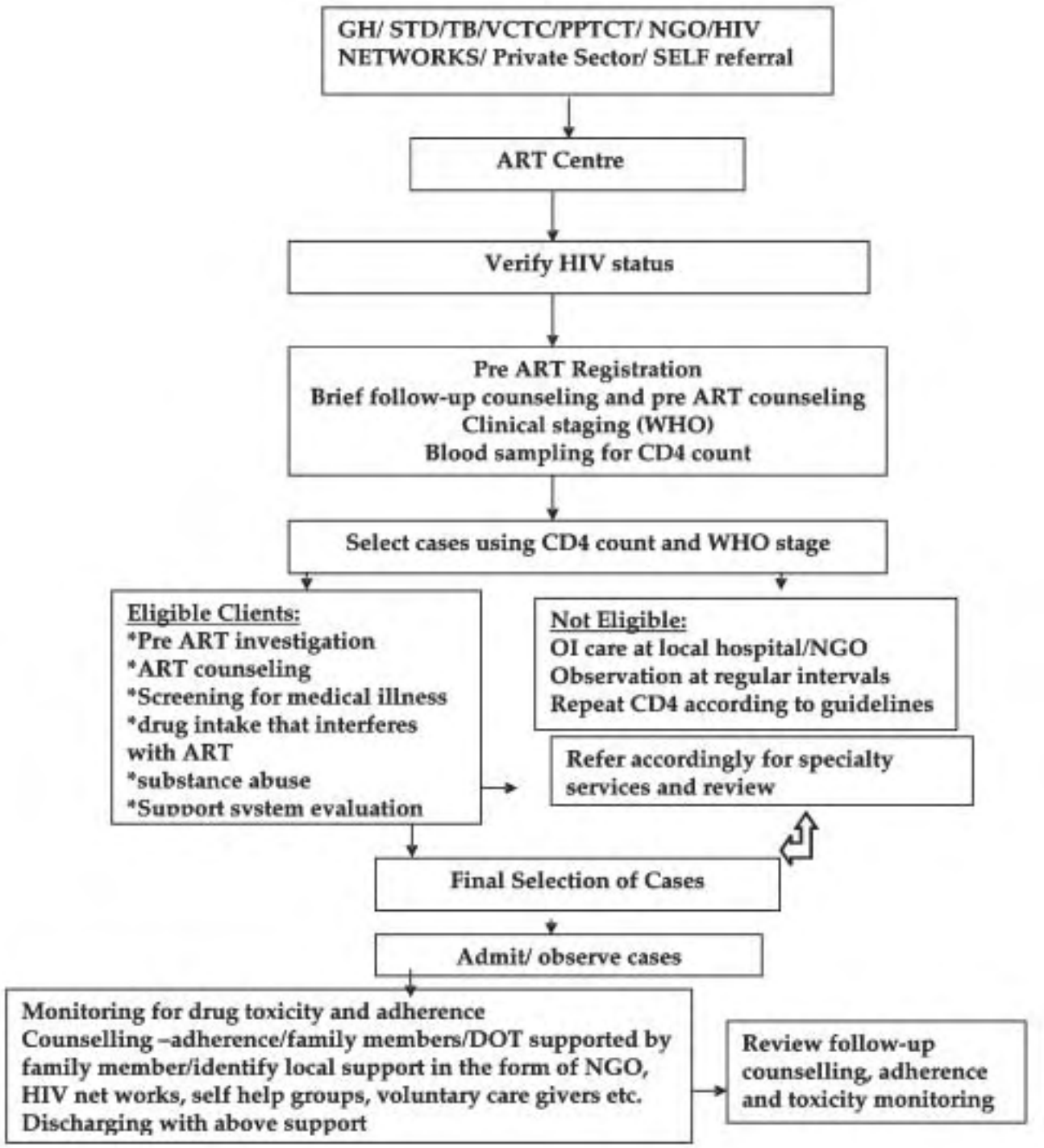
Slide 3



Reader's Notes:

- The ART team will be based in medicine, but will cater to children and pregnant mothers also.
- The infrastructure for the ART centre should be provided by the hospital and can be improved through SACS support. The existing guidelines and protocols should be clearly understood to ensure optimal functioning.
- Ensure that the documentation process is clearly understood and designate forms that are easy to use.
- There should be linkages with key departments like microbiology (for CD4 testing), the VCTC (for patient flow), PPTCT (for pregnant clients), DOTS (for patients with TB) and etc.
- Paediatric IP/OI care will be done through pediatric ward/OP.
- According to local situation, an ART centre may function within Medicine OP premises or outside the med OP. (if so, linkage should be strong with Medicine OP to prevent loss of clients referred from Medicine OP to ART Center.)

Handout 1 : Steps in ART Programme Implementation



The flow chart given above gives the steps in the ART implementation programme

- The first box lists the entry points for PLWA into ART centres
- Each client's HIV status will be verified upon entering the ART centre. Depending on their baseline knowledge, give post test/ART counselling before drawing blood for CD4 count.

Ensure that clients attending the ART centre:

- Understand their status
- Have adequate knowledge/understanding of their illness
- Have been provided with post test counselling
- Have been provided with risk reduction counselling to avoid engaging in high risk behaviour
- Are not already on ART at a private sector clinic

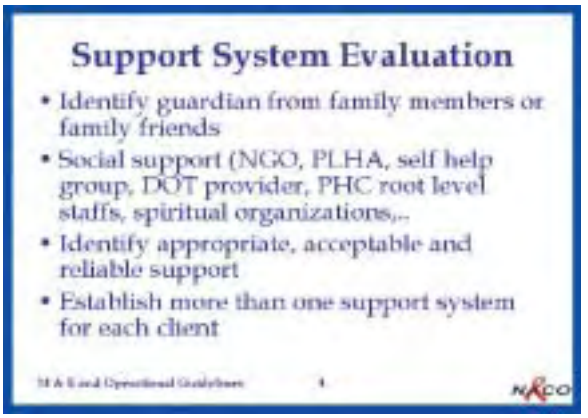
Based on staging and CD4 results, clients will be selected for ART. Those not eligible will be given counselling on OI care and follow up.

- A client is referred to local government hospital for OI care and encouraged to avail services of local NGO/PLHA network in patient's locality. With OI care at local GH/NGO setting, a client is advised to review to ART at stipulated intervals. For example, a patient that is STAGE III with CD4 360 needs to be followed more frequently than a client with STAGE II with CD4 600.
- Those clients eligible will undergo pre ART investigation and counselling and screening for concurrent medical illness (TB, Hepatitis B), drug intake (ART, seizure drug etc), substance abuse (alcoholism) as all these factors determine regiment and outcome of ART. They need to be referred to speciality services and ART initiated under specialist supervision.

NACO has revised the ART guidelines and provides guidelines on how often to repeat CD4 for non-ART cases.

- Observe clients for the first 14 days of ART (to monitor for Nevirapine sensitivity).
- In congested medical wards, it may be difficult to admit all clients on ART initiation. Hence NGOs with IP facility, drop in centers, and service oriented hospitals located around ART centres (within city limits) may be utilized during observation phase of ART especially for IP care of OIs like diarrhoea.
    - Medical officers/staff of above centres/organizations should be trained in this type of care and active coordination and linkages should be established.
    - Some technical and ethical issues related to admission are: overcrowded medical wards, stigma and discrimination, and breaches in confidentiality at ward.
- Utilise the time available during the observation phase for (along with toxicity monitoring) adherence counselling, developing adherence strategies, and strengthening/establishing/linking to support systems.

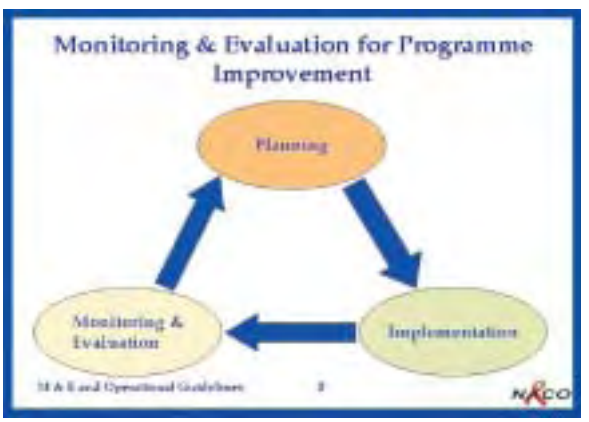
Slide 4



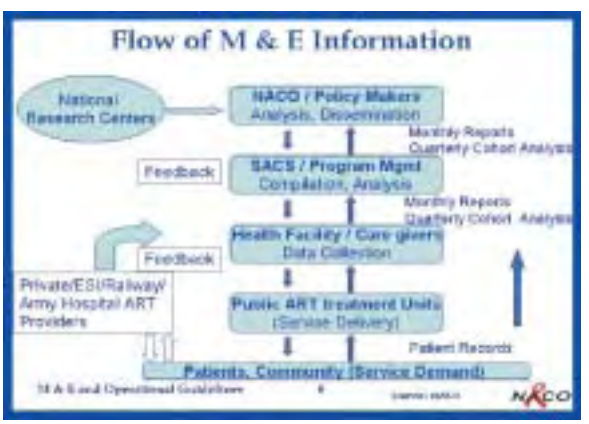
Reader's Notes:

- Support system evaluation:
- Once client becomes medically eligible for ART, he needs to be assessed of his support system. List of support system may be endless, and through discussion with patient, we need to link to appropriate reliable system.
- **Family support:** Relatives/Family friends/Work place friends, colleagues (who shows interest on sufferer's well being).
- **Government network:** Village health nurse, PHC staffs, …
- **Social support system:** NGOs, PLWHA networks, self help groups, service based organizations (rotary club etc), family physician.
- For patient with poor family support, social support should be established.
- Guardian should be identified preferably from close relatives (parents, spouse, son, daughter..) ,who takes interest on taking care of the sufferer. Its good to have a guardian to be educated/ with understanding capacity.
- Client need periodic review of the support system as he might have missed the support of already identified guardian. Death of a identified guardian, migration of the guardian, migration of patient and hence loosing care of identified NGO support.

Slide 5



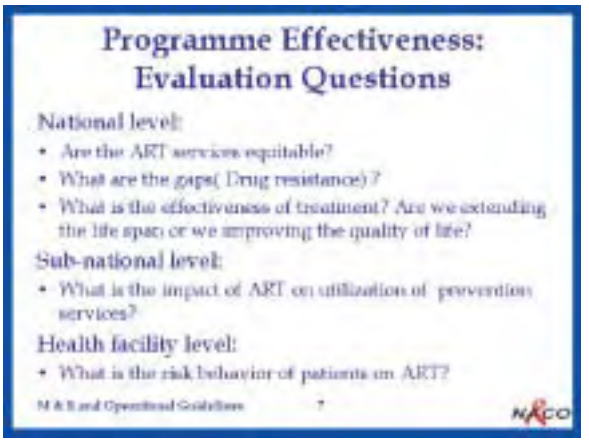
Slide 6



Reader's Notes:

- In the current monitoring and evaluation plan, there is two way flow of information between the individual centres, SACS and NACO in the form of various reports and feedback.

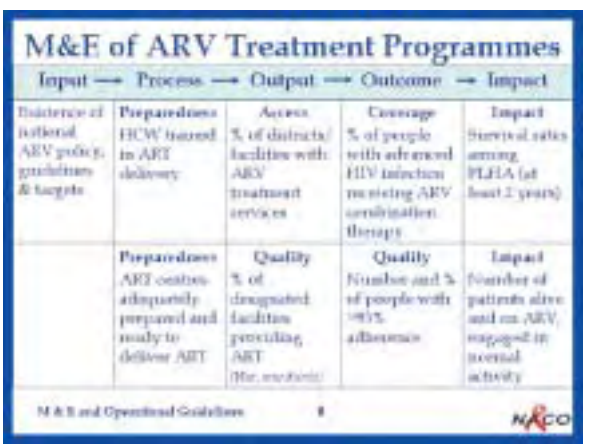
Slide 7



Reader's Notes:

- This slide lists important evaluation questions that can be used to assess programme effectiveness at the national, sub-national and health facility level.
- N**ational level (at NACO):**
  - Equitable service means equal coverage by gender, geographical location (urban/rural), below poverty line, and risk group.
  - The gaps- ART Drug resistance
  - Effectiveness of treatment refers to type of regimen, age, sex, weight, clinical staging, CD4 cell count.
  - Cohort Analysis of data source is done to know the answers for the questions: Did we enable the patients on ART to return to their normal activities?, and Did we extend the life span of patients on ART?.
- **Sub-national level (at SACS):**
  - The impact of ART on utilization of prevention services is measured by the % increase in number of VCT clients after introduction of ART.
- **Health facility level (at ART centre):**
  - The risk behaviour of patients on ART can be measured by the incidence of sexually transmitted infections among patients on ART.

Slide 8



Reader's Notes:

- The M & E process is a dynamic and continuous process, with indicators at all phases. The ultimate impact goal of the process is the number of patients surviving with HAART, and the percentage of them gainfully employed.
- Refer the participants to **Handout 2: Indicators of Programme Monitoring at Health Facility (F), State (S) and National (N) levels** to review M & E indicators.
- Refer the participants to the **Annexure: Handbook of Indicators for Monitoring National AIDS Control Programme — II,** NACO (Ministry of Health & Family Welfare, Government of India Chandralok Building, 36, Janpath, New Delhi - 110 001) for further information.

Handout 2 : Indicators of Programme Monitoring at Health Facility (F), State (S) and National (N) levels

The following list contains the indicators used in programme monitoring:

(*Some of the indicators are explained in detail)*

1. **Cumulative number enrolled in HIV care (F)**

2. **No. of PLWHA screened for ART eligibility each month (F)**

3. **No. started on ART during a period (F,S,N)**

4. **Cumulative no. ever started on ART (F,S,N)**

5. **Cumulative no. eligible for ART but not started on ART(F,S,N)**

6. **Total no. currently on ART (F,S,N)**

7. **Total no. currently on substituted first line treatment (F,S)**
   Due to Nevirapine toxicity, starting ART, ART toxicity (zidovudine to Stavudine in case of AZT induced anaemia).

8. **Total no. currently on switched second line treatment (F, S)**

9. **Proportion of people with >95% adherence (F, S, N)**
   - N(numerator): No. of patients who missed less than 3 number of drug doses during the month
   - D (denominator): No of patients who made a scheduled visit to the health facility to collect their drugs.

10. **Proportion of patients who consistently picked their drugs each month (F)**
    - N: No. of patients who did not collect scheduled monthly drugs
    - D: Total no. of patients scheduled to collect drugs in the month

11. **Proportion of patients with CD4 counts >200 (F)**
    - N: No. of patients showing an increase in CD4 count after starting treatment
    - D: Total no. of patients alive in the cohort

12. **Proportion of patients showing 10% weight gain (F)**
    - N: No. of patients showing gain in weight of >10% after starting treatment
    - D: Total no. of patients alive in the cohort

13. Proportion of patients alive and on treatment(6,12, 24 months) (F,S,N)

- N: No. of patients alive after initiating therapy after 6, 12, 24 months
- D: Total no. of patients in the cohort (initiating therapy during the same month and year)

14. Proportion of patients whose functional status is working/normal activity (6, 12, 24 months) (F,S,N)

- N: No. of patient alive after initiating treatment after 6, 12,24 months
- D: Total no. of patients in the cohort (initiating treatment during the same month and year)

15. Sufficient drug stock for existing patients for 6 months (F,S)

Assessed by comparing total 6 months drug requirement for the no. of patients on ART currently with the total number of drugs in stock

16. No of NGOs on ART delivery (F)

No. of NGOs delivering service (referrals, treatment education, home based care... as mentioned in ART TEAM session)

Indicators of Programme Monitoring at State(S) and National (N) levels

1. Existence of national policy, guidelines targeting ART patients
2. No. of health care workers trained in ART delivery
3. Proportion of designated facilities providing ART treatment according to national guidelines
4. Proportion of ART centres reporting a drug stock out in the past month
5. Proportion of patients with advanced HIV infection receiving ART

Slide 9

Slide 10

Reader's Notes:

- The purpose of the pre-ART screening register is:
- To provide standardized and systematic information regarding the profile of ART patients.
- To document the process from care to ART (checklist).
- To feed a monthly report.
- Patient monitoring and follow up before ART.
- To plan and assess demand for ART (program management).
- This is to be completed at first visit; at start of TB, PCP prophylaxis, at ART eligibility; at start of ART; at end of follow up (e.g., death of patient).
- This will be completed by a doctor, counsellor, data clerk, nurse depending on the data (e.g. WHO stage to be filled in by doctor).

Slide 11

Reader's Notes:

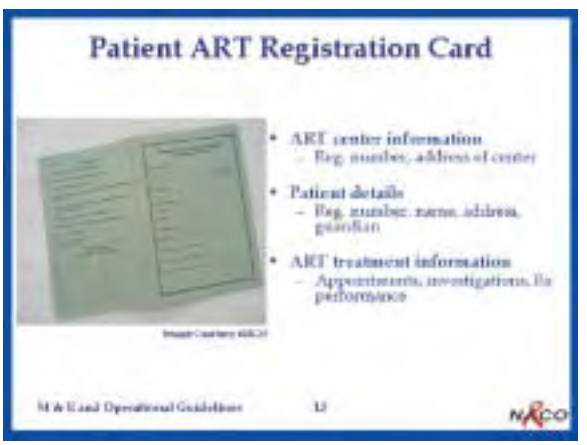
- The image shows a patient care and treatment record. It is a triple folded card for patient information.
- The patient care and treatment record provides information on key variables of patient and is used in both patient monitoring and program monitoring for effectiveness and impact indicators.
- Information feeds into the monthly ART centre report.
- This should be completed at each visit by health care providers (counsellors, nurses and doctors).
- This is the "master card' of the ART programme which contains all data about the individual patient through out the course of treatment.

Slide 12

Reader's Notes:

- CD4 percentage is taken into account and recorded in case of pediatric population.
- **Monthly visits:**
- **1st row**, write patient outcome:
  - On Treatment (OT) - if patient picked up ART drugs.
  - Stopped (ST) - if ART was stopped by the doctor.
  - Missing (MIS) - if the patient missed the scheduled visit.
  - Lost to follow-up (LFU) - if the patient is missing for =3 successive months.
  - Restart (RS) - if ART was restarted after an interruption.
  - Transferred out (TR) - transferred to another ART centre.
  - Dead (D) - client expired.
  - (NA) - if the patient was not scheduled to visit this month and came to ART centre for OI care, clarification of ART issues etc.
- **2nd row,** write adherence for the patients on treatment (A=>95%, B=80-95%, C=<80%):
  - > 95% (0-3 dosages missed).
  - 80-95% (4-12 dosages missed).
  - <80% (12 or more dosages missed).

Slide 13



Reader's Notes:

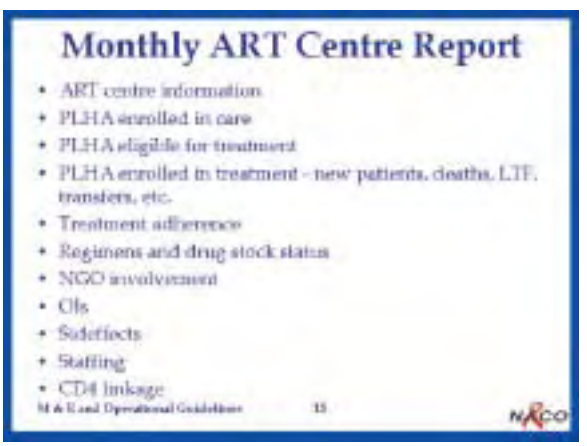
- Previously the ART registration card was used, now it has been replaced by a green booklet because:
- It is easy to carry.
- It can be kept in pocket and minimizes stigma in hospital.
- It still serves its purpose (consists of all required information. E.g., ART number to search patient master card from locked cabin at ART centre on patient's visit; regimen — so that patient can avail appropriate OI treatment, avoiding drug interaction, at local health care facility; appointment date-check for adherence).
- Photograph of patient is not needed (a column for photo of patient was there in previous card) which increases confidentiality.

Slide 14

Reader's Notes:

- **Drug Dispensing Register:**
  - Is maintained by pharmacist.
  - Monitors daily drug consumption.
  - Contains name of patient, drugs and no. of tablets dispensed.
  - The purpose is to monitor patient adherence through pill-count.
  - Should be completed at time of dispensing drug by the pharmacist/officer in charge of dispensing drugs.
  - Has the daily list of drugs dispensed to each patient which allows pharmacists to monitor drug consumption. As the drugs are expensive, this ensures accountability, and data is transferred to the drug stock register.
  - Requires signature of the patient after receiving pill. This also may add to the accountability.
- **Drug Stock Register:**
  - Monitors drug stock.
  - Alerts regarding stock-outs.
  - Feeds into monthly report that monitors drug consumption and demand assessment.
  - Is maintained by pharmacist in ART unit.
  - Should be completed on a daily basis by pharmacist/officer in charge of dispensing drug.
  - Instruction for filling out drug stock register:
  - Stock at beginning of the month=A.
  - Stock received during the month=B.
  - Stock dispensed during the month=C.
  - Stock expired/discarded during the month=D.
  - Stock at the end of the month= (A+B) — (C+D).
  - Maintain separate page for each day and each drug.
  - The pills collected from patients in case of death, poor adherence etc need to be discarded under supervision.

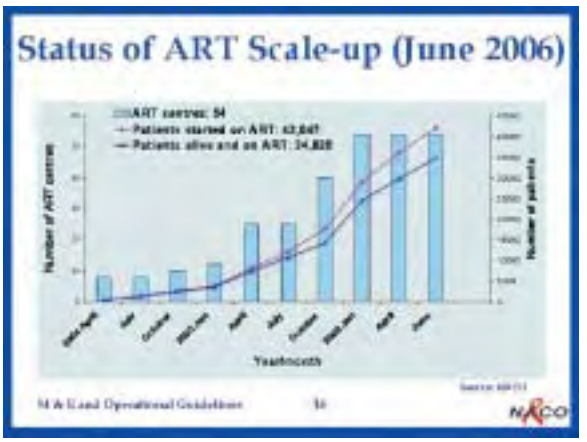
Slide 15



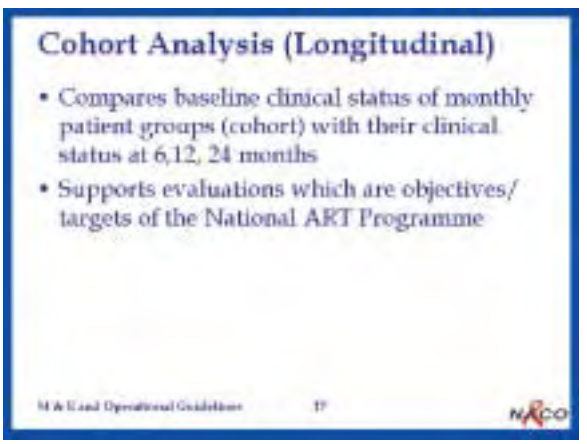
Reader's Notes:

- The monthly ART centre report compiles indicators for program monitoring.
- This is completed each month by the ART in-charge.
- Care should be taken to ensure that appropriate pre defined terminology is used in preparing the report.
- Clear definitions should be used, for example:
  - Loss to follow-up is defined as patients that do not return for 3 or more continuous months (90 days) / miss 4th drug packet in a row.
  - Transfers in and out.
  - Re-enrollment after loss to follow-up.

Slide 16



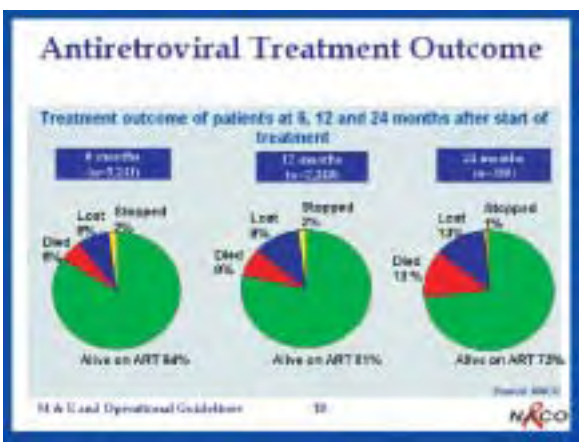
Slide 17

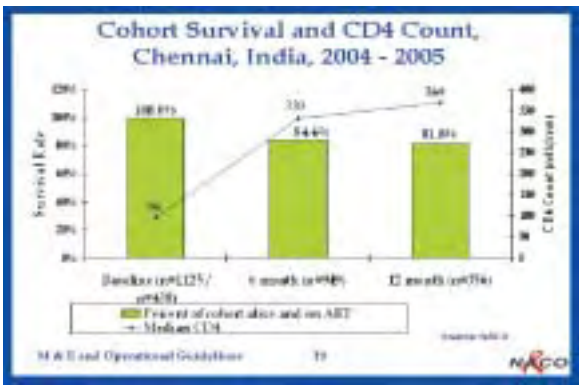
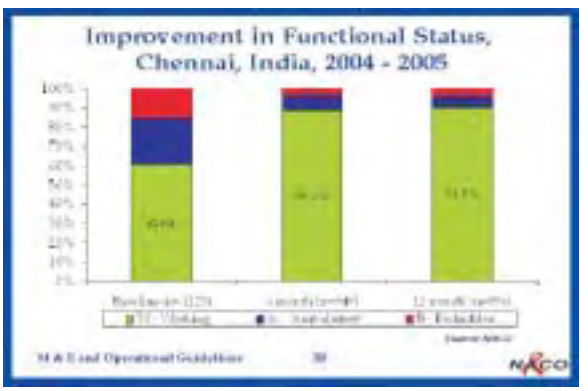
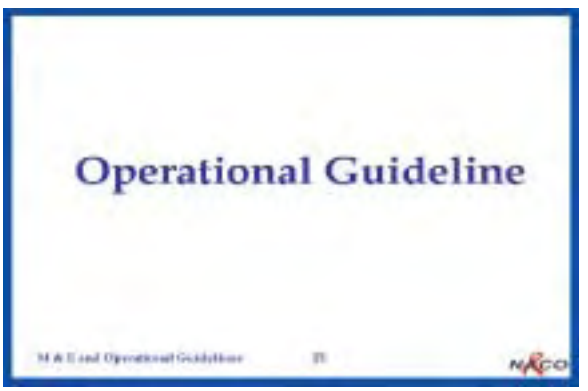
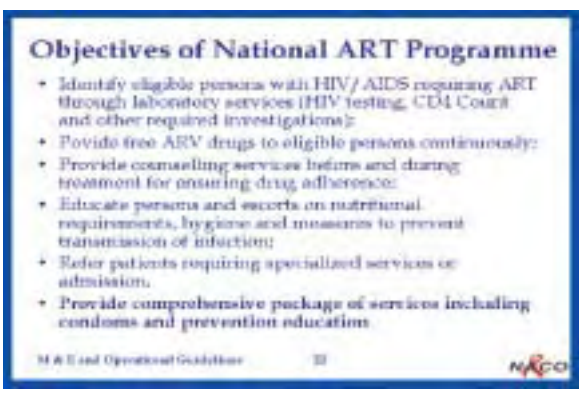


Reader's Notes:

- Cohort analysis is a longitudinal analysis which follows a group of patients who started treatment in the same month and year over time. It allows comparison of treatment status/ outcome over time and between groups of patients who have had equal duration of ART either form the same or between different ART centres.
- Cohort follow-up is important to assess the effectiveness of the program. The program targets to be measured are:
  - Proportion of cohort alive and on 1st line regimen at 6, 12, 24 months (alternative 1st line / 2nd line).
  - Proportion of cohort able to work at 6, 12, 24 months (ambulatory, bed ridden).
  - Proportion of cohort who picked up their ARVs 6 out of 6 months (12 out of 12 months).
  - Proportion of cohort with CD4 counts above 200 mm3 at 6, 12, 24 months.

Slide 18



Slide 19		**Reader's Notes:** • Note: The "Baseline" and "6 months" were based on 13 cohorts and the "12 months" was based on 6 cohorts.
Slide 20		
Slide 21		
Slide 22		

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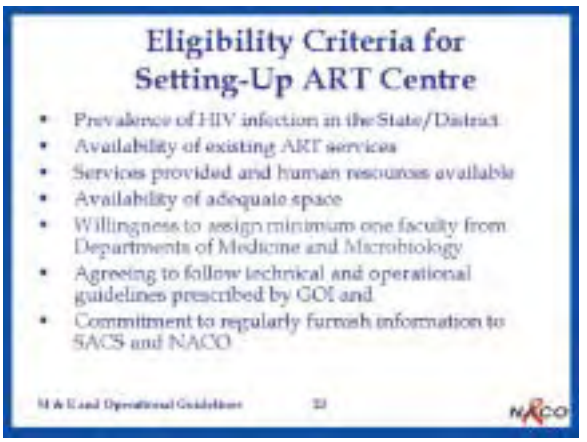
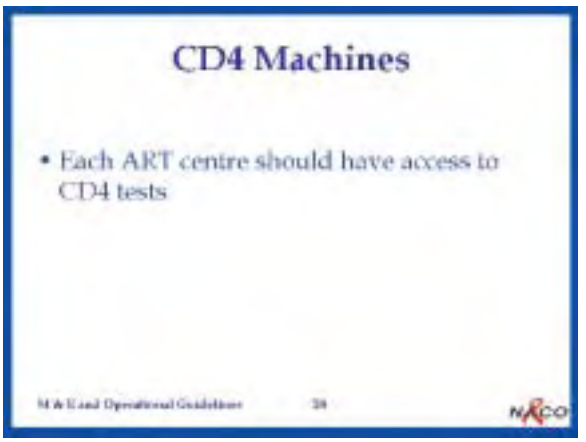


Reader's Notes:

- The following are the eligibility criteria for setting up an ART centre;
  1) Prevalence of HIV infection in the State/District (preference given to category "A' & 'B' districts) and estimated number of persons with HIV/ AIDS;
  2) Availability of existing ART services in the State/ Region/District;
  3) Services provided and human resources available in critical departments in the hospital (Medicine, Microbiology, Obstetrics & Gynaecology, Paediatrics, Dermatology / Venereology);
  4) Availability of adequate space for setting up ART Centre within the hospital area;
  5) Willingness to assign minimum one faculty from Departments of Medicine and Microbiology to support ART Centre on a daily basis;
  6) Agreeing to follow technical and operational guidelines prescribed by GOI; and

  Commitment to regularly furnish information on facilities, services and outcomes in prescribed formats to SACS and NACO.

Slide 24



Reader's Notes:

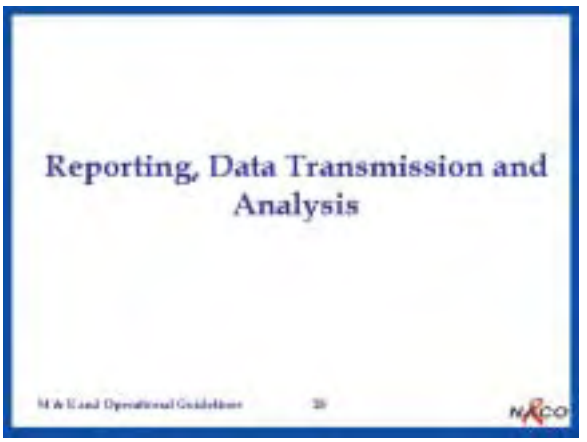
- Each ART centre should have access to CD4 tests either directly or by a clear linkage mechanism for conducting regular uninterrupted CD4 count at a designated centre. The centre must follow the instructions on collection and transport of samples **(and not patients)** from testing site to the identified site where the test is to be conducted. The reagents and other consumables needed for CD4 test would be procured by NACO or SACS and supplied to the Centres. The machines should be utilised optimally to ensure that there is minimal waiting period for CD4 test.
- All those patients who are started on ART will have their subsequent CD4 count done free of cost to a maximum of two per year unless desired by the clinician. CD4 test for all BPL patients and all HIV+ children would also be free of cost. Those who are being screened for eligibility of ART would be charged Rs.250/- per test
- It is recommended that the SACS should publish receipt books and supply these to the testing centres. The receipt should be prepared in three copies, one copy should be given to the patient, one should be retained at the institution where the sample has been collected / ART centre. The third copy should be sent to the SACS monthly along with a consolidated statement of money collected.
- The money collected for CD4 testing at collection centre should be deposited into Account of ART centre. The money thus collected can be used for purchase of vacoutainers, disposables and other consumables etc

Slide 25

Reader's Notes:

- All ART centres are provided with ARV drugs directly by NACO. The number of patients for which drugs are supplied is estimated in consultation with the ART centre concerned. The drugs are generally procured annually. The different types of ARV drugs and their proportions being supplied to ART centres are as below: The ratio of Stavudine vs. Zidovudine based combination is 40:60; Among the Stavudine based combinations, Stavudine 30 mg is 90% and 40 mg is 10% (very few of our patients have weight more than 60 kg); The proportion of Efaviranz is 20% of total (as many of our patients have TB co-infection and need simultaneous ATT and ART). The patient should be shifted to NVP after ATT is complete.
- The drugs are supplied in 3 instalments in a year. All centres should ensure that they have a minimum stock of drugs for three months at their centre. New patients should not be enrolled for ART without having 3 months stock of medicine. In such situations, information should be sent regarding non-availability of drugs to the following:
  - **SACS:** Joint Director I/c ART with copy to PD, SACS
  - **NACO:** Joint Director I/c ART with copy to National Consultant (ART) and AS&DG.
  - **Process for requisition and acceptance of ARV drugs;** Nodal Officer of ART Centre should send requisition for ARV drugs to NACO under information to SACS. The requisition should indicate full consignee address (Nodal Officer, ART) with pin code, phone/fax numbers and e-mail and quantity of each drug received, utilized, balance available and additional requirement. Supply would be made to the consignee of ART centre who would accept and receive drugs and store in medical store of the hospital/ institution.Weekly/fortnightly indents would be sent by the ART centre to the Store. Drug stock register should be kept with the store-keeper and a sub-stock register should be maintained at the ART centre by Staff Nurse/Pharmacist.
  - **Impending drug expiry; (1)** Poor planning, over supply, lack of communication, decrease in patient load, faulty expected number could lead to impending drug expiry. (2) Regular reporting and timely intimation to SACS and NACO is necessary to avoid such situations. (3) ART centre should inform NACO/SACS when expiry date of drugs supplied is within 6 months.

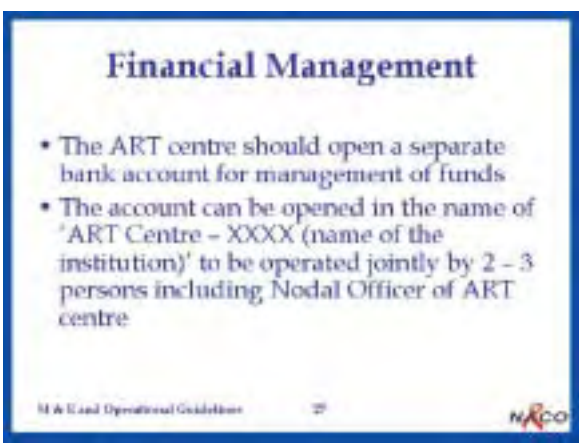
Slide 26



Reader's Notes:

- Information from the prescribed records and registers is compiled and used in filling up various monitoring reports, which are forwarded to SACS and NACO. (2) **Monthly reports should be forwarded electronically/fax to NACO by 2nd of every month without fail.** (3) Quarterly reports are to be forwarded in the months of July, October, January and April every year. It is intended to use electronic means of data recording and reporting system wherein ART data will be fed into the CMIS at the state, district or even ART centre level.(4) A pilot project using an electronic smart card system for ART patients is also being tested and will be implemented under NACP-III.
- The responsibility for information collection, reporting, management and analysis rests at four levels.
- **ART centres:** Data generation, maintenance of patient records and registers, reporting to SACS and NACO and using the information in patient management, drug stocking and referral.
- **State AIDS Control Societies (SACS)**: Data analysis, quality control, assessment of ART centres, supervision, feedback and dissemination of information to state-level stakeholders and NACO.
- **NACO:** Compilation, analysis, monitoring, evaluation, planning, advocacy resource allocation, drug supply and dissemination of information to national and international stakeholders.
- **National Research Institutions:** Conducting special evaluation studies and operational research.

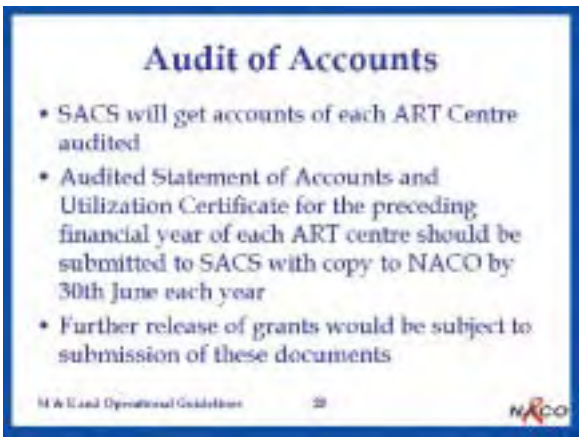
Slide 27



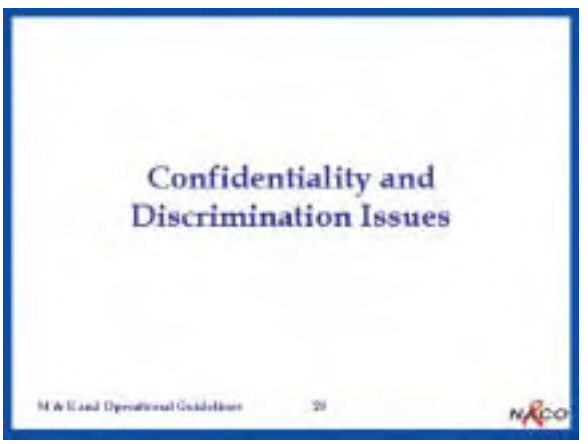
Reader's Notes:

- Opening a Back account for the ART centre is essential for proper and timely utilization of funds made available to ART centre.
- Payment should be made by cheques except for small contingent expenses.
- A cash book will be maintained by ART centre to meet petty cash expenses. For this purpose, the nodal officer may draw imprest money not exceeding Rs. 5000 at a time

Slide 28



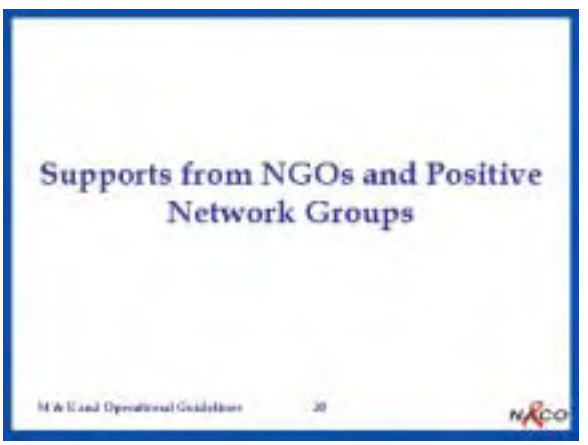
Slide 29



Reader's Notes:

1) Irrespective of HIV status of a person, all patients are entitled to receive general and specialty out-patient and in-patient services in a hospital.
2) Confidentiality should be maintained at all levels irrespective of HIV status as per accepted medical ethics and the law. Maintenance of confidentiality should help to reduce discrimination against PLHA during the management of the patient in any hospital.
3) It may also be noted that hospital infection control policies and measures, when observed properly and maintained at all levels and Post Exposure Prophylaxis (PEP) for all staff, if followed as per norms, will create a safe environment for health care providers to manage PLHA appropriately.

Slide 30



Reader's Notes:

1) In order to improve the quality of care provided to HIV/AIDS patients, the hospital should have effective linkages with Community Based Organisations (CBO), Faith Based Organisations (FBO) and with Positive Network Groups in the region.
2) Rapport building and development of positive relationships with these organisations will also help reduce the burden on the hospital.
3) Such NGOs may provide vocational (or occupational) rehabilitation to deserving PLHA and family members, support children affected with AIDS (CAA) and children infected with AIDS (CIA) by providing educational support and/or care homes.

- They could also provide legal support when PLHA or their family members are deprived of their rights. In addition, they are often well equipped to provide psychosocial support and even nutritional support to the patients and, if necessary, their families.

Slide 31		


Key Points
• M&E is an ongoing process that informs programme development and implementation
• Adhering to M&E formats will lead to greater programme improvements
• Current evaluation data demonstrates that ART programmes are attaining impact goals

SESSION 17-19

DAY - FIVE

SESSION 17

SESSION

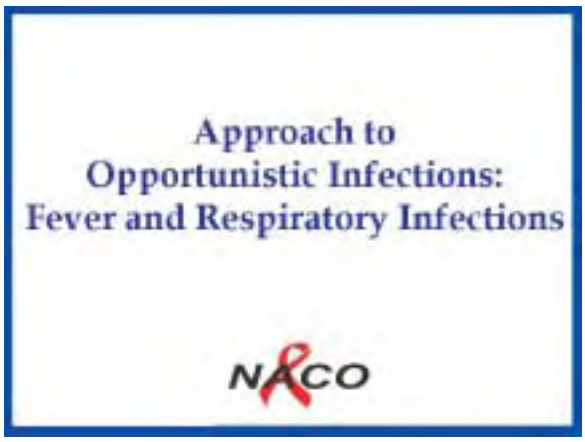
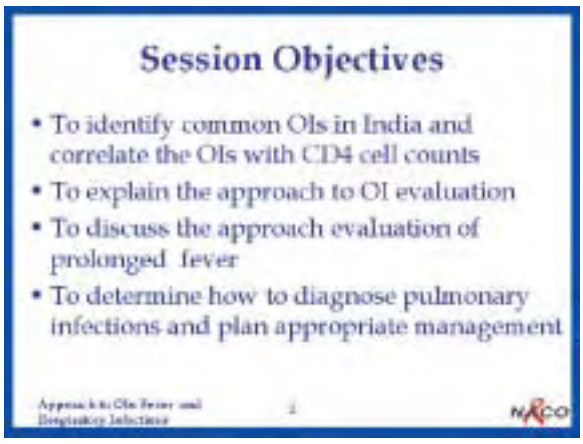
APPROACH TO OPPORTUNISTIC INFECTIONS: FEVER AND RESPIRATORY INFECTIONS

17

Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Identify common OIs in India and correlate the OIs with CD4 cell counts
- Explain the approach to OI evaluation
- Discuss the approach evaluation of prolonged fever
- Determine how to diagnose pulmonary infections and plan appropriate management

Slide 1		
Slide 2		

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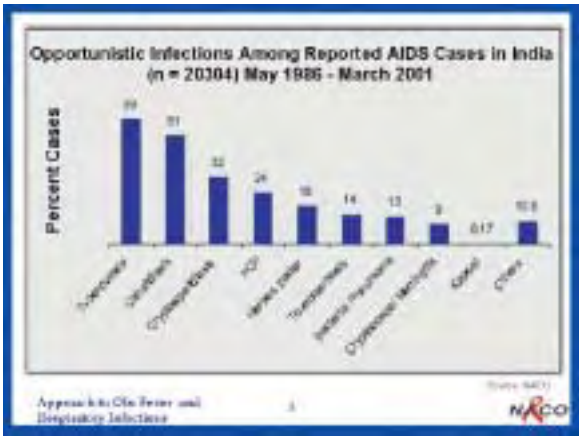
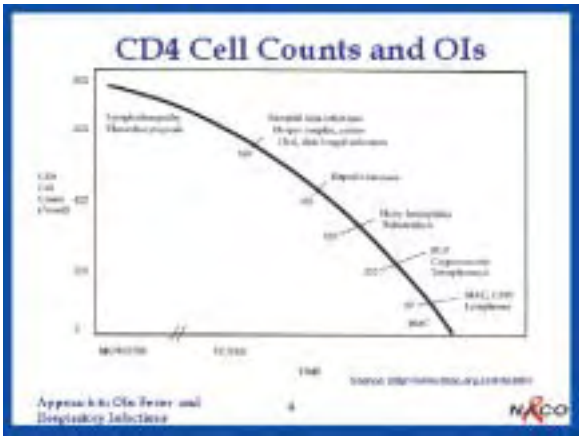


Reader's Notes:

- The most important reason for a PLHA to access health care is illness.
- According to national statistics, the leading pathogen co-infecting PLHA is tuberculosis.
- Other important pathogens are candida, cryptosporidium and other diarrhoeal pathogens, pneumocystis and herpes zoster.
- Kaposi's sarcoma is very rare.
- **Source**: http://www.nacoonline.org/publication /1.pdf :Combating HIV/AIDS in India 2000-2001.
- Guidelines for Prevention and Management of common opportunistic Infections/ Malignancies among adults/ adolescents PLHAs- Final draft, November 2006, NACO, Ministry of Health and Family Welfare, Govt of India, figure 1.1, page 9.

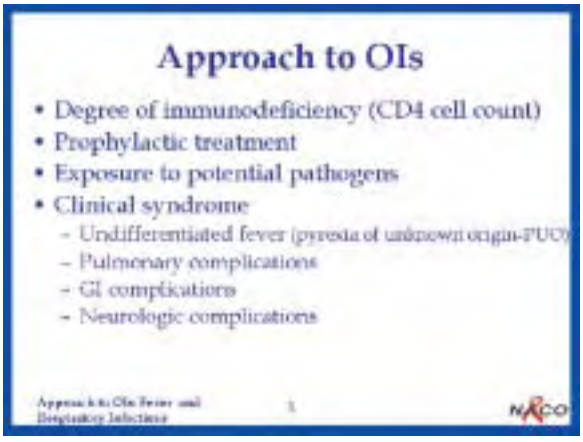
Slide 4



Reader's Notes:

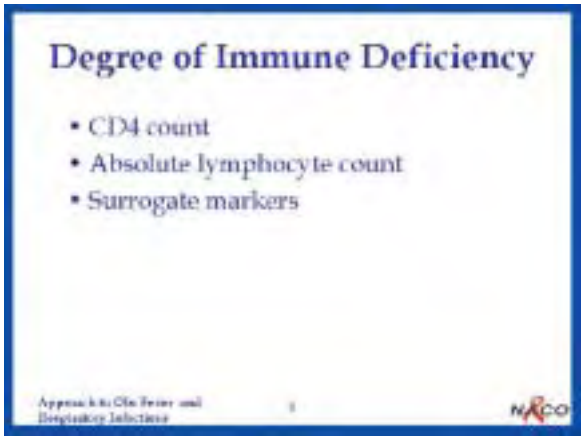
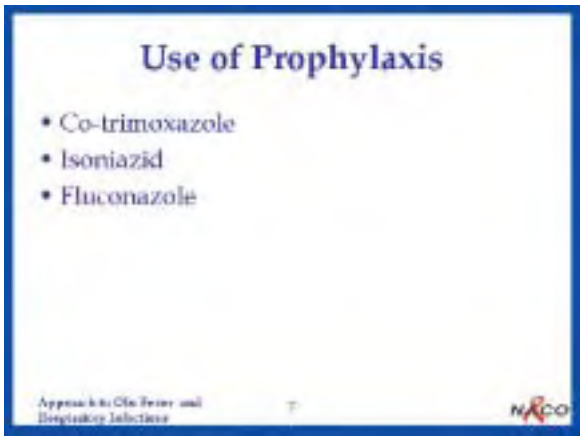
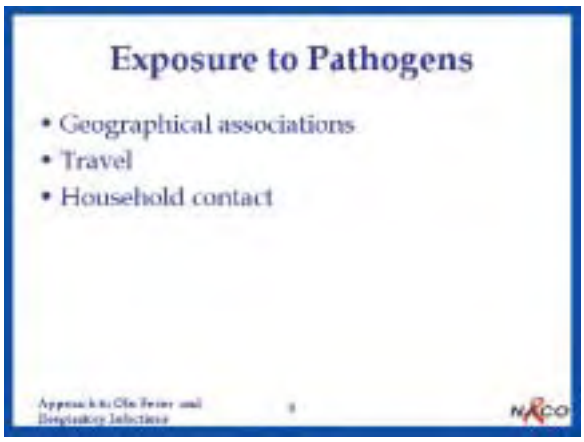
- This graph is an example of the kind of infections that a patient may develop over the course of a life time of living with HIV in the absence of ART.
- Remember that with advancing immune suppression, the risk of developing these infections increases several fold.
- For example, the risk of developing pneumococcal pneumonia is higher for a PLHA with a CD4 count of 350 cells/mm3 than a normal host, but the risk is still higher for a PLHA with a CD4 of less than 200 cells/ mm3.

Slide 5

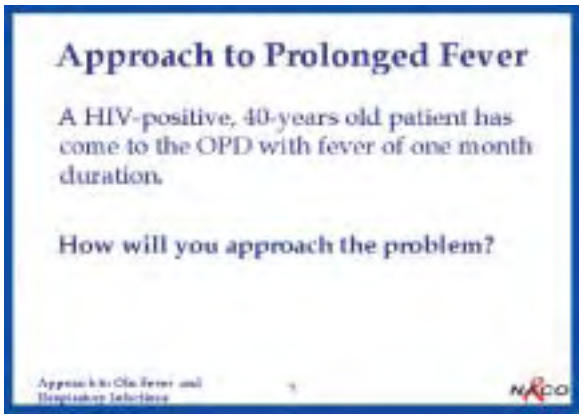


Reader's Notes:

- The general principle in the approach to OIs is based on various factors.
- The most important of these is the immune status of the host.
- Other factors that can influence decision making in diagnosis in symptomatic PLHA are: use of prophylaxis and the possibility of exposure to certain pathogens.

Slide 6		**Reader's Notes:** • As has been already discussed, the CD4 cell count is a good marker to assess the risk of all diseases. • CD4 estimation may be very useful in certain cases. • One example is a situation where PCP is considered, a CD4 level of more than 200 cells/mm3 will make the possibility unlikely. • It may not always be possible to do such estimations, due to cost considerations. • The value of absolute lymphocyte count is not standardized, therefore uncertain. • The presence of other co-morbidities could serve as surrogate markers - for example, the presence of disseminated cryptococcosis suggests a CD4 of less than 100 cells/mm3.
Slide 7		**Reader's Notes:** • Prophylaxis for certain infections is possible, and they extend considerable benefit against many other infections. • The best example of this is the use of co-trimoxazole for PCP, which has also been shown to protect against toxoplasmosis, non-typhoidal salmonella, and many diarrhoeal pathogens. • There is no role for prophylaxis against tuberculosis, as will be discussed later in the session on HIV and TB. • Routine prophylaxis for mycobacterium avium complex (MAC) is presently not recommended in our country. • The only situation in which fluconazole is recommended is in the setting of secondary prophylaxis for cryptococcosis, and in this situation, it makes infection by candida unlikely.
Slide 8		**Reader's Notes:** • Another important issue is the possibility of exposure to the potential pathogen. • Penicillium marneffei is found only in the north eastern parts of India and has not been reported for other areas. • Similarly, histoplasmosis appears to be clustered in the Gangetic delta, so it is less likely to be considered for people in other parts of the country. • It is important to obtain history of travel, as this can occur in mobile population, where the stay in areas of endemicity of the disease is adequate to cause infection. • It is also important to assess for domestic exposure, especially when a child is found to be infected. Transmission of certain infections like tuberculosis in children mandates screening of household contacts. This is similar to partner screening in STD care.

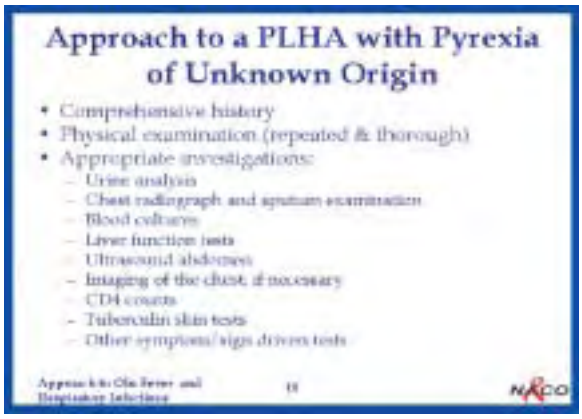
Slide 9



Reader's Notes:

- Very often, the PLHA presents with fever to health care facility, and assessing the cause of fever can be diagnostic challenge.
- Fever is a very common symptom or sign in PLHA presenting to medical care, and in many cases, it is due to a treatable pathogen.

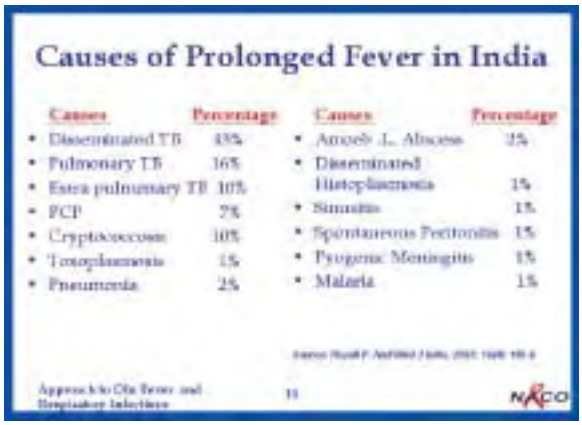
Slide 10



Reader's Notes:

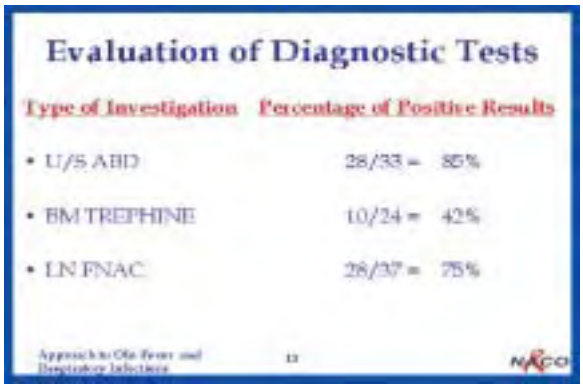
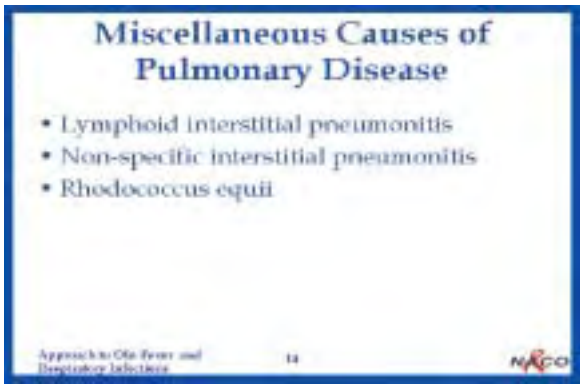
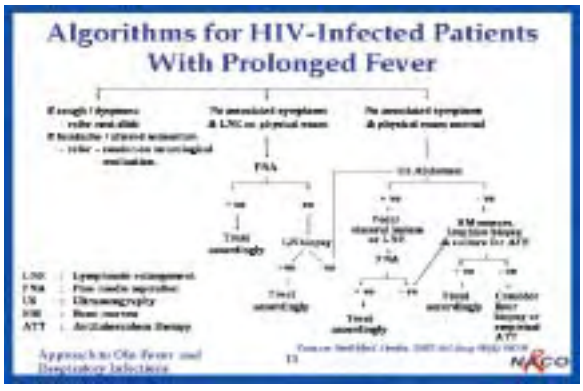
- For the evaluation of a PLHA with fever of 1 month duration, it is necessary to document a good history.
- Following this, the patient should be examined thoroughly at baseline and repeat examinations should be performed if the cause cannot be determined. The appearance of new findings (like lymph nodes) is of great value and significance.
- Blood counts should be performed at baseline, along with at least 3 blood smears for malaria.
- Other useful tests are urine analysis, chest X ray and sputum examination, liver functions (at least liver enzymes - aspartate transaminase (AST), alanine aminotransferase (ALT) and alkaline phosphatase), and blood culture.
- If these tests do not yield an answer, the options of an ultrasound examination of the abdomen and imaging of the chest should be considered. CD4 counts will help stage the patient and help in assessing the possibility of the illness being due to a particular pathogen (refer the natural history for correlation of CD4 to pathogen causing infection).
- The tuberculin skin test may be mentioned here only to highlight it's negative impact.
- It is very difficult to interpret the test in the presence of HIV, and a negative result can occur frequently even in those with extensive TB, if the patient in advanced stage of disease.

Slide 11



Reader's Notes:

- In a study carried out at a tertiary institution in India, the most common pathogen causing prolonged fever was found to be tuberculosis.
- Other important pathogens include pneumocystis and cryptococcus.
- **Source:** Rupali P, Abraham OC, Zachariah A, Subramanian S, Mathai D. Aetiology of prolonged fever in antiretroviral-naive human immunodeficiency virus-infected adults. Natl Med J India. 2003 Jul-Aug; 16(4): 193-9.

Slide 12		**Reader's Notes:** • Useful investigations that have a high yield are lymph node fine needle aspiration for cytology, ultrasound examination for nodes, and bone marrow examination. • A significant number of patients can be diagnosed based on the judicious use of these tests. • This approach is of greatest use in evaluating patients who have no localizing features.
Slide 13		**Reader's Notes:** • Of course, not all causes of fever are HIV-related. • Malaria needs to be considered as a possibility, although co-trimoxazole use protects against falciparum malaria. • Among injection drug users, right heart endocarditis should be a possibility. Infection by salmonella and pneumococcus is more frequent in this population.
Slide 14		
Slide 15		**Reader's Notes:** • This is a simplified algorithm for evaluation of PLHA. This can be used even when there are no symptoms referable to any particular organ system. • If there is no clue indicating involvement of a specific organ system, a lymph node aspiration is best done if adenopathy is present. • In the absence of adenopathy, an ultrasound of the abdomen may be performed followed by aspiration of any nodes or lesions, if found. • In the absence of lesions on ultrasound, the best option is a bone marrow examination. • If the evaluations are negative, the alternative is to do either a liver biopsy or an empirical ATT.

Handout 1: OI Algorithms

MANAGEMENT ALGORITHMS FOR HIV-INFECTED PATIENTS WITH PROLONGED FEVER

Fig. 1 Prolonged Fever

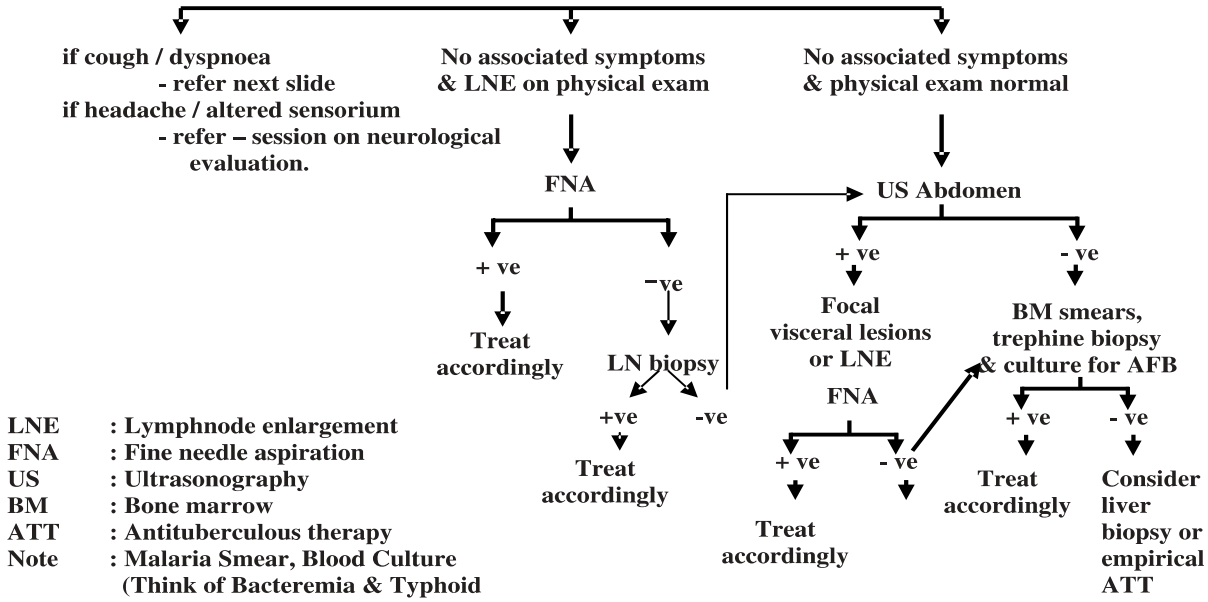
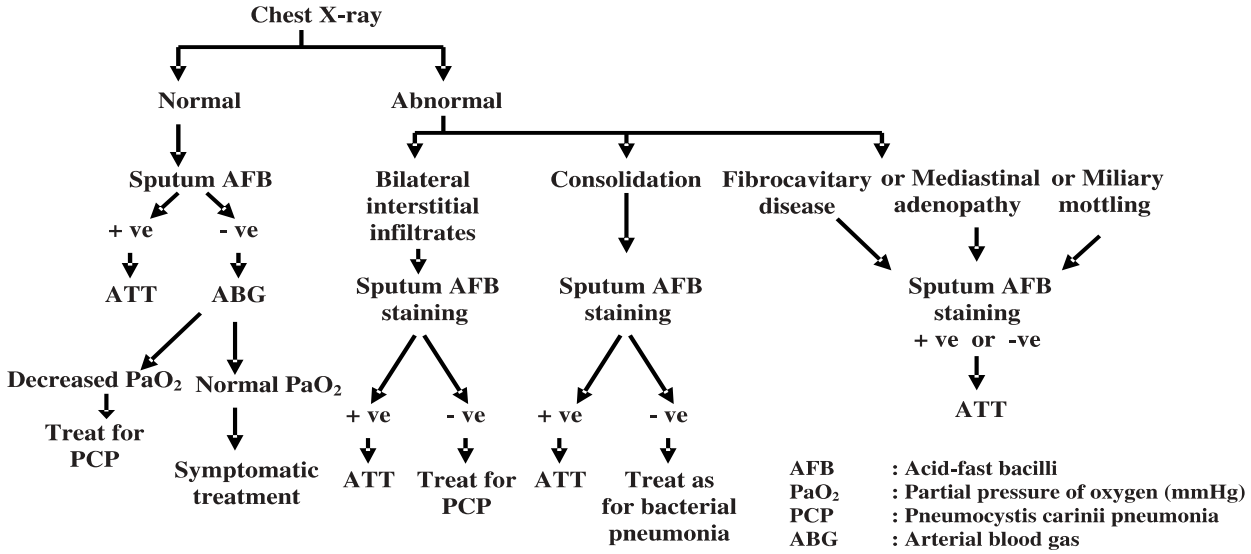
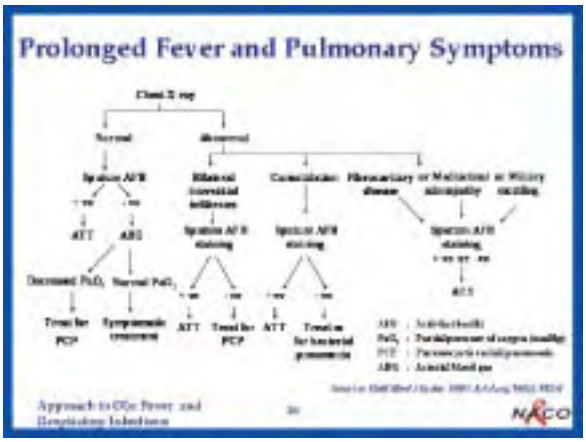


Fig. 2 Prolonged Fever and Pulmonary Symptoms



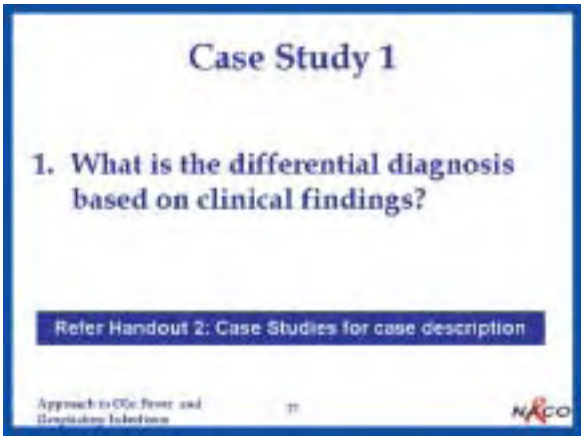
Slide 16



Reader's Notes:

- In the presence of pulmonary symptoms, the most important investigation is a chest X ray.
  - If this is normal and sputum AFB is negative, PCP should be considered strongly in a patient found hypoxic by blood gas or by pulse oximetry.
- In case of radiological changes, the decision on treatment is dependent on the type of anomaly noted.
  - Likely possibilities in such a situation are: tuberculosis, PCP and bacterial pneumonia.
  - In a resource restricted setting, it may not be possible to have a bronchoscopy done for all patients.
  - However, such tests should be considered in case of non response to empiric therapy.
- Another option would be to start with sputum examination to rule out community acquired pneumonia and nocardiosis and then proceed to a chest x-ray; that approach is also acceptable.

Slide 17



Handout 2: Case Studies

Case Study 1

- 27 year-old PLHA (detected 8 years ago) was diagnosed with pulmonary TB 3 years ago and received complete treatment after which he improved.
- He was doing well until 2 weeks ago.
  - Received TMP/SMX prophylaxis, but took tablets irregularly.
  - Presented with 2 weeks of progressive breathlessness and mild cough with minimal sputum production.
- O/E: Pulse rate 102/min.
- Respiratory rate 22/min.
- Temp 99°F.
- Weight 45 Kg.
- Oral candidiasis present.
- No cyanosis.
- Respiratory system: No areas of dullness, vesicular breath sounds, bil. fine early inspiratory crepitations.
- Cardiovascular, GIT, CNS : No abnormality detected.

Question and Answers:

Q.1. Discuss the differential diagnosis based on clinical findings.

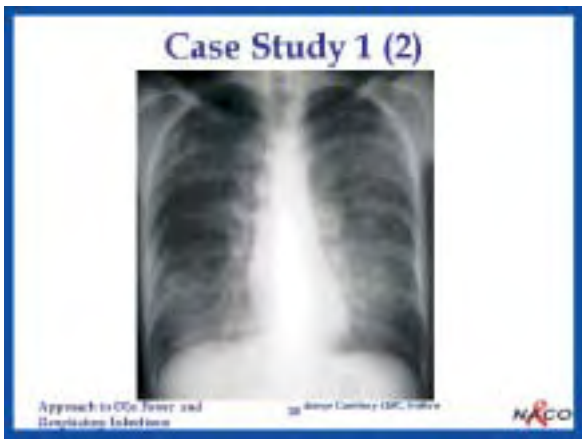
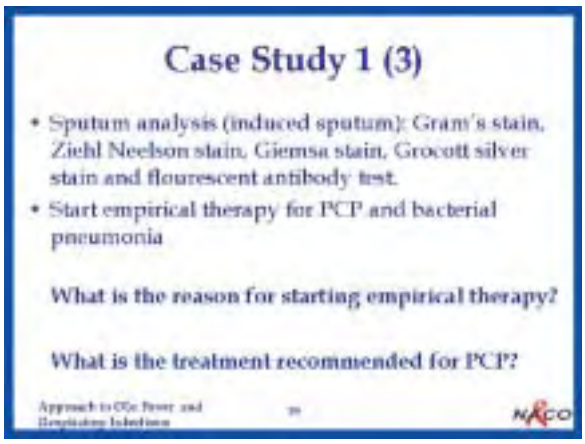
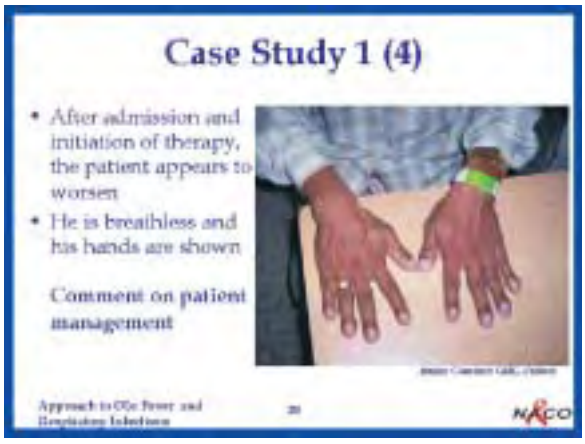
Case Study 2

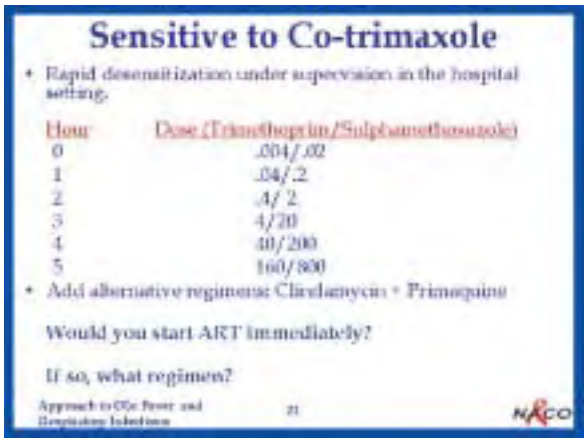
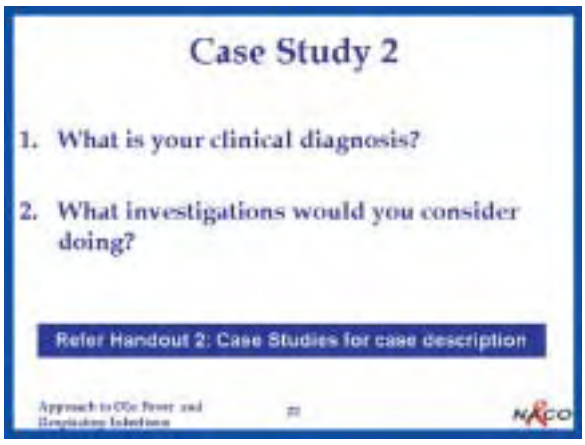
- A 43 year-old man who is HIV-positive (detected during blood donation screening 5 years ago) presented with high grade fever, cough with purulent expectoration of 6 days duration and breathlessness (This is his second episode in 6 months).
- He has had multi-dermatomal herpes zoster in the past.
- O/E: Tachypnoeic with a RR- 30/mt.
- Temp-104º F.
- Respiratory system examination - decreased breath sounds in the right mammary and infra-axillary regions.

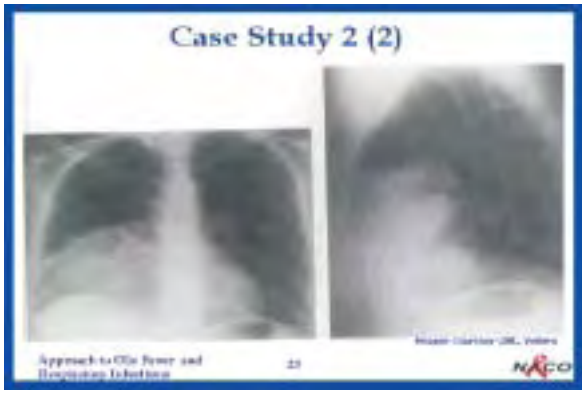
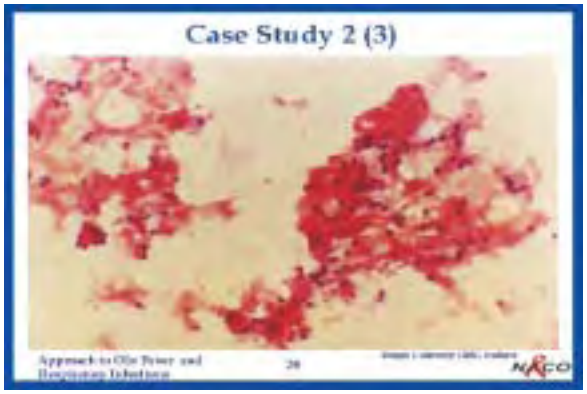
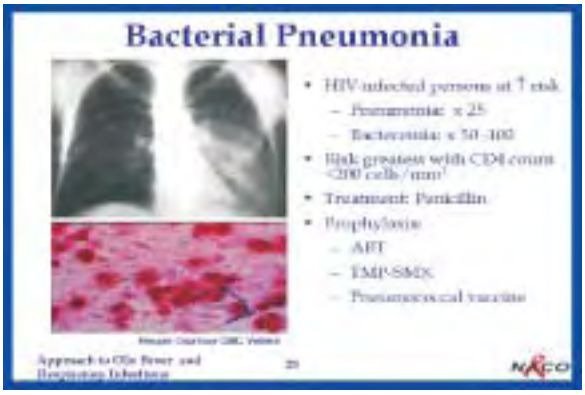
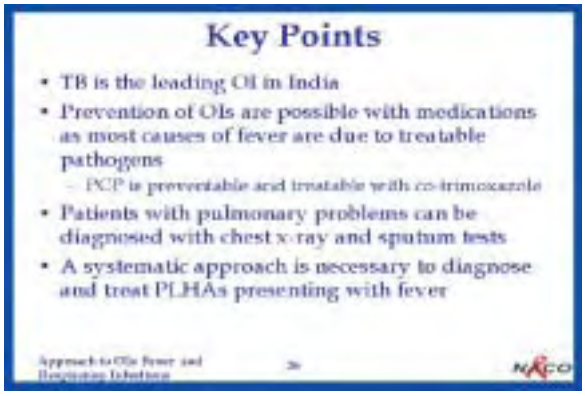
Questions with Answers:

Q.1. What is your clinical diagnosis?

Q.2. What investigations would you consider doing?

Slide 18		
Slide 19		**Reader's Notes:** • Source:http://www.nacoonline.org/publication/9.pdf, Specialist's Training and Reference Module. • Source:http://www.cdc.gov/mmwr/preview/mmwrhtml/00001409.htm. • MMWR: Supplement June 16, 1989 / 38(S-5);1-9. • Guidelines for prophylaxis against pneumocystis carinii pneumonia for HIV-positives.
Slide 20		

Slide 21		
Slide 22		

Slide 23		
Slide 24		
Slide 25		**Reader's Notes:** • Sources: For further study refer to: Global strategies to prevent bacterial pneumonia in adults with HIV disease Feikin DR, Feldman C, Schuchat A, Janoff EN, The Lancet Infectious Diseases - Vol. 4, Issue 7, July 2004, Pages 445-455.
Slide 26		

SESSION 18

SESSION

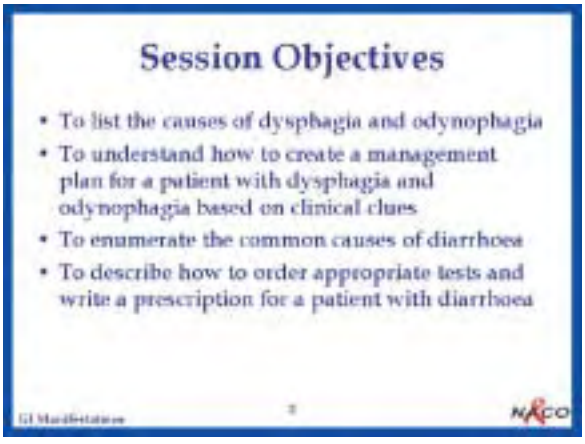
GASTROINTESTINAL MANIFESTATION

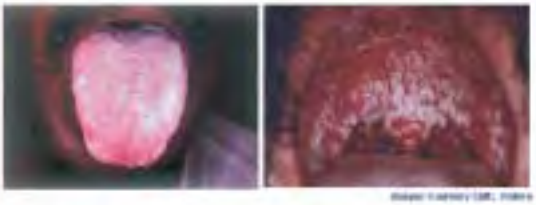
18

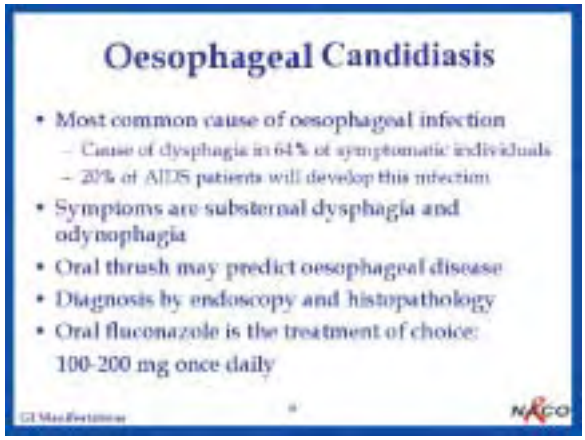
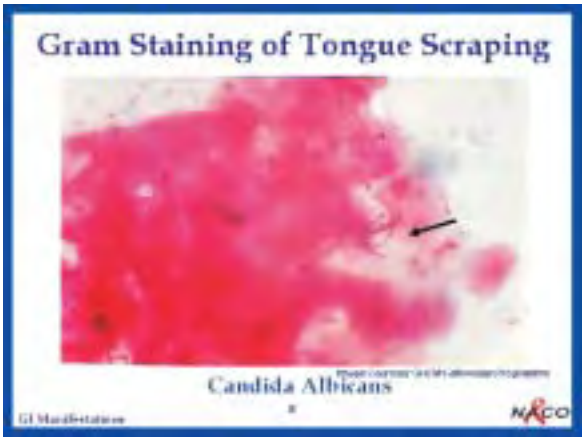
Total Session Time: 45 minutes

Session Objectives: At the end of the session, the participant should be able to:

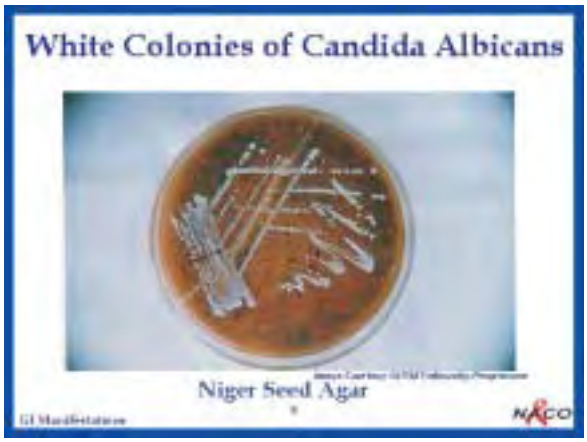
- List the causes of dysphagia and odynophagia
- Understand how to create a management plan for a patient with dysphagia and odynophagia based on clinical clues
- Enumerate the common causes of diarrhoea
- Describe how to order appropriate tests and write a prescription for a patient with diarrhoea

Slide 1		
Slide 2		

Slide 3	**Case Study 1** • 32 year-old Mr. M., HIV-positive, presents with progressive difficulty in swallowing and retrosternal pain while swallowing, of two weeks duration • A year ago, he presented with history of TB; he received regular treatment for 6 months • Since then he has been on co-trimoxazole prophylaxis and vitamins **What are the clinical problems in this patient?**	
Slide 4	**Case Study 1- Findings: Oral Cavity**  **Symptoms: Thrush, Sore mouth**	
Slide 5	**Causes of Odynophagia** **Common causes:** • Fungal (e.g., Candida) • Viral (e.g., CMV, HSV) • Others (e.g., Idiopathic HIV ulcers) **Less common:** • Bacteria (e.g., Staphylococcus, TB) • Fungus (e.g., Aspergillus) • Virus (e.g., EBV) • Parasites (e.g., Cryptosporidium) • Drugs (e.g., AZT, NSAIDs) • Gastroesophageal reflux disease (GERD)	

Slide 6		**Reader's Notes:** • The most common cause of odynophagia in PLHA is Candidiasis. It is the cause of dysphagia in nearly two thirds of symptomatic patients. An estimated fifth of all PLHA will experience oesophageal Candidiasis in their lifetime. • Suspect candidiasis in all PLHA presenting with substernal dysphagia and odynophagia. • The presence of oral thrush significantly increases the chance of Oesophageal Candidiasis; hence oral cavity examination is mandatory in all patients with dysphagia.
Slide 7		
Slide 8		**Reader's Notes:** • Gram's staining showing the fungal filaments. • It is a simple test to perform and patient can be treated based on evidence. • The scrapping of tongue can be done at the bedside and the fungal filaments can be demonstrated by Gram's staining or by other special staining procedures depending upon the facilities available at the medical centre.

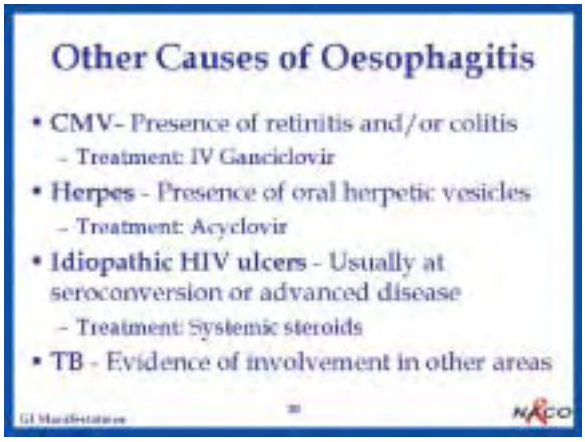
Slide 9



Reader's Notes:

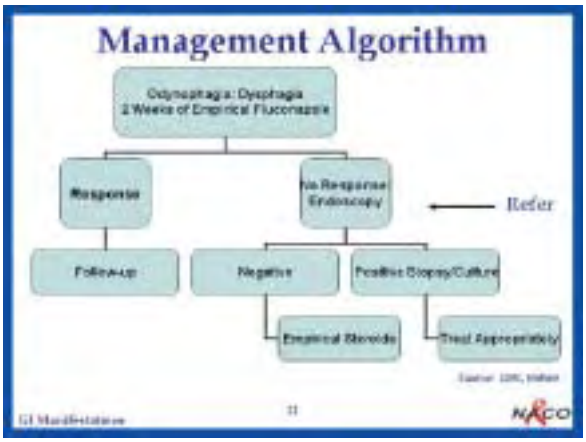
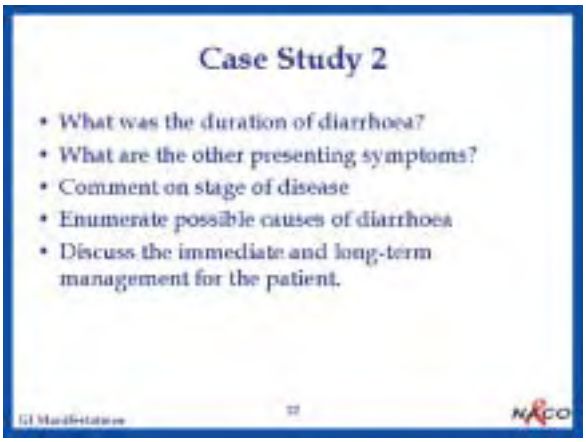
- During the 1980s and 1990s, numerous reports emerged describing the development of fluconazole (Diflucan)-resistant oropharyngeal candidiasis in AIDS patients following prolonged exposure to fluconazole.
- Source: Powderly WG, Mayer KH, Perfect JR. Diagnosis and treatment of oropharyngeal candidiasis in patients infected with HIV: a critical reassessment. AIDS Res Hum Retroviruses. 1999;15:1405-12.
- Investigators have identified low CD4 cell count, advanced immune suppression, greater number of fluconazole-treated episodes, and longer median duration of fluconazole therapy as the most important risk factors.
- Source: Maenza JR, Keruly JC, Moore RD, Chaisson RE, Gallant JE. Risk factors for fluconazole-resistant candidiasis in HIV-infected patients. J Infect Dis 1996;173:219-25.
- In recent years, clinicians have observed a major decrease in the number of patients with fluconazole-resistant oropharyngeal candidiasis, predominantly as a result of the widespread use of ART [7].
- Source:Martins MD, Lozano-Chiu M, Rex JH. Declining rates of oropharyngeal candidiasis and carriage of Candida albicans associated with trends toward reduced rates of carriage of fluconazole-resistant C. albicans in human immunodeficiency virus-infected patients. Clin Infect Dis.1998;27: 1291-4.

Slide 10



Reader's Notes:

- Suspect CMV in a PLHA with retinitis or colitis and confirmed by classical histological appearance.
  - Endoscopic biopsy classical.
  - Treatment with Ganciclovir can induce remission, but requires prophylaxis; long term cure requires use of ART.
- Herpes viruses are known to cause Oesophagitis and should be suspected when herpetic vesicles are seen in the oral cavity.
  - Diagnosis is confirmed by biopsy and treated with acyclovir.
- Idiopathic HIV ulcers are seen in seroconverting illness and advanced HIV infection.
  - Biopsy and cultures are negative, and treatment is by systemic steroids.

Slide 11		**Reader's Notes:** • The algorithm is ideal for management of odynophagia when resources are limited. • In such a situation, try a two week trial of fluconazole, if there is a good response, only follow up is required. If there is no response, then referral for endoscopy can be done. • If the biopsy, histopathology and cultures are negative, then try systemic steroids. If a specific aetiology is identified, the therapy is pathogen directed.
Slide 12		

Handout 1: Case Study 2

- Mrs. A. HIV-positive, presented with a history of diarrhoea of 9 months duration that had worsened in the last 2 months.
- The initial episodes of diarrhoea stools were 1-2 per month, each lasting for 4-5 days with 4-5 stools per day. In the past two months this worsened to loose watery stools on most days of the week, about 8-9 times a day.
- She gave no history of fever or vomiting.
- She lost 10kg in weight in the last 6 months.
- Her husband died 3 years ago of TB.

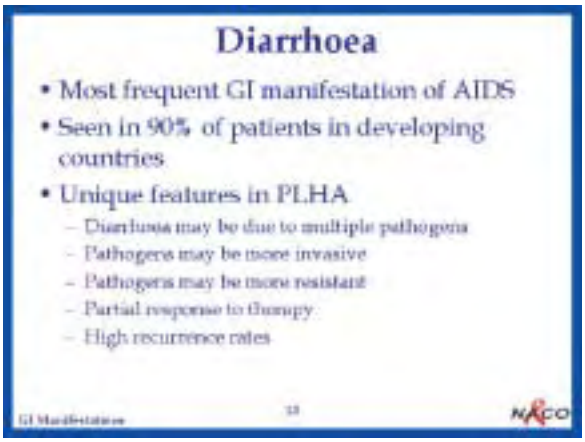
Examination Findings

- Emaciated
- Pulse — 120/min, regular
- BP — 80 systolic
- Respiratory rate — 14/min, regular
- Temperature — 99F
- Dehydrated
- Oral candida present
- Abdomen - scaphoid, no other abnormalities
- Other systems-no abnormality seen

Fill in the following information given with answers:

1. Duration of Diarrhoea: ……
2. Other symptoms: ……
3. Stage of disease: ……..
4. Possible causes of diarrhoea: ……
5. Immediate management: ……
6. Long term management: ……

Slide 13



Reader's Notes:

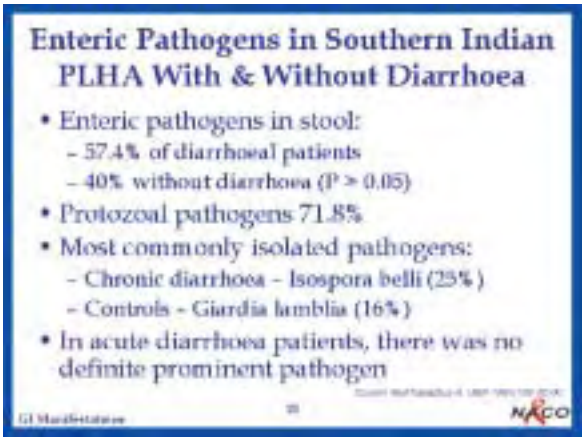
- There are multiple reasons for the high occurrence of diarrhoea:
- Immune dysfunction of the intestinal epithelial cells.
- Reduced Ig A levels.
- Poor gastric acid secretion and nutritional deficiencies.

Slide 14

Reader's Notes:

- The pathogens causing diarrhoea in PLHA can be classified into bacterial, protozoal, helminths and viral causes.
- In some patients, there is no demonstrable pathogen in the stool and the cause of diarrhoea is probably due to the enteropathy of HIV/AIDS.
- The commonest class of pathogens causing diarrhoea is protozoal and of these, Isospora belli is the most frequent.
- Other pathogens include Cyclospora, Microsporidia, Cryptosporidia and Giardia. Bacterial pathogens like Salmonella and Shigella are also common causes.
- Of the helminthes, the pathogen of importance is Strongyloides.

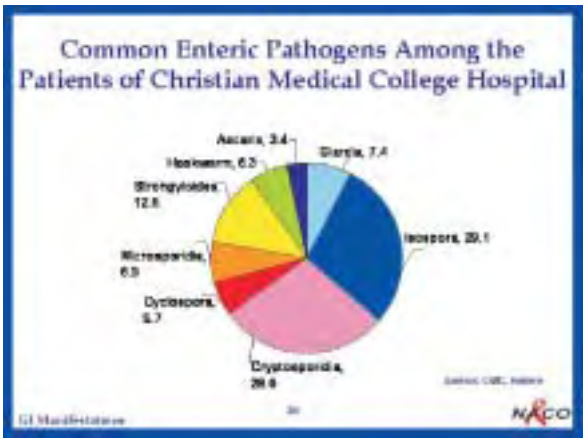
Slide 15



Reader's Notes:

- Studies done in India have shown that these pathogens may be isolated from the stools of PLHA without any symptoms, although the isolation of parasites was shown to be more common in patients with diarrhoea.
- The most common pathogen identified in those with diarrhoea was **Isospora belli**.
- On the other hand, asymptomatic patients were more likely to shed Giardia in their stools.
- **Source:** Enteric pathogens in southern Indian HIV-infected patients with & without diarrhoea, Mukhopadhya A. Indian Journal of Medical Research 1999; 109: 85-90.

Slide 16



Reader's Notes:

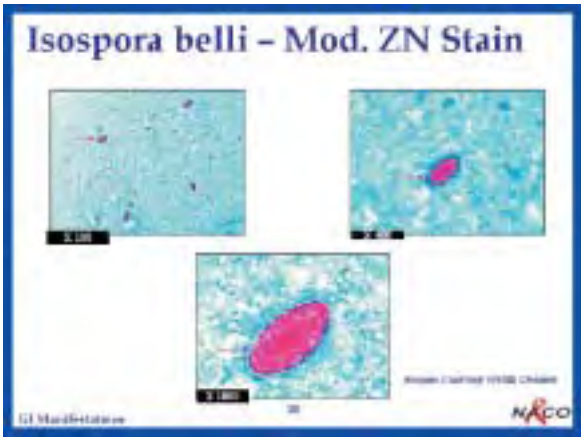
- The common pathogens identified in the stools of PLHA with diarrhoea are Isospora, Cryptosporidia, Strongyloides, Microsporidia and others.
- Other than pathogen specific therapy, the importance of symptomatic therapy to ensure adequate hydration should not be forgotten.
- ART also makes a big impact, especially in the case of Cryptosporidium, where no good treatment is available.
- **Source:** Enteric pathogens in southern Indian HIV-infected patients with & without diarrhoea, Mukhopadhya A. Indian Journal of Medical Research 1999; 109: 85-90.

Slide 17

Reader's Notes:

- Stool examination stained with modified Ziehl-Neelsen's Staining demonstrates the oocysts of cryptosporidium.

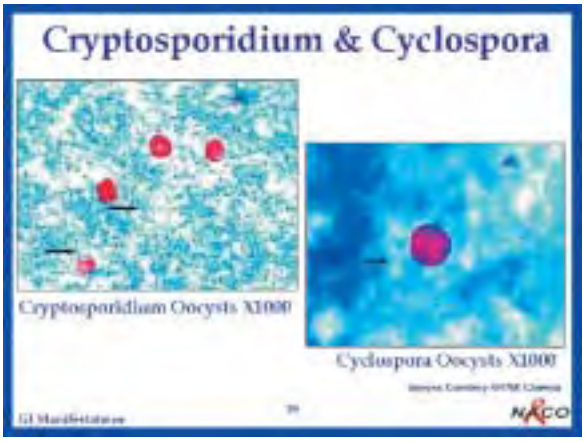
Slide 18



Reader's Notes:

- **Isospora Belli — Modified Acid Fast Stain:**
  1. Isosporabelli will stain pink to deep purple, while other fecal matters take the counter stain (depends upon the counter stain if it is methylene blue background will be blue, if it is malachite green background will be green)
  2. It measures 25 to 30 µm will have ellipsoidal shape.
  3. It is auto fluorescence.
- **Cryptosporidium — Modified Acid Fast Stain:**
  1. Cryptosporidium will stain pink to deep purple other take the counter stain.
  2. It measures 4-6 µm round in shape.
  3. Auto fluorescence absent in cryptosporidium.

Slide 19



Reader's Notes:

- **Cyclospora — Modified ZN Stain:**
  1. It will stain pink to deep purple, others than cyclospora take the counter stain colour.
  2. It measures 8- 10 µ, may not be perfectly round, some may appear collapsed or distorted on one side.
  3. Auto fluorescence present.

Slide 20

Reader's Notes:

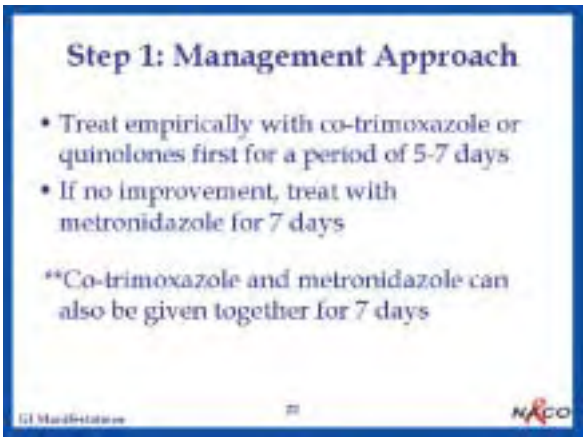
- The principles of management are similar to that for a normal patient.
- The most important step is ensuring adequate hydration, with fluids and electrolytes.
- Once this is achieved, it is preferable to treat with specific therapy as determined by the pathogen causing diarrhoea.
- Stage-wise evaluation is ideal for evaluation of patients with diarrhoea.

Slide 21

Reader's Notes:

- Cryptosporidia: Nitazoxanide- 500 mg orally twice daily.
- Isospora: Co-trimoxazole- 2DS tablet twice daily for 10 days and then 1DS tablet three times daily for three weeks.
- Cyclospora: Co-trimoxazole- DS tablet orally twice daily for 10 days followed by once orally three times weekly for maintanence.
- Micosporidia: Albendazole, Nitazoxanide- 400-800mg orally twice daily for 30 days and then 200-400 mg daily orally for maintanence.
- Giardia: Metronidazole- 250 mg orally three times daily for 5-10 days.
- Strongyloides: Thiabendazole- 25 mg per kg orally twice daily for two days.

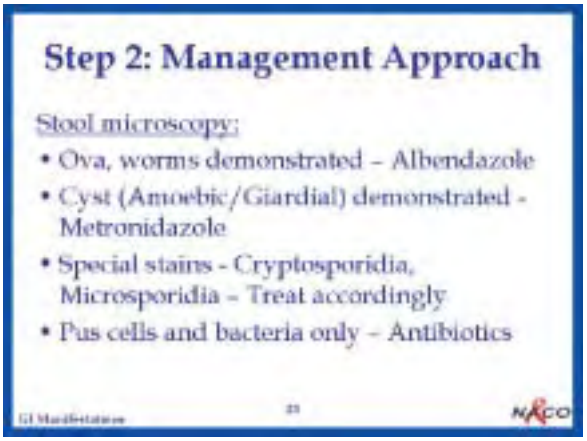
Slide 22



Reader's Notes:

- If no facilities are available at the health care facility, like in PHC, options include: Giving empirical therapy with co-trimoxazole and then if necessary metronidazole or give the combination of both the drugs.

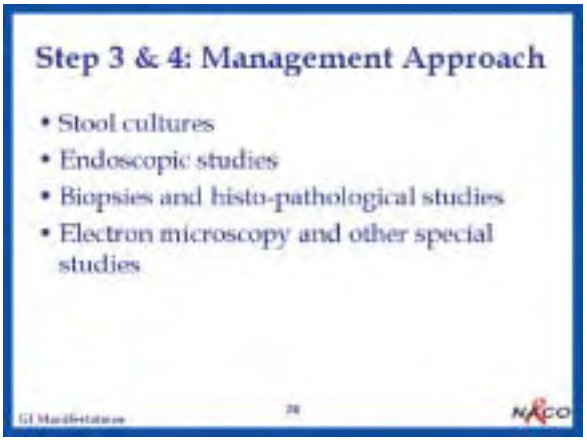
Slide 23



Reader's Notes:

- If facilities are available, the patient's stool should be examination for pathogens (with special stains if possible).
- Depending upon the diagnosis, appropriate treatment can be initiated.
- Special stains: Modified acid fast stain, Trichrome and monoclonal stains.

Slide 24



Reader's Notes:

- If no pathogen can be isolated, perform next step investigations- endoscopy for biopsies and cultures. These are to be examined under light and electron microscopy.
- The flow chart may be used for management of PLHA with chronic diarrhoea.
- Refer to **Handout 2: Management of HIV Related Diarrhoea**.
- In the absence of availability of any investigative facilities, the option is to use empirical therapy, but a baseline knowledge of pathogens is necessary to decide on the choice of antimicrobials that is most likely to be efficacious.
- To establish this data, evaluation of some patients by this flow chart will help understand the microbiology in the community studied.

Handout 2: Managing HIV-Related Diarrhoea

Fig 1: Approach to Acute Diarrhea in HIV positive Patients

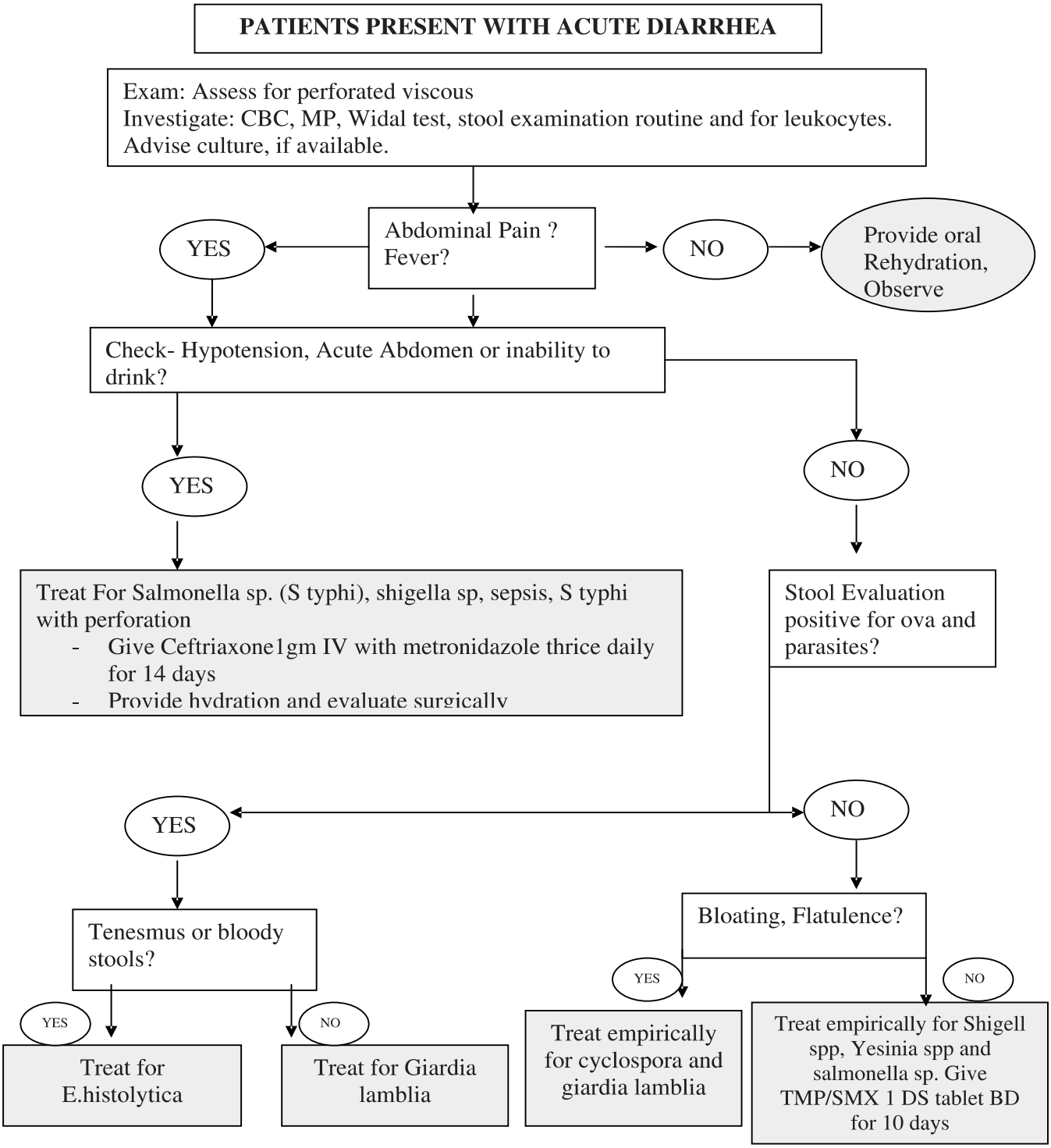
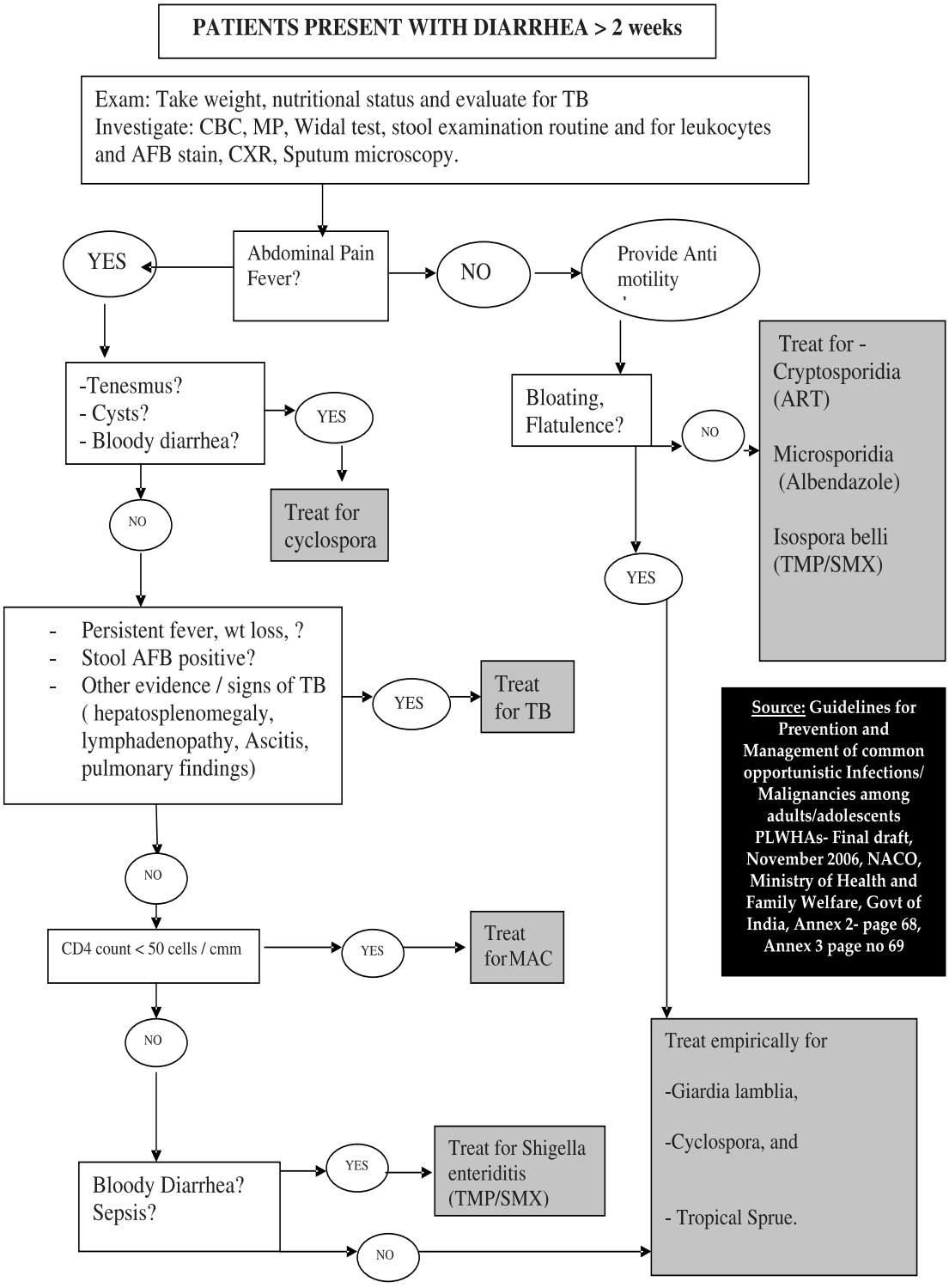
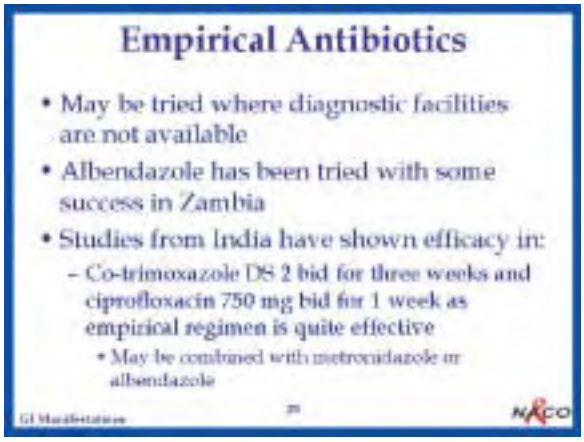


Fig 2: Approach to Chronic Diarrhea (> 2 weeks) in HIV Positive Patients



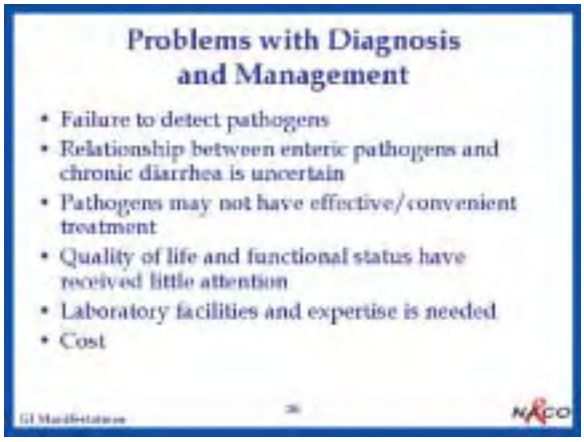
Slide 25



Reader's Notes:

- Empirical antibiotics should ideally be used only in areas where basic diagnostic facilities are not available.
- Various agents have been tried with some success in treatment of diarrhoea in different parts of the world.
- Studies from India have evaluated the efficacy of co-trimoxazole and ciprofloxacin and found them to be quite effective.
- Combining this with Metronidazole or Albendazole or both are options for empirical therapy, but as mentioned earlier, a good knowledge of the spectrum of diarrhoeal pathogens in the community will make empirical therapy more effective.
- Sources: Indian Pediatrics 2002; 39: 941-944, Isosporiasis in Children Bijay R. Mirdha, S.K. Kabra*, J.C. Samantray and BioMedCentral Infect Dis. 2006; 6: 39, Diarrhea, CD4 counts and enteric infections in a hospital — based cohort of HIV-infected patients around Varanasi, India, Suresh VS Attili, 1 AK Gulati, 2 VP Singh, 1 DV Varma, 3 M Rai, 1 and Shyam Sundar1, website:http://www.biomedcentral.com/1471-2334/6/39.

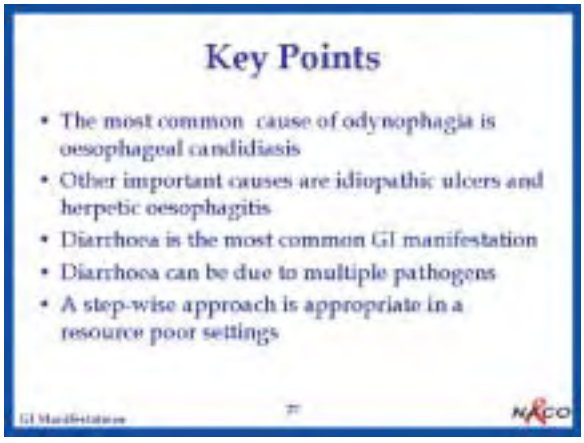
Slide 26



Reader's Notes:

- Although many of the pathogens can be detected by simple stool examination, the diagnosis and management of diarrhoea in a PLHA is a major challenge.
- Sometimes even after repeated stool testing, no pathogen can be isolated.
  - May not be related to technique, but due to fact that the shedding of pathogens may be intermittent.
- The relationship between the pathogen and diarrhoea is unclear.
  - Many of the pathogens have been isolated from stools of asymptomatic PLHA.
  - This is probably because the bowel may be colonized fairly early in the life of the PLHA by the pathogen, and it produces diarrhoea when the immunity wanes.
- Some of the pathogens do not have effective treatment, or it may not always be available.
  - A classic example is the pathogen **Cryptosporidium.parvum**, which responds poorly to therapy and the mainstay of treatment is symptomatic or ART.

		• Very often, the episodes of diarrhoea are recurrent and severely compromise the quality of life.
		  • This can cause frequent absence from work and need to access medical care.
		  • This has not been well studied.
		  • Although the initial evaluation is quite simple, if no pathogen is isolated, then further testing may be required and this is expensive.
		  • Lab facilities and expertise of this nature is not available in most institutions.
		• Finally, the cost needs to be considered.
		  • These include cost to the health care, to the patient- both direct and indirect (due to loss of wages).

Slide 27		

SESSION 19

SESSION

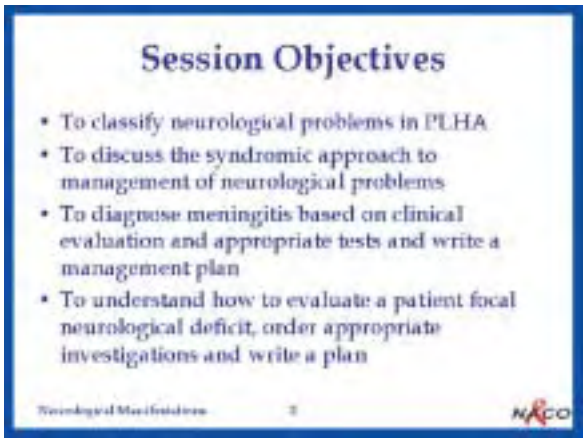
NEUROLOGICAL MANIFESTATIONS

19

Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Classify neurological problems in PLHA
- Discuss the syndromic approach to management of neurological problems
- Diagnose meningitis based on clinical evaluation and appropriate tests and write a management plan
- Understand how to evaluate a patient focal neurological deficit, order appropriate investigations and write a plan

Slide 1		
Slide 2		

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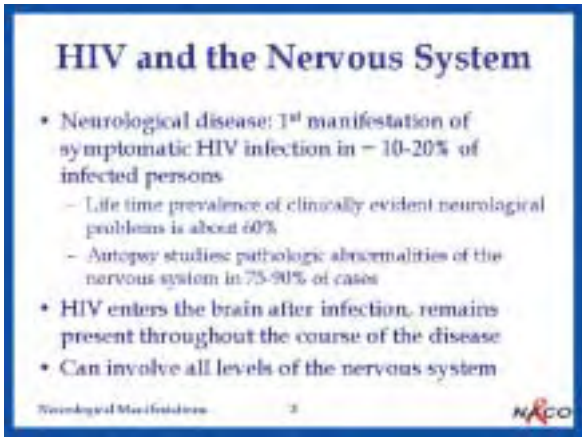


Reader's Notes:

- HIV invades the CNS (central nervous system) fairly early during the course of infection, and progresses with the advancement of the infection in the host.
- It has the capability to affect all parts of the neural axis, and the use of HAART may not always be associated with improvement.
- Studies from Western countries have shown that the neurological system is the first to show manifestations of HIV in up to 20% of infected individuals.
- The life time prevalence of clinically evident neurological problems in HIV infected patients is about 60%. Autopsy studies have shown that more than 75% of PLHA with advanced disease have pathological changes in the nervous system attributable to HIV.

Handout 1 : Neurological Complications of HIV

The neurological manifestations seen in HIV can be classified in two ways:

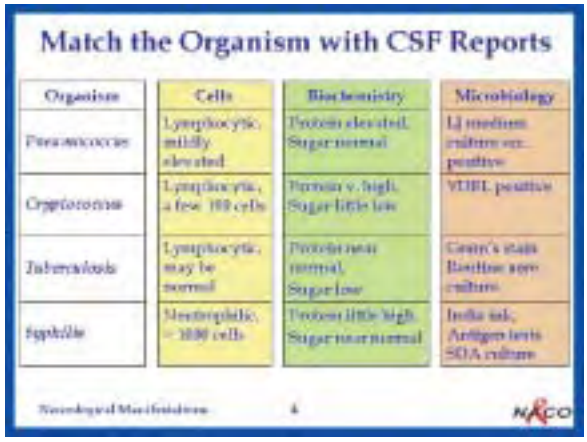
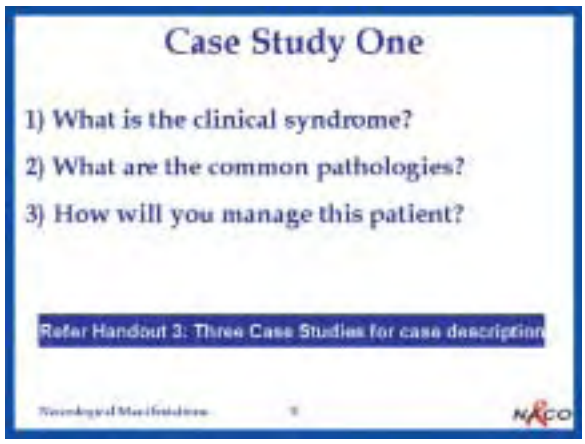
1. **Opportunistic Infections:** Those seen as a result of opportunistic infections:
   - Cryptococcal meningitis
   - Cerebral toxoplasmosis
   - CMV retinitis & encephalitis
   - PMLE
   - Primary CNS lymphoma
   - TB
   - Syphilis
   - The most important of the truly opportunistic infections of the nervous system is cryptococcal meningitis.
   - Although syphilis and tuberculosis can also cause chronic meningitis, these are not strictly opportunistic pathogens, and these problems may be seen in normal hosts as well.

2. **HIV Related:** Those caused by HIV itself
   - Acute aseptic meningitis
   - Chronic meningitis
   - HIV encephalopathy (AIDS dementia)
   - Vacuolar myelopathy
   - Peripheral neuropathy (sensory)
   - Myopathy
   - Acute aseptic meningitis is well described in acute seroconverting illness and is self limiting like any viral meningitis.
   - Other manifestations related directly to HIV usually occur with advanced disease.
     - HIV is known to cause chronic meningitis, but this is rarely fatal.
     - A diagnosis of exclusion and a long follow up is required to rule out other causes like tuberculosis, cryptococcosis and syphilis.
   - **Common** HIV related manifestations are:
     - HIV encephalopathy
     - AIDS dementia complex
     - Peripheral neuropathy
     - Vacuolar myelopathy and myopathy occur very infrequently
   - **Less common** manifestations include:
     - CNS lymphoma
     - Cerebral toxoplasmosis
     - CMV disease
     - Progressive multifocal leucoencephalopathy (PMLE)

Handout 2 : Common Neurological Problems in HIV

Syndrome	Clinical features	Etiology
Chronic Meningitis	Headache, fever, nausea/ vomiting, neck stiffness, altered consciousness	Cryptococcosis, TB, Syphilis
Focal Cerebral Lesions	Headache, focal neurological deficits, seizures	Toxoplasmosis, TB, Cysticercosis PMLE
Encephalitis	Cognitive impairment, psychiatric features, altered consciousness	CMV
Dementia	Cognitive impairment, psychomotor slowing, behavioral disturbance	HIV
Myelopathy	Paraparesis, sensory changes, sphincter disturbances	CMV HIV

- It is best to evaluate the neurological problems seen in PLHA syndromically. The approach can be tailored to resource restricted settings, as in STIs.
  - The commonest serious neurological problem is global cerebral syndrome, where the patient presents with changes to sensorium and/or orientation without focal neurological defects.
    - This is commonly due to chronic meningitis or meningo encephalitis, with tuberculosis, cryptococcosis and syphilis as usual causes.
  - Focal neurological defects may be noted in PLHA with space occupying lesions in the brain parenchyma. An example of this includes toxoplasmosis, PMLE, and lymphoma.
- Cognitive decline in PLWA could be the result of dementia, but infections and other factors such as toxic and nutritional need to be excluded first. Myelopathy is seen rarely and is usually due to vacuolar degeneration secondary to HIV itself. It occurs rarely due to disseminated CMV disease.

Slide 4		
Slide 5		

Handout 3: Three Case Studies

Case Study One

- 38 year-old male, HIV-positive since '98 presents with headache of 3 weeks and confusion of 3 days duration.
- Diagnosed with disseminated TB in Dec 2001, received ATT for 1 year.
- On Co-trimoxazole prophylaxis since then.
- Exam: Oral thrush, but no focal neurological deficits or neck stiffness.

Questions with Answers:

Q.1. What is the clinical syndrome?

Q.2. What are the common pathologies?

Q.3. How will you manage this patient?

Case Study Two

- 32 year-old Mr. J., known PLHA presents with seizures after an episode of clonic movements of the left arm progressingly involving the rest of the body, followed by an unconscious period.
  - Had herpes zoster involving the trunk 6 months ago.
- O/E: moderately built person, not reacting to call.
  - Pupils are equal and reacting to light.
  - Some weakness of the left upper limb as compared to the right, and the planter responses are extensor.
  - Given Diazepam and Phenytoin IV after which his seizures became controlled.

Questions with Answers:

Q.1. What is the clinical syndrome?

Q.2. What are the common pathogen?

Case Study Three

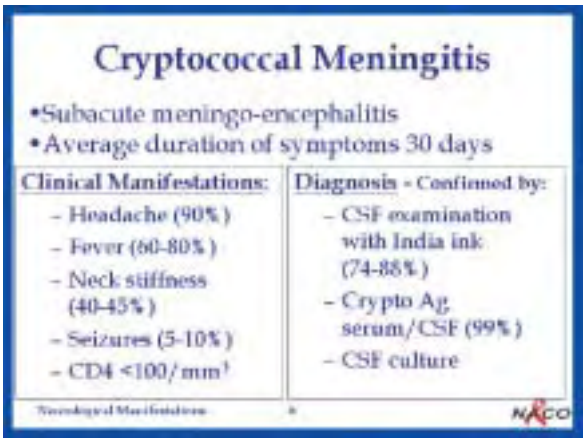
- 45 year-old Mr. Y., an attender at a hotel has been brought for evaluation of strange behaviour.
  - Progressively behaving differently over the last 6 months.
  - Started with loss of recent memory and progressed over time to inability to identify people.
  - Now presents with difficulty in remembering orders and been noted to treat customers to songs.

Questions with Answers:

Q.1. What is the probable diagnosis?

Q.2. How can it be confirmed?

Slide 6



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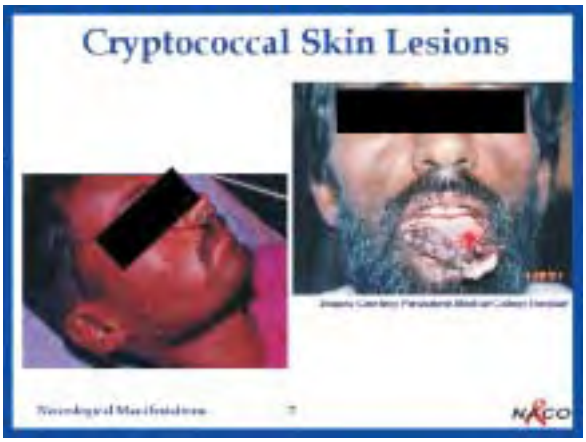


Reader's Notes:

- These slides show Cryptococcal skin lesions. These skin lesions are prognostically important.

Slide 8

Handout 4: NACO Treatment Recommendations for Cryptococcal Infections

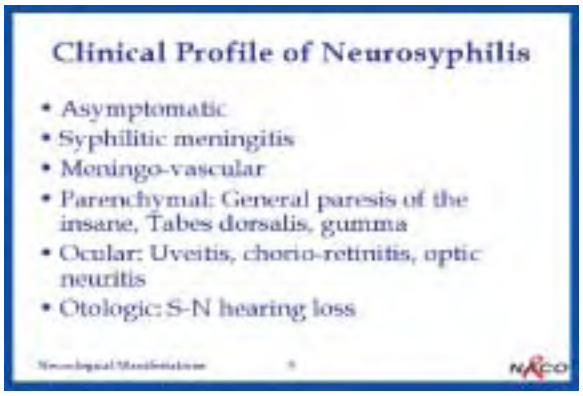
1st Line Treatment for Severe Cases

Antifungal Agent	Dose	Frequency	Route	Duration
Amphotericin B	0.7-1.0 mg/kg	QD	IV	14 days
PLUS				
Flucytosine	25 mg/kg	QD	PO	14 days
THEN				
Fluconazole	400 mg	QD	PO	8-10 weeks
THEN				
Fluconazole	200 mg	QD	PO	For life

Treatment for Mild Cases

Antifungal Agent	Dose	Frequency	Route	Duration
Loading Dose: Fluconazole	800 mg	Single dose	PO	Single dose
THEN				
Fluconazole	400 mg	OD	PO	4-6 weeks
Maintenance Therapy: Fluconazole **OR** Itraconazole	200 mg/kg	OD	PO	For Life

Slide 9



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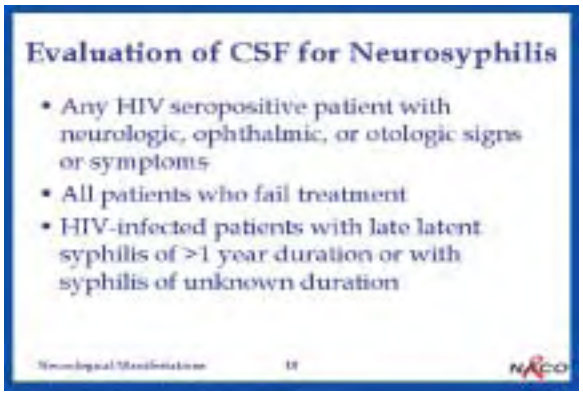
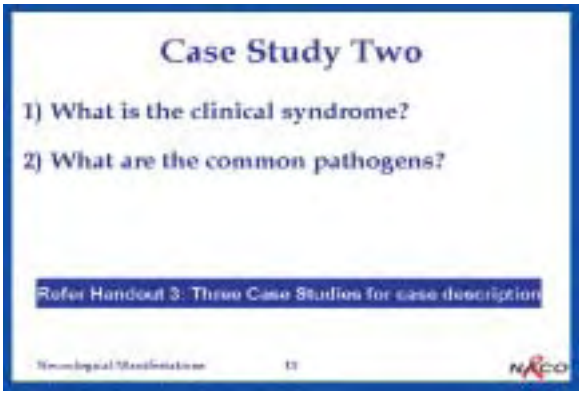


Reader's Notes:

- **Diagnosis** of Neurosyphilis is by:
  - CSF VDRL with abnormal CSF - Pleocytosis (usually 10-400 cells/mm3) and mildly elevated protein (46-200 mg/dL)- confirmatory.
  - Sensitivity of CSF VDRL only ~70%.
  - Abnormal CSF ± positive CSF VDRL + positive peripheral syphilis serology.
- **Treatment** is Penicillin G 30 L units Q4H i.v. x 10-14 days.

Slide 11



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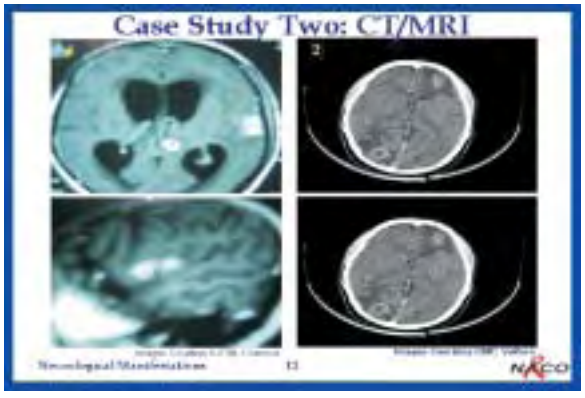


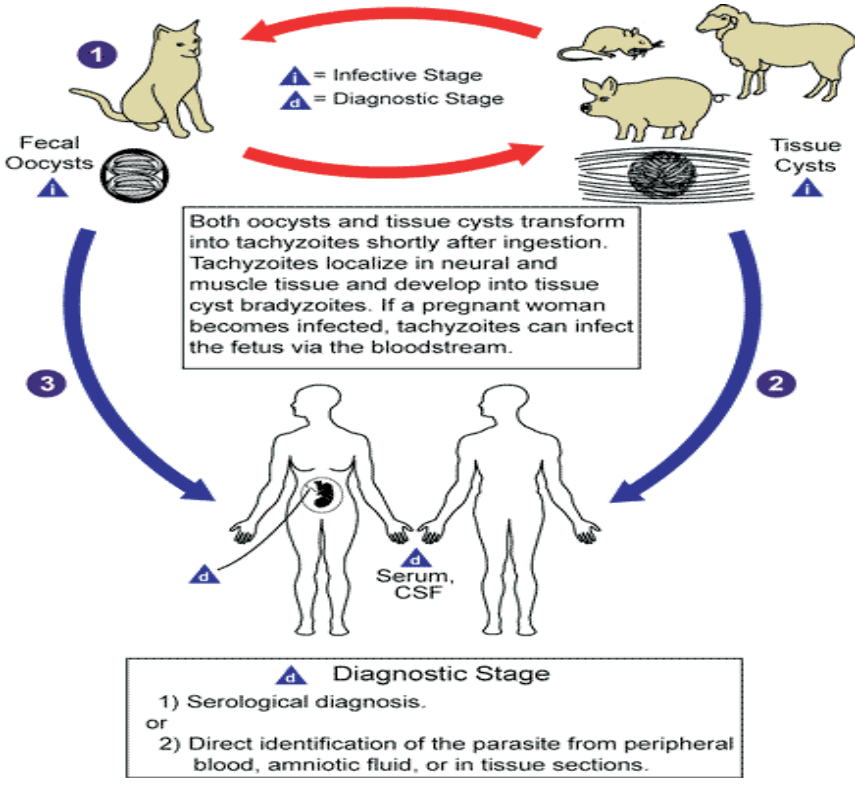
Reader's Notes:

- **Images 1:** A patient with ring enhancing lesion. There is significant oedema around the lesions, which excludes the possibility of a lumbar puncture.
- **Images 2:** Differential diagnosis — Cerebral cysticercosis.

Handout 5: Toxoplasma Encephalitis

Toxoplasma gondii

- Obligate intracellular protozoan
- Commonest cause of CNS mass lesion in AIDS.
- Incidence 5-20%; CD4 <100/mL
- Clinical presentation:
  - Focal neurological deficits (50-89%),
  - Seizures (15-20%), Fever (56%), Generalized
  - Cerebral dysfunction (confusion, coma),
  - Neuro-psychiatric manifestations.
- Diagnosis
  - Presumptive- based on clinical presentation, characteristic lesions, risk strata & positive serology.
  - Serum Toxoplasma IgG usually positive (~97%).
  - Presumptive diagnosis confirmed by tissue sample or response to TOXO therapy in appropriate time frame.



Treatment (for at least 6 weeks, 80-90% response)

Acute:
Sulfadiazine (4-8 gm/d in four divided doses) + Pyrimethamine (100-200 mg x 1st dose; then 50-75mg/d) with Folinic acid (10-20 mg/d).

Alternatives:
Clindamycin /Macrolides (Azithromycin, Clarithromycin) + Pyrimethamine and Folinic acid; TMP-SMX.

Maintenance:
Pyrimethamine 25-50 mg/day + Sulfadiazine 0.5-1.0 g Q6H (life long).

- Consider stopping in patients who have completed primary treatment, are asymptomatic, and have sustained (>6 months) increase in CD4 cell count to >200/µL with HAART.
- ~ 86% patients show clinical improvement by day 7 of treatment & 95% show radiographic improvement by day 14.
  Failure to respond within 14 days - consider alternative diagnosis; indication for brain biopsy.
- The treatment of choice is a combination of sulfadiazine 1-1.5 gm every 6 hours with high dose Pyrimethamine.
- The next best option is high dose Co-trimoxazole, but other options are less efficacious.
- All patients require life long suppressive therapy following cure. This may be withdrawn only after improvement with HAART- CD4 being above 200 cells/µl for at least 3 months.

Prophylaxis
Toxoplasmosis may be prevented by use of Co-trimoxazole as for prevention of PCP. Other drugs are not well studied for primary prophylaxis.

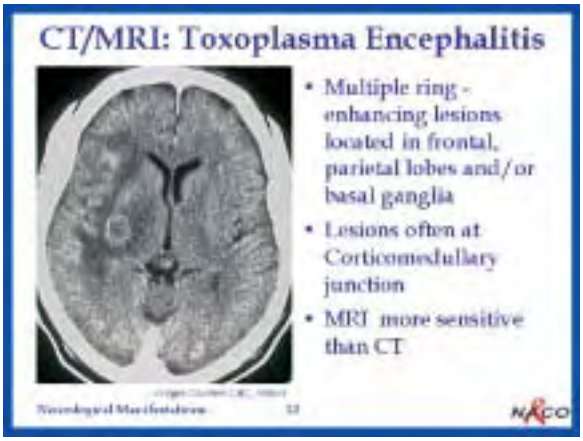
Supportive therapy
Supportive therapy is also important.

- The need for steroids is based on mass effect and oedema as seen on imaging. Anti epileptics may also be needed for control.

Response to therapy

- Response to therapy is both prompt and predictable. Progressive clinical improvement occurs by a week and there is usually a marked reduction in the size of the lesion, if not complete disappearance, when the patient is re-imaged 2 weeks after starting therapy.
- Failure to respond should prompt a search for alternative causes.
- A steriotactic brain biopsy should be considered.

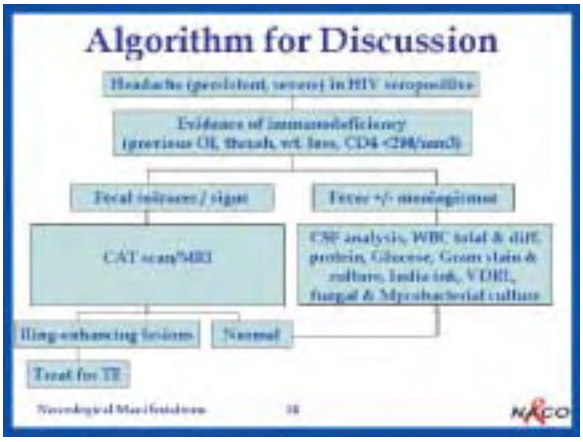
Slide 13

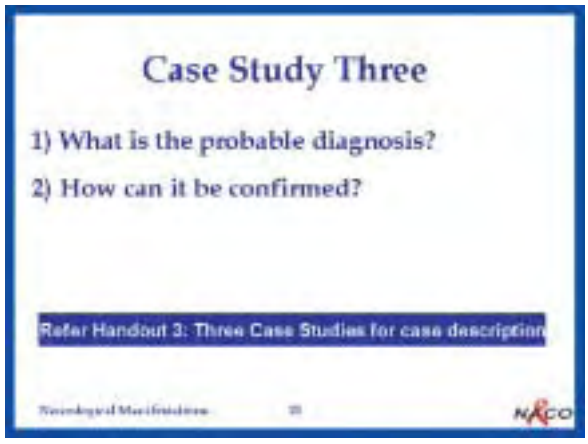


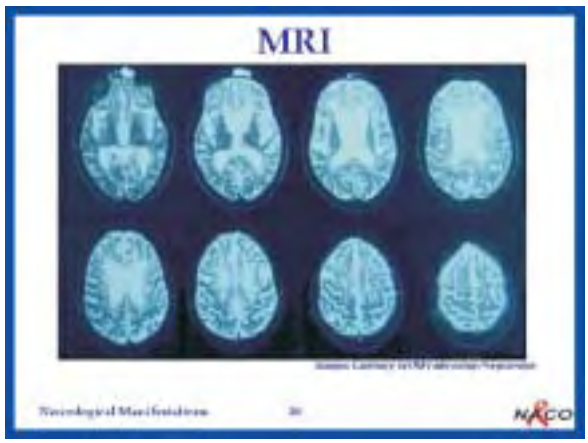
Reader's Notes:

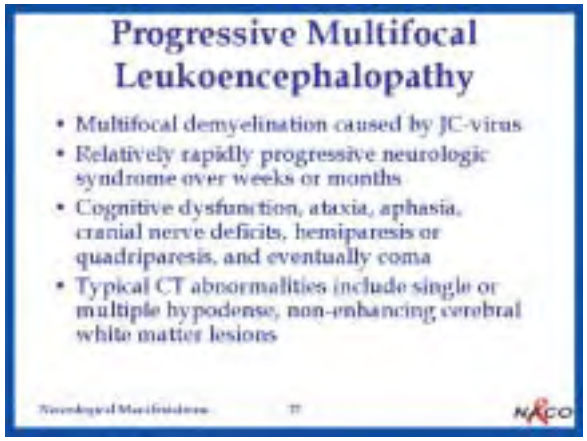
- This slide shows a classic lesion of Toxoplasma gondii infection, with the lesion in the left basal ganglia. There is pronounced perilesional oedema, and the lateral ventricle on the same side is slightly deformed indicating an elevated intracranial tension. In such cases, it is important to assess if there are additional lesions elsewhere.
- ***Toxoplasma gondii*** is an intracellular parasite that causes disease in PLHA when their CD4 count falls below 100 cells/µl.
  - The usual manifestations are focal neurological deficits, fever and seizures, but other manifestations may occur rarely.
  - Imaging by CT scan or MRI is the investigation of choice, as this can give a good estimate of the number and location of the lesions. The lesions have some areas of preference as listed.
- It is important to remember that the **diagnosis** is **presumptive**, based on the presence of a typical presentation, lesions in the classical areas, suggestion of profound immune compromise in the host (or a CD4 <100 cells/µl) and a positive serology for toxoplasma.
  - Confirmation is either by response to therapy or by steriotactic biopsy.
  - Serum toxoplasma IgG titer is an important tool to assist diagnosis.

Slide 14

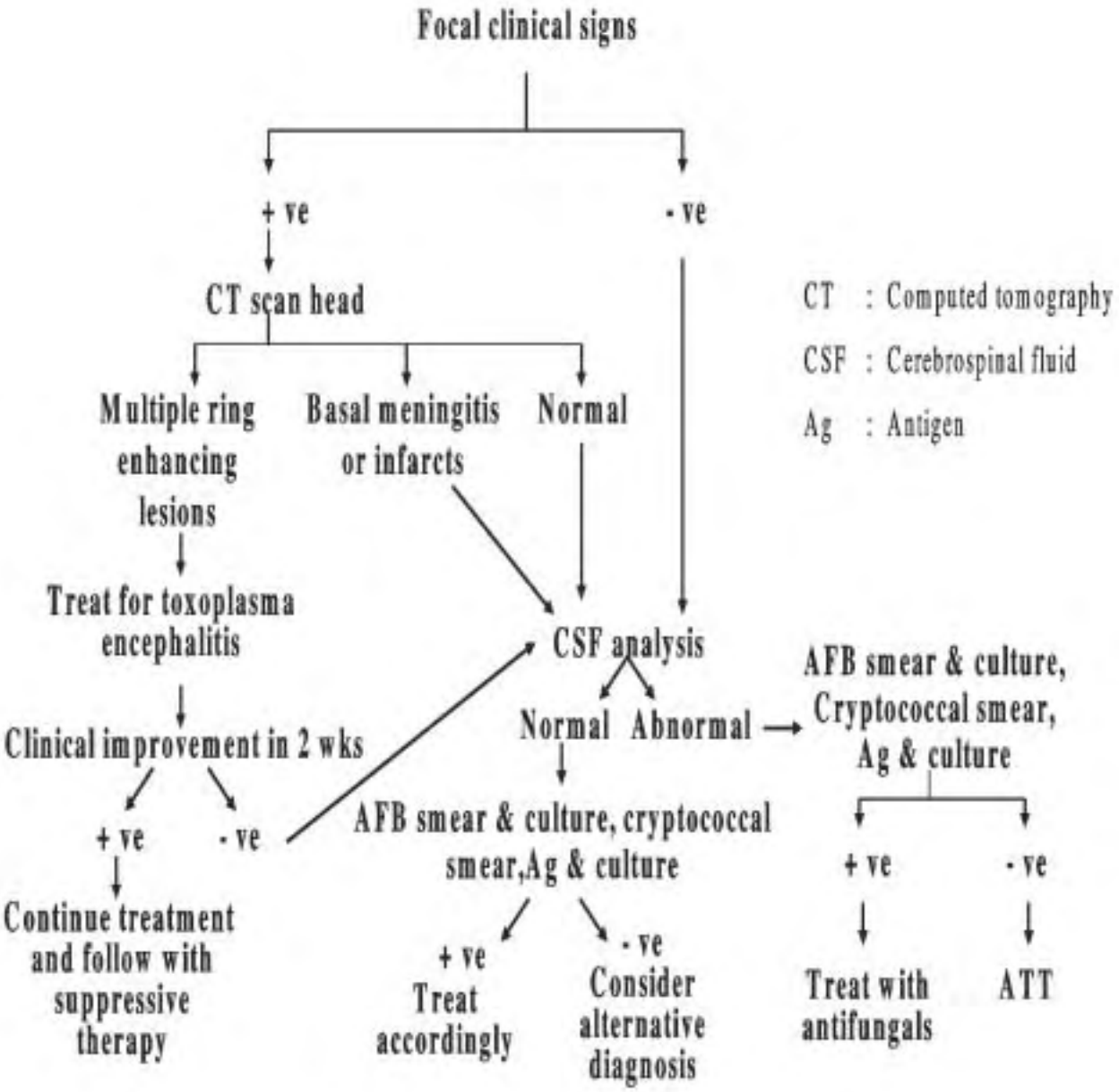


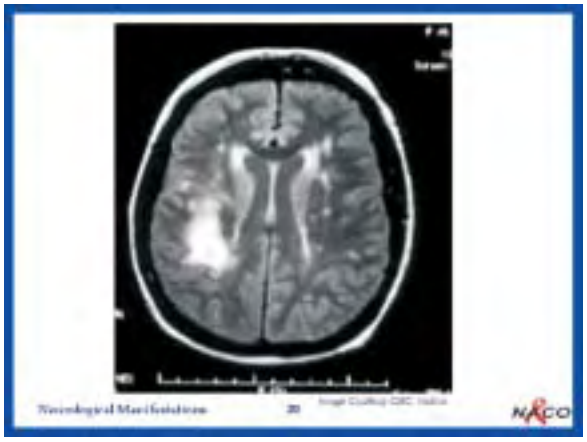
Slide 15		

Slide 16		**Reader's Notes:**
		• This slide shows an MRI of a patient with **AIDS dementia** showing cortical atrophy and also enlargement of the ventricles.
		• Salient features of AIDS dementia include:
		  • CD4 <200 cells/mL.
		  • Slowly progressive.
		  • Acquired, persistent cognitive decline, with motor & behavioural changes.
		  • Neurological exam: alert, with non-focal or diffuse signs.
		  • CSF examination: non-specific.
		  • CT/MRI: cerebral atrophy, ventricular dilatation.
		  • Therapy: HAART; include drugs which cross blood brain barrier.

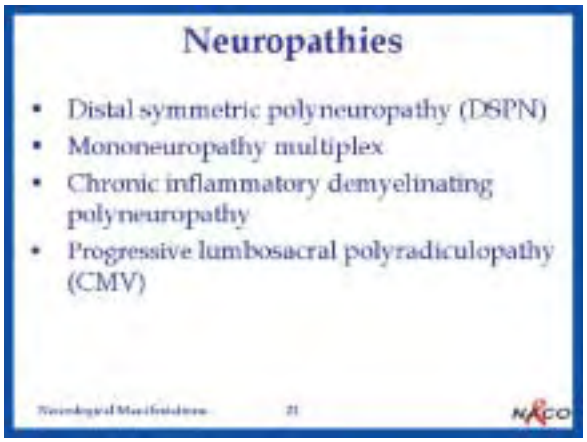
Slide 17		**Reader's Notes:**
		• Progressive multifocal leukoencephalopathy (PML) is caused by
		  • The reactivation of a common virus in the central nervous system of immune-compromised individuals.
		  • Polyomavirus JC (often called JC virus) is carried by a majority of people and is harmless except among those with lowered immune defenses.
		  • The disease occurs, rarely, in organ transplant patients; people undergoing chronic corticosteroid or immunosuppressive therapy; and individuals with cancer, such as Hodgkin's disease, lymphoma, and sarcoidosis.

Handout 6: Algorithm for PLHA with Neurological Problems



Slide 18		**Reader's Notes:** • CT of a patient before developing PMLE. The CT scan was almost normal.
Slide 19		**Reader's Notes:** • The CT scan repeated after 2 years demonstrates the typical picture of PMLE.
Slide 20		**Reader's Notes:** • When a PLHA presents with a neurological problem, the flow chart in **Handout 6: Algorithm for PLHA with Neurological Problems** can be used. • In the presence of focal signs, imaging by CT scan is mandatory to rule out a space occupying lesion. • If there is no such lesion, the most valuable investigation is a CSF analysis by lumbar puncture. The CSF picture will guide the choice of therapy. • In the presence of multiple focal lesions, the patient may be treated empirically with anti toxoplasma therapy, and will need more detailed evaluation if there is no improvement in two weeks.

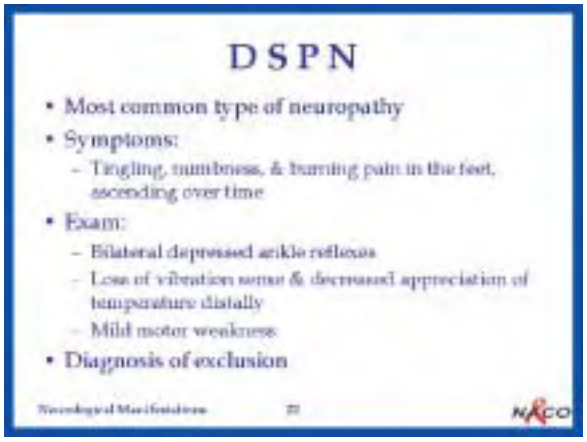
Slide 21



Reader's Notes:

- PLHA have many types of neuropathy that affect the quality of life in a major way. They are classified into four types, as the treatment is different.
- We will discuss **distal symmetric polyneuropathy** (DSPN) on the following slide.
- **Mononeuritis multiplex**, or **multiple mononeuropathies**, can occur as an immune phenomenon and should invoke a search for vasculitis, Hansen's disease and diabetes.
- **Demyelinating polyneuropathy** has been reported and needs steroids for treatment.
- Finally, the occurrence of **radiculopathies** should prompt the consideration of CMV infection.

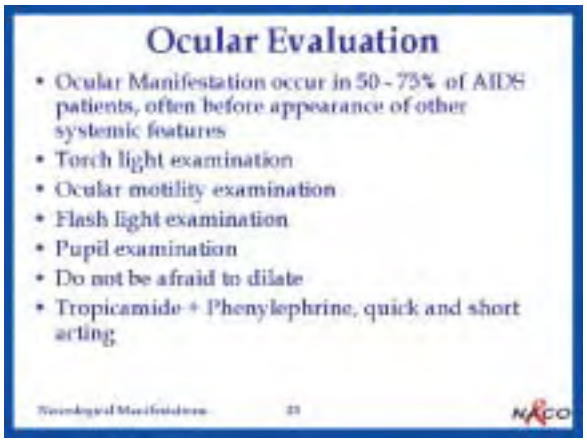
Slide 22



Reader's Notes:

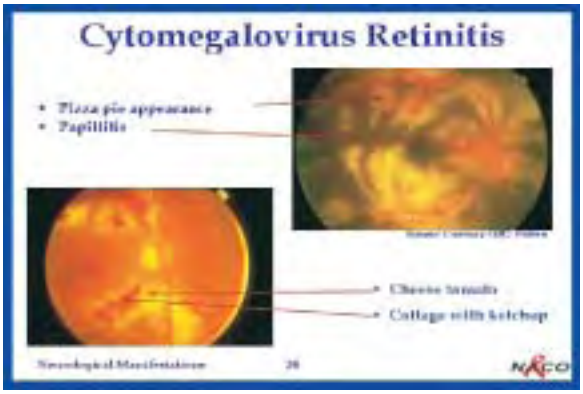
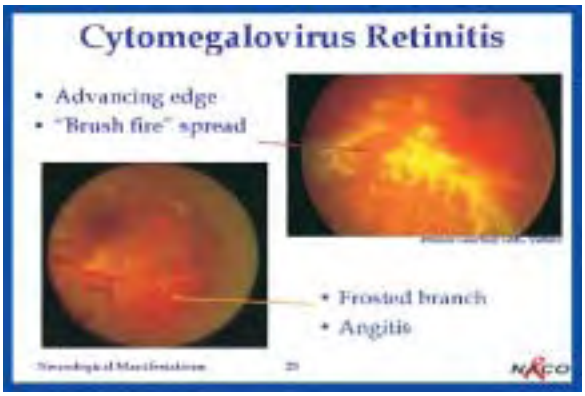
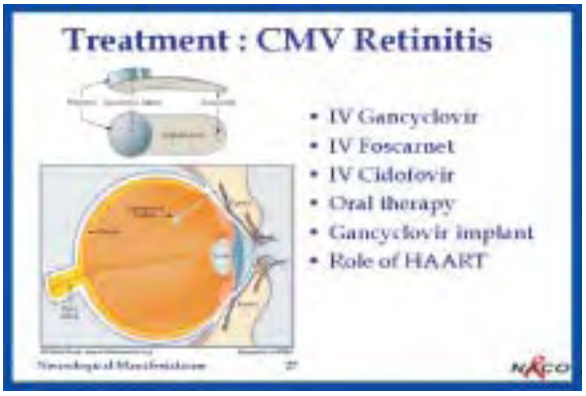
- Distal symmetric polyneuropathy (DSPN) is the commonest form of neuropathy seen.
  - It has predominantly sensory symptoms that are progressive and symmetrical.
  - Motor findings are minimal, and usually not severe.
  - The diagnosis is of exclusion, and very often this is not possible.
  - Patients with this problem are very often on multiple drugs, many of which can cause this problem. (e.g., Isoniazid, Stavudine, and ddI.)
- ***Q.1: "What would you offer a patient with severe neuropathy?"***
- **Answer:**
  - Avoid drugs that cause neuropathy; replace if possible (switch to zidovudine in place of Stavudine).
  - Increase dose of vitamins (in case of nutritional deficiency, or as with Isoniazid).
  - Use of tricyclic drugs like Amitryptylline- no anti epileptics like Carbamazepine - they are enzyme inducers.
  - Support during periods of extreme symptoms.

Slide 23

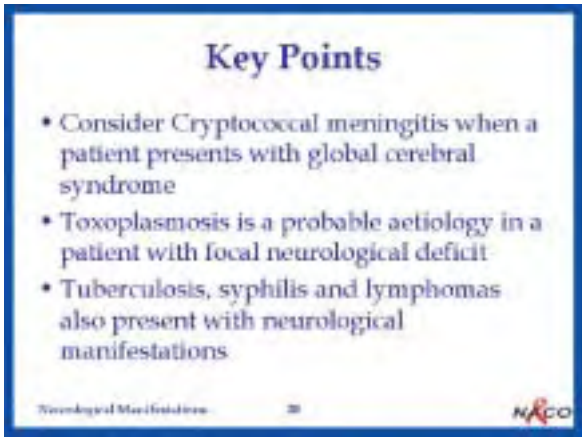


Reader's Notes:

- Dilatation of the pupil is not dangerous unless the patient is at risk for glaucoma, which is rare in younger age groups.
- A dilated pupil yields better visualization of the fundus. This can be achieved by a combination of phenyl ephrine and tropicamide.

Slide 24		
Slide 25		
Slide 26		
Slide 27		**Reader's Notes:** • Treatment of CMV infection of the eye presents two options- systemic therapy (iv or oral) and implant therapy. • Systemic therapy is toxic and expensive. • The incidence of serious, life threatening side effects is about one third of all patients receiving IV ganciclovir. Foscarnet is very nephrotoxic. Cidofovir is still not available in India. • Oral drugs are being developed for convenience and the oral analog, valganciclovir, is preferred for suppressive prophylaxis. • Intravitreal implants are preferred due to decreased

		• toxicity, but this requires availability of materials and technical expertise for administering the drug. **Intra-vitreal injection - in 0.1ml.**
		• Gancyclovir:
		  • Induction — 200-4000mcg 3/week.
		  • Maintenance — 200-4000mcg weekly.
		• Foscarnet
		  • Induction — 1.2-2.4mg 2/week.
		  • Maintenance — 1.2mg/week.
		• Cidofovir
		  • Induction/maintenance — 20mcg/5weeks.
		• Remember that all patients recovering from invasive CMV disease require life long suppressive prophylaxis. The only situation where this can be discontinued is after initiation of HAART.
		• Starting HAART in such a patient improves the chances of clearing the virus, but will not restore the damage to the tissue. If HAART is started without anti CMV therapy, there is high risk of IRIS, and this can result in complete damage to the eye. If IRIS were to occur, steroids for a short duration is likely to be of benefit.
		• **Source:** website: http://www.cognitionstudio.com/anatomy/042506_vitrasert.jpg.

Slide 28		

SESSION 20-22

DAY - EIGHT

SESSION 20

SESSION

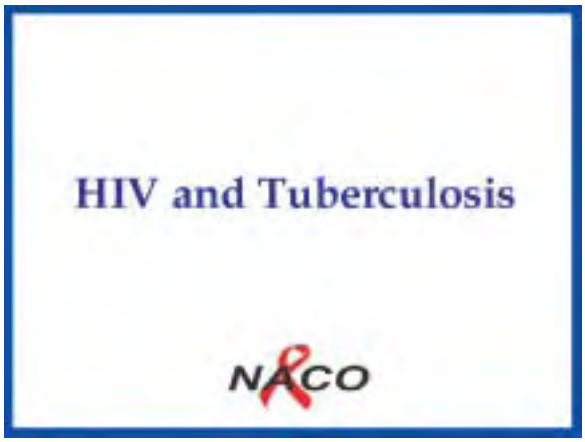
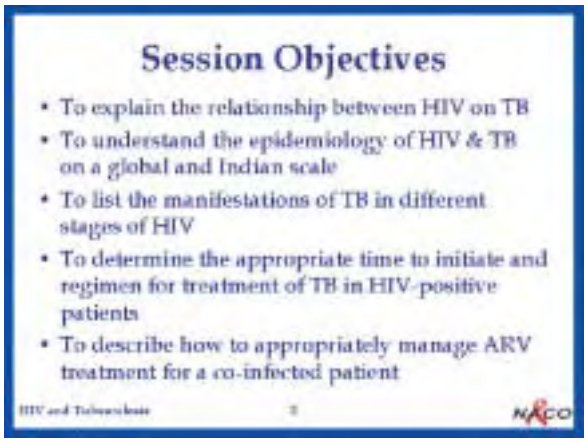
HIV AND TUBERCULOSIS

20

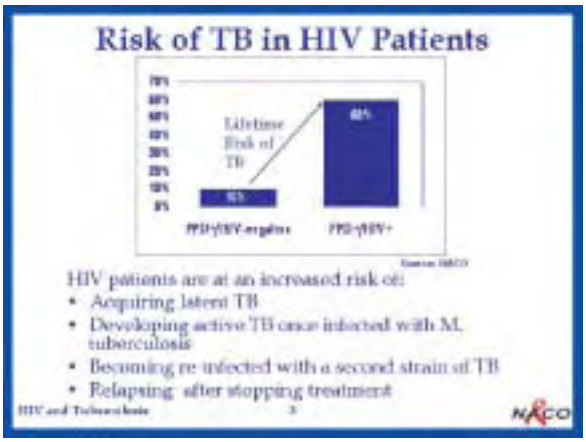
Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Explain the relationship between HIV on TB
- Understand the epidemiology of HIV & TB on a global and Indian scale
- List the manifestations of TB in different stages of HIV
- Determine the appropriate time to initiate and regimen for treatment of TB in HIV-positive patients
- Describe how to appropriately manage ARV treatment for a co-infected patient

Slide 1		
Slide 2		

Slide 3

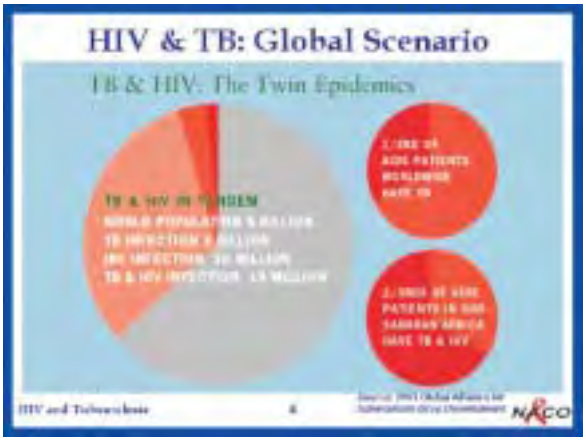


Reader's Notes:

Risk of tuberculosis associated with HIV:

- The life time risk of developing active tuberculosis in PPD positive normal host is about 10%; in comparison, the risk of active tuberculosis in a PPD positive HIV infected person is about 60%.
- HIV can be a powerful driver of the tuberculosis epidemic. This effect has been noted in many populations and studies. One example is a study done in Chiang Mai, Thailand.
- The number of HIV negative tuberculosis patients has remained more or less constant, but with the HIV epidemic, the total number of cases of tuberculosis has increased, as a reflection of the driving force that HIV has on tuberculosis. On further follow up, it was noted that the number of cases of tuberculosis noted in those HIV negative also increased.
- **Source:** WHO/GTB. Second Review of the National Tuberculosis Programme in Thailand, July 1999. Department of Communicable Disease Control, Ministry of Public Health Thailand & WHO 1999. HO/CDS/TB/99.273. http://www.who.int/tb/publications/en.

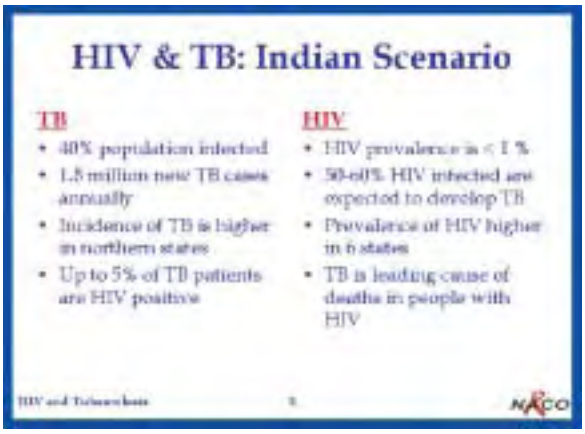
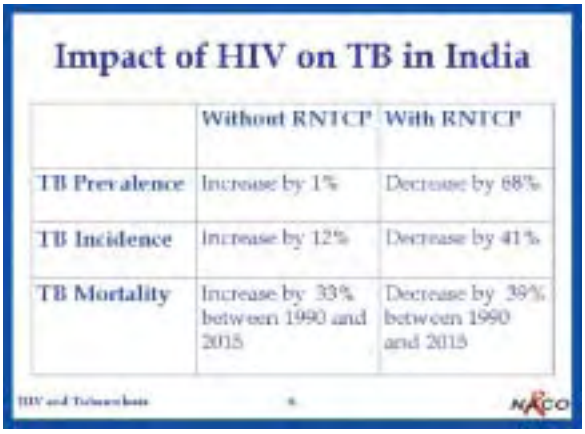
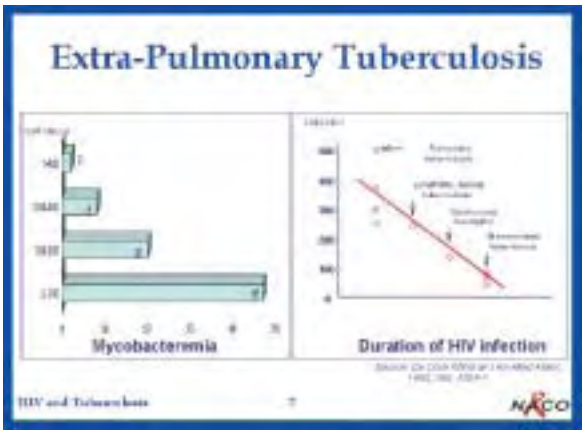
Slide 4



Reader's Notes:

- On average, about half of HIV patients will develop tuberculosis in their lifetime.
- Tuberculosis is still the leading cause of death in PLHA.
- More than 1.5 crore people are co-infected with HIV and tuberculosis globally.
- Half of all new global cases of TB (4.5 million of 9 million) each year are in six Asian countries — Bangladesh, China, India, Indonesia, Pakistan and the Philippines. (Source: www.stoptb.org - WHO and Stop TB Partnership, The Global Plan to Stop TB 2006-2015.)
- Worldwide, 15 million people are co-infected with TB and HIV — 70% of them are concentrated in Africa.
  - In 2003, an estimated 9% of all new tuberculosis patients were HIV co-infected.
  - In some regions of Africa, 75% of TB patients are HIV-infected.
- Effect of HIV on TB is most striking in Africa where 29% of TB is attributable to HIV.
- Rising TB incidence in Africa is offsetting the stable or falling TB incidence in the rest of the world.

		• Global TB incidence continues to rise by 1% per annum.
		  • In 2003, an estimated 15% (~230,000) of all TB deaths (1.7million) were HIV positive.
		  • TB causes at least 13% of AIDS deaths and possibly as many as 50%. (Source: http://www.who.int/mediacentre/factsheets/fs104/en/).

Slide 5		**Reader's Notes:** • In the Indian context, about 40% of the population is infected with tuberculosis, whereas less than 1% with HIV. • 1.8 million patients develop TB annually, most are in the north, although HIV is seen more in the south. • ***Ask participants to think about the future impact of HIV on TB in India and predict the TB trends in prevalence, incidence and mortality. Ask participants what other factors might impact these trends. (See next slide for two different scenarios).*** • Source: www.nacoonline.org/publication: HIV-TB Co-infection: A Guide for Medical Officers (2004).
Slide 6		
Slide 7		**Reader's Notes:** • This graph shows the relationship between the immune status of the PLHA and the mycobacteremia (graph on the left side) and the type of tuberculosis (graph on the right side). • Primary tuberculosis occurs more often when the immune status is very good, like in a normal host. As the immunity wanes, the chance of developing tuberculosis in other areas increases- notably lymphatic, meningeal and disseminated forms. • Source: De Cock K M, Soro B, Coulibaly I M, Lucas S B. Tuberculosis and HIV infection in sub-Saharan Africa. JAMA 1992; 268:1581—1587.

Handout 1 : Extra-Pulmonary Tuberculosis

Presentations of Extra-pulmonary TB:

Lymphatic

- Commonest extra-pulmonary site.
- Peripheral.
- Intrathoracic.
- Intra-abdominal with necrosis (accompanying visceral involvement).

Disseminated

- Miliary or more than one XP site.
- Mycobacteremia.

TB Meningitis

- CSF findings may be normal.

Skin

- May co-exist with pulmonary TB.
- Erythematous papules, purpura, subcutaneous nodules, pustules.
- Biopsy- little granuloma, AFB+.

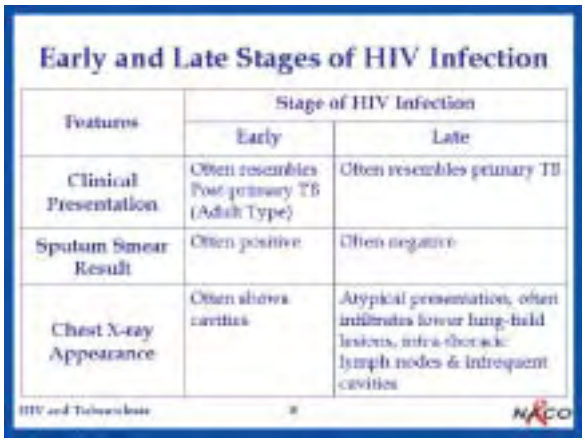
Hepatosplenic

- Round, hypo echoic, multiple lesions <1 cm.

Laryngeal

- Highly contagious, usually sputum positive, make presents as throat clearing or cough.

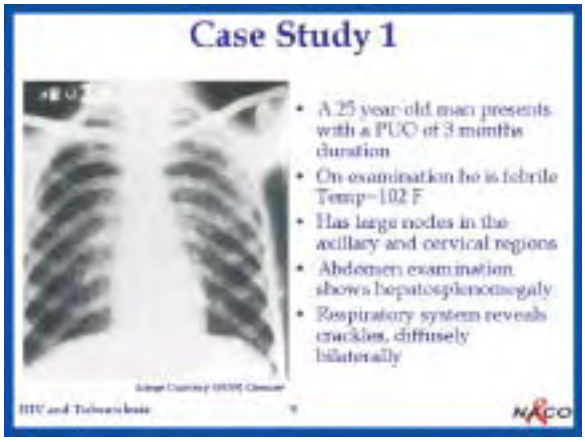
Slide 8



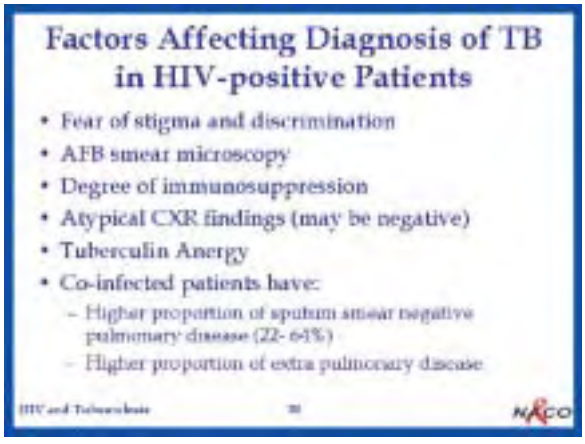
Reader's Notes:

- This slide describes the clinical presentation, sputum status and the radiological pictures of TB in early and late HIV disease.
- In HIV negative patients, pulmonary involvement is very common. Upper lobe involvement with cavitation and sputum positivity are also very common.
- In late HIV infection, adenopathy, pleural effusion, lower lobe involvement and miliary pattern are seen. Although pulmonary involvement is seen, the incidence of disseminated disease is more common and these patients are less likely to be sputum positive.
- In early HIV, tuberculosis presents between these two ends of the spectrum.
- **Source:** www.nacoonline.org/publication: HIV-TB Co-infection: A Guide for Medical Officers (2004).

Slide 9



Slide 10

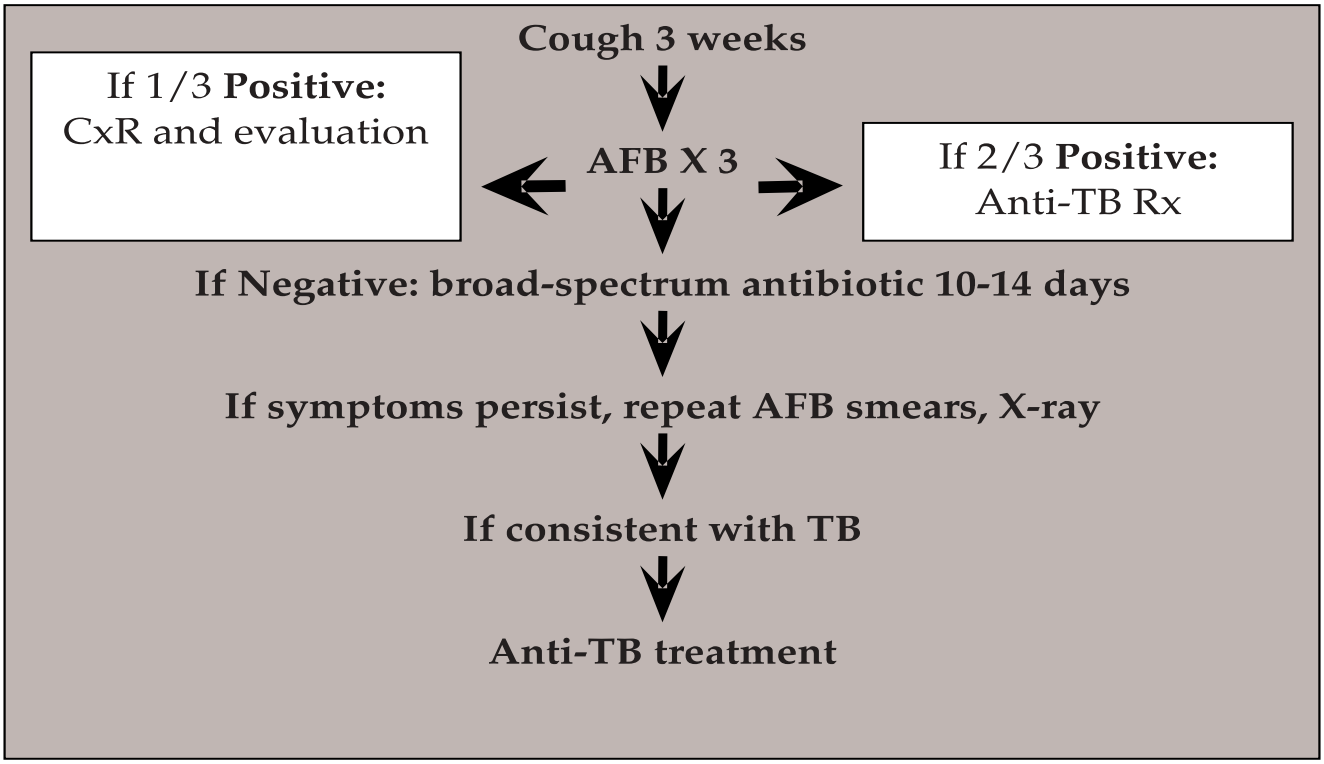


Source: R. Colebunders, I. Bastian. A review of 0diagnosis and treatment of smear-negative pulmonary tuberculosis. 2000. Int J Tuberc. Lung Dis.4(2):97—107.

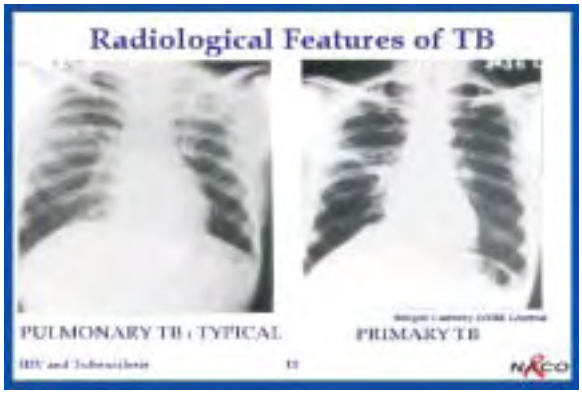
Handout 2: Diagnosis of Pulmonary TB

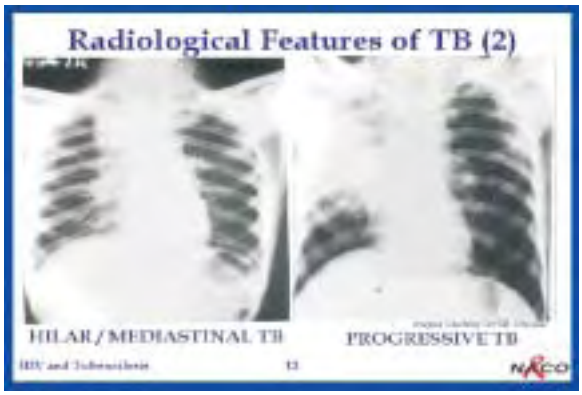
- The diagnostic algorithm recommended by WHO allows for rapid diagnosis. If patient's symptoms like cough persist for more than 3 weeks, sputum smears should be taken and tested.
- If negative, even after a course of antibiotics, an x-ray is obtained.
- If x-ray finding is consistent with TB, anti-TB treatment should be given.

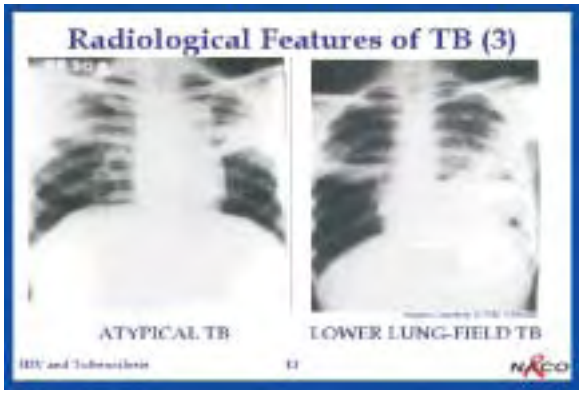
This diagnostic approach will result in diagnosis of tuberculosis more rapidly than culture in most settings. If this approach is followed, there should be no more than one new smear-negative case of pulmonary tuberculosis for each new smear-positive case of tuberculosis, except in situations where there are a large number of persons with advanced HIV disease.

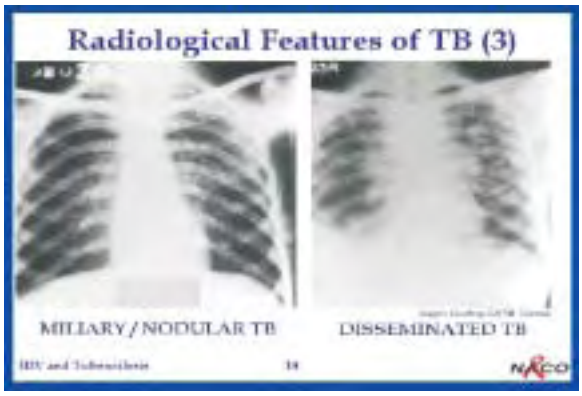


- **Source:** Global Tuberculosis Control: WHO Report 1999 (WHO/TB/99.259) and World Health Organization. Treatment of tuberculosis. Guidelines for national programs. (Second Edition.) WHO/TB/97.220,1997.

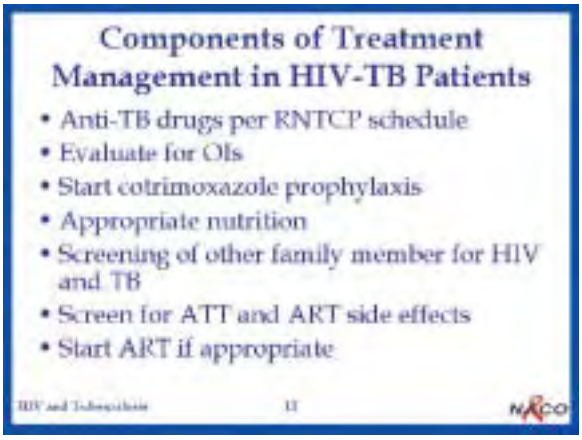
Slide 11		**Reader's Notes:**
		• The x-rays show the different radiological features of tuberculosis in HIV patients:
		  • Left side: A typical picture of left apical cavitary TB.
		  • Right side: Picture resembling primary complex with pleural, parenchymal and hilar components.
		• **Source:** Government Hospital of Thoracic Medicine, Tambaram Sanatorium, Chennai, India.

Slide 12		**Reader's Notes:**
		• The x-rays shows
		  • Left side : A picture of hilar and mediastinal tuberculous lymphadenopathy.
		  • Right side : A picture of progressive pulmonary TB, with hilar and parenchymal involvement.

Slide 13		**Reader's Notes:**
		• The x-rays show atypical involvement:
		  • Left side : Billateral apical involvement with superior mediastinal widening due to mediastinal lymphadenopathy.
		  • Right side: bilateral lower lobe involvement.

Slide 14		**Reader's Notes:** • The x-rays depict the miliary (left side) and disseminated form (right side) of TB.

Slide 15



Reader's Notes:

- In a patient with HIV-TB co-infection, the treatment components are:
  1. Anti-TB drugs as per RNTCP guidelines.
  2. Exclude other opportunistic infections.
  3. Co-trimoxazole prophylaxis.
  4. Appropriate nutrition.
  5. Screening of other family members not only for HIV but also for TB.
  6. Screen for the drug toxicities, both ATT and ART.
  7. Start ART at the appropriate stage depending upon the CD4 count, as per the NACO ART guidelines.

Handout 3a: Revised National Tuberculosis Control Programme (RNTCP) Treatment Categories and Schedules

Category of treatment	Type of patient	Regimen
CAT I	New sputum smear positive	$2(HRZE)_3\ 4(HR)_2$
	Seriously ill smear negative	
	Seriously ill extra pulmonary	
CAT II	Sputum smear positive positive relapse	$2(HRZES)_3/1(HRZE)_3/5(HRE)_3$
	Sputum smear positive failure	
	Sputum smear positive treatment after default	
CAT III	Sputum smear negative not seriously ill	$2(HRZ)_3/4(HR)_3$

*The number before the letters (e.g. 2(HRZ)3/4(HR)3) refers to the number of months of treatment. *The subscript after the letters refers to the number of doses per week. *HRZE stands for: H: Isoniazid (600mg), R: Rifampicin(450mg) , Z: Pyrazinamide (1500mg), E: Ethambutol (1200mg).

- Patients who weigh more than 60Kg receive additional Rifampicin 150 mg.
- Patients more than 50 years old receive Streptomycin 500mg.
- Patients in categories I and II who have positive sputum smear at the end of the initial intensive phase receive an additional month of intensive treatment.
- Examples of seriously ill extrapulmonary cases are meningitis, disseminated TB, tuberculous Pericarditis, peritonitis, bilateral extensive pleurisy, spinal TB with neurological complications and intestinal and genitourinary TB.
- In rare and exceptional cases, patients who are sputum smear negative or who have extra pulmonary disease can have relapse or failure. This diagnosis in all such cases should always be made by an MO and should be supported by culture or histological evidence of current active tuberculosis. In these cases, the patient should be categorized as "Other" and given Category II treatment.
- Any patient treated with Category I or Category II who has a positive smear at 5, 6, or 7 months of treatment should be considered a failure and started on Category II treatment afresh.

Phases and Duration of Treatment

Category	Duration(Number of doses)		Total
	Intensive phase	Continuation phase	
CAT I	8 weeks(24 doses)	18 weeks(54 doses)	26 weeks(78 doses)
CAT II	12 weeks(36 doses)	22 weeks(66 doses)	34 weeks(102 doses)
CAT III	8 weeks(24 doses)	18 weeks(54 doses)	26 weeks(78 doses)

- Source: http://www.tbcindia.org/documents: Technical and Operational Guidelines for Tuberculosis Control.
- According to the RNTCP Guidelines, all patients with sputum positive pulmonary tuberculosis and those with extensive parenchymal involvement or those with severe forms of extra pulmonary involvement can be considered for category I ATT.
- Patients with sputum negative pulmonary tuberculosis and less severe forms of extra pulmonary disease qualify for category III ATT.
- Patients who have failed therapy- remain sputum positive after 3 months of continuous therapy or have relapsed or have treatment interruption are candidates for category II ATT.
- All HIV infected patients co infected with tuberculosis will be classified as severe involvement, making them automatically eligible for category I ATT. Besides, there is an option for extending the maintenance phase by another 2-3 months at the discretion of the physician and this could be valuable in the instance of severe involvement like meningitis.
- Moreover the category 3 in the RNTCP guideline is no longer useful in HIV-TB coinfection.

Treatment Schedule for TB in HIV-Positive Patients

Treatment Category Phase	TB Patients	Regimen	
		Intensive Phase	Continuation
CAT I	• New smear-positive pulmonary TB • New smear-negative pulmonary TB with extensive parenchymal involvement • New cases of severe forms of extra-pulmonary TB with HIV disease	$2(EHRZ)_3$ (24 doses)	$4(HR)_3$ (54 doses)
CAT II	• Sputum smear-positive relapses • Sputum smear-positive treatment failure cases • Sputum smear-positive cases requiring treatment after interruption	$2(SEHRZ)_3$ + $I\ (EHRZ)_3$ (24+12 doses)	$5(HRE)_3$ (66 doses)

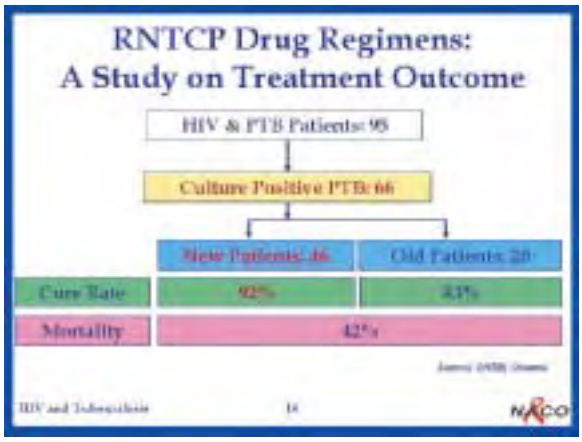
Handout 3b : Role of Steroid Therapy

There are few situations where steroid medications are indicated in HIV-TB co-infection. They are listed below.

- Indications:
  - TB meningitis/cerebral involvement.
  - TB pericardial effusion.
  - TB adrenal involvement.

- Schedule:
  - Prednisolone 60 mg OD for 2 weeks and then taper over four weeks.

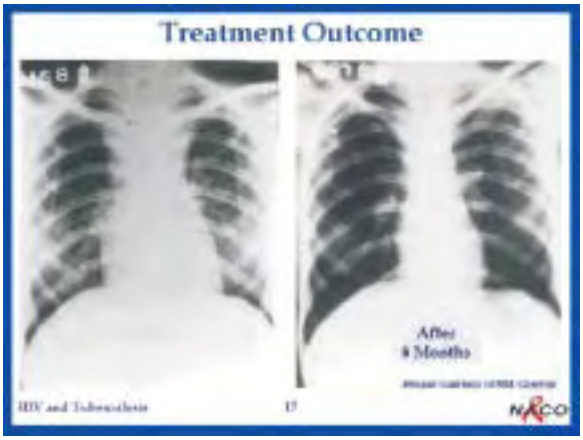
Slide 16



Reader's Notes:

- In this study from Tuberculosis Research Center, Chetpat, Chennai and the Government Hospital of Thoracic Medicine, Tambaram Sanatorium, Chennai the cure rates for pulmonary tuberculosis with DOTS therapy was found to be very good, favoring the use of shorter duration (6 months-RNTCP guideline) of treatment.
- In a review of six month therapy for tuberculosis, the authors concluded that the cure of tuberculosis was not influenced by the HIV status of the host. Treatment success and effectiveness were also similar; however, there was marked increase in relapse rates for PLHA, as noted earlier.
- The two studies clearly show that standard DOTS therapy is ideal. Duration of six months is acceptable in most cases; treatment is as effective as in normal hosts; relapse rates are higher and survival is lower, and not related to duration of treatment.
- **Source:** Abstract 764 Recurrent Tuberculosis and Mortality Are High in Patients with Advanced HIV Disease Treated with Short-course Chemotherapy S Swaminathan*1, S Rajasekar2 et al : 11th Conference on Retroviruses and OIs, 2004.

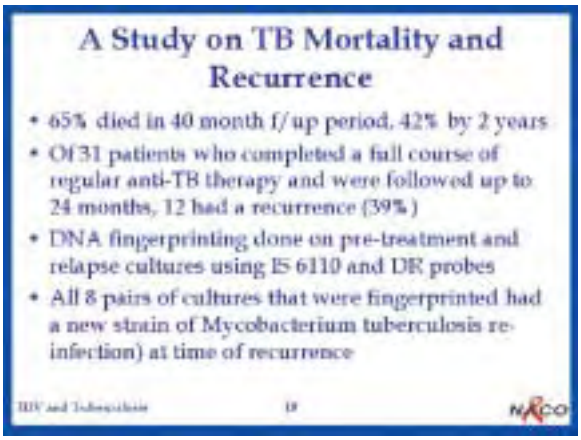
Slide 17



Reader's Notes:

- This x ray shows the effectiveness of a 6-month treatment. The TB mediastinal lymphadenopathy and the opacities on both the lower zones have cleared after a 6 month course of Anti-TB Treatment.

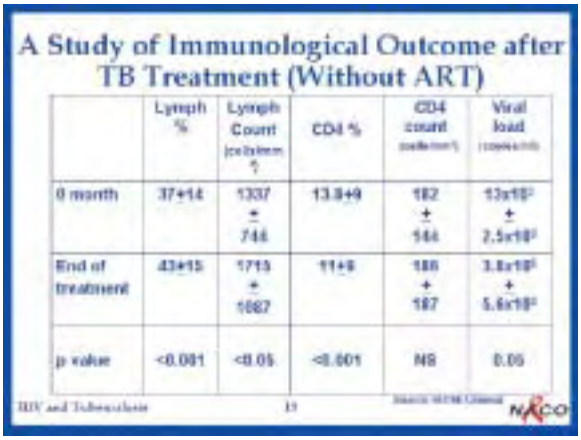
Slide 18



Reader's Notes:

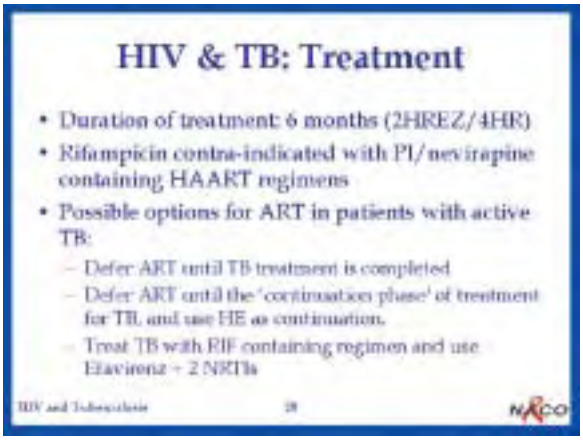
- In the same study cited earlier in slide 16 done at Tambaram, patients who had a relapse of tuberculosis after successful cure were re-analyzed using advanced molecular techniques (DNA fingerprinting) and it was noted that at least a significant number of these recurrences are actually re-infection with a new strain of mycobacterium tuberculosis.
- Source: Abstract 764 Recurrent Tuberculosis and Mortality Are High in Patients with Advanced HIV Disease Treated with Short-course Chemotherapy S Swaminathan*1, S Rajasekaran et al 11th Conference on Retroviruses and OIs, 2004.

Slide 19



Reader's Notes:

- This study researched immunological and the viral outcome.
- It revealed that there is no improvement in the immunological profile after treatment with only Anti-TB Treatment and the virological outcome is also poor. It indicates the need for concomitant ART to have a good immunological and virological outcomes in HIV-TB coinfection.
- Source: Pulmonary Tuberculosis in HIV Positive Individuals : Preliminary Report on clinical Features and Response to Treatment, Soumya Swaminathan, M. Sangeetha, N. Arunkumar, P.A. Menon, Beena Thomas, K. Shibi , Ponnuraja and S. Rajasekar Ind.J Tub.,2002,49,189.

Slide 20		

HIV & TB: Treatment
• Duration of treatment: 6 months (2HREZ/4HR)
• Rifampicin contra-indicated with PI/nevirapine containing HAART regimens
• Possible options for ART in patients with active TB:
– Defer ART until TB treatment is completed
– Defer ART until the 'continuation phase' of treatment for TB, and use HE as continuation.
– Treat TB with RIF containing regimen and use Efavirenz + 2 NRTIs

Handout 4: ART Recommendations for Individuals with Tuberculosis Disease andHIV Coinfection

CD4 cell count (cells/ mm3)	Timing of ART in relation to start of TB treatment	ART recommendations
CD4 < 200	Start ATT first. Start ART as soon as TB treatment is tolerated (between 2 weeks and 2 months) (i)	Recommend ART. (ii) EFV containing regimens (iii)
CD4 between 200-350	Start ATT first. Start ART after 8 weeks of ATT.(ie. completion of TB intensive phase)	Recommend ART (vi)
CD4 > 350	Start ATT first.Re-evaluate patient for ART at 8 weeks and at end of TB treatment	Defer ART (iv)
CD4 not available	Start ART between 2 and 8 weeks after ATT initiation	Recommend ART (i,v)

Notes:

i Timing of ART initiation is based on clinical judgment as per other signs of immunodeficiency and WHO clinical staging. For extra pulmonary TB, ART should be started as soon as TB treatment is tolerated irrespective of CD4 cell count.

ii ART should be started as soon as TB treatment is tolerated, particularly in patients with severe immunosuppression

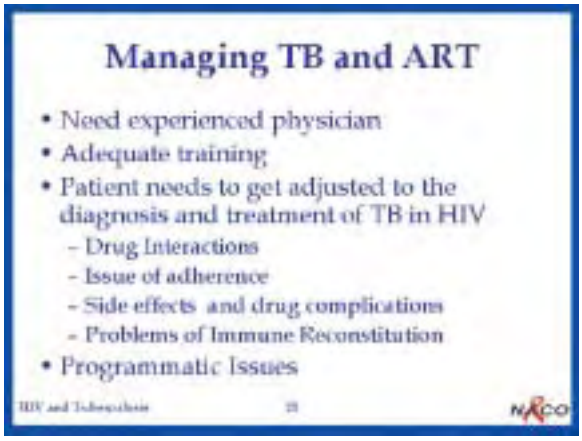
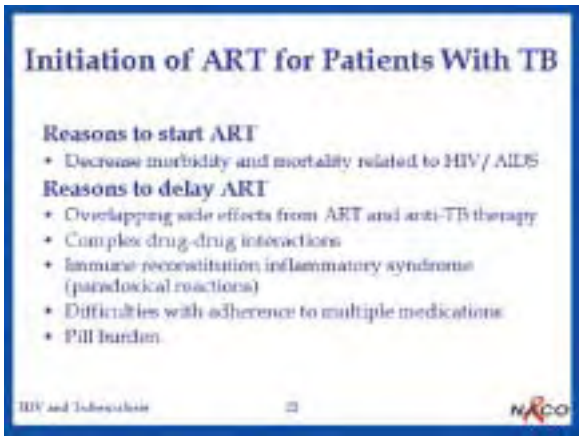
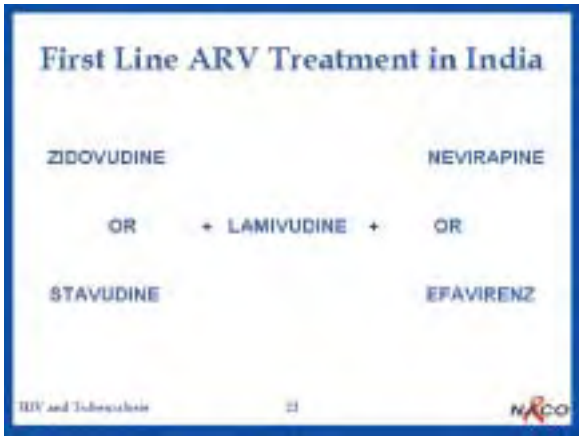
iii EFV containing regimens include d4T/3TC/EFV or AZT/3TC/EFV.

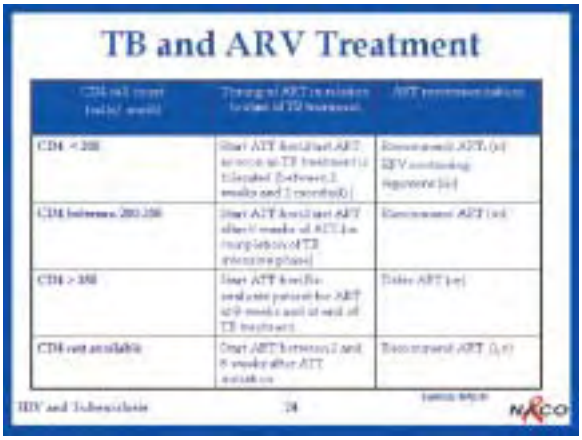
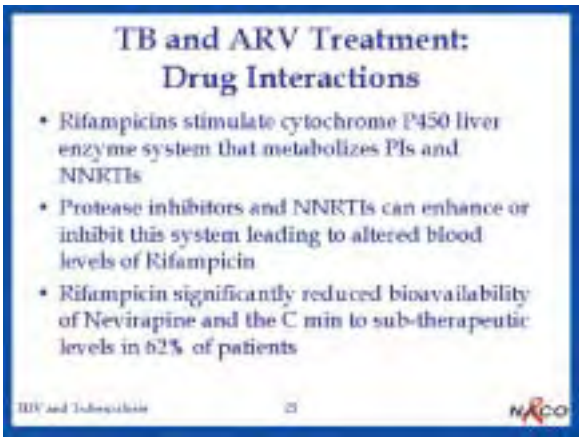
iv ART should be started if other non-TB stage 3 or 4 events are present

v For some TB diagnoses that generally respond well to anti-TB therapy (ie lymph node TB, uncomplicated pleural effusion) or some cases where uncomplicated pulmonary TB disease is responding well to TB treatment, consider deferring ART initiation.

vi **Rationale for ART recommendation during TB treatment (6,7,8,9,10,11)**

- HIV infected patients with CD4 cell count 200-350 cells/mm^3 are at increased risk to develop active tuberculosis, even in regions with high baseline TB prevalence.
- HIV-infected patients with CD4 cell count between 200-350 cells/mm^3 and active tuberculosis are at greater risk for AIDS and death, in comparison to HIV-infected patients without TB with the same CD4 cell counts.
- In the absence of ART, TB therapy alone does not significantly increase CD4 cell counts, nor significantly decrease HIV viral load among TB-HIV infected patients. Thus, CD4 counts measured during active TB are likely to reflect the actual level of immunosuppression.
- The use of HAART among patients with TB can lead to sustained reductions in HIV viral load, immunologic reconstitution, decrease in AIDS defining illness, and decreased mortality. This benefit is seen across CD4 cell counts.
- Source : NACO

Slide 21		
Slide 22		
Slide 23		

Slide 24		
Slide 25		**Reader's Notes:** • **Source:** J Acquir Immune Defic Syndr 2006 Apr26 (Epub ahead of print), Increasing Nevirapine dose can overcome Reduced Bioavailability due to Rifampicin Co-administration. Ramachandran G, Hemanthkumar AK, Rajasekaran S, et al.

Handout 5: TB and ARV Drug Interactions

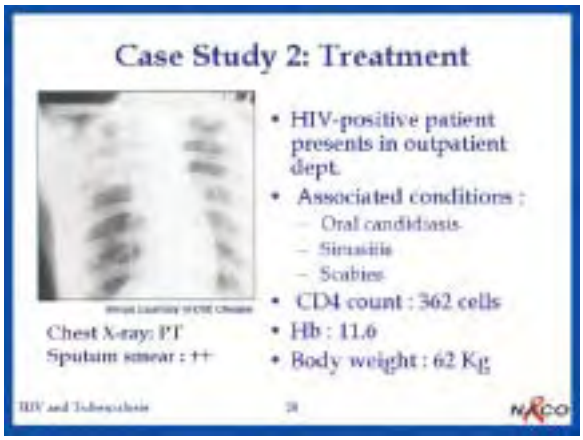
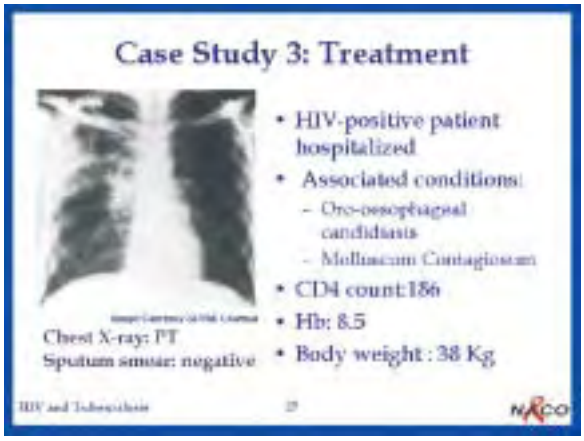
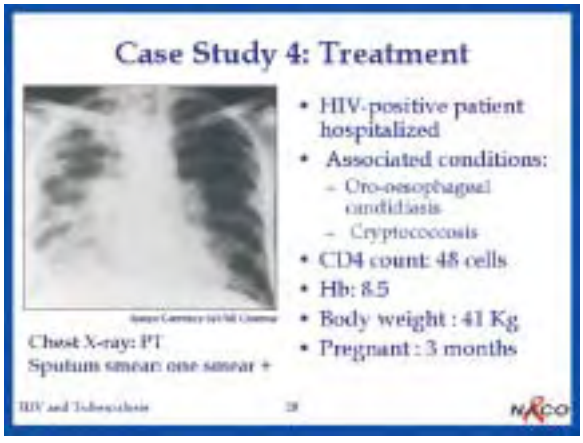
Rifampicin Interactions for NNRTIs & PIs

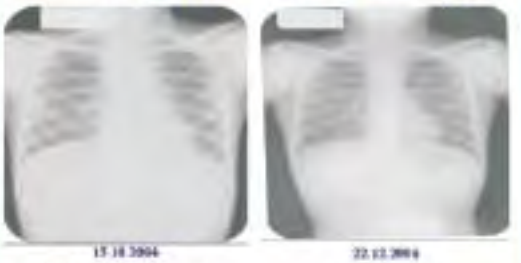
Antimycobacterials	NVP	EFV	IDV
Rifampin Recommendation	Decreased 40% Do not co-administer	Decreased 25-33% Consider EFV 800 mg daily	Decreased 89% Do not co-administer

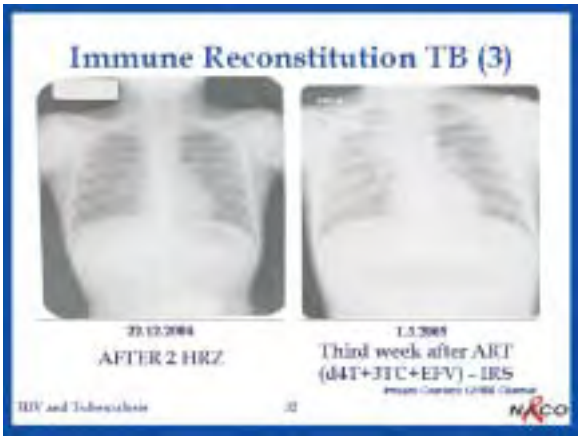
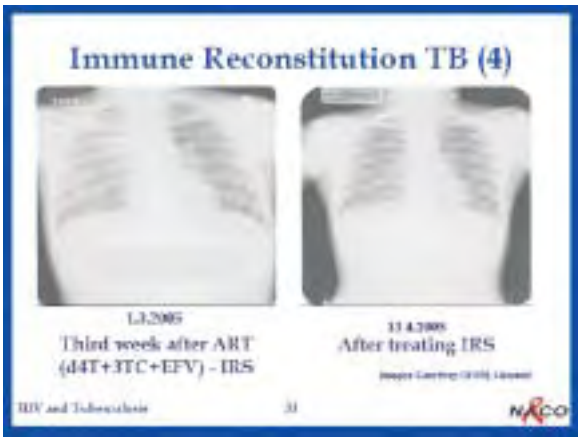
Rifampicin Interactions for NNRTIs & PIs

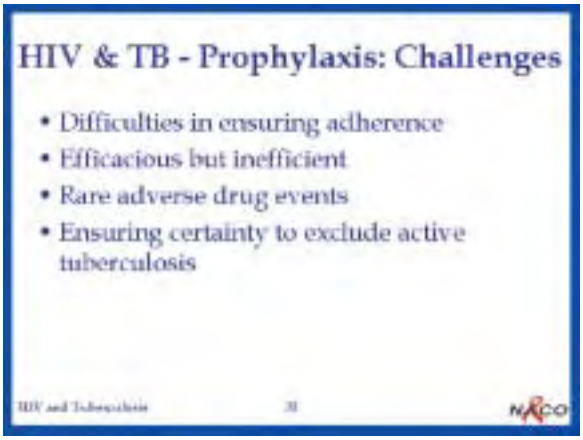
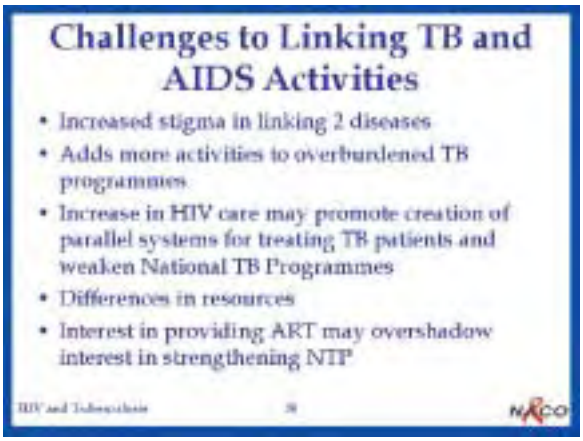
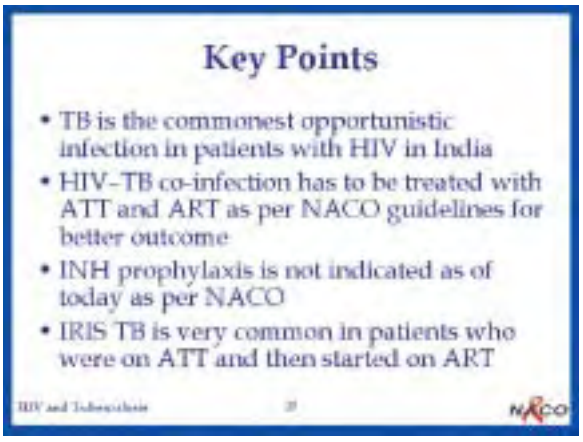
Antimycobacterials	LPV AUC	NFV	SQV	Amprenavir
Rifampin	Decreased 75%	Decreased 82%	Decreased 84% when given without RTV	Decreased by 81%
Recommendation	Do not co-administer	Do not co-administer	If using SQV/RTV can use Rifampin 600 mg/day or 2-3 times weekly	

- **Source for further reference:** http://www.ucsf.edu/hivcntr/Clinical_Resources/Guidelines/PDFs/tbhiv.pdf, 2004.

Slide 26		
Slide 27		
Slide 28		

Slide 29	**Immune Reconstitution Inflammatory Syndrome** • Can happen with any antiretroviral regimen • Mean onset of symptoms is 2 weeks • Mean duration of symptoms is 3 weeks • Most common symptoms include fever, cervical lymphadenopathy, Intrathoracic lymphadenopathy • Associated with restoration of tuberculosis reactivity	
Slide 30	**Immune Reconstitution TB**  • Master AB, 7 years • HIV-positive presenting with fever, loss of appetite, loss of weight and oral candidiasis • Mantoux Test : 0 mm. • Sputum Smear AFB : Negative • CD4 COUNT : 84 Cells (4%) • Treatment : 2HRZ + 4HR	
Slide 31	**Immune Reconstitution TB (2)**  PRE-TREATMENT AFTER 2 HRZ	

Slide 32		
Slide 33		
Slide 34		

Slide 35		**Source:** David Wilkinson, S B Squire, Paul Garner. Effect of preventive treatment for tuberculosis in adults infected with HIV: systematic review of randomised placebo controlled trials. BMJ 1998;317:625-629.
Slide 36		
Slide 37		

SESSION 21

SESSION

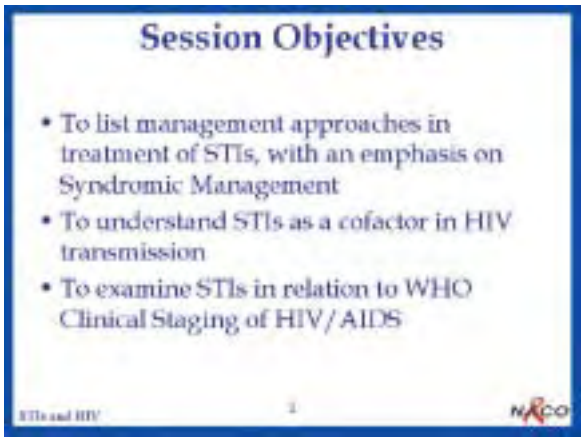
STIs AND HIV

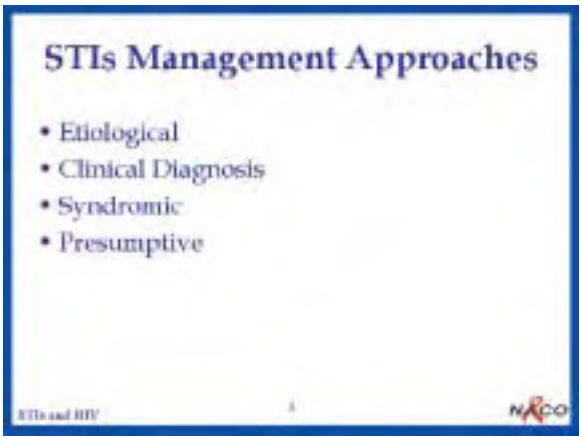
21

Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

- List management approaches in treatment of STIs, with an emphasis on Syndromic Management
- Understand STIs as a cofactor in HIV transmission
- Examine STIs in relation to WHO Clinical Staging of HIV/AIDS

Slide 1		
Slide 2		

Slide 3	 STIs Management Approaches • Etiological • Clinical Diagnosis • Syndromic • Presumptive	

Handout 1: STIs Management Approaches

Management approaches in the treatment of STIs have evolved to address individual, group and community levels of intervention.

1. Etiologic Approach:

- The **etiologic approach** stresses identifying causative organism and treating the specific etiology identified. Problems with this approach include:
  - The need for expensive laboratory support (dark field microscopy)
  - The need for sophisticated tests (e.g., Chlamydia)
  - The delay in initiation of treatment of cases until the results return
  - Loss of follow up of cases
  - Interpretation of results may be difficult (Quality control of results and testing procedures needs to be an ongoing process.)
  - Partner treatment is difficult to ensure.

2. Clinical Approach:

- The **clinical approach** focuses on the clinical experience of the treating physician, who relies on specificity of clinical manifestations and appearance of lesions to make a diagnosis.
  - Studies have documented the unreliability of clinical diagnosis to provide STI treatment.
  - In studies done abroad, only 30% of patients with chancroid and 10% of patients with mixed infections were identified correctly.
  - **Source**:

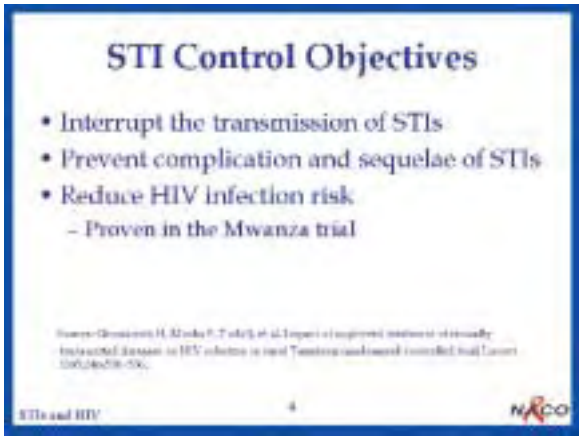
3. Syndromic Approach:

- The **syndromic approach** gives treatment to all possible STIs that cause the syndrome based on epidemiological and laboratory data. This is a simple, easy to follow method, which can be practiced by community health workers.
  - Patients are treated at the first visit
  - Minimal equipment/lab support is necessary
  - It is effective in the presence of mixed infections.
  - Presence of STI complications or conditions not included within flowchart algorithms necessitate referral to STI specialists for individual assessment and correct treatment.

4. Presumptive Approach:

- The **presumptive approach** aims to treat asymptomatic STIs within high risk groups.
- Presumptive approach treats all prevalent STIs in the community at the time of first visit, irrespective of whether patients are symptomatic or not. Single dose therapy is given.
- The risk of dissemination of resistance within the community needs to be considered.

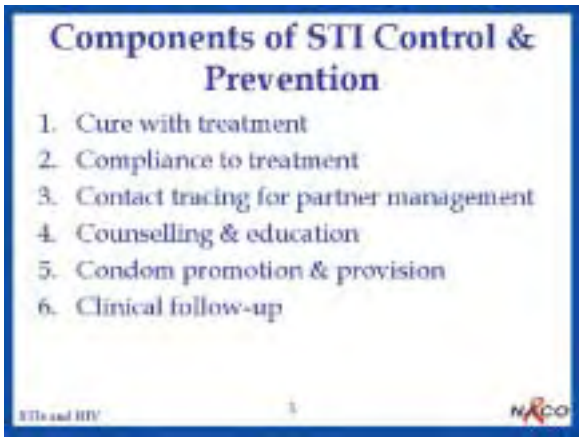
Slide 4



Reader's Notes:

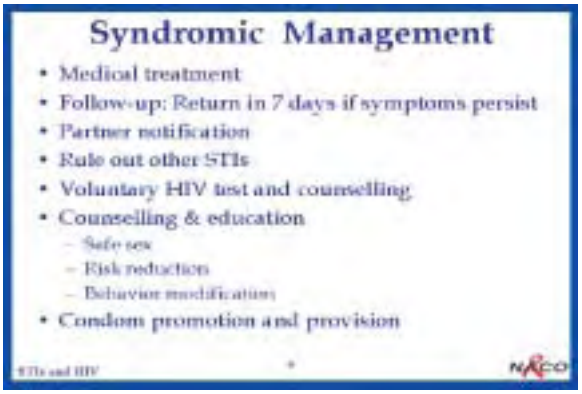
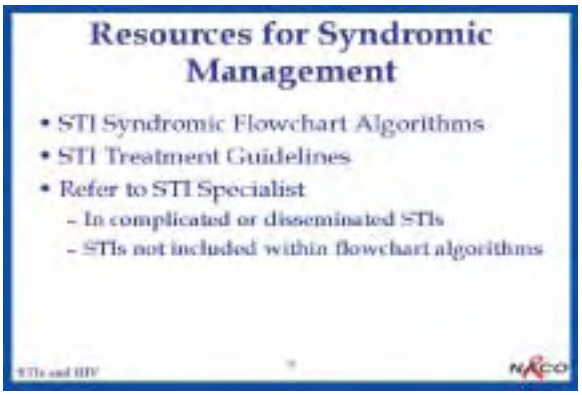
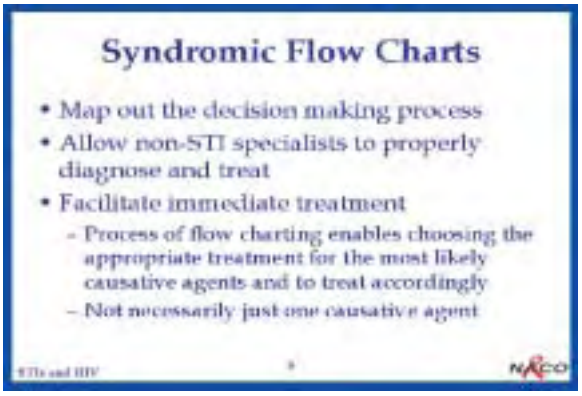
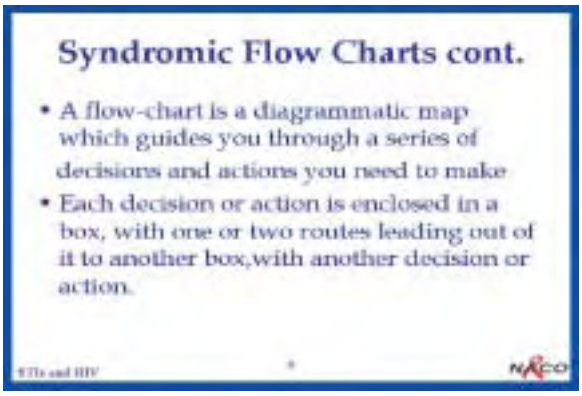
- There are three main objectives of STI control, the most important being to ***prevent the transmission of STIs to reduce HIV infection risk***.
- The ***Mwanza trial*****,** conducted in Tanzania, was a landmark trial reported in 1995 which demonstrated the effectiveness of Syndromic Management as a STI intervention program for the reduction of HIV transmission.
- Over a two year period during which the study was conducted, there was a 42% reduction in HIV incidence.
- Community health workers (CHWs) were trained in syndromic management of STIs and were able to correctly diagnose STI syndromes at an individual level. The treatment was based on STI Flowchart Algorithms which were provided to CHWs. The study was based out of an STI referral centre.
- Reference:Source: Grosskurth H, Mosha F, Todd J, et al. Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. Lancet 1995;346:530—536.

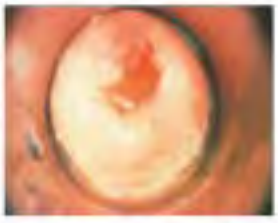
Slide 5

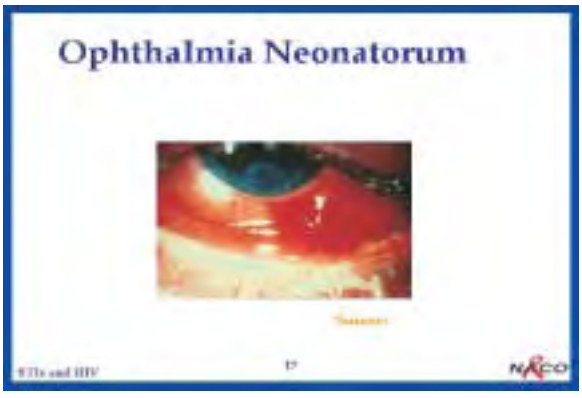


Reader's Notes:

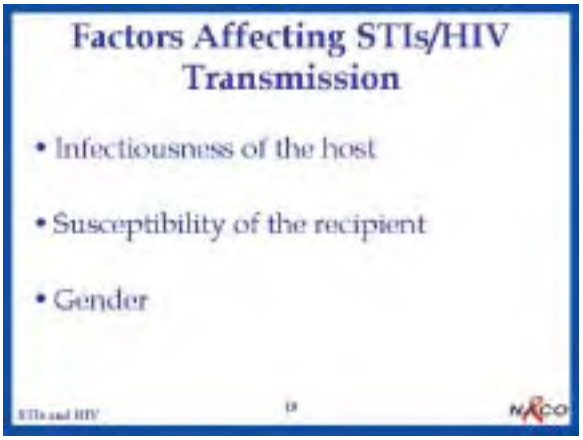
- **Treatment** regimens are designed to be effective, even in the face of widespread drug resistance. Syndromic Management Flowchart algorithms should utilise available laboratory and epidemiological data to ensure appropriate treatments.
- Single dose regimens are given whenever possible to increase **compliance** to treatment. This should be weighed against clinical efficacy of regimen. Cost effectiveness is another factor in proscribing single dose regimens.
- Using **condoms** is not 100 percent effective in preventing transmission of STIs and HIV, but they are still the best method of protection to prevent transmission. Patients should be counselled that condoms need to be used 100 percent of the time to be effective.

Slide 6		**Reader's Notes:** • Because of the advantages of the syndromic management approach, it is the first choice in the management of STIs even at the individual level. This also leads to community level benefits, as we shall see subsequently. • Syndromic management is not only about giving medical treatment to individual patients, but is a comprehensive set of measures which help to control STIs.
Slide 7		**Reader's Notes:** • Within a STI Syndrome Flowchart, history is elicited, risk is assessed, clinical examination performed and treatment is given based on the STI syndrome. • For certain STIs, no Flowchart Algorithm is provided, e.g., genital warts. In cases such as these, follow guidelines for the individual STI. • Draft STI Treatment Guidelines on individual STIs are found on the NACO website's publications: www.nacoonline.org/publications.htm
Slide 8		
Slide 9		

Slide 10	**Syndromes** • Syndromic approach uses flow charts to identify causes of 7 common syndromes associated with STIs: – Urethral discharge/Burning micturition – Genital ulcer – Vaginal discharge – Scrotal swelling – Lower abdominal pain – Inguinal bubo – Neonatal conjunctivitis – Anorectal	
Slide 11	**Urethral Discharge** 	
Slide 12	**Complications** • Epididymitis • Periurethral abscess • Urethral stricture • Prostatitis • Gonococcal arthritis	
Slide 13	**Vaginal Discharge (With Speculum)** 	

Slide 14		**Reader's Notes:** • Risk factors associated with cervical infection include: • Younger than 21 years • Not married • Multiple (more than one) sex partner in the last three months • A new partner in the last three months • Current sex partner has a sexually transmitted infection • Recent use of condoms by the partner
Slide 15		
Slide 16		
Slide 17		**Reader's Notes:** • **Ophthalmia Neonatorum** • This condition results from exposure to infected cervical secretions during parturition. • The clinical manifestations are acute and begin 2 to 5 days after birth. • Initially nonspecific conjunctivitis with a serosanguinous discharge is followed by tense edema of both eyelids, chemosis, and a profuse, thick, purulent discharge. • Corneal ulcerations may result in nebulae or perforation which leads to anterior synechiae, anterior staphyloma, panophthalmitis, and blindness if not properly treated.

Slide 18



Reader's Notes:

- Ro=bDC : For diseases spread sexually, whether it is HIV or syphilis, the transmission equation is related to a complex interplay between:
  - **b (beta),** which represents **efficiency of transmission which is a biological event** (e.g., vaginal intercourse is less likely to transmit than rectal intercourse),
  - **D is the duration of infectiousness**,
  - and **C is the number of partners**.
- Probabilities for efficiency of sexual transmission of HIV vary from 1 in 700 to 1 in 3000 sexual acts depending on nature of sexual act and varying efficiencies of transmission.
- Sexual behaviours that increase the risk for acquiring HIV also increase the risk for acquiring other STIs.
- Biological factors that could increase the risk of STI/ HIV transmission:
  - Infectiousness of the host is increased with the following: 1.High viral load — seen in Acute(Primary) HIV infection, as well as in more advanced stages of untreated HIV infection, 2.Presence of genital tract changes — bacterial vaginosis, STIs, 3.Systemic co-infections eg tuberculosis, 4.Presence of blood during contact, 5.If they are breastfeeding (an infant).
  - Susceptibility of recipient is increased with the following: 1.Presence of STI, 2.Exposure to infected blood, semen or other genital secretions, 3.Poor state of health, 4.Co-infection with other diseases.
  - Gender: women are more biologically prone to HIV than men because of Increased mucosal surface area, Pooling of semen, Presence of genital ulcers or other STI, Thinning of vagina (due to menopause or progestin contraceptives), Immature genital tract of young girls.
- *References for further reading: 1.* Source: Sena, Cates and Cohen, New England Journal of Medicine,336:1072-1078,1997. 2.) Gray RH, Wawer MJ, Brookmeyer R, Sewankambo NK, Serwadda D, Wabwire-Mangen F, et al. Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda. Lancet 2001; 357: 1149-1153.

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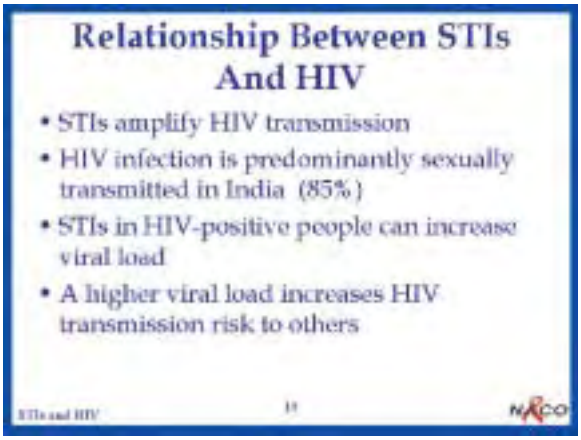
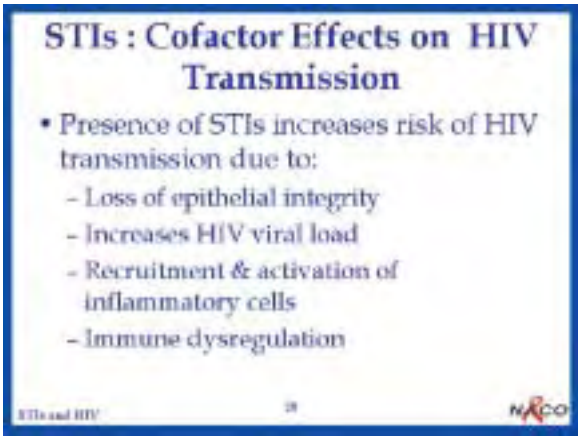


Reader's Notes:

- STIs amplify HIV transmission 3 to 22-fold depending on the presence of an inflammatory or ulcerative STI.
- Statistics from NACO illustrate that the predominant mode of transmission of infection in AIDS patients is sexually transmitted (heterosexual contact) in about 85.7% of total reported cases, followed by Injecting drug use (2.2%), blood transfusion and blood product infusion (2.6%), perinatal transmission as 2.7% and others as 6.8%.
  - Source Available at: http://www.nacoonline.org/facts_overview.htm .
- Treatment of STIs reduces HIV transmission.
- HIV care/STI care should be integrated. Prevention of STIs prevents HIV.

Slide 20



Reader's Notes:

- The loss of epithelial integrity results in disruption of surface/mucosal epithelium, which provides an entry route for STI/HIV pathogens.
- HIV viral load is increased in the genital tract in the presence of STIs. This increases the infectiousness of HIV transmission.
- Recruitment and activation of inflammatory (receptor CD4 cells) increases the susceptibility of HIV transmission as does immune dysregulation in the host.
- References for further reading:
- Rottingen JA, Cameron DW, Garnett GP. A systematic review of the epidemiological interactions between classical STDs and HIV. Sexually Transmitted Diseases 2001; 28: 579-597.
- Korenromp EL, de Vlas SJ, Nagelkerke NJD, Habbema, R. Estimating the magnitude of STD cofactor effects on HIV transmission: how well can it be done? Sexually Transmitted Diseases 2001; 28: 613-621.5.

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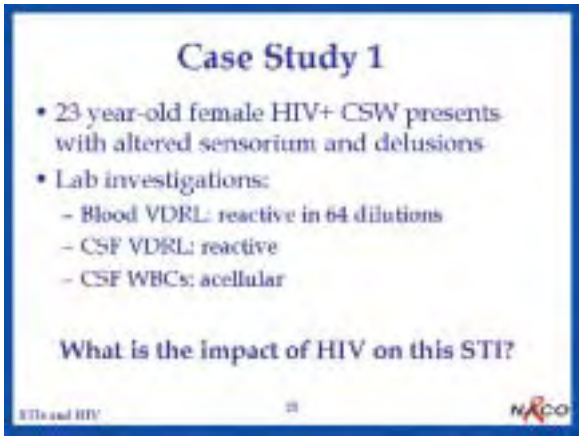
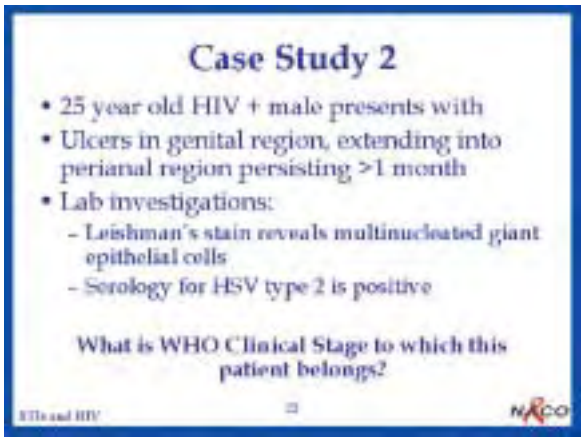


Reader's Notes:

- The interaction of syphilis and HIV infection is reportedly complex.
- Isolated case reports have suggested that coexistent HIV infection may alter the natural history of syphilis and the dosage or duration of treatment required to cure syphilis.
- These anecdotal reports have led to the hypothesis that in patients co-infected with HIV, T. pallidum, cutaneous lesions may be more severe, symptomatic Neurosyphilis may be more likely to develop, the latency period before the development of meningovascular syphilis may be shorter, and the efficacy of standard therapy for early syphilis may be reduced.
- The impairment of both cell-mediated and humoral immunity by HIV, could limit the host's defences against T. pallidum, thereby enhancing susceptibility to syphilis and also altering the clinical manifestations or natural course of the infection.
- It is worth noting that infection with HIV may not only alter the clinical presentation of syphilis, but also the performance of syphilis serologic tests.
    - Thus the diagnosis of syphilis may be more complicated in HIV-infected patients because of false-negative and false-positive serologic results for T. pallidum.
- Co-infection with HIV and syphilis however, does not generally impair the sensitivity of syphilis testing, although there are sporadic reports of absent or delayed response to nontreponemal tests.

Slide 22



Reader's Notes:

- For the case studies 2 and 3, Refer to **Handout 1: WHO Clinical Staging HIV/AIDS in session " Natural History of HIV infection and WHO Clinical Staging"** for more information on WHO Clinical Staging of HIV/AIDS.

Slide 23	**Case Study 3** • If this patient presents with pain in the scrotum, with swelling, how would you manage? 	
Slide 24	**Key Points** • The Syndromic Management approach provides a great advantage in the management of STIs as it benefits both the individual and the community • NACO's Syndromic Flowchart Algorithms and STI Treatment Guidelines are two resources used in managing STIs • The presence of STIs increases risk of HIV transmission • Chronic, severe, resistant, atypical lesions are common presentations in HIV	

SESSION 22

SESSION

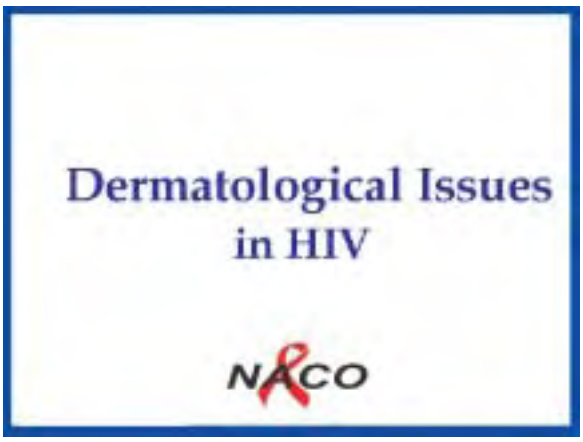
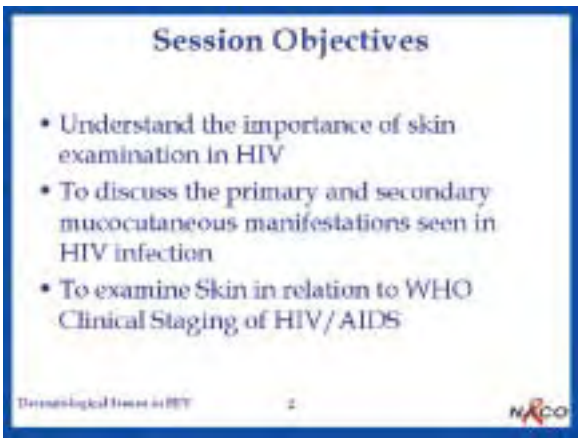
DERMATOLOGICAL ISSUES IN HIV

22

Total Session Time: 45 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Understand the importance of skin examination in HIV.
- Discuss the primary and secondary mucocutaneous manifestations seen in HIV infection.
- Examine Skin in relation to WHO Clinical Staging of HIV/AIDS.

Slide 1		
Slide 2		

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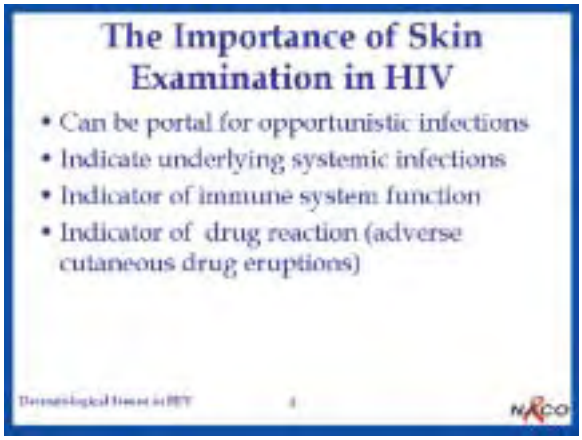
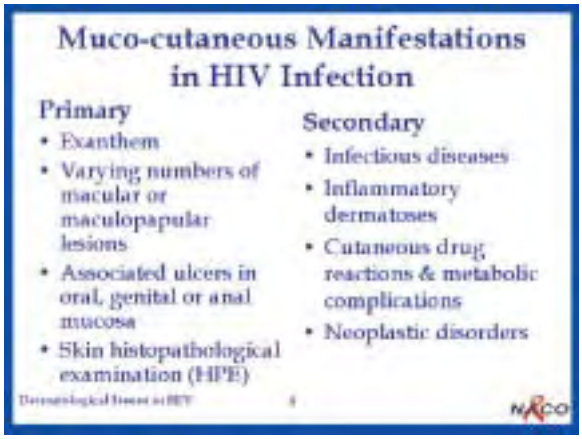


Reader's Notes:

- Certain skin conditions like Oral Hairy Leukoplakia,Kaposi's are specific indicators of the immune system.
- While no skin condition is specific to HIV, the occurrence of certain muco-cutaneous lesions have high positive predictive value for the presence of HIV infection.
- A variety of drugs used in HIV disease including ART causes adverse cutaneous drug eruptions(ACDE). The incidence of ACDE is 100 times more common than in general population.
- The skin problems are commonly seen in more than 90% of HIV+ patients, demonstrating the importance of the skin examinations not only to identify lesions correctly, but to also provide an entry pathway into HIV prevention and care.
- A proper history, close inspection and correct interpretation are important during examination of the skin. The morphology, evolution and distribution of lesions needs to be clearly described.
- Secondary muco-cutaneous manifestations seen commonly throughout course of HIV infection.

Slide 4



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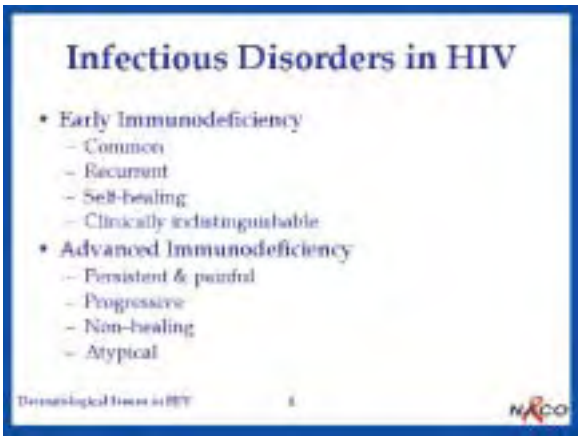
Slide 5



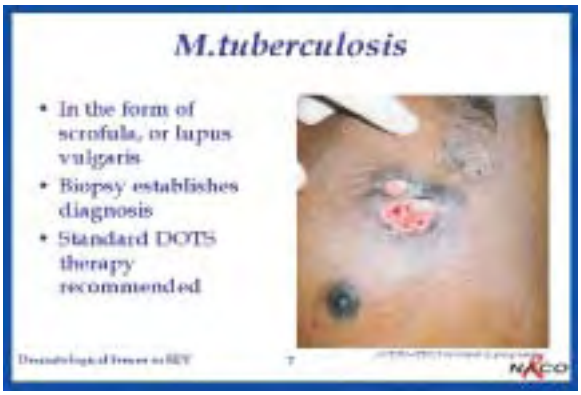
Reader's Notes:

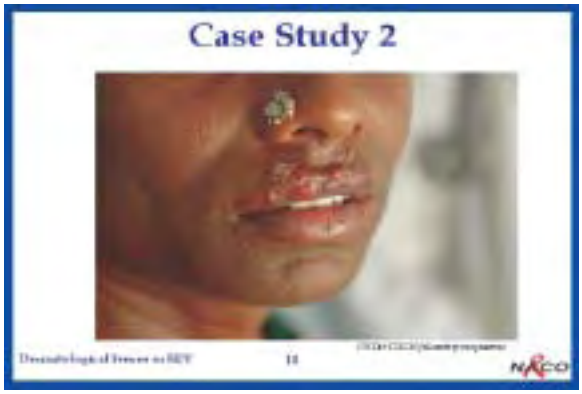
- In early immunodeficiency, infectious disorders are commonly recurrent, self healing and clinically indistinguishable from lesions in immunocompetent individuals. As immunodeficiency progresses, lesions are persistent, progressive, non healing and painful. E.g. Oral/anogenital herpes simplex virus (HSV) infection.
- Multiple infections are common.
- Cutaneous mycobacterial infections occur in the form of scrofuloderma or lupus vulgaris. Viral infections are commonly seen due to Herpes simplex virus (HSV), Varicella zoster, Molluscum contagiosum, Human Papilloma Virus (HPV).
- Fungal infections due to Candida species, Dermatophytes and Malassezia furfur are the most common pathogens causing superficial/muco-cutaneous mycoses in HIV infected patients.
- Clinical course is often atypical and may be masked by other infections

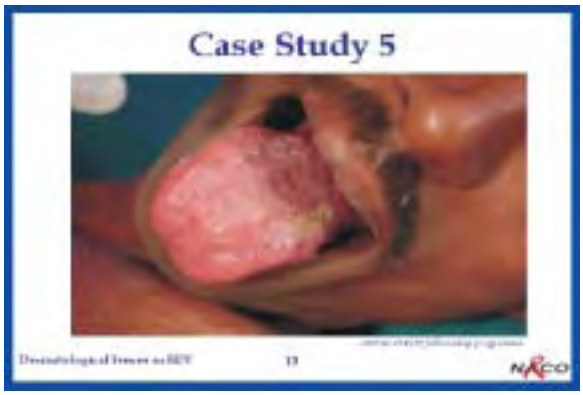
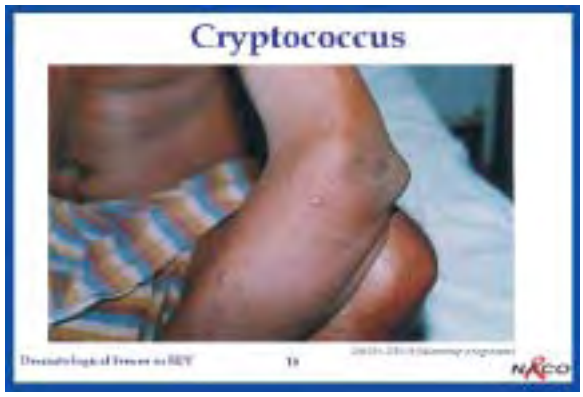
Handout 1: Common Skin Manifestations in HIV-Infected

List of common skin manifestations seen in HIV-infected persons

SL	Infectious conditions	Examples
1	**Bacterial**	
a.		*Staphylococcal*
b.		Pseudomonas
c.		Bacillary angiomatoses
2	***Mycobacterial***	
a.		M. *tuberculosis*
b.		*M. leprae*
c.		Atypical mycobacteria
3	***Viral***	
a.		HIV at Seroconversion
b.		*Herpes simplex*
c.		Varicella zoster
d.		H P V
e.		Molluscum contagiosum
f.		E B virus
4	***Fungal***	
a.		Dermatophytes
b.		Candida
c.		Pityrosporium
d.		Deep seated mycoses
e.		Cryptococcus
f.		Histoplasma
g.		Aspergillus
h.		Pencillium
5	***Ectoparasitic***	
a.		*Scabies*

Slide 6		**Reader's Notes:** • Bacterial Infections commonly are due to Staphylococcus aureus. • Clinical manifestations are impetigo, folliculitis, furuncles, carbuncles, cellulitis, as well as secondary infections of underlying inflammatory dermatoses. Staphyloccal folliculitis needs to be differentiated from other causes of folliculitis like eosinophilic folliculitis and pityrosporum folliculitis. • Treatment is with appropriate anti staphylococcal antibiotics.
Slide 7		
Slide 8		**Reader's Notes:** • Hansen's disease may be seen occasionally in PLHA. • They tend to present more in the lepromatous part of the spectrum in patients with advanced infection. • Identification may be difficult, and if HAART is started, they may present in reaction as an IRIS. • Diagnosis is established by skin smears, and treatment is as for multibacillary disease. • This may present a problem for patients with HD who also requires HAART, given the interaction between Nevirapine and Rifampicin. • An acceptable alternative would be the use of Efavirenz based regimen.
Slide 9		

Slide 10		**Reader's Notes:** • Infection that persists more than a month indicates progression to AIDS • In early stages, the classical grouped vesicles on an erythematous base may be noted, but as immunity falls, the ulcers become painful, deep and large. • Herpetic infections in PLHA are more extensive and recurrent; treatment may need to be prolonged. • In severe cases, suppressive prophylaxis may be considered. • As the person is increasingly immunosuppressed Acyclovir-resistant infections may be seen, which may require specialist therapy with Foscarnet.
Slide 11		**Reader's Notes:** • Occurs in younger age group. Patients with history of Zoster in last 5 years are staged in WHO stage 2 disease. • Zoster can also be commonly seen as an IRIS occurring a few weeks after initiation of HAART. • Treatment is ideally with acyclovir 800 mg 5 times a day for two weeks.
Slide 12		
Slide 13		**Reader's Notes:** • They are often widespread, persistent and recur after treatment. The severity of the infection is an indicator of the degree of immune deficiency. • Treatment is with iodine cautery

Slide 14		**Reader's Notes:** • Widespread, resistant lesions are commonly seen with advanced immunodeficiency. Diagnosis is by skin scraping and identifying fungal hyphae. • Single small lesions respond to topical antifungal like Clotrimazole. Extensive resistant infections may need systemic antifungal.
Slide 15		
Slide 16		
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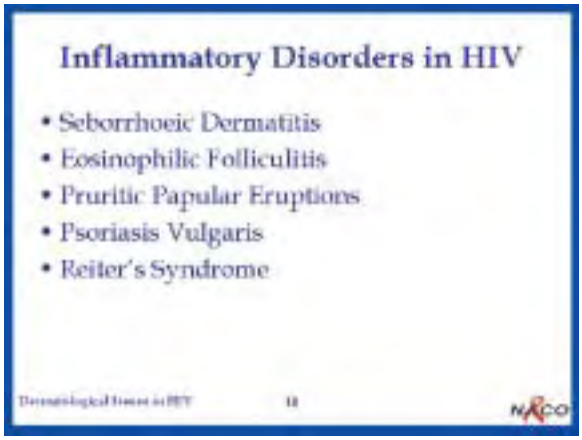
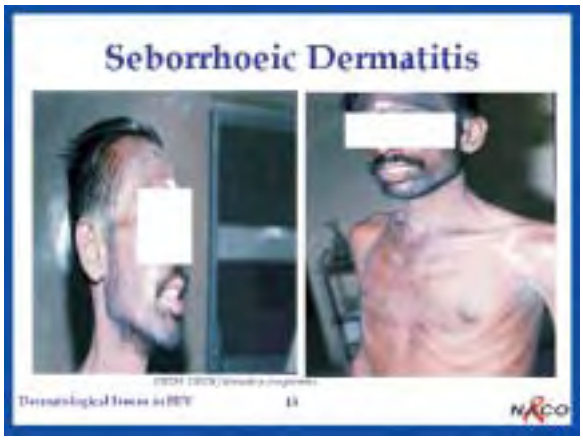


Reader's Notes:

- Pruritic Papular eruptions are a significant cause of HIV related morbidity. Empirical therapies provide only minimal relief and the associated pruritus and resultant scars subject patients to stigma in the community. The typical primary lesion is a firm, discrete, erythematous papule, concentrated mostly in the extremities, but also distributed over the face and trunk. Severe Pruritus leads to secondary excoriated papules, marked post inflammatory hyperpigmentation and formation of scarred nodules.
- Differential diagnosis for PPE needs to be kept in mind. Conditions like Staphylococcal folliculitis, Demodex folliculitis, drug eruptions, exuberant reaction to arthropod bites, crusted scabies, secondary syphilis and papulonecrotic tuberculid have to be ruled out.

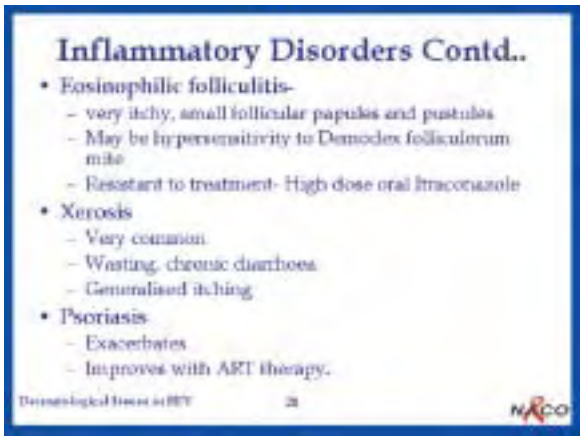
Slide 19



Reader's Notes:

- Seborrhoeic dermatitis is exceedingly common in HIV infection.
- Early in the course of infection, it is morphologically typical, with greasy scaly erythematous patch.
- More severe in late stage of disease. Patients with Seborrhoeic dermatitis have defective CMI response to Pityrosporum sp, and are often refractory to treatment.
- Treatment :
  - Selenium sulfide, Zinc Pyrithione, Ketoconazole shampoo
  - Hydrocortisone, Clotrimazole, Ketoconazole cream

Slide 20



Reader's Notes:

- Eosinophilic folliculitis is also called as "prurigo nodularis," "itchy red bump disease," and "papular pruritic eruption of AIDS"
- Eosinophilic folliculitis is a chronic, pruritic, culture negative folliculitis, which is seen in advanced HIV infection.
- Clinically it is characterized by multiple follicular and non follicular, urticarial papules, most commonly involving the upper trunk, face and proximal extremities.
  - Lesions most often present on the face (especially the forehead), the neck, the area behind and below the ears, the chest, the back, and the lateral surfaces of the upper arms.Sometimes axillae, buttocks and thighs are affected
- Some treatments may which provide relief:
  - Oral metronidazole, Topical permethrin (Elimite), Isotretinoin (accutane), Systemic corticosteroids may also be effective
- Xerosis is very commonly seen in hiv patients.
  - It is due to diminished sweating and sebaceous gland secretion possibly due to malabsorption of essential fatty acids.
  - Treatment include Emollient creams, Soap substitutes, Bath oils and Nutritional supplements
- Psoriasis-Presentation: Red plaques with thick silvery scale over the elbows, knees, and/or lumbosacral areas.
  - May also include nail pitting, dystrophy, and arthritis and possible pruritus
  - Treatment: Improvement of immune system.Same treatment as HIV-ve
  - UVA and UVB therapies can lead to serious complications in HIV+ individuals with psoriasis

Slide 21

Reader's Notes:

- All skin reactions are considered drug eruptions when they occurred with in 30 days after the onset of treatment with drugs like sulfa. In the event of a rash with Nevirapine, there are many options; the first is to assess the severity.
- If it is generalized, or has mucosal involvement, or systemic involvement (like jaundice), all drugs should be stopped.
  If the rash is mild, a wait and watch policy may be applied. In this situation, the patient should be reviewed daily to ensure that it is not worsening, **and the nevirapine dose should not be escalated to twice daily until the rash settles**.
  It has been noted that the rash will settle in nearly half the patients, if given time and observed carefully

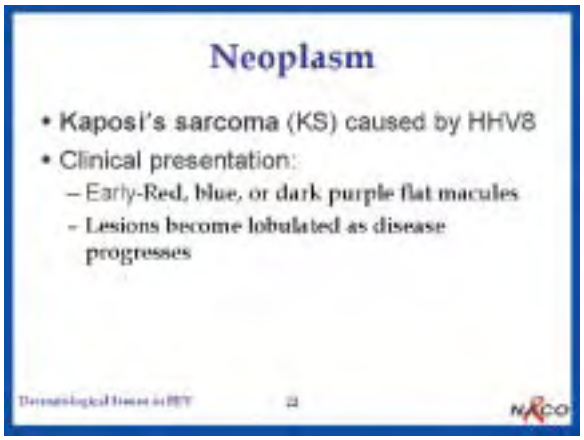
Handout 2: Cutaneous Drug Reactions & Metabolic Complications

- Multiple drugs cause cutaneous drug reactions
  - Most reactions occur within 30 days after the onset of treatment of drug.
- Morphology of muco-cutaneous lesions is not predictable
  - None of the muco-cutaneous manifestations are specific for a drug.
  - The cutaneous reaction in an individual patient may be mild to severe.
    - Associated features include pruritus and urticaria.
    - Morphology may be in the form of a maculopapular eruption, exfoliative dermatitis or fixed drug eruption.
    - In severe cases of mucosal involvement, Stephen Johnson syndrome may result with scarring and threat to life as in Toxic epidermal necrolysis.
    - The likelihood of rashes with Nevirapine is increased in female patients and in those with CD4 cell counts >350 cells/cu.mm
    - Although Nevirapine is classically quoted as a drug causing rash, it should be remembered that all drugs can cause a hypersensitivity rash; Efavirenz being of the same class is also likely to produce a rash.
- Careful monitoring & immediate cessation
  - In patients taking multiple classes of drugs, it is appropriate to stop all drugs, and gradually introduce needed drugs one at a time, under careful medical supervision.
- Metabolic complications of HAART
  - In certain cases, where decision to continue the drug is made in spite of moderately severe maculopapular eruption, provision of intensive care to take care of SJS, TEN is necessary.
- **Metabolic complications of HAART** are like
    - Stavudine induced or PI induced **Lipodystrophy** is manifested as changes in body appearance.
    - Nail hyperpigmentation is seen with Zidovudine, as is anaemia manifest as pallor in conjunctiva.
    - Long term metabolic complications of HAART such as protease inhibitor induced lipodystrophy manifests as visible alterations in body such as wasting of cheeks, buffalo hump appearance, thinness of limbs, and abdominal obesity.

Multiple groups of drugs cause cutaneous drug reactions:

Examples: **Sulfonamides (TMP-SMZ, Sulfonamide)**, Penicillins, Amoxicillin, anti—epileptics (Carbamazepine, Eptoin), anti tuberculosis (INH, Rifampicin), antivirals (Foscarnet), Pentamidine, NNRTIs (**Nevirapine**, Efavirenz), NRTIs (Abacavir, Zidovudine) can all cause cutaneous drug reactions.

Slide 22



Reader's Notes:

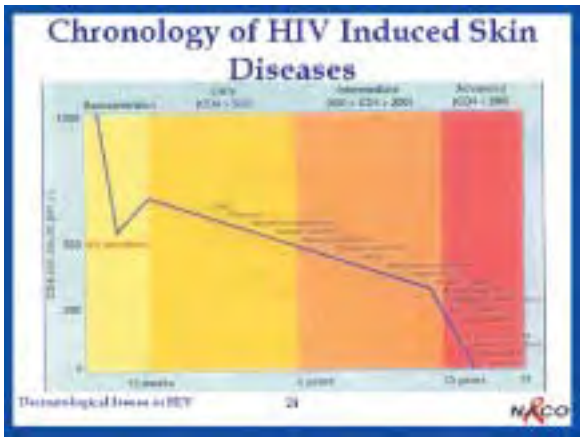
- Kaposi's sarcoma (Which is not common in India) manifests as red, purplish or brown coloured macules, nodules or plaques, which may be localized or typically follow an aggressive course with widespread cutaneous and systemic lesions.
- Lesions may resemble dermatofibromas, pyogenic granulomas, or nevi.
- Any site of the body may be affected, but common sites are the trunk, legs, face and oral cavity.
- Prognosis has improved with initiation of HAART. Diagnosis is through biopsy and histopathological examination.
- Treatment:
  - Topical treatment (e.g., Aliretinoin) in patients with CD4+ cell counts greater than 400/iL and plasma HIV RNA levels below detection limits.
  - Liposomal Doxorubicin or Paclitaxel infusions should be given in patients with eruptive KS or lymphedema who are on antiretroviral therapy.

Slide 23

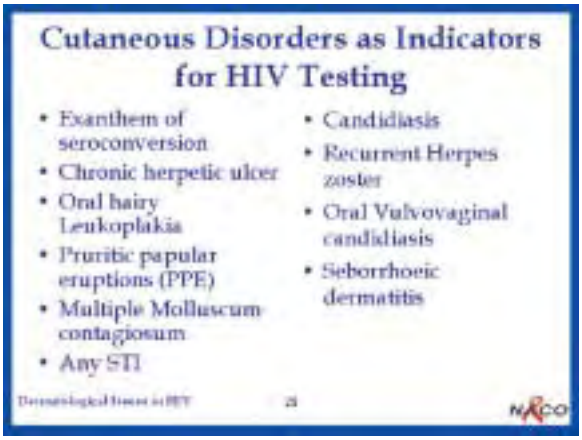
Reader's Notes:

- List the other common muco cutaneous manifestations like
- Recurrent apthous ulcer
- Pigmentary skin changes
- Xerostomia and exfoliative cheilitis
- Patchy depapillation of tongue
- Gingivitis and periodontitis
- Acquired trichomegaly of eye lashes

Slide 24



Slide 25


Cutaneous Disorders as Indicators for HIV Testing
• Exanthem of seroconversion
• Chronic herpetic ulcer
• Oral hairy Leukoplakia
• Pruritic papular eruptions (PPE)
• Multiple Molluscum contagiosum
• Any STI
• Candidiasis
• Recurrent Herpes zoster
• Oral Vulvovaginal candidiasis
• Seborrhoeic dermatitis

Handout 3: Skin Conditions Indicative of HIV Infection

- **Highly Indicative of HIV Infection**
  - Exanthem of acute retroviral syndrome
  - Proximal subungual onychomycosis
  - Chronic herpetic ulcers
  - Oral hairy leukoplakia
  - Kaposi's sarcoma
  - Eosinophilic folliculalitis
  - Molluscum contagiosum, multiple facial in adult

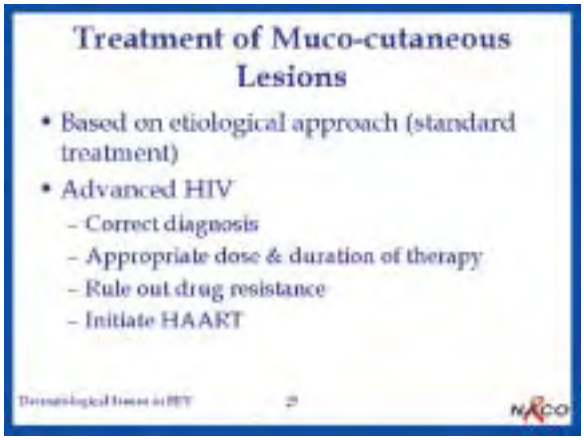
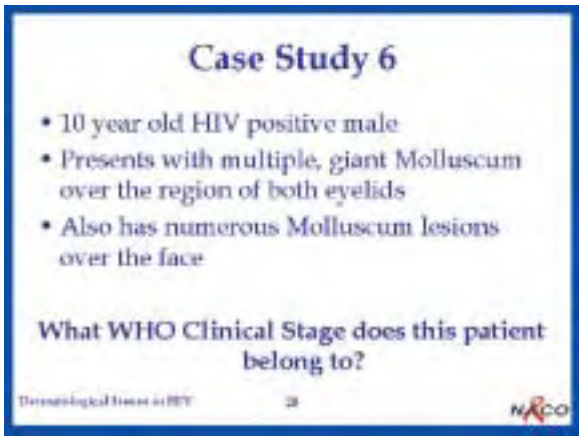
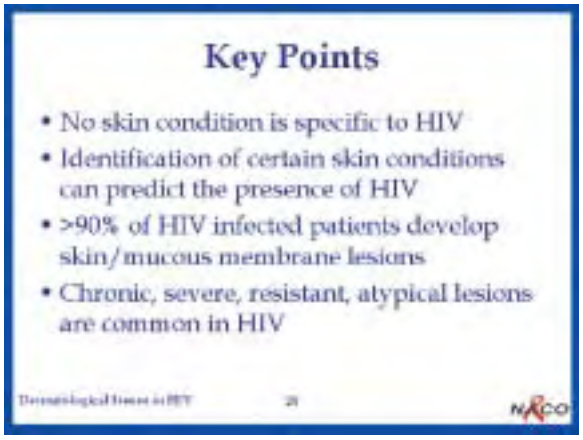
- **Strongly Associated with HIV Infection**
  - Any STI
  - Herpes zoster
  - Signs of injecting drug use
  - Candidiasis: oropharyngeal or recurrent vuvovaginal

- **May be Associated with HIV Infection**
  - Generalized lymphadenopathy
  - Seborrheic dermatitis (extensive, refractory to treatment)
  - Aphthous ulcers (recurrent, refractory to therapy

Slide 26

Reader's Notes:

- Visual inspection of lesions and clinical experience helps the physician to narrow down the differential.
  - Biopsy of lesions aids to complement and correctly provide therapy.
  - Always conduct good clinical practice to work up the differential diagnosis of lesions.
- Cost effectiveness needs to be balanced with optimized therapy.
  - For example, in ulcers preceded by appearance of vesicles, herpes (reactivational) zoster needs to be differentiated from herpes simplex virus, since the dosage of acyclovir would differ in both conditions.

Slide 27		**Reader's Notes:** • In advanced HIV, challenges of treatment of muco-cutaneous lesions are likely to be met, due to the persistent, recalcitrant nature of lesions or non healing state. • To overcome these challenges, amongst the four measures outlined, the most important challenge is to initiate the patient on HAART. • Stage the patient and after screening for ARV, HAART should be instituted as per the NACO guidelines. Treatment of mucocutaneous lesions should proceed concurrently.
Slide 28		**Reader's Notes:** • Age, living in close proximity, skin-to-skin contact, sharing of fomites, and residence in tropical climates were also associated with higher rates of infection with Molluscum contagiosum, while sex, seasonality, and hygiene showed no such association. • Observational studies have reported a correlation between the appearance of facial lesions of Molluscum contagiosum in adults and immune deficiency, with CD4 cell counts less than 200 cells per cumm. The correlation in children is not well defined. • In shared home facilities, transmission by fomites may also take place. • Reference: Braue A.,Ross G., Varigos G., et al., Epidemiology and Impact of Childhood Molluscum Contagiosum: A Case Series and Critical Review of the Literature. Pediatric Dermatology: 2005; 22:4, 287-294
Slide 29		

SESSION 23-26

DAY - NINE

SESSION 23

SESSION

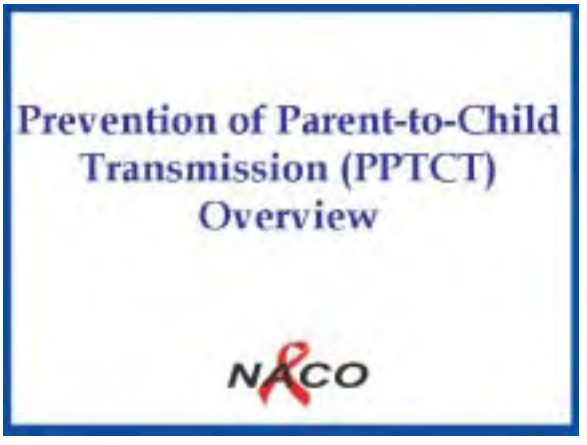
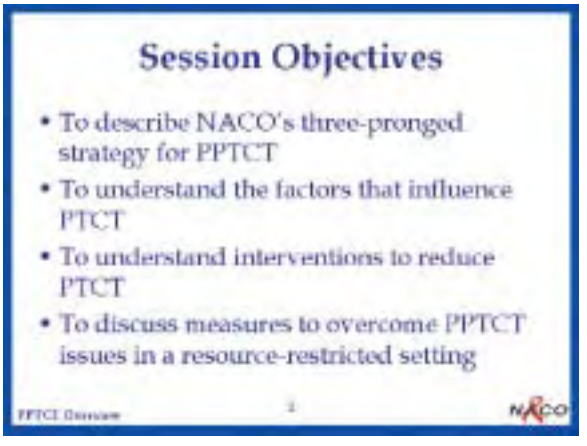
PREVENTION OF PARENT-TO-CHILD TRANSMISSION (PPTCT) OVERVIEW

23

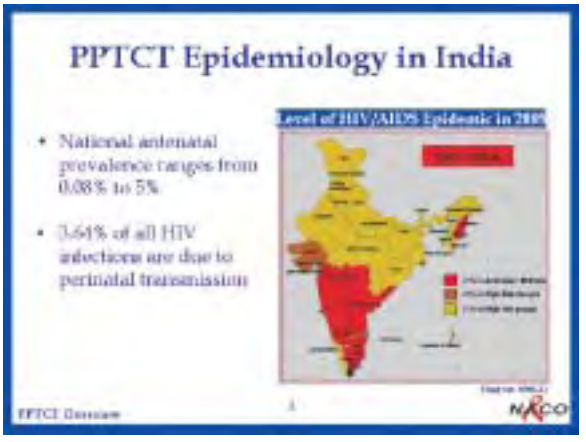
Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Describe NACO's three-pronged strategy for PPTCT
- Understand the factors that influence PTCT
- Understand interventions to reduce PTCT
- Discuss measures to overcome PPTCT issues in a resource-restricted setting

Slide 1		
Slide 2		**Reader's Notes:** • This session aims to provide knowledge and skills to care for women living with HIV, with special emphasis on intervention to prevent mother to child transmission of HIV infection. You will have the opportunity to discuss the challenges to implementing intervention to prevent PTCT in your setting. • PTCT- parent-to-child transmission is known as vertical or perinatal transmission. In most other countries this is referred to as MTCT (mother-to-child-transmission). There are proven interventions to reduce the likelihood of PTCT.

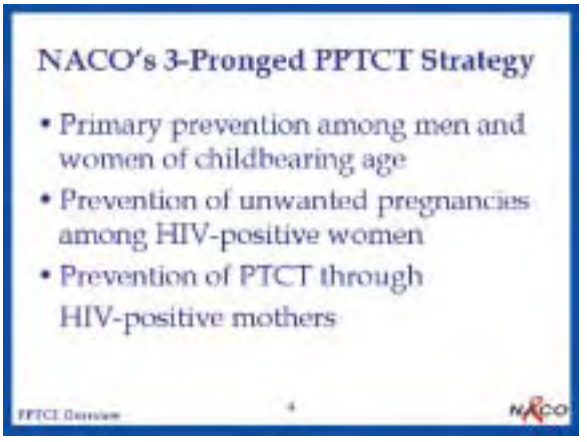
Slide 3



Reader's Notes:

- According to NACO data, the antenatal prevalence is lowest in Kerala 0.08 % and highest in Manipur 5%. Average prevalence rate in pregnant women in cities such as Hyderabad, Mumbai, Pune, Sangli and Manipur is 2-2.5%. In three states: Goa, Gujarat and Tamil Nadu, the prevalence of HIV exceeds 5% among groups engaging in high risk behaviour. These groups are truckers and migrant workers, CSWs and IDUs.

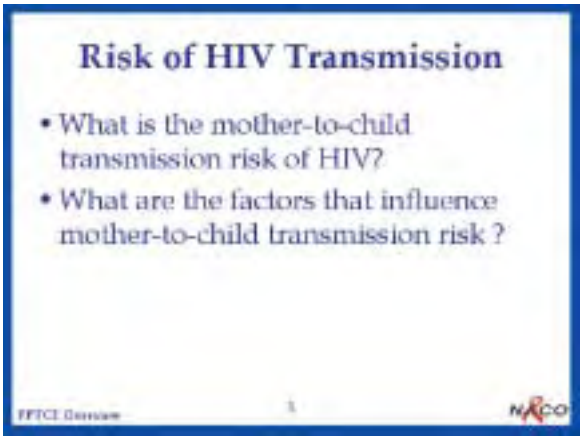
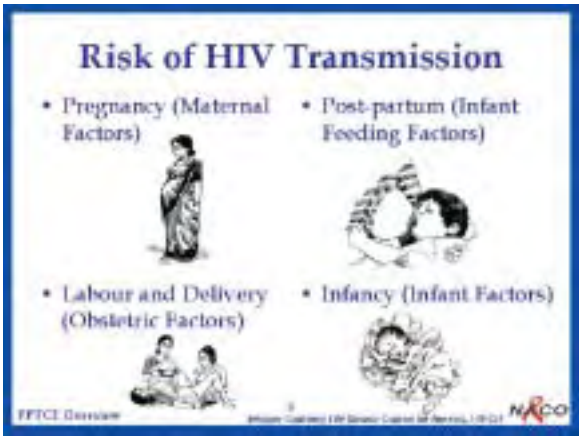
Slide 4



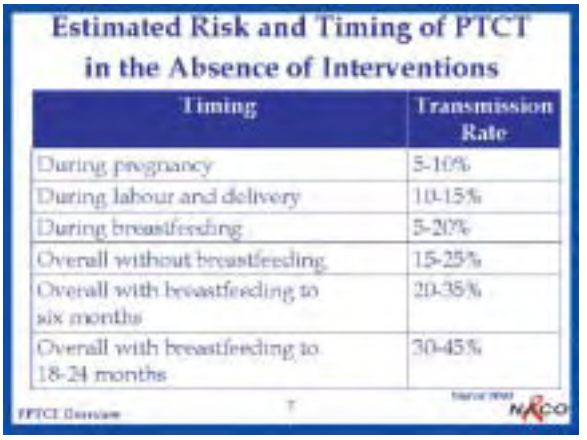
Reader's Notes:

NACO has a three-pronged strategy for the PPTCT.

1) The first, primary prevention, focuses on preventing HIV among women and men of childbearing age. This can only be achieved as part of a general population-based HIV prevention strategy as discussed in the epidemiology module. Some components of primary prevention include:
   - **Promoting condoms through social marketing and community-based distribution system.** The social marketing strategy has helped in increasing the use of condoms in the country at large. There is greater need to ensure availability of condoms at places (hospitals and clinics) and times where they are needed.
   - **Behaviour change communication (BCC) and social mobilisation campaigns**. While there is general awareness about the disease, specific aspects like mode of transmission, method of protecting oneself from getting infected, etc. are still not known to a large section of the population. There is an urgent need to generate appropriate programmes which stress interpersonal communication for targeted groups (e.g. students, youth, women, migrant workers and children).
   - **Prevention, diagnosis, and treatment of sexually transmitted infections (STIs).** The presence of STDs, specially with ulcers or discharge, facilitates transmission of HIV infection. The risk of transmission is 8 to 10 times higher in case of persons with STDs compared with others. Two approaches for STD control adopted by the government are: incorporate management of STDs through syndromic approach into the general health service and integrate services for treatment of reproductive tract infections (RTIs) and sexually transmitted infections (STIs) at all levels of health care.
2) The second strategy involves preventing unwanted pregnancies in HIV infected women. This strategy requires provision of VCT services and voluntary, safe, and effective contraception, sterilization, or abortion. HIV positive women should have complete choice in making decisions regarding pregnancy and childbirth. Proper counselling should be provided to women to enable her to make an appropriate decision either to continue the pregnancy or terminate the pregnancy.

		3) The third strategy is to promote interventions to prevent PTCT by HIV-positive mothers**.** PPTCT programmes can reduce the risk of transmission from the mother to the child. Examples include: Comprehensive maternal and child health services (antenatal, postnatal, and child health), voluntary, confidential counseling and testing (VCT), antiretroviral (ARV) prophylaxis, counselling and support for safe infant feeding and optimal obstetrical practices. • Source: NACO. National AIDS Prevention and Control Policy. Available at: http://www.nacoonline.org/prog_policy.htm, 3 Preble E, Piwoz E. Academy for Educational Development.
Slide 5		
Slide 6		**Reader's Notes:** • Clinicians' job is to minimise the risk associated with each of these factors. The following slides review each factor— the risks involved as well as the interventions to decrease the risks.

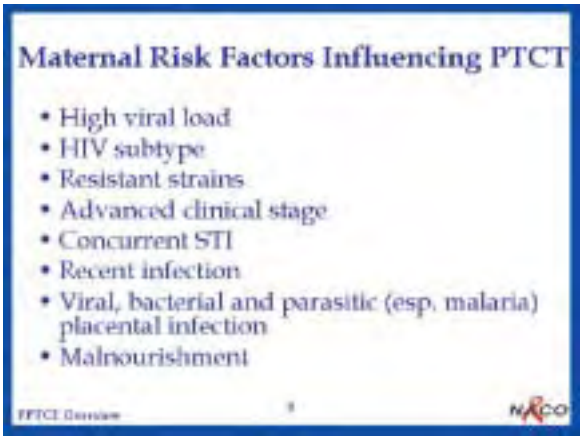
Slide 7



Reader's Notes:

- **Rates vary because of differences in population characteristics such as maternal CD4+ cell counts, RNA viral load and duration of breastfeeding.**
- In the absence of any interventions, transmission from the mother to child is likely to be about 15-45%. Transmission occurs during the intrapartum period, through contact and ingestion of infected maternal secretions and maternal blood and foetal maternal micro transfusion in labour. Transmission also occurs antenatal due to trans placental infection and post partum due to infant feeding practices.
- Source: World Health Organisation. HIV transmission through breastfeeding. A review of available evidence. 2004. Available at http://www.who.int/child-adolescent-health/ publications/Nutrition/ ISBN_92_4_156271_4.htm. (Table adapted from De Cock KM et al. Prevention of mother-to-child HIV transmission in resource-poor countries: Translating research into policy and practice. JAMA. 2000 Mar 1; 283(9) : 1175-82).

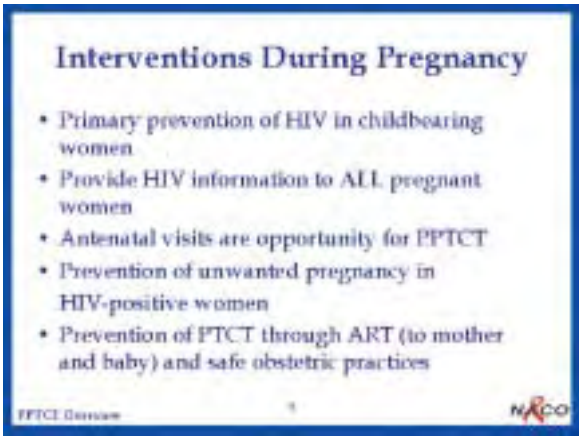
Slide 8



Reader's Notes:

- There is a correlation between the maternal blood viral loads and the risk of transmission. There is no lower limit below which there is absolute safety and upper limit above which there will be definite transmission. Studies have shown that the viral load, the phenotype and genotype of the virus found in the plasma may be different from what is present in cervicovaginal secretion. Other factors like viral resistance to nevirapine may also influence transmission.
- The lower the CD4 count, the greater risk of transmission. Women who are recently infected and those in clinical stage 3 & 4 have high viremia. Their infants are at higher risk of acquiring the infection. Any infection that induces the presence of immune mediators influences transmission. Sexually transmitted infections in the mother increases genital viral shedding.
- While pregnancy does not appear to hasten HIV progression, it is clearly an important additional stress on the body above and beyond the effects of HIV and OI, and ARV side effects. Data on the impact of HIV and pregnancy are difficult to interpret, as so many factors may affect the outcome. Most pregnancy complications appear to be related to advanced HIV disease.

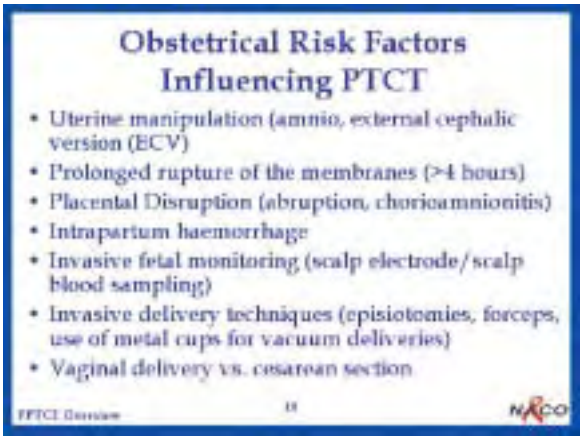
Slide 9



Reader's Notes:

- Primary prevention includes:
- Education about safe sex with use of condoms for mother AND father.
- Early treatment of STIs.
- Encouraging safe sex during pregnancy and lactation.
- Physicians should provide similar care to HIV-positive women as for HIV-negative women. They should have the same number of antenatal visits. Antenatal visits are vital opportunities for PPTCT for both HIV-positive and HIV-negative women. Whether positive or negative, all women should recognise the risk of initial infection, super-infection if they are already infected, and STIs in terms of increased burden on the immune system.
- Pregnancy is not necessarily high risk in HIV-positive women. Invasive antenatal test and procedures must be avoided and voluntary counselling and testing (VCT) to be given all pregnant women. The eventual goal is no mother-to-child transmission. While this may not be possible currently, we can greatly reduce transmission by using the practices described in this unit.

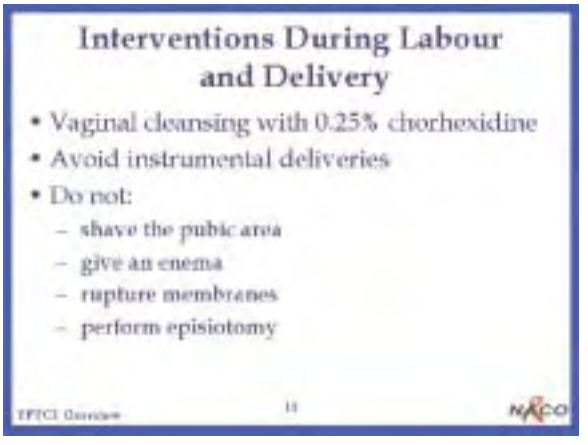
Slide 10



Reader's Notes:

- Studies have shown that uterine manipulations like amniocentesis and external cephalic version increase the risk of transmission of HIV.
- Long duration of rupture of membranes increase the transmission risk. It has been estimated that with every hour, the risk of transmission increases by 2%.
- Placental disruption and infections also adversely affect transmission.
- Invasive fetal monitoring should be avoided, as should all invasive obstetric procedures.
- Where facilities are available, elective LSCS should be offered. Where not feasible, obstetricians should learn safer ways to deliver babies of HIV positive women.
- If instrumental delivery is necessary, then forceps are a better option than vacuum suction cup delivery. Emergency LSCS is associated with high transmission of mother to child transmission.

Slide 11

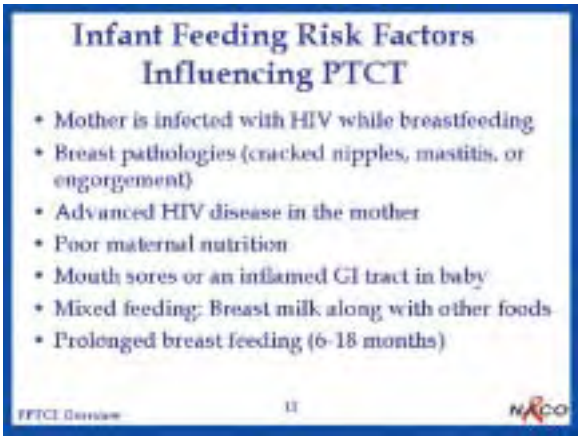


Reader's Notes:

- Delivery can be an emotional time for pregnant women. It could be even more so for women who have fears about disclosure, confidentiality, and transmission of HIV to the baby. The staff must be extremely sensitive and respectful in making these stressful situations less traumatic for the mother and her family.
- General practice recommends that an elective C-section is **NOT** considered a standard PPTCT intervention. Benefits of protecting the baby from HIV are better understood than risk to mothers (i.e., infection, wound dehiscence) and risk to health-care workers. It is a complex issue that must be discussed.
- Clinical judgment and the mother's wishes should guide the decision. It is indicated and effective in certain clinical situations such as when the viral load of mother is extremely high, and should be done before onset of labour preferably at 38 weeks and electively based on mothers wishes and facilities available, but is not standard practice. In India — normal delivery is recommended unless the woman has obstetric reasons (like foetal distress, obstructed labour, etc) for a C-section.
- Use of ART can reduce risk of PTCT better and with less risk than a C-section.

Slide 12	**Infant Risk Factors Influencing PTCT** • Born premature • Low birth weight (<2.5kg) • First infant of multiple birth • Altered skin integrity • Immature GI tract • Genetic susceptibility – HLA genotype – CCR5 karyotype deletion • Immature Immune System – Preterm baby	
Slide 13	**Intervention for Newborns** • Cut cord under cover of light gauze • Determine mother's feeding choice before attaching to breast • Clean injection site with surgical spirits before administering injections • Do not use suction unless absolutely necessary	
Slide 14	**Interventions During Infancy** • Observe for signs and symptoms of HIV infection • All HIV exposed infants should receive cotrimoxazole at 4-6 weeks of age • Follow standard immunisation schedule • Routine well baby visits • DNA PCR if necessary and available • 18-month visit for HIV testing 	

Slide 15



Reader's Notes:

- The factor conferring the greatest risk is the mother becoming infected herself during pregnancy or lactation.
- Advantages of exclusive breast feeding over mixed feeding need to be emphasised during infant feeding counselling sessions. When replacement feeding (infant formula) is acceptable, feasible, affordable, sustainable and clean water is available, HIV-infected mothers should avoid breastfeeding completely.
- Conditions to consider during feeding options counselling: Home environment refers to resources such as fridges, cooking facilities, fuel, electricity, etc. For example, difficulty in boiling water 8 times a day or safe storage of milk. Education on how to manage breastfeeding or prepare breast milk substitute and the importance of not mixing the feeds. Income refers to capacity to buy supplies, or taking break during work to breastfeed. Do they have resources to boil water, type of contamination during transport and to store water safely. It may also be difficult to get water.
- Family and community support is very important for successful feeding of the child. Breastfeeding support groups and health worker support also play a role. Time available for child care is important. If the mother is working, who takes care of child for exclusive breastfeeding/ preparing and feeding of replacement milk.
- Access to counselling is especially important during the management of breastfeeding problems or artificial feeding problems.

Slide 16

Reader's Notes:

- **Refer to Handout 1: Strategies Focused on Prevention of Breast Milk Transmission of HIV** for Options in India.
- The highest risk of HIV transmission during lactation occurs in women who acquire HIV while breastfeeding. When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected mothers is recommended. Otherwise, exclusive breastfeeding is recommended during the first months of life, with early abrupt weaning at 3-4 months or 6 months of age. If breastfeeding exclusively, minimise HIV risk to baby through the following:
  - Use only breast milk for the period.
  - Not even water, tea, or kanji to be given.
  - Infants weaned before 6 months needs alternative feeding with formula - use a cup to feed, not bottle with nipple, for hygiene purposes.

Handout 1: Strategies Focused on Prevention of Breast MilkTransmission of HIV

WHO and UNAIDS (1993): Breastfeeding can lead to an additional risk of HIV transmission of up to 20%, depending on duration of breast feeding, mode of infant feeding and breast health. However, breastfeeding also provides infants with optimal nutrition, reduces morbidity and mortality associated with infections other than HIV, and delays the mother's return to fertility. Therefore, all HIV-infected women should receive counseling and support to be able to choose the infant feeding option most appropriate to their situation.

Three options that could be told to the mother about feeding the baby:
No breast feeding at all (Exclusive Artificial Feeds)

1. Breast feeding exclusively (no other feeds even water) till 4 months and then stop abruptly and move to other milk.
2. Breast feeding for 6 months exclusively and the stop abruptly and move to weaning foods.

Factors that increase the risk of breast milk transmission (BMT) of HIV
Remember the word — DICE

- **D : D**uration of breast feeding
- **I : I**ntegrity of the mucosa of the gastrointestinal system
- **C : C**olostrum
- **E : E**xpressed versus direct breast feeding

- **Duration of breast feeding:**
  - The longer the duration of the breast feeding the higher the risk of transmission.
  - If this factor were to be considered then the 1st option is better than the 2nd option and the 2nd is better than the 3rd option.
  - However considering the Indian situation (poor hygienic practices, ignorance of mother, lack of enough money to buy materials for feeding, etc.) the chance of baby dying due to gastroenteritis is higher than the chance of the child dying of HIV. If this were to be considered then the 2nd option is better than the 3rd is better than the 1st option.

- **Integrity of baby's gastrointestinal (gut) mucosa:**
  - The baby's gut is safe from any mucosal injury with breast milk.
  - If this were considered the 2nd and third option is better than the 1st option.
  - If any artificial feed is given the chance of small microscopic mucosal injury of the gut is very high.
  - Hence it is safer to feed only exclusive breast feed so that the mucosa of the gut is safeguarded and the chance of infection is reduced.

- **If mixed feeds** (i.e breast milk and other milk such as cow's milk is given) the chance of mucosal injury is very high and this could increase the risk of breast milk transmission of HIV.
- Considering the options again, the risk of giving **mixed feeds** is higher in the 1st option than the 2nd and third options. Consideration of social implications of not breast feeding or the pressure to breast feed by other family members increases chances of giving mixed feeds under option 1.

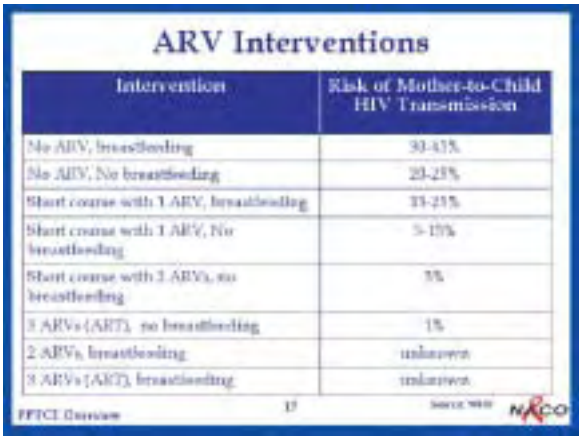
Never mix breast feeds and artificial feeds. Follow any one option correctly, after

- **Colostrum versus no colostrum:**
  - The chance of the baby getting natural immunity against many infections increases with the baby being fed with colostrums.
  - Hence if this is considered then the 2nd or 3rd option is better than the first option. However colostrums is also considered to be highly infectious.
- **Expressed versus direct breast feeding (DBF):**
  - The risk of the mother having **cracked nipples, mastitis** is possibly higher with direct breast feeding than expressed breast feeding.
  - Cracked nipples, mastitis could increase the risk of BMT of HIV due to the chance of blood being mixed with breast milk.
  - Hence if 2nd or 3rd options are chosen it is preferable to give expressed breast milk than DBF.
  - The advantage of expressed breast milk is that when breast milk has to be stopped suddenly/ abruptly at either 4 months or 6 months the chance that the baby will not give trouble as well as the mother having engorged breasts is reduced.
  - But if the mother wants to give DBF, she must be taught how to reduce the chance of cracked nipples and this during the antenatal period itself:
    - Examine for inverted or flat nipples and take measures to correct it in the antenatal period itself by oil massage and drawing it out or by the negative suction syringe method.
    - Assume the correct position for herself and the baby when feeding
    - Avoid use of soaps that dry the skin.
    - Daily bath and change of inner wear is sufficient to keep the breast clean and maintain the suppleness of the nipples.
    - Avoid washing the breast every time she feeds the baby.

Important aspects on counseling HIV-positive mothers who opt to breast-feed :

- Prevent breast problems:
  - Increased risk of transmission with mastitis, abscesses, and bleeding, cracked nipples. Examination and correction of problems at pregnancy time.
  - HIV-infected women who breastfeed should be assisted to ensure that they use a good breastfeeding technique to prevent breast pathologies, which should be treated promptly if they occur.
- Safer sex while breastfeeding:
  - "Super-infection" with different HIV can increase mother's viral load and increase risk of HIV transmission to baby.
- Seek medical care for any illness.
- Benefits of expressing the breast milk and feeding over direct breast feeding. How to stop breast feeding abruptly: How to avoid mixed feeding.

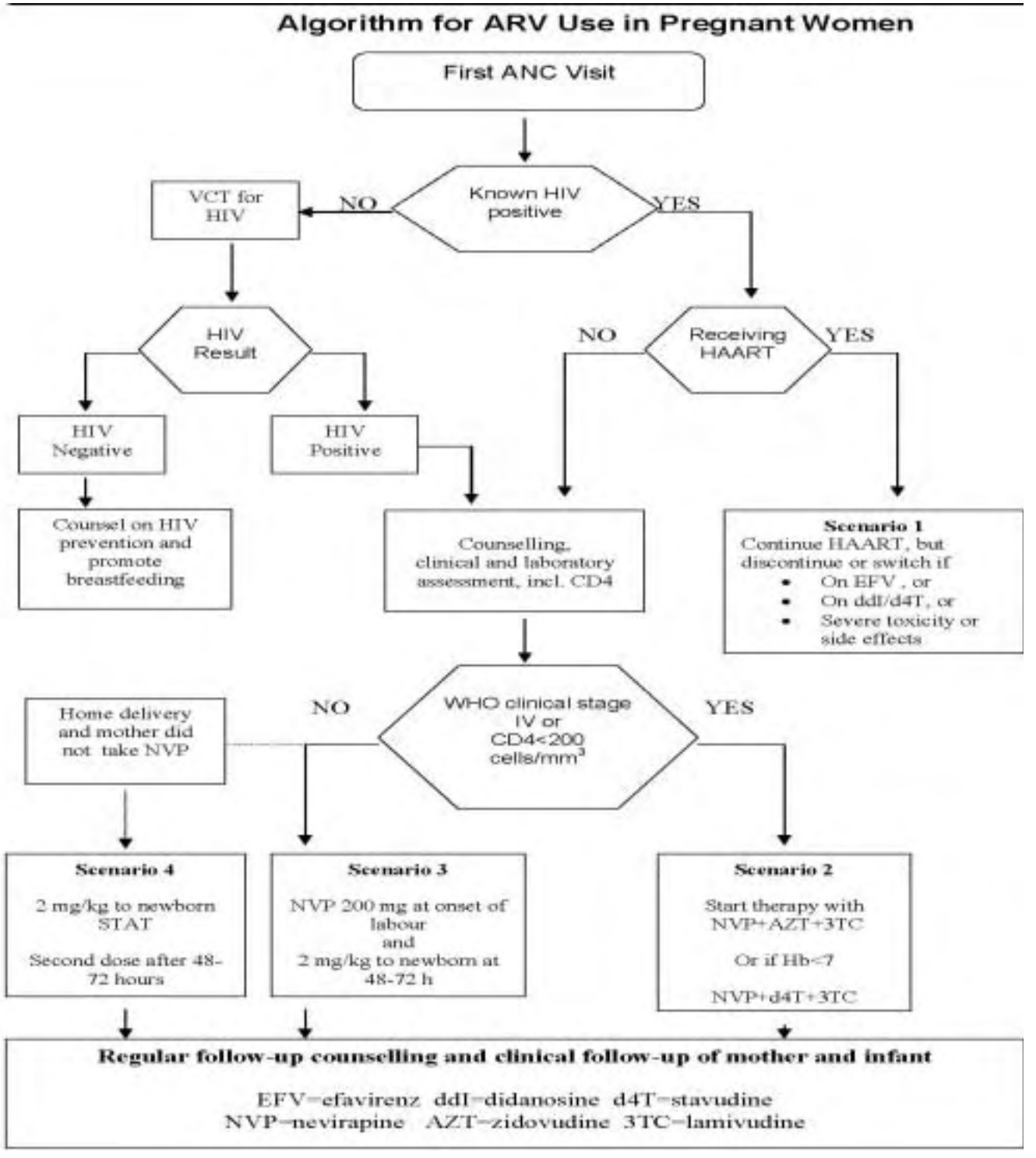
Slide 17



Reader's Notes:

- Adequate and appropriate ARV prophylaxis, safe methods of delivery and good care of the mother during the antenatal period will help to decrease risk of transmission.
- This is a review of ARV interventions that summarise efforts to decrease the risk to babies. Our goal is to prevent HIV transmission.
- Refer to **Handout 2: Algorithm for ARV Use in Pregnant Women for Specific ARV Treatment for Details.**
- ARV's require ongoing care and monitoring and reduce risk of PTCT in the following ways:
  - Reduces viral replication and viral load.
  - Treats maternal infection.
  - Protects the HIV-exposed infant.
  - Improves overall health of mother.
- Advantages of ART during pregnancy:
  - Antiretroviral therapy reduces risk of transmission even in mothers with low baseline viral loads. Combination therapy with 3 drugs called ART can reduce transmission risk to <2% in many cases. Combination ART is the best way to prevent PTCT.
  - Remember that in developed countries vertical transmission rarely happens, especially for women on ART (less than 70 nationwide in the U.S., 2003).
  - ARV's are safe, well tolerated and easy to use in a pregnant woman who is carefully monitored.
  - It is economical because it eliminates the need for the HIV care and treatment of infected babies (there won't be any, or they will be few in number).
  - Reduces the risk of the mother developing resistance, thereby preserving her future treatment options.
  - GOI guidelines for PPTCT include single dose of Nevaripine for all pregnant positive women.
  - Risks to infant (teratogenicity, preterm labour) appear to be minimal for most regimens. EFV has a teratogenic effect and is contraindicated in pregnancy. It should be avoided in women of child-bearing age who are not on effective contraceptives.

Handout 2: Algorithm for ARV Use in Pregnant Women (2006)



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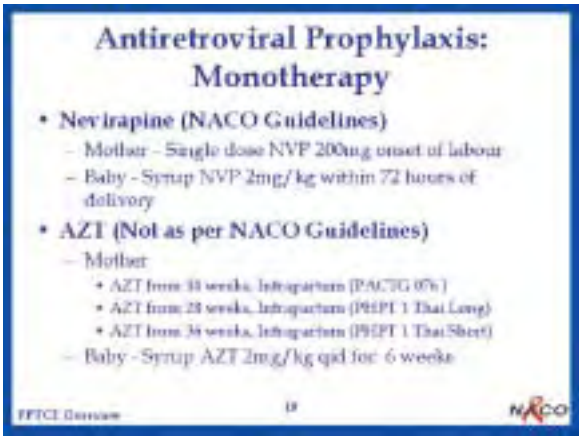


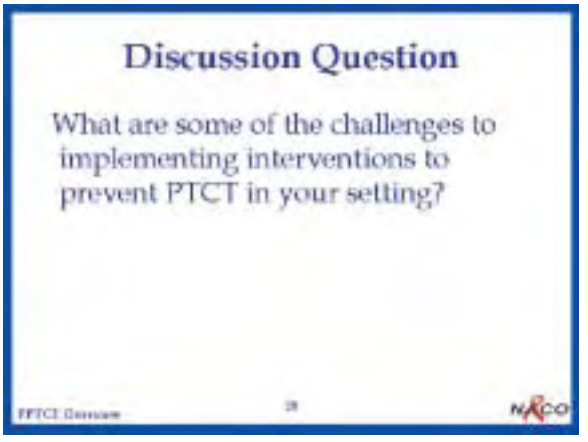
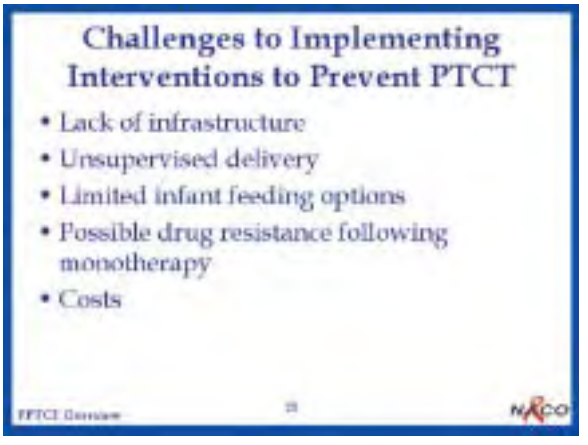
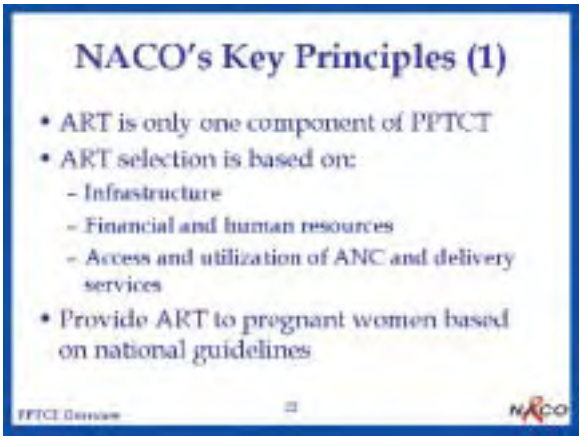
Reader's Notes:

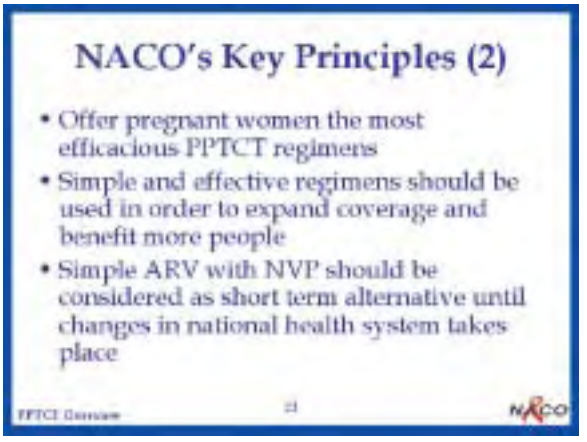
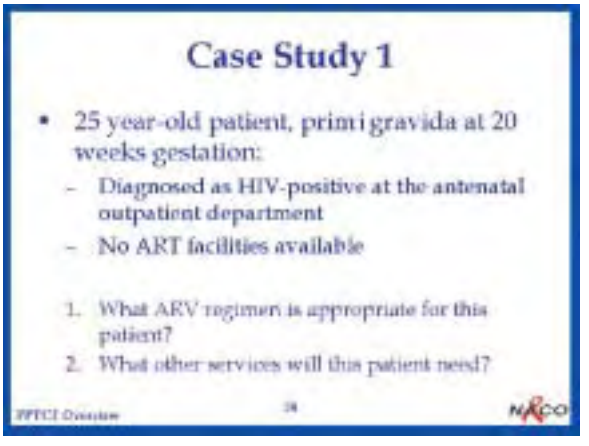
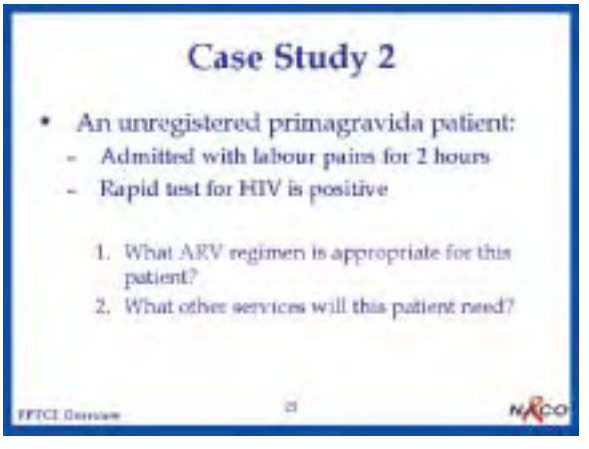
- ARV drugs decrease the viral load and thus decrease the transmission rates. Single dose NVP 200mg given at the onset of labour and single dose of syrup NVP 2mg/kg weight to the baby within 72 hours decreases risk of transmission by 13.1% (breast feeding).
- **Advantages:** Affordable, single dose easy administration, appropriate for resource poor settings.
- **Disadvantages:** Resistance even with single dose of NVP, which makes it difficult to treat mother if she needs HAART for her own health in the near future. Baby may get infected with NVP resistant strains. If the women delivers within 2 hours of administering NVP, the baby needs syrup NVP 2mg/kg soon after delivery and a second dose at 72 hours of age. If a women gets NVP and the labour turns out be false labour, there is need to repeat NVP only if does not deliver in the next seven days.
- Studies have proved beyond doubt that AZT is most effective pre exposure prophylaxis for the baby. The drug is metabolized into its active form in the placenta and the mother to child drug concentration is also high. The first study PACTG 076 demonstrated starting AZT from 14 weeks, and the Thai studies started at 28 weeks and 36 weeks, which have proved very effective in preventing transmission in women that choose to breast feed as well as non breast feeding women. Transmission rates 8.3 %, 6.5%, 8.6 % (non breastfeeding).

Slide 19

Reader's Notes:

- With the changing policies world wide , the NACO is shifting its emphasis from just prevention of infection to the baby to care of the maternal health with the baby. Hence all HIV positive antenatal women who attend antenatal clinics need to be assessed by the HIV physician to the stage of the disease or based on the CD 4 count and be started on HAART therapy. Efavirenz is contra indicated in first trimester.

Slide 20		
Slide 21		**Reader's Notes:** • In low resource settings there is generally a lack of infrastructure to provide antenatal counseling and testing, ART prophylaxis and safe delivery. There is also the possibility of drug resistance following intermittent monotherapy with each pregnancy. The cost of India's national perinatal prevention program is 3 times higher than the program that provides basic maternal and neonatal care. • A significant number of deliveries still occur unsupervised or by days at home and extending the services to this population would be a great challenge. Breast feeding is still done due to economic and cultural reasons. Getting good and uninterrupted supply of formula feeds will need to be a priority in the future. • There are also concerns for the mother. The risk of inducing nevirapine resistance is being studied and there is data that subsequent therapy for the mother is likely to be less effective. Finally, there is the huge bill for the program that is being subsidized by the Government. Any modification to this simplified protocol increases the financial burden excessively.
Slide 22		

Slide 23		
Slide 24		
Slide 25		

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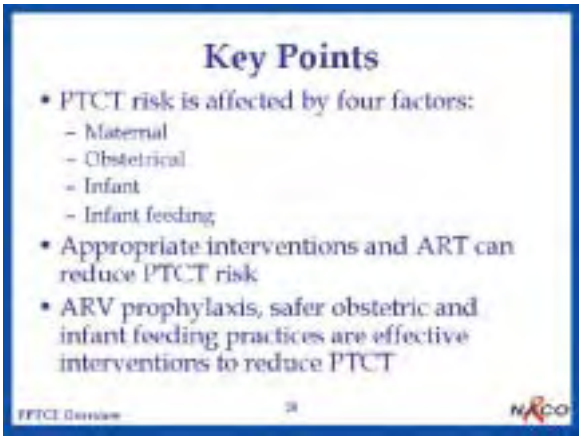


Reader's Notes:

- Further reading:

1. NACO Guidelines for HIV Care & Treatment in Infants and Children — November 2006

SESSION 24

SESSION

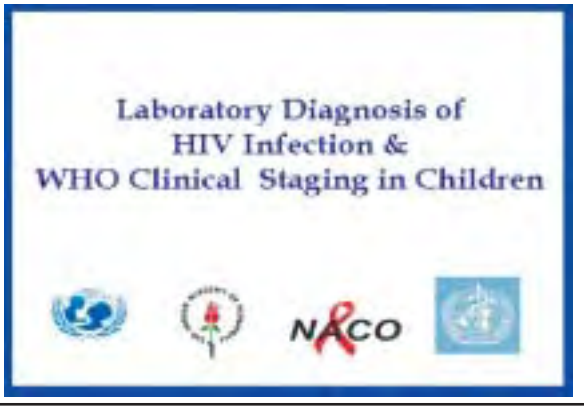
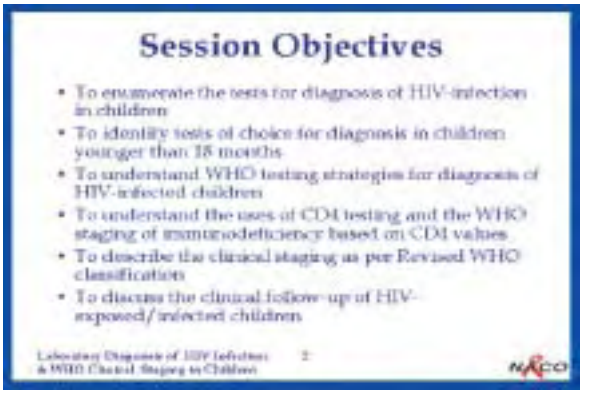
LABORATORY DIAGNOSIS OF HIV INFECTION & WHO CLINICAL STAGING IN CHILDREN

24

Total Session Time: 45 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Enumerate the tests for diagnosis of HIV-infection in children
- Identify tests of choice for diagnosis in children younger than 18 months
- Understand WHO testing strategies for diagnosis of HIV-infected children
- Understand the uses of CD4 testing and the WHO staging of immunodeficiency based on CD4 values
- Describe the clinical staging as per Revised WHO classification
- Discuss the clinical follow-up of HIV-exposed/infected children

Slide 1		
Slide 2		

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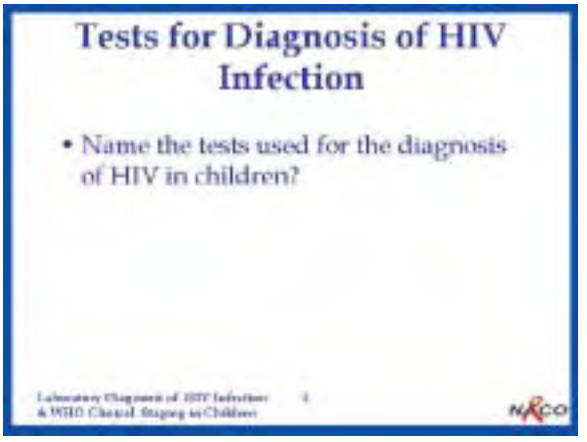

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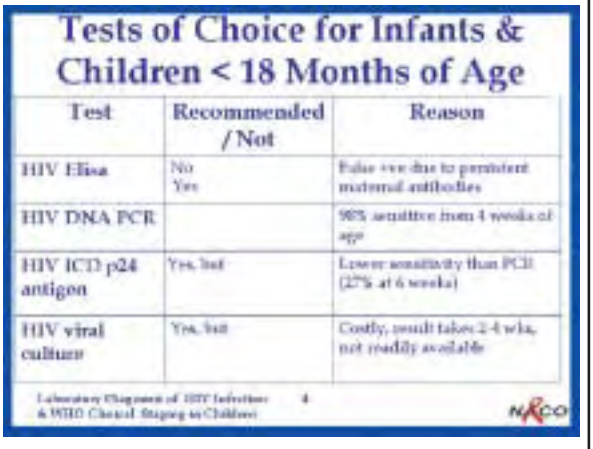


Reader's Notes:

- For children < 18 months old, both breastfed and non-breastfed, born to a HIV positive mother – the following testing strategy applies according to the NACO programme:The first HIV DNA PCR shall be conducted at 6 weeks of age. If the PCR test is positive,the test is to be repeated immediately (or as early as possible) for confirmation.
- If the first PCR is negative in a non-breastfed baby, confirm with a second PCR test at 6 months.
- If the child is breastfed and initial PCR test at 6 weeks is negative, PCR testing should be repeated at 6—8 weeks after cessation of breastfeeding to rule out HIV infection. In case of mixed -feeding the same strategy to be applied as for a breast fed baby.
- If symptoms develop at any time, the child should be tested appropriately (PCR or ELISA/rapid) at that age.
- A report of "HIV Positive" is given when 2 PCR tests are positive; and a report of "HIV negative" is given when 2 PCR tests are negative.

Handout 1: Presumptive and Definitive Criteria for Recognizing HIV/AIDS-Related Clinical Events in Infants & Children with Confirmed HIV Infection

Primary HIV infection	Presumptive	Definitive
Asymptomatic infection Acute retroviral syndrome	Acute febrile illness 2-4 weeks post-exposure, often with lymphadenopathy, pharyngitis and skin rashes	In children 18 months or over sero-conversion from HIV antibody negative to antibody -positive. A positive virological test for HIV virus or its components (RNA or DNA or ICD HIV p 24 antigen) confirmed by a second virological test obtained from a separate determination. Profound temporary lymphopaenia and other transient blood abnormalities may occur.
Clinical Stage 1		
Asymptomatic	No HIV related symptoms reported and no signs on examination.	Not required.
Persistent generalized lymphadenopathy (PGL)	Swollen or enlarged lymph nodes >1 cm at two or more non-contiguous sites, without known cause.	Not required.
Clinical Stage 2		
Unexplained persistent hepatosplenomegaly	Enlarged liver and spleen without obvious cause.	Not required.
Papular pruritic eruptions	Papular pruritic vesicular lesions. Also common in uninfected children: scabies and insect bites should be excluded.	Not required.
Fungal nail infections	Fungal paronychia (painful, red and swollen nail bed) or onycholysis (painless separation of the nail from the nail bed).	Not required

	Presumptive	Definitive
	Proximal white subungual onchomycosis is uncommon without immunodeficiency.	
Angular cheilitis	Splits or cracks on lips at the angle of the mouth with depigmentation, usually responding to antifungal treatment but may recur.	Not required.
Lineal Gingival Erythema (LGE)	Erythematous band that follows the contour of the free gingival line; may be associated with spontaneous bleeding.	Not required.
Extensive wart virus infection	Characteristic warty skin lesions; small fleshy grainy bumps, often rough, flat on sole of feet (plantar warts); facial, more than 5% of body area or disfiguring.	Not required.
Extensive molluscum contagiosum infection	Characteristic skin lesions: small fleshcoloured, pearly or pink, dome-shaped or umbilicated growths, may be inflamed or red; facial, more than 5% of body area or disfiguring.	Not required.
Recurrent oral ulcerations (two or more in six months)	Aphthous ulceration, typically with a halo of inflammation & yellow-grey pseudo-membrane.	Not required.
Unexplained parotid enlargement	Asymptomatic bilateral swelling that may spontaneously resolve and recur, in absence of other known cause, usually painless.	Not required.
Herpes zoster	Painful rash with fluid-filled blisters, dermatomal distribution, can be haemorrhagic on erythematous background, and can become large and confluent. Does not cross the midlines.	Not required
Recurrent upper respiratory tract infection (URTI)	Current event with at least one episode in past 6 months. Symptom complex; fever with unilateral face pain and nasal discharge (sinusitis) or painful swollen eardrum (otitis media), sore throat with productive cough (bronchitis), sore throat (pharyngitis) and barking crouplike cough (LTB). Persistent or recurrent ear discharge.	Not required.

	Presumptive	Definitive
Clinical Stage 3		
Unexplained moderate malnutrition	Weight loss: low weight-for-age, upto 2 standard deviations (SDs), not explained by poor or inadequate feeding and or other infections, and not adequately responding to standard management.	Confirmed by documented loss of bodyweight of —2SD, failure to gain weight on standard management and no other cause identified during investigation.
Unexplained persistent diarrhoea	Unexplained persistent (14 days or more) diarrhoea (loose or watery stool, three or more times daily), not responding to standard treatment.	Confirmed by stools observed and documented as unformed. Culture and microscopy reveal no pathogens.
Unexplained persistent fever(intermittent or constant, for longer than one month)	Reports of fever or night sweats for longer than one month, either intermittent or constant, with reported lack of response to antibiotics or anti-malarials. No other obvious foci of disease reported or found on examination. Malaria must be excluded in malarious areas.	Confirmed by documented fever of>37.5 0C with negative blood culture, negative malaria slide and normal or unchanged CXR, and no other obvious foci of disease.
Oral candida (outside first 6—8 weeks of life)	Persistent or recurring creamy white to yellow soft small plaques which can be scraped off (pseudomembranous), or red patches on tongue, palate or lining of mouth, usually painful or tender(erythematous form)	Confirmed by microscopy or culture.
Oral hairy leukoplakia	Fine small linear patches on lateral borders of tongue, generally bilaterally, which do not scrape off	None
Lymph node TB	Non acute, painless “cold” enlargement of lymph nodes, usually matted, localized to one region. May have draining sinuses. Response to standard anti-TB treatment in one month.	Confirmed by histology or fine needle aspirate for Ziehl Neelsen stain. Culture.

	Presumptive	Definitive
Pulmonary TB.	Nonspecific symptoms, e.g. chronic cough, fever, night sweats, anorexia and weight loss. In the older child also productive cough and haemoptysis. Abnormal CXR. Response to standard anti-TB treatment in one month	Confirmed by positive sputum smear or culture.
Severe recurrent presumed bacterial pneumonia.	Cough with fast breathing, chest indrawing, nasal flaring, wheezing, and grunting. Crackles or consolidation on auscultation. Responds to course of antibiotics. Current episode plus one or more in previous 6 months	Confirmed by isolation of bacteria from appropriate clinical specimens (induced sputum, BAL, lung aspirate).
Acute necrotizing ulcerative gingivitis or stomatitis, or acute necrotizing ulcerative periodontitis	Severe pain, ulcerated gingival papillae, loosening of teeth, spontaneous bleeding, bad odour, and rapid loss of bone and/or soft tissue	None
Symptomatic LIP	No presumptive diagnosis.	Diagnosed by CXR bilateral reticulonodular interstitial pulmonary infiltrates present for more than two months with no response to antibiotic treatment and no other pathogen found. Oxygen saturation persistently <90%. May present with cor pulmonale and may have increased exercise induced fatigue. Characteristic histology
Chronic HIV-associated lung disease (including bronchiectasis)	History of cough productive of copious amounts of purulent sputum bronchiectasis only), with or without clubbing, halitosis, and crepitations and/or wheezes on auscultation	Confirmed by CXR may show honeycomb appearance (small cysts) and/or persistent areas of opacification and/or widespread lung destruction, with fibrosis & loss of volume

	Presumptive	Definitive
Unexplained anaemia (<8g/dl), or neutropenia (<1000/mm3) or chronic thrombocytopenia (<50 000/ mm3)	No presumptive diagnosis.	Diagnosed on laboratory testing, not explained by other non-HIV conditions, or not responding to standard therapy with haematinics, antimalarials or anthelminthics as outlined in IMCI.
Clinical Stage 4		
Unexplained severe wasting, stunting or severe malnutrition not adequately responding to standard therapy	Persistent weight loss not explained by poor or inadequate feeding, other infections and not adequately responding in two weeks to standard therapy. Characterized by: visible severe wasting of muscles, with or without oedema of both feet, and/ or weight-for -height of —3 SDs, as defined by WHO IMCI guidelines.	Confirmed by documented weight oss of>-3 SD +/- oedema
Pneumocystis pneumonia (PCP)	Dry cough, progressive difficulty in breathing, cyanosis, tachypnoea and fever; chest indrawing or stridor. (Severe or very severe pneumonia as in IMCI). Usually of rapid onset especially in infants under six months of age. Response to high-dose co-trimoxazole+/- prednisolone.	Confirmed by: CXR typical bilateral perihilar diffuse infiltrates; microscopy of induced sputum or BAL or NPA, or histology of lung tissue.
Recurrent severe presumed bacterial infection, e.g. empyema, pyomyositis, bone or joint infection, meningitis but excluding pneumonia	Fever accompanied by specific symptoms or signs that localize infection. Responds to antibiotics. Current episode plus one or more in previous 6 months.	Confirmed by culture of appropriate clinical specimen.
	Presumptive	**Definitive**
Chronic herpes simplex infection; (orolabial or cutaneous of more than one month's duration or visceral at any site).	Severe and progressive painful orolabial, genital, or anorectal lesions caused by HSV infection present for more than one month	Confirmed by culture and/or histology

	Presumptive	Definitive
Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)	Chest pain and dysphagia (difficulty in swallowing), odynophagia (pain on swallowing food and fluids), or retrosternal pain worse on swallowing (food and fluids) responds to specific treatment. In young children, suspect particularly if oral candida observed and food refusal occurs and/or difficulties/ crying when feeding	Confirmed by macroscopic appearance at endoscopy, microscopy of specimen from tissue or macroscopic appearance at bronchoscopy or histology.
Extrapulmonary/ disseminated TB.	Systemic illness usually with prolonged fever, night sweats, weight loss. Clinical features of organs involved, e.g. sterile pyuria, pericarditis, ascites, pleural effusion, meningitis, arthritis, orchitis. Responds to standard anti-TB therapy	Confirmed by positive microscopy showing AFB or culture of Mycobacterium tuberculosis from blood or other relevant specimen except sputum or BAL, biopsy and histology.

Handout 2: Monitoring HIV-infected Children not on ART (Pre-ART Care)

Assessment and management after confirmed HIV diagnosis include the following:

- Assess growth and nutritional status, and intervention needs.
- Assess immunization status and provide appropriate immunization.
- Assess for signs and symptoms of opportunistic infections and TB exposure. If opportunistic infection is suspected, diagnosis and treatment of OIs take priority over ART initiation.

- Assign WHO clinical stage

- Ensure that the child is on cotrimoxazole prophylaxis
- Identify any concomitant medication use that may have drug interactions with ART.

- Staging of HIV disease using immunological criteria (see WHO stage from "not significant" to "severe immune suppression")
  - Perform CD4 (% CD4 is preferred in children < 5 years and CD4 count is preferred in children = 5 years).
  - In order to calculate % CD4, full blood cell count (FBC) needs to be performed as well (ideally automated).

- Assess whether the child fits the criteria for starting ART
- Assess family situation including but not limited to number of persons with or at risk for HIV infection and their current health/treatment status.
  - Identify primary caregiver for the child and his/her ability and willingness to adhere to follow up and HIV treatment especially ART
  - Assess family member's understanding of HIV disease and treatment
  - Assess disclosure status of HIV diagnosis within the family (whether the child knows his/her diagnosis and whether anyone else knows, and also if the child knows the parent(s)' HIV status)
  - Assess family financial status including ability to pay for transportation to clinic, ability to afford adequate food/nutritional supplements for the child, ability to pay for any treatment needed etc.

- Caregivers should be advised to bring back the child if sick. If child has missed a visit, attempts should be made to call or visit the child's home to see what has happened.
- Regular monitoring of children not requiring ART yet (Pre-ART care) is essential in order to maintain a healthy positive living status until they require therapy:
- Good pre-ART care of the infected child with support to the family as comprehensive care for the family unit is important as this sets the stage for future care and better response to treatment.

Monitoring and follow-up schedule for children on pre-ART care						
Items	Baseline	Month 1	**Month 2**	**Month 3**	**Month 6**	Every 6 months
Clinical Evaluation						
Clinical Evaluation [a]	X	X	X	X	X	X
Weight, Height	X	X	X	X	X	X
Nutritional status and needs	X	X	X	X	X	X
Cotrimoxazole needs & adherence	X	X	X	X	X	X
Counselling for prevention of STIs and pregnancy in adolescents [b]	X				X	X
OI prevention and treatment needs [e]	X	X	X	X	X	X
Laboratory						
Hb WBC	X					X
ALT [C]	X					
CD4% or count [d]	X					X

Notes:

a. Includes history taking and physical exam and assessment of neurodevelopment. Children <12 months of age have a higher risk of HIV disease progression and should be followed more frequently than older children.

b. See section A2 of Pedialric guideline (NACO) pg 7; for cotrimoxazole prophylaxis.

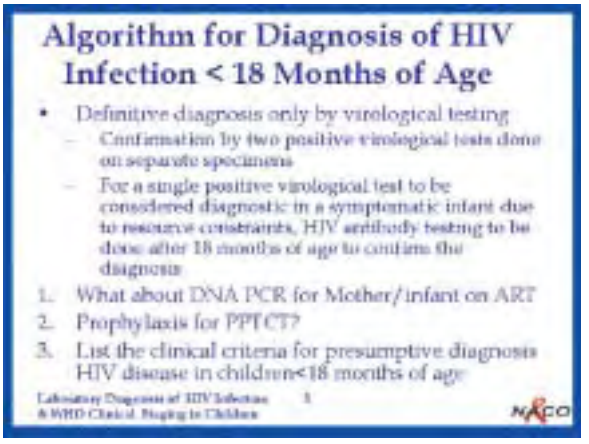
c. ALT at baseline is the minimum monitoring for possible liver impairment. Children with high ALT (> 5 times upper limit of normal) should have full liver function test performed as well as assessment for hepatitis B, hepatitis C or other hepatic disease. Other chemistry tests depend on symptoms.

d. CD4% is used in children < 5 years of age. For children > 5 years of age, CD4 count is mainly used.

e. Counselling and access to birth control measures and sexually transmitted infections prevention in teenagers should be part of every visit. Counselling should also include prevention of transmission of HIV to others, and in girls who are in reproductive age, the risk of transmitting HIV to their infants

f. Assessing TB exposure is important.

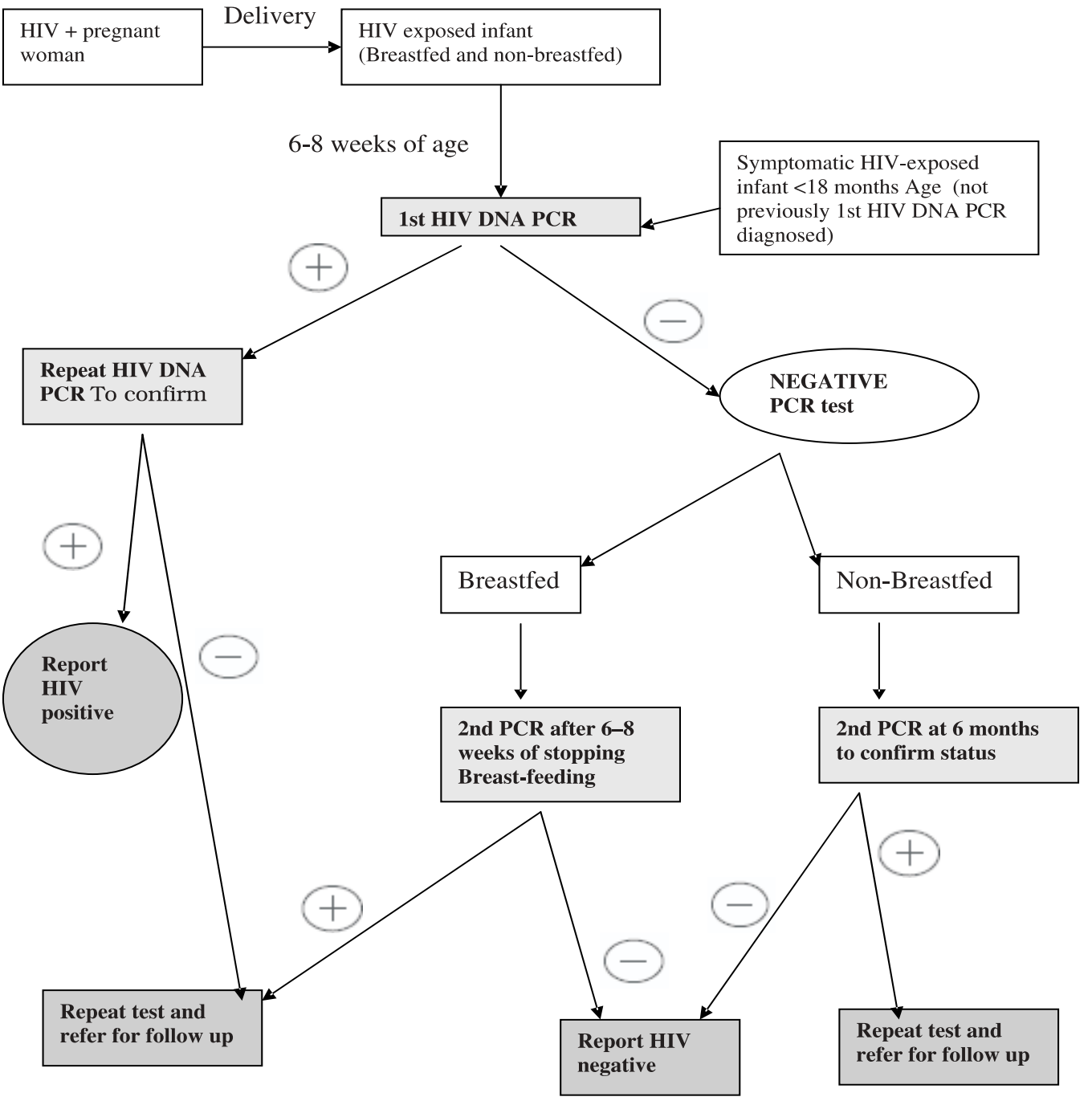
Slide 5



Reader's Notes:

- Clinical criteria for presumptive diagnosis of severe HIV disease in infants and children < 18 months of age, requiring ART is to be applied in infants and children without a confirmed diagnosis of HIV infection.
- In such infants and children, presence of certain criteria are sufficient to consider them to have severe manifestation of HIV infection.This infant should be ELISA positive (antibody test positive), & should have any AIDS defining disease OR the infant has two or more of three criteria listed.
- Also, one needs to have other supportive evidence to consider HIV infection in the child. The trainer may request the participants to refer to the below mentioned reference for the IMCI (Integrated Management of Childhood Illnesses) definitions of oral thrush, severe pneumonia and severe sepsis.
- Reference(Handout 5): Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO pg 10.
- Reference:(Handout 6): Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO pg 12.

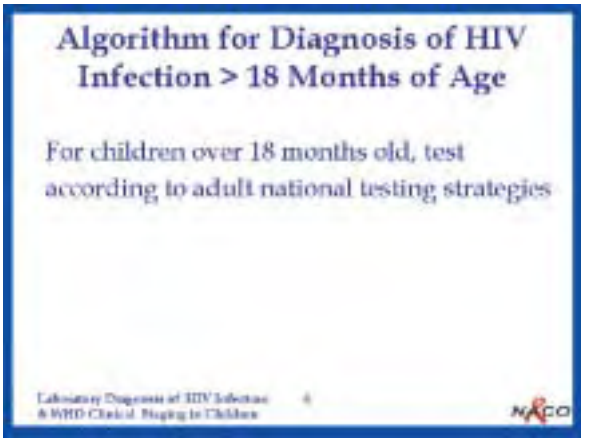
Handout 3: HIV diagnosis in children < 18 months with DNA-PCR



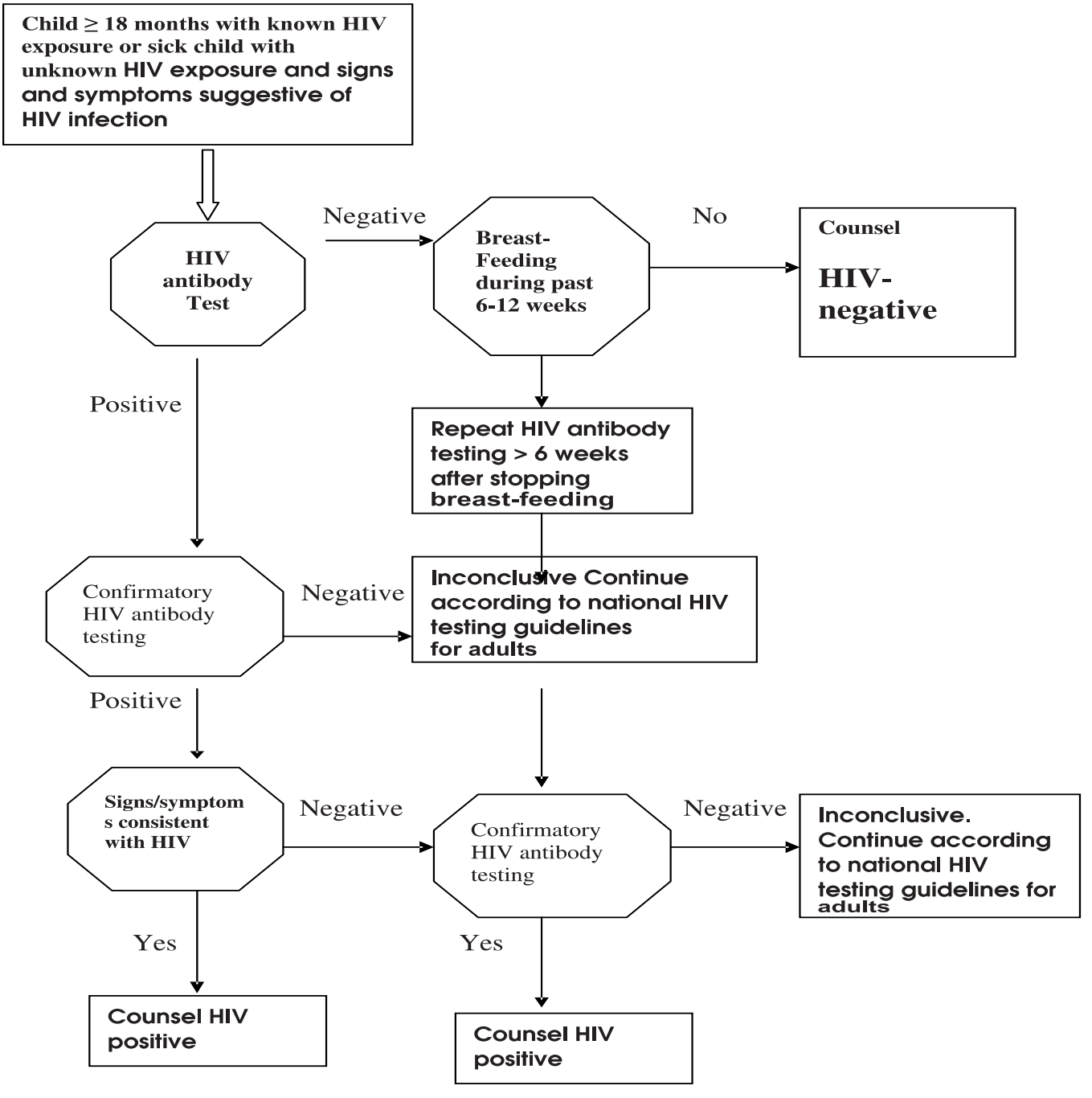
If Child 12 months old, can use adult testing strategies such as rapid test or ELISA however, definitive and confirmatory testing is only possible after 18 months of age

Handout 4: Clinical criteria for presumptive diagnosis of severe HIV disease in infants and children less than 18 months of age requiring ART in situations where virological testing is not available

Clinical criteria for presumptive diagnosis of severe HIV disease in infants and children less than 18 months of age requiring ART in situations where virological testing is not available
A presumptive diagnosis of severe HIV disease should be made if: • The infant is confirmed HIV antibody positive; *and* • Diagnosis of any AIDS-indicator condition (s) can be made; *or* • The infant is symptomatic with two or more of the following: – Oral thrush [a]; – Severe pneumonia [a]; – Severe sepsis [a]. Other factors that support the diagnosis of severe HIV disease in an HIV sero-positive infant include: • Recent HIV-related maternal death; or advanced HIV disease in the mother; • CD4 < 20% Confirmation of the diagnosis of HIV infection should be sought as soon as possible.
Notes: As per Integrated Management of Childhood Illnesses (IMCI) definition: 1. Oral thrush: Creamy white to yellow soft small plaques on red or normally coloured mucosa which can often be scraped off (pseudo membranous), or red patches on tongue, palate or lining of mouth, usually painful or tender. Not responding to topical antifungal treatment. 2. Severe pneumonia: Cough or difficult breathing in a child with chest indrawing, stridor or any of the IMCI general danger signs; i.e., lethargic or unconscious, not able to drink or breast-feed, vomiting, and presence or history of convulsions during current illness; responding to antibiotics. 3. Severe sepsis: Fever or low body temperature in a young infant with any severe sign such as fast breathing, chest indrawing, bulging fontanelle, lethargy, reduced movement, not feeding or sucking breast milk, convulsions, etc. a. It is unclear how often CD4 is lowered in the above conditions in HIV-uninfected children.

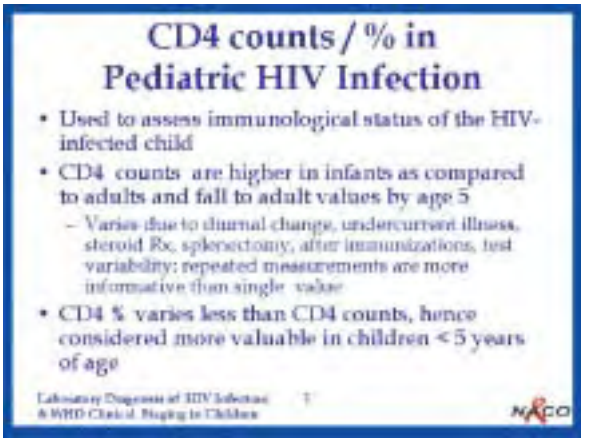
Slide 6		**Reader's Notes:** • Refer participants to **Handout 5 : HIV Diagnosis in Children > 18 months** and Guidelines for HIV Care and Treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO page 11.

Handout 5: HIV Diagnosis in Children > 18 months



See annex 1 for detailed algorithm for HIV testing in children > 18 months and adults

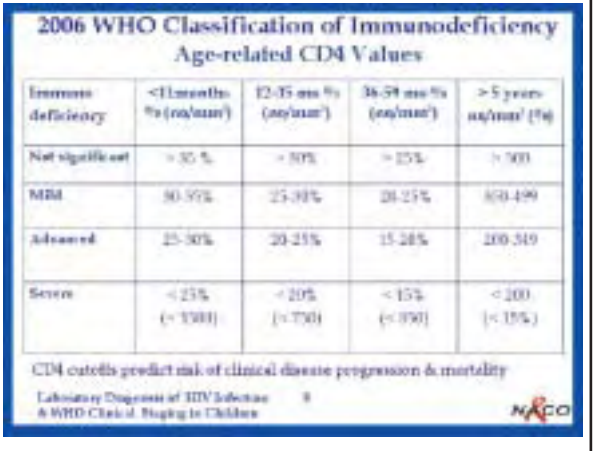
Slide 7



Reader's Notes:

- CD4 is the best measurement for assessing immune deficiency.
- CD4 should be used in conjunction with clinical assessment; however, CD4 allows an earlier detection of worsening of HIV disease as CD4 decline usually occurs prior to clinical progression.
- CD4 monitoring can aid in the decision to initiate or switch ART.
- Younger children normally have higher CD4 than older children and adults.
- %CD4 cells varies less in children < 6 years old and is the preferred measurement.
- Reference: Table-9, Page 16; Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO.)

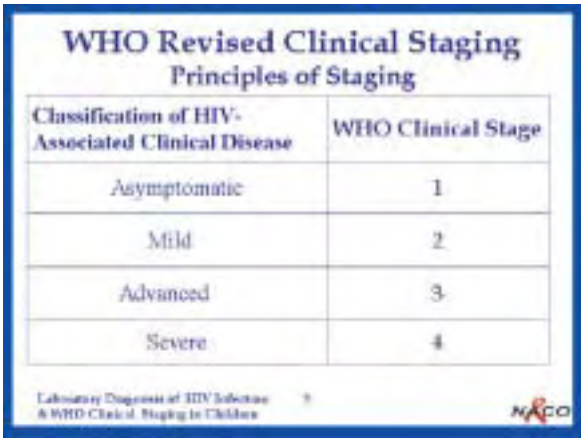
Slide 8



Reader Notes:

- At age ≤ 5 years, CD4% can be used.
- The threshold CD4 cell levels for severe immuno-deficiency in children age 1 year and up corresponds with a 12-months mortality risk of = 5%. In children younger than 1 year and especially < 6 months, CD4 is less predictive of mortality and there is high risk for death even at high %CD4.
- Normal CD4 count/% in children are:
  (a) <11 months:- >= 35%
  (b) 12-35 months: >=30%
  (c) 36-59 months: >= 25%
  (d) > 5 years: >500 cells/mm3
- Long-term prognosis related to CD4 value (degree of immunocompromise) Therefore, CD4 value used for
  1. Initiation of ART
  2. Monitoring response to ART
- Reference: Page 16; Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO.)

Slide 9



Reader's Notes:

- Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006, developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO.

Handout 6: WHO Clinical Staging of HIV for Infants andChildren with Confirmed HIV Infection

Clinical Stage 1

- *Asymptomatic* (No HIV related symptoms reported and no signs on examination)
- *Persistent generalized lymphadenopathy*

Clinical Stage 2

- Unexplained[1] persistent hepatosplenomegaly
- Papular pruritic eruptions
- Extensive wart virus infection
- Extensive Molluscum Contagiosum
- Recurrent oral ulcerations
- Unexplained persistent parotid enlargement
- Lineal gingival erythema
- *Herpes zoster*
- *Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)*
- *Fungal nail infections*

Clinical Stage 3

- Unexplained moderate malnutrition not adequately responding to standard therapy
- *Unexplained persistent diarrhoea (14 days or more)*
- *Unexplained persistent fever (above 37.5oC intermittent or constant, for longer than one month)*
- *Persistent oral candidiasis (after first 6-8 weeks of life)*
- *Oral hairy leukoplakia*
- *Acute necrotizing ulcerative gingivitis/periodontitis*
- Lymph node TB
- *Pulmonary TB*
- Severe recurrent bacterial pneumonia
- Symptomatic lymphoid interstitial pneumonitis
- Chronic HIV-associated lung disease including bronchiectasis

- *Unexplained anaemia (<8g/dl), neutropenia (<500/mm³) or chronic thrombocytopenia(<50 000/ mm³)*

Clinical Stage 4[2]

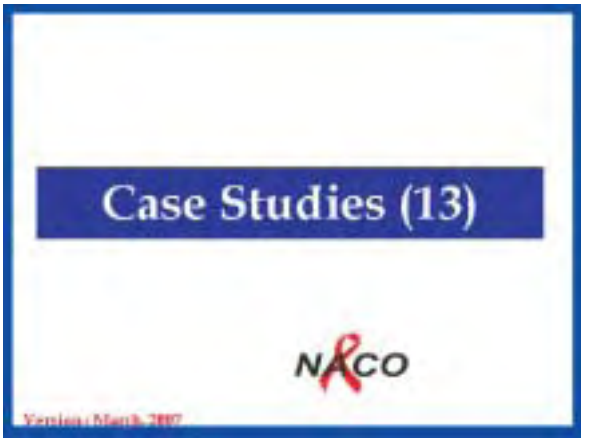
- *Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy*
- *Pneumocystis pneumonia*
- *Recurrent severe bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)*
- *Chronic herpes simplex infection; (orolabial or cutaneous of more than one month's duration or visceral at any site)*
- *Extrapulmonary TB*
- *Kaposi sarcoma*
- *Oesophageal Candidiasis (or candidiasis of trachea, bronchi or lungs)*
- *Central nervous system Toxoplasmosis (after one month of life)*
- *HIV encephalopathy*
- *Cytomegalovirus infection: retinitis or CMV infection affecting another organ, with onset at age over 1 month.*
- *Extrapulmonary Cryptococcosis (including meningitis)*
- *Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis)*
- *Chronic Cryptosporidiosis*
- *Chronic Isosporiasis*
- *Disseminated non-tuberculous mycobacterial infection*
- *Cerebral or B cell non-Hodgkin lymphoma*
- *Progressive multifocal leukoencephalopathy*
- ***Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy***

Note: The conditions in **Italics** are common to both. Others are specific to paediatric HIV.

1. Unexplained refers to where the condition is not explained by other conditions (Unexplained persistent Hepatosplenomegaly means enlarged liver and spleen without obvious cause).

2. Some additional specific conditions can also be included in regional classifications (e.g. reactivation of American trypanosomiasis [meningoencephalitis and/or myocarditis] in Americas region, Penicilliosis in Asia and HIV associated rectovaginal fistula in Africa).

- Reference: Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006, developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO. Annexure 2.

Slide 10		
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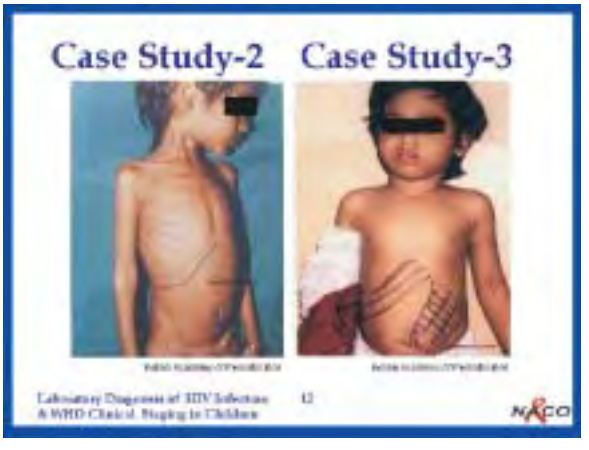
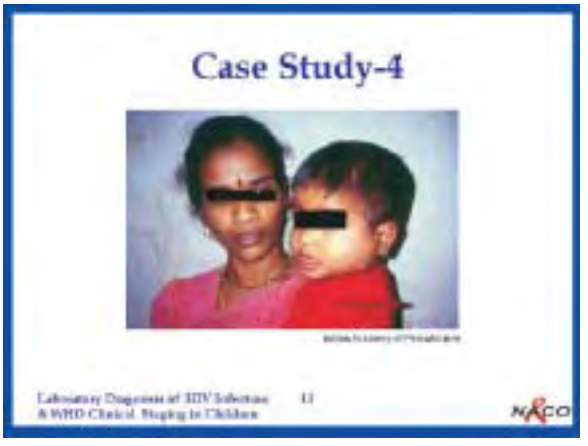
Slide 12		

Slide 13		
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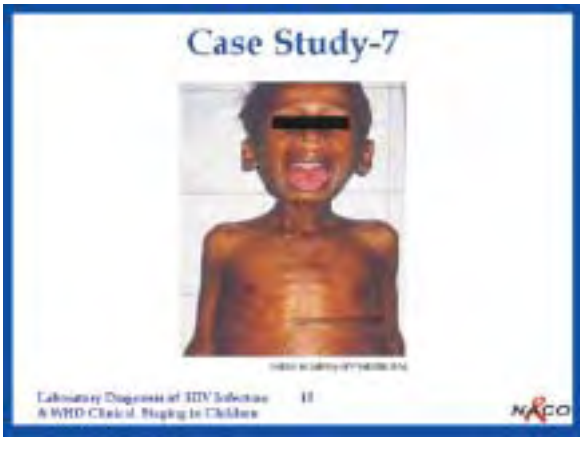
Slide 15		

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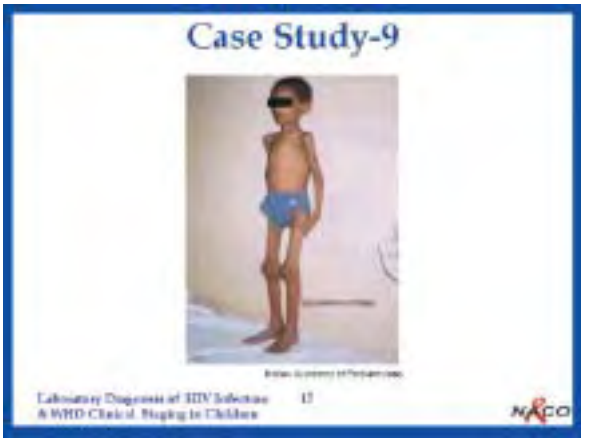
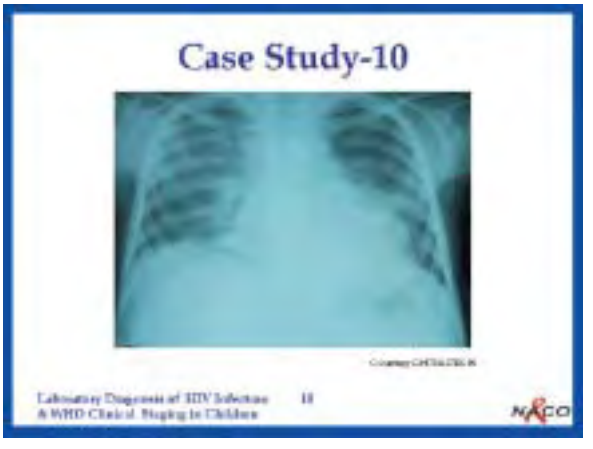
Slide 17		
Slide 18		

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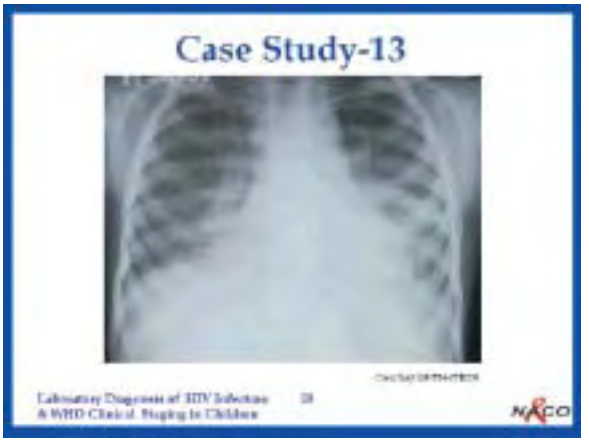
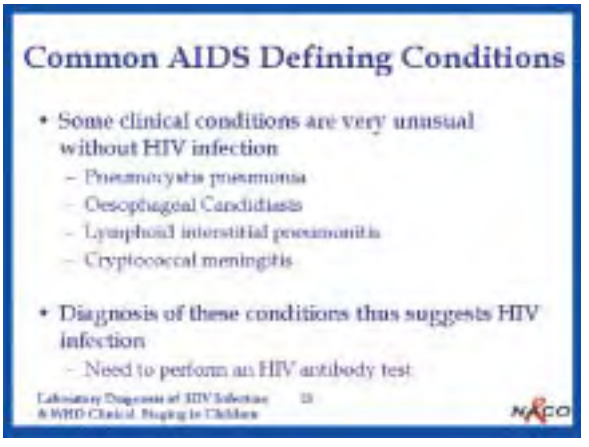
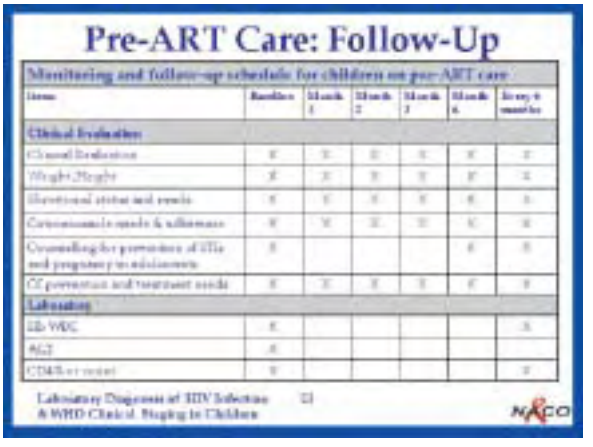
Slide 20		
Slide 21		

Slide 22

Reader's Notes:

- Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO. Page 13, section A-4, Monitoring HIV-infected Children , not on ART.

Slide 23



Reader's Notes:

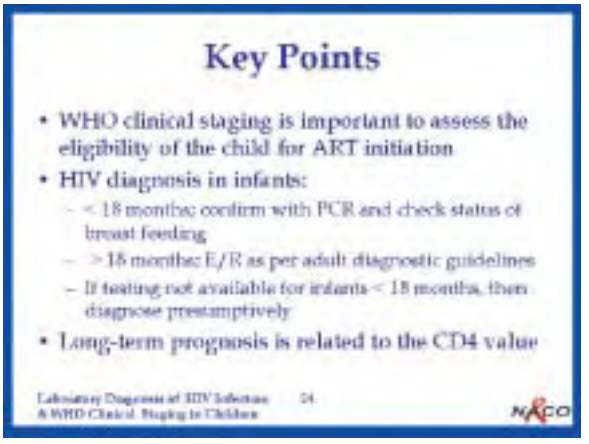
- Reference (Table-Handout 3): Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO.Section A4 Page 14, Table-6: Monitoring and follow up schedule for children on Pre ART care, section A-4, Monitoring HIV-infected Children , not on ART.
- Reference (Handout 4): Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO Section A-5 page 15)

Handout 7: Pre-enrolment Details: History/Physical Examination

Details of history and physical examination to be done	
History	**Physical Examination**
• Current symptoms and concerns of the patient • Co-existing medical conditions and their treatments • Developmental milestones • History suggestive of any opportunistic infections (OI) • History of contact with tuberculosis • Current and past OI prophylaxis • Ability to adhere to OI prophylaxis and/or anti-t uberculous treatment (ATT)/ART in the past • Past history of ART and details thereof • Ability to keep scheduled appointments in the past • Psychosocial, financial and family support status	• Nutritional and growth status • Brief developmental assessment • Neurological examination • Detailed general physical examination with emphasis on cutaneous manifestations such as herpes zoster, papular pruritic eruptions (PPE), diffuse skin dryness, warts, Molluscum angular cheilitis and parotitis • ENT examination • Lymphadenopathy • Oropharyngeal mucosa examination — candidiasis, oral hairy leucoplakia (OHL) etc. • Exclude active tuberculosis: respiratory system, abdominal lymphadenopathy etc. • Hepatosplenomegaly • Examination of eye and optic fundus • Examination of genito-urinary tract

* Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006, developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO. Section A-5 page 15 Table 7: Details of history and physical examination to be done

Slide 24


Key Points
• WHO clinical staging is important to assess the eligibility of the child for ART initiation
• HIV diagnosis in infants:
– < 18 months: confirm with PCR and check status of breast feeding
– > 18 months: E/R as per adult diagnostic guidelines
– If testing not available for infants < 18 months, then diagnose presumptively
• Long-term prognosis is related to the CD4 value

SESSION

PAEDIATRIC ART: INITIATION AND FOLLOW-UP

25

Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

- To provide ART to children based on the national guidelines
- To know when, how and what to start ART in children
- To prescribe appropriate ARV dosages and formulations for children
- To apply criteria for success and failure and to know what to do in case of failure

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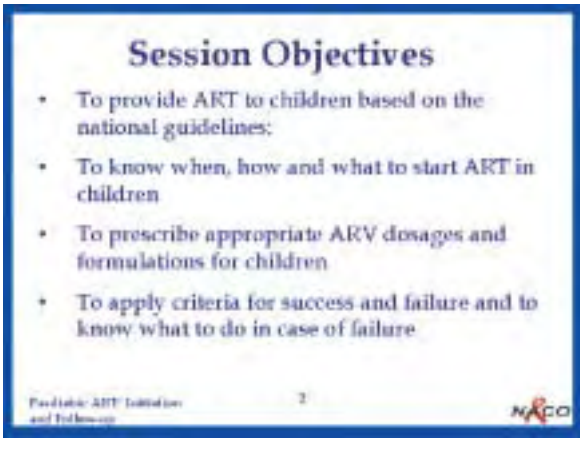
Slide 2		

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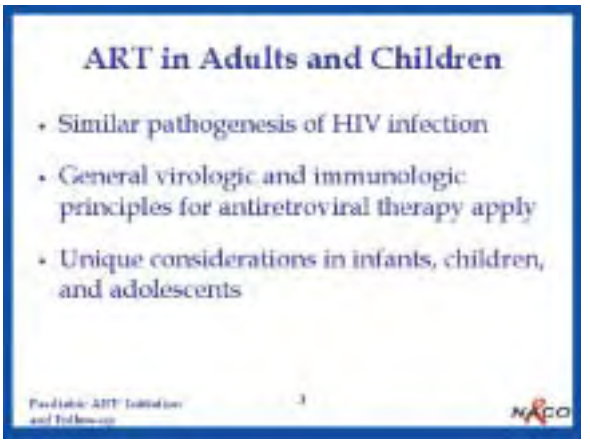
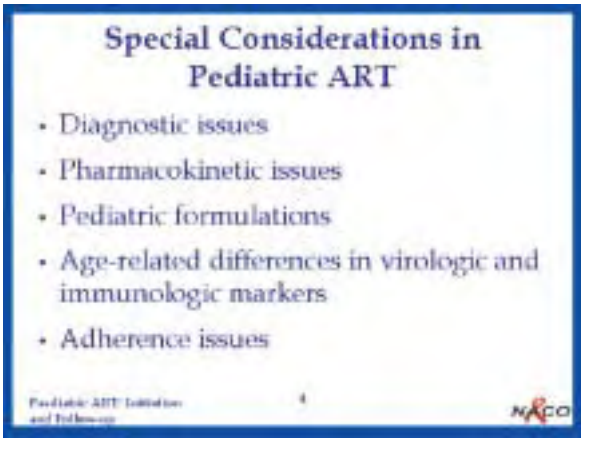


Reader's Notes:

- Although the pathogenesis of HIV infection and the general virologic and immunologic principles underlying the use of antiretroviral therapy are similar for all HIV-infected persons, there are unique considerations needed for HIV-infected infants, children, and adolescents.
- Most HIV infections in children are acquired perinatally, and most perinatal transmission occurs during or near the time of birth, which raises the possibility of initiating treatment in an infected infant during the period of initial (i.e., primary) HIV infection (if sensitive diagnostic tests are used to define the infant's infection status early in life).
- Perinatal HIV infection occurs during the development of the infant's immune system; thus, both the clinical manifestations of HIV infection and the course of immunologic and virologic markers of infection differ from those for adults.
- Treatment of perinatally infected children will occur in the context of prior exposure to ZDV and other antiretroviral drugs used during pregnancy and the neonatal period, for maternal treatment, to prevent perinatal transmission, or both.
- Additionally, drug pharmacokinetics change during the transition from the newborn period to adulthood, requiring specific evaluation of drug dosing and toxicity in infants and children.
- Finally, optimizing adherence to therapy in children and adolescents requires specific considerations.

Slide 4



Reader's Notes:

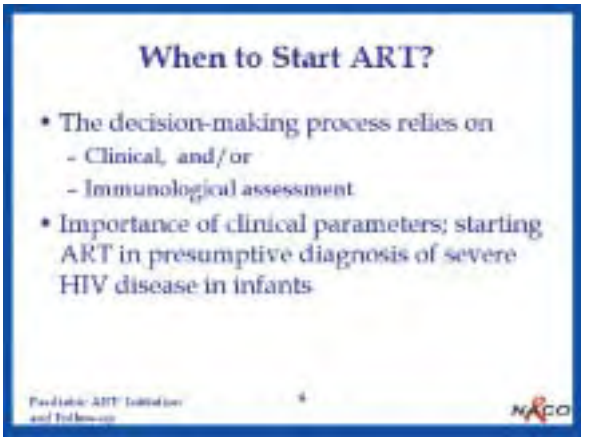
- Perinatal HIV-infection occurs when the infant's immune system is developing.
- Both the clinical manifestations of HIV infection and the course of immunologic and virologic markers of infection differ from those for adults.
- Children have higher lymphocyte and CD4 counts than adults and HIV thus has a larger pool of cells that can be infected
- Viral load levels are generally very high in infancy and do not correlate well with prognosis

Slide 5

Reader's Notes:

- Aggressive antiretroviral therapy with at least three drugs is recommended for initial treatment of infected children because it provides the best opportunity to preserve immune function and delay disease progression.
- The goal of antiretroviral therapy is to maximally suppress viral replication, preferably to undetectable levels for as long a time as possible, while preserving and/or restoring immune function and minimizing drug toxicity.

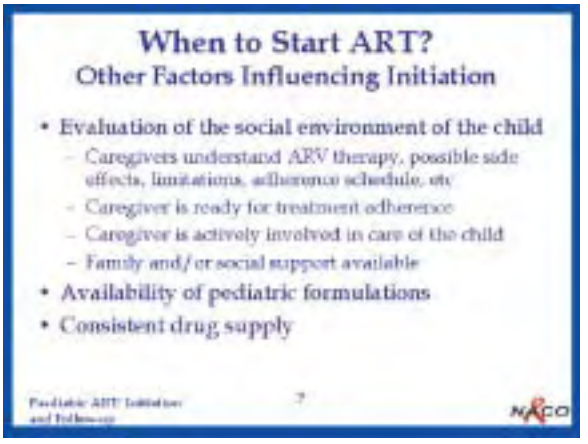
Slide 6



Reader's Notes:

- The decision-making process for initiation of ART in infants and children relies heavily on clinical or immunological assessment; to facilitate scale up to universal access of ART, WHO emphasizes the importance of clinical parameters.
- This approach aims at enabling all children needing treatment to receive it, even if the diagnosis is presumptive and if CD4 measurement and total lymphocyte count (TLC) assays are not available. However, where possible, using the results of CD4 measurements is valuable, particularly for decisions about the need for starting therapy in less sick children, and WHO encourages national programmes to increase access to CD4 measurement technologies.
- Enabling decision-making on starting treatment is particularly important for children less than 12 months; the probability of death in untreated HIV-infected children is high, with reported mortality rates of about 50% within the first year of life

Slide 7



Reader's Notes:

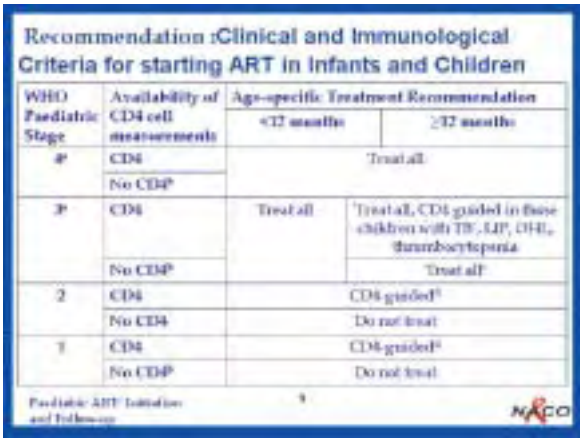
- The decision on when to start ART should also involve the evaluation of the social environment of the child.
- This should include the identification of a clearly defined caregiver who understands the prognosis of HIV and the implications of ART (i.e., the fact that it is a life-long therapy; implications of non-adherence; administration, side effects and storage of drugs).
- Access to nutritional supplements and family support groups, including, ideally, identification of a secondary (back up) informed caregiver, are important parameters when making decisions on initiation of ART.
- Availability of appropriate paediatric formulations is a very important issue in initiation of therapy in eligible patients. With the supply of paediatric fixed-dose combinations in the NACO ART centres, this is not a major issue now.

Slide 8

Reader's Notes:

- ART once started has not only to be taken lifelong, but also has to be taken strictly as per schedule. Besides, it takes regular monitoring.
- All these factors demand careful patient selection and thorough counselling to ensure adherence.
- Before enrollment, it is necessary to have 2 or 3 counselling visits to confirm their preparedness for ART and ensure long-term adherence to the therapy.
- Thus, a detailed history and examination including clinical staging are manadatory prior to enrollment into ART.

Slide 9



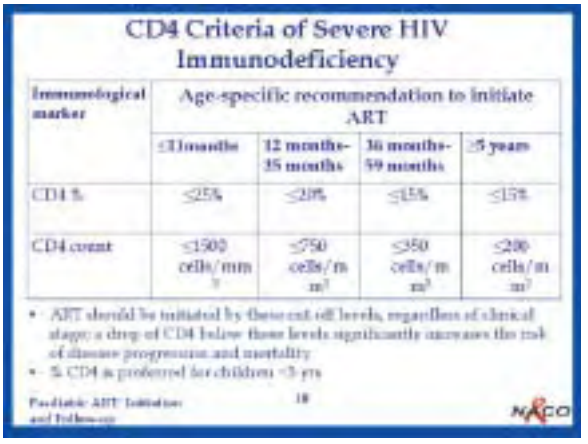
Recommendation :Clinical and Immunological Criteria for starting ART in Infants and Children

WHO Paediatric Stage	Availability of CD4 cell measurements	Age-specific Treatment Recommendation	
		<12 months	≥12 months
4	CD4	Treat all	
	No CD4		
3	CD4	Treat all	Treat all, CD4 guided in these children with TB, LIP, OHL, thrombocytopenia
	No CD4		Treat all
2	CD4	CD4 guided[b]	
	No CD4	Do not treat	
1	CD4	CD4 guided[b]	
	No CD4	Do not treat	

Reader's Notes:

- Initiation of ART based on presumptive diagnosis of severe HIV disease is not recommended for use by clinical care providers who are not appropriately trained in HIV care or administration of antiretroviral therapy.
- Viral load is also not required for use in children 18 months of age and older as antibody testing is confirmatory.
- Explanations for the contents in the slide: Abbreviations: LIP - Lymphocytic interstitial pneumonia; OHL- oral hairy Leukoplakia; TB — tuberculosis
- Notes: Superscripts in the table refer to:
  - a) Stabilize any opportunistic infection prior to initiation of ARV therapy.
  - b) Baseline CD4 estimation is useful to monitor ART even if it is not required to initiate ART.
  - c) In children with pulmonary or lymph node tuberculosis, the CD4 level and clinical status should be used to determine the need for and timing of initiation of ART in relation to tuberculosis treatment (see Table 13).
  - d) For CD4 count %, refer to Table 10. page 17, chapter 5.2 in the NACO Paediatric Guidelines.

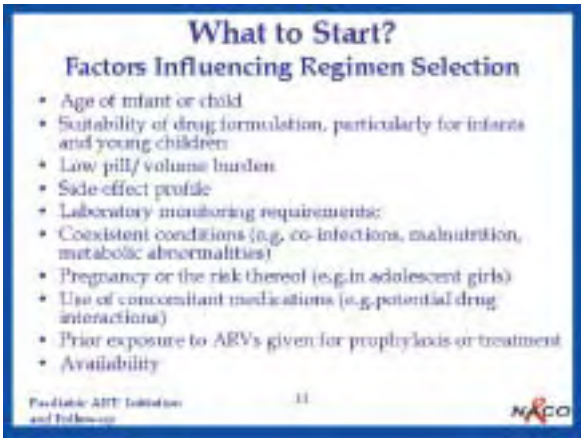
Slide 10



Reader's Notes

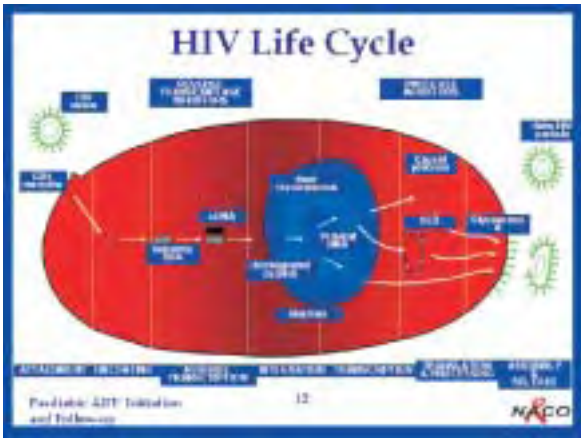
- CD4 is the best measurement for assessing immune deficiency.
- CD4 should be used in conjunction with clinical assessment; however, CD4 allows an earlier detection of worsening of HIV disease as CD4 decline usually occurs prior to clinical progression.
- CD4 monitoring can aid in the decision to initiate or switch ART.
- Younger children normally have higher CD4 than older children and adults.
- %CD4 cells varies less in children < 6 years old and is the preferred measurement.
- At age = 6 years, either %CD4 and/or absolute CD4 count can be used.
- The threshold CD4 cell levels for severe immuno-deficiency in children age 1 year and up corresponds with a 12-months mortality risk of = 5%. In children younger than 1 year and especially < 6 months, CD4 is less predictive of mortality and there is high risk for death even at high %CD4.
- Normal CD4 count/% in children are:
  (a) <11 months:- >= 35%
  (b) 12-35 months: >=30%
  (c) 36-59 months: >= 25%
  (d) > 5 years: >500 cells/mm3

Slide 11



Reader's Notes:

- Potential for infection with a virus strain with diminished susceptibility to one or more ARVs, including that resulting from prior exposure to ARVs given for prophylaxis or treatment, especially single-dose Nevirapine must be kept in mind. However, at present only NNRTI-containing regimens are available in the program and have to be used even if there is prior exposure to Nevirapine.
- Lack of pharmacokinetic data in children prevents the use of certain drugs, e.g Efavirenz in children < 3 years/10kg.
- Important to choose regimen that caregivers can follow easily.
- Though data exists about development of NVP resistance mutations in children exposed to single dose NVP given as PPTCT, there is not much information available on the response of such children to standard ART. Research is urgently required in this area.

Slide 12		
Slide 13	**What to Start?** **1st line Antiretroviral Drugs** • Nucleoside reverse transcriptase inhibitor – Zidovudine (AZT) – Stavudine (d4T) – Lamivudine (3TC) – Abacavir (ABC) • Non-nucleoside reverse transcriptase inhibitor – Nevirapine (NVP) – Efavirenz (EFV)	

Handout 1: Pharmacology of First Line ARV Drugs

Nucleoside Reverse Transcriptase Inhibitors

- Lamivudine (3TC) is a potent NRTI (i.e. a cytidine analogue) with an excellent record of efficacy, safety and tolerability in HIV-infected children, and is a core component of the dual NRTI back bone of therapy.
  - It is usually given twice daily in children and has been incorporated into a number of fixed-dose combinations.
  - The choice between d4T, AZT or ABC to be combined with 3TC should be made at the country level on the basis of local considerations but it is recommended that at least two of these NRTIs be available to allow substitution of one drug for the other should there be toxicity.

- Stavudine (d4T) is a NRTI (i.e., a thymidine analogue) that is initially better tolerated than AZT and does not require haemoglobin or laboratory monitoring.

  - However, among the NRTIs, it has been consistently most associated with lipoatrophy and lactic acidosis. In addition, elevated hepatic transaminases and pancreatitis have been observed. d4T can also cause peripheral neuropathy, though these complications are less common in children than in adults.
  - d4T liquid formulations require a cold chain and capsule size starts at 30 mg only.
  - While less laboratory monitoring requirements may be a good reason to favour d4T over AZT as the chosen nucleoside component, in particular during rapid scale up of programmes, the risk of widespread lipoatrophy in populations treated with d4T-containing regimens remains.

- Zidovudine (AZT) is a thymidine analogue in the NRTI class that has its greatest activity in replicating cells.
  - Although AZT is generally well tolerated in children; it has also been associated with metabolic complications of therapy but to a lesser extend than d4T.
  - Initial drug-related side-effects (headache, nausea) are more frequent with AZT and the drug can cause severe anaemia and neutropaenia; haemoglobin monitoring before and during treatment with AZT is thus useful. This is particularly important in areas with stable malaria where anaemia is highly prevalent in young children.
  - Large volumes of AZT liquid are often poorly tolerated. d4T can be substituted for AZT in the event of intolerance to the latter and vice versa, except in cases of suspected lactic acidosis in which instance neither drug should be prescribed.

- However, as noted above, AZT should not be administered in combination with d4T.

- Abacavir (ABC), a guanosine analogue, has been included in theses guidelines as an alternative nucleoside agent in first-line therapy, representing a change from the 2003 guidelines that recommended reserving the use of ABC as part of second-line regimens.
  - Clinical trial results in antiretroviral-naïve persons demonstrating efficacy, availability of ABC in paediatric formulation and the resulting potential to deliver family-based care of HIV-infected parents and children with ABC/3TC are overriding concerns about the need for availability of additional first line drugs in countries.
  - Reports from a randomized, partly blinded multi-centre trial comparing dual NRTI regimens (PENTA-5) have shown that ABC-containing dual NRTI backbone regimens (ABC/3TC or ABC/AZT) are more effective than AZT+3TC-containing regimens in children with HIV-1 who have not been previously treated. The results have also suggested a similar safety profile in children to that in adults, with very little haematologic toxicity.
  - NRTI combinations containing ABC therefore provide a good NRTI backbone for use with NNRTI or as part of a triple nucleoside regimen. Of all the NRTI drugs, ABC has the least effect on mitochondrial DNA, and would be the preferred substitute for d4T in a child who developed lactic acidosis while receiving a d4T-containing regimen.
  - ABC could also be substituted for AZT in the event of intolerance. However, ABC is associated with a potentially fatal hypersensitivity reaction in a small proportion of children who receive the drug (about 3%).
  - In infants and children suspected of having a hypersensitivity reaction, ABC should be stopped and not restarted.
  - Children and/or their caregivers should be advised about the risk of this serious hypersensitivity reaction and the need to immediately consult their care provider if signs or symptoms of a hypersensitivity reaction occur.

    Abacavir is not currently available in the NACO ART program

Non-nucleoside Reverse Transcriptase Inhibitor

- Nevirapine (NVP) is highly lipophylic and widely distributed in the body. As with EFV, NVP is metabolized via cytochrome P 450.
  - NVP should only be given in combination with other retroviral drugs, except for when used as prophylaxis to reduce perinatal HIV transmission.
  - NVP is currently the only NNRTI syrup available for infants. It also exists as part of three-drug FDC which could be used for older children.
  - NVP may be the preferred choice in adolescent girls when there is potential for pregnancy, or during the first trimester of pregnancy when EFV cannot be used because of its teratogenic effect. But because of an increased risk of adverse events associated with Absolute CD4 counts >350 cells/mm3 in adolescent girls NVP should not be given.

- NVP has a higher incidence of rash than other ARVs. NVP related rash may be severe and life-threatening, including Stevens-Johnson syndrome, and it is associated with a great risk of potentially life-threatening hepatotoxicity.
- In these rare situations, NVP should be permanently discontinued and not restarted. This makes the drug less suitable for treating patients who use other hepatotoxic medications, or drugs that can cause rash, or both, such as rifampicin for the treatment of tuberculosis.

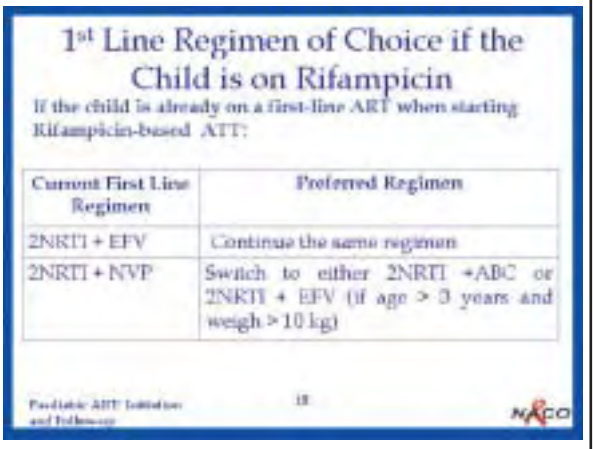
- Efavirenz (EFV) is metabolized via the cytochrome P450 pathway. It may be considered as the NNRTI of choice in children with TB/HIV coinfection.
  - However, EFV should not be given to infants and children younger than 3 years of age (or weighing less than 10 kg) as there is no established dosing recommendation and
    - o It should be avoided in children with a history of severe psychiatric illness,
    - o When there is a potential for pregnancy (unless effective contraception can be assured) and during the first trimester of pregnancy in adolescent girls.
    - o In the latter two situations, NVP may be the best choice.
  - EFV is mostly associated with toxicities related to the central nervous system (CNS), teratogenicity and rash. Rash is more frequent in children than adults, is generally mild, and usually does not require discontinuation of therapy.
  - The CNS symptoms typically abate after 10 to 14 days in the majority of patients; observational studies reported the transient CNS disturbance in 26%-36% of children receiving EFV.

Slide 14

Reader's Notes:

- The first two regimens are used as first line therapy in India. Since no AZT-containing fixed-dose paediatric formulations are available at present for children < 20kg, d4T based FDCs are considered as the first choice drugs for all children < 15kg weight. Studies have increasingly shown long term adverse effects with d4T based therapy and hence with availability of paediatric formulations of FDCs with AZT, these would be preferred except in those with moderate to severe anemia.
- AZT and d4T are antagonists as both have a thymidine backbone.
- Currently only d4T and AZT based regimens are available under the National Paediatric Initiative. Second line regimen has been mentioned in the current guidelines for the sake of completeness only.

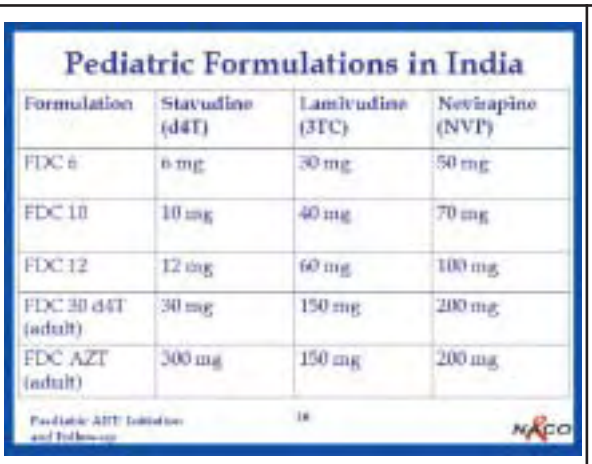
Slide 15



Reader's Notes:

- There is no drug interaction between NRTI and Rifampicin. Rifampicin lowers NVP drug level by 20-58% and EFV drug level by 25%. In children, there is no information on appropriate dosing of NVP and EFV when used with Rifampicin. EFV is the preferred drug with ATT in children > 3 years and > 10kg.
- Another option is to use a triple NRTI combination (AZT+3TC+ABC); however ABC is not available in the program
- Apart from Rifampicin, other anti-TB drugs do not have drug interaction with ART.
- Rifampicin is the best bactericidal anti-TB drug and should be part of anti-TB regimens especially during the first 2 months of treatment.
- Consideration to change from Rifampicin-based to non-Rifampicin-based anti-TB treatment during the maintenance phase is up to the discretion of the treating physician and should follow the National TB treatment guidelines.
- Both Anti-TB drugs and NNRTI (especially NVP) can cause hepatotoxicity; therefore, close monitoring is required. After 2 weeks of completing Rifampicin-based anti-TB treatment, switch back to standard line regimen with 2NRTI + NVP.
- Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO Table 13 in the chapter 5.6, page no 20

Slide 16



Pediatric Formulations in India

Formulation	Stavudine (d4T)	Lamivudine (3TC)	Nevirapine (NVP)
FDC 6	6 mg	30 mg	50 mg
FDC 10	10 mg	40 mg	70 mg
FDC 12	12 mg	60 mg	100 mg
FDC 30 d4T (adult)	30 mg	150 mg	200 mg
FDC AZT (adult)	300 mg	150 mg	200 mg

Reader's Notes:

- Stavudine-containing 3 drug FDC's is used as first line therapy currently in India. Syrups and solutions remain necessary to treat infants and very young children who cannot swallow whole tablets or capsules but they have shortcomings; these may include limited availability, increased cost, difficulties in storage, need for refrigeration, reduced shelf life, and poor palatability.

Single Drug Preparations:

- Zidovudine (10 mg/mL, 100 mg cap, 300 mg tab), Lamivudine (10 mg/ mL, 150 mg), Stavudine (1 mg/ mL, 30 mg cap, 40 mg cap), Nevirapine (10 mg/ mL, 200 mg tab), Efavirenz (200 mg cap, 600 mg cap, 30 mg/ mL)
- The paediatric guideline, the dosing disc, and the desk reference indicate Efavirenz syrup contains 50 mg in 2.5 ml of EFV solution. But at present we have only 30mg/ml preparation available.

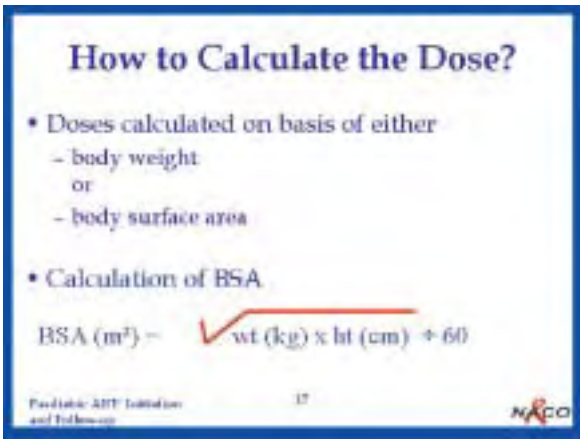
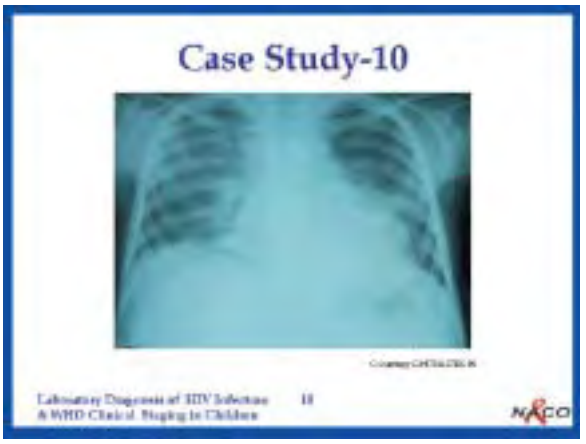
Dual Drug Preparations:

- AZT + 3TC (AZT 300 mg + 3TC 150 mg), d4T + 3TC (d4T 30 mg + 3TC 150 mg, d4T 40 mg + 3TC 150 mg, d4T 12 mg + 3TC 60 mg DT, d4T 10 mg + 3TC 40 mg DT, d4T 10 mg + 3TC 40 mg/ 5 mL (needs refrigeration)
- **3 Drug FDCs:**
- **AZT + 3TC + NVP (**300 mg + 150 mg + 200 mg)
- **d4T + 3TC + NVP (**30 mg + 150 mg + 200 mg, 40 mg + 150 mg + 200 mg)

Handout 2: NRTIs and NNRTIs

3 different NRTIs to use in combination with 3TC		
2 NRTI	**Pros**	**Cons**
AZT + 3TC	-AZT causes less lipodystrophy and lactic acidosis than d4T - AZT does not need refrigeration	- AZT has more initial GI side effects - Large volume of AZT liquid is often poorly tolerated - Severe anemia and neutropenia can occur. - CBC monitoring before and after treatment is useful particularly in areas with stable malaria
2 NRTI	**Pros**	**Cons**
d4T + 3TC	- d4T causes less GI side effects and anemia than AZT	- d4T causes more lipodystrophy, lactic acidosis and peripheral neuropathy - d4T liquid needs refrigeration. - The smallest size of d4T capsule is 30 mg which is appropriate for children weighing 30 kg and up
2 NNRTIs to chose from		
1 NNRTI	**Pros**	**Cons**
NVP	- NVP can be given to children at any age - NVP does not have teratogenic effect - NVP is available in both pill and liquid formulations. Both do not need refrigeration. - NVP is part of several three -drug fixed dose combinations that can be used in older children	- NVP has higher incidence of rash than EFV. NVP rash may be severe and life-threatening - NVP is associated with rare but potentially life-threatening risk of hepatotoxicity- - Symptomatic NVP-associated hepatic or serious rash toxicity is more frequent in women with CD4 > 250 cells/mm3; therefore, if used in adolescent girls, careful monitoring is needed during the first 12 weeks. - NVP should be avoided in pregnant women with CD4 > 250 cells/mm3 as they appear to be at highest risk for these toxicities. - Rifampicin lowers NVP level more than EFV
** Younger children require a higher per kg dose of Nevirapine. The genetic barrier for resistance is low and a single mutation (K103N) causes cross-resistance with all NNRTIs. Hence, correct dosing is crucial.*		

1 NNRTI	Pros	Cons
EFV	- EFV causes less rash and hepatotoxicity than NVP. Rash that occurs is generally mild. - EFV level is less affected by rifampicin and can be considered the NNRTI of choice in children receiving rifampicin-based anti-TB treatment. - For children unable to swallow pills, EFV capsule can be opened and added to liquid or small amount of food	- EFV can only be used in children of age > 3 years old or weigh >10 kg - Transient CNS disturbance can occur in 26-36% of children; therefore, patients should be warned. - EFV should be avoided in children with a history of severe psychiatric illness. - EFV has teratogenic effect and should be avoided in adolescent girls with potential for pregnancy.
** CNS side effects with Efavirenz are generally mild and transient in children. However, caregivers should be warned about their occurrence.*		

Slide 17		
Slide 18		

Handout 3: Antiretroviral - Paediatric Formulations, Doses and Common Side Effects

Zidovudine - AZT

Syrup 10mg/ml, caps 100 mg, tabs 300 mg

- < 4 w: 4mg/kg/dose bd or 2 mg/ kg q 6hr
- 4 w - 13 y : 180- 240 mg/m2/dose bd
- Max dose: 300 mg bd

Caps may be opened and mixed with drink or food

Adverse effects:

- Common: Hematologic toxicity- anemia, neutropenia, headache
- Other: Myopathy, myositis, liver toxicity

Lamivudine - 3 TC

Syrup 10mg/ml, caps 150 mg tab

- < 4 w: 2 mg/kg/dose bd
- >4 w - 60 kg: 4 mg/kg/dose bd
- Max dose: 150 mg bd

Adverse effects:

- Common: Nausea/diarrhea, headache, fatigue, abdominal pain
- Severe: pancreatitis, lactic acidosis with hepatic steatosis

Stavudine — d4T

Solution 1mg/ml, caps 30 and 40 mg

- < 30 kg: 1 mg/kg/dose bd
- 30-60 kg : 30 mg/dose bd
- Max dose (>60kg): 40 mg bd

Caps may be opened and mixed with drink or food

Adverse effects:

- Common: headache, nausea, vomiting, diarrhea, increased transaminases
- Severe: peripheral neuropathy, pancreatitis, lactic acidosis

Abacavir - ABC

- 3m- 13 yr: 8 mg/kg/ dose q12 hr
- 13 yr: 300 mg/ dose q12 hrly (max: 300 mg/ dose)

Adverse effects:
- Common: Nausea, vomiting, diarrhea, loss of appetite, malaise, rash
- Severe: Hypersensitivity (Do not rechallenge)

Nevirapine - NVP:

Suspension 10 mg/ml, tabs 200 mg
- >30 days -13 y :
  - 120 mg/m2/dose od during first 2 weeks,
  - then 150 - 200 mg/m2/dose bd

- Max dose (if >13y): 200mg/d during first 2 weeks, then 200mg bd

- Tabs may be crushed and mixed with drink or food

Adverse effects:
- Common: Rash, sedative effects, headache, nausea
- Other: Increased transaminases; rare-hepatitis

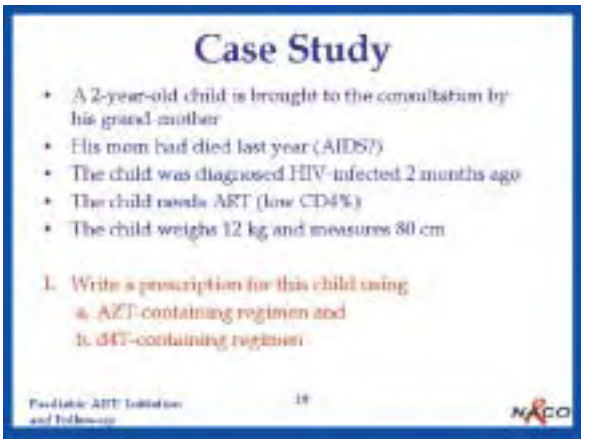
Efaviranz -EFV:

Only if >3 years old and >10KG !!!!
Capsules 200, 600mg

- **10-15 kg: 200 mg od**
- **15-20 kg: 250mg od**
- **20-25kg: 300 mg od**
- **25-33kg: 350 mg od**
- **33-40kg: 400 mg od**
- **Dose max : >40kg, 600mg 1x/d od**

Caps may be opened and mixed with drink or food; Bad taste, best with sugar
Administer at night
Adverse effects:
- Common: Rash, Central nervous system (dizziness, etc)
  Other: Increased transaminases

Slide 19


Case Study
• A 2-year-old child is brought to the consultation by his grand-mother
• His mom had died last year (AIDS?)
• The child was diagnosed HIV-infected 2 months ago
• The child needs ART (low CD4%)
• The child weighs 12 kg and measures 80 cm
1. Write a prescription for this child using
a. AZT-containing regimen and
b. d4T-containing regimen
19

Handout 4: Paediatric ARV Drug Formulations and Dosage Calculation as per National Guidelines

Calculation of Body Surface Area (BSA)

$$BSA\ (m^2) = \sqrt{wt\ (kg) \times ht\ (cm) \div 60}$$

Example:

- Weight x Height = 12 x 80
- v 960 = 31
- 31/60 = 0.52 m^2

* Nomograms to calculate BSA are available and should be used where possible

Calculation for Zidovudine based Regimen (AZT, 3TC and NVP)

AZT

- The dose is 180-240 mg/m^2, bid;
- The dose for the above child can be calculated using the above formula
- For 1 m^2 of the body surface the dose is 180 to 240 mg
- For 0.52 m^2 of the body surface, the dose is 94 (180 x 0.52 = 94 mg) to 125(240 X 0.52= 125 mg) mg.
- AZT is available as 10 mg/ml syrup or 100 mg capsules
- The child needs 94 to 125 mg of AZT, so the dose is one 100 mg capsule bid or 10 ml of syrup bid.

3TC

- The dose is 4mg/kg bid
- The dose for the above child is 48 mg bid(4 X 12)
- 3TC is available as 10 mg/ml syrup or 150 mg tablets
- The child needs 5 ml bid
- Change to tablets when appropriate

NVP

- The dose is 120 mg/m², od for two weeks, then 150 to 200 mg/m² bid
- The dose for the above child can be calculated using the above formula
- For 1 m² of the body surface the dose is 120 mg
- For 0.52 m² of the body surface, the dose is 62.4 (120 x 0.52 = 62.4 mg)
- For 1 m² of the body surface the dose is 150 to 200 mg
- For 0.52 m² of the body surface, the dose is 78 (150 x 0.52 = 78 mg) to 104 (200 X 0.52 = 104 mg) mg.
- NVP is available as 10 mg/ml suspension or 200 mg tablets
  — The child needs 6.5 ml during first two weeks as lead-in dose and then 7.5 to 10 ml bid or ½ a tab bid. Change to tab when appropriate

Conclusion

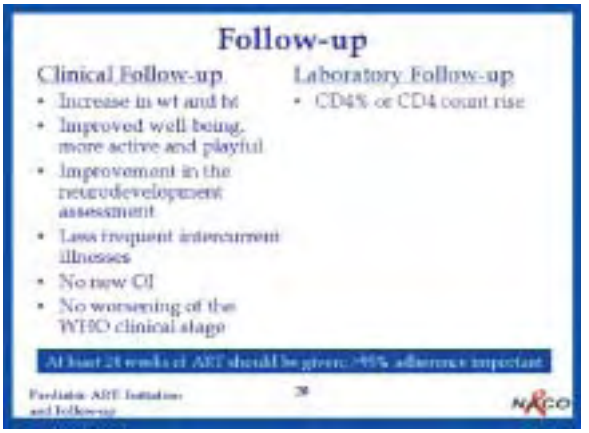
	Morning	**Evening**
ZDV caps 100 mg 3TC syrup	1 5 ml	1 5 ml
NVP syrup After 14 days	6.5 ml 7.5- 10 ml or ½ tab (200 mg)	7.5- 10 ml, or ½ tab (200 mg)

Calculation for Stavudine based Regimen (d4T, 3TC and NVP)

Stavudine

- The dose is 12 mg bid (1 mg/ kg/ dose bid)
- The dose for the above child is 12 mg bid (12 X 1) since the child weight is 12 kg.
- Now d4T containing 3-drug FDC can be used, choosing the dosage in the appropriate weight band. A simple paediatric HIV dosing disk and desktop reference is available for reference in the national programme. The same (dosing disk and desktop reference) can be demonstrated during the above calculation

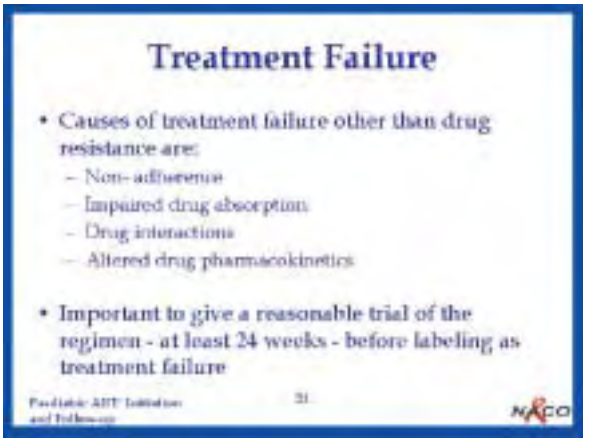
Slide 20



Reader's Notes:

- Children may have rapid weight and height gain after ART in addition to expected normal growth; therefore, re-calculation of
- ART dose should be done at every visit. Under dosing of ART can lead to rapid development of resistance. WHO Clinical
- staging for clinical monitoring after ART initiation must be done at all visits
- Check for concomitant drug intake at every visit such as appropriate cotrimoxazole prophylaxis (if indicated) and other drugs.
- Check for potential drug interactions with ART

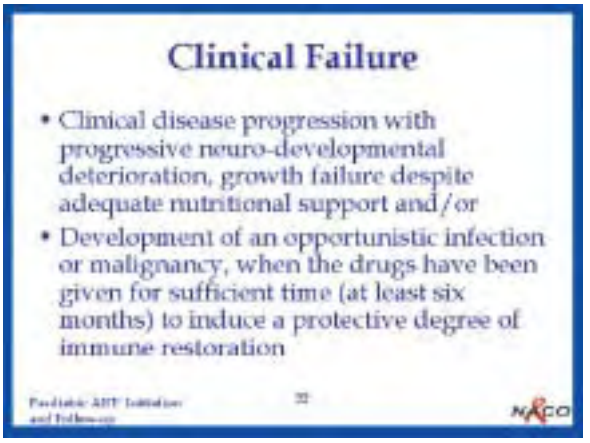
Slide 21



Reader's Notes:

- Poor adherence, inadequate drug levels or drug interactions can all contribute to ARV treatment failure, genetic differences in drug metabolism and pharmacokinetics may also be important. It is recommended that programmes primarily use clinical criteria, supported, where possible, with CD4 criteria, in order to define treatment failure. When treatment failure is confirmed, switching to a new second-line regimen becomes necessary.
- It should not be concluded, on the basis of clinical criteria, that an ARV regimen is failing until the child in question has had a reasonable trial on the therapy, i.e. the child should have received the regimen for at least 24 weeks, and adherence to therapy has been assessed and considered to be optimal. Additionally, before considering changing treatment because of growth failure, it should be ensured that the child is failing to grow despite receiving adequate nutrition, and that any intercurrent opportunistic infections have been treated and resolved.

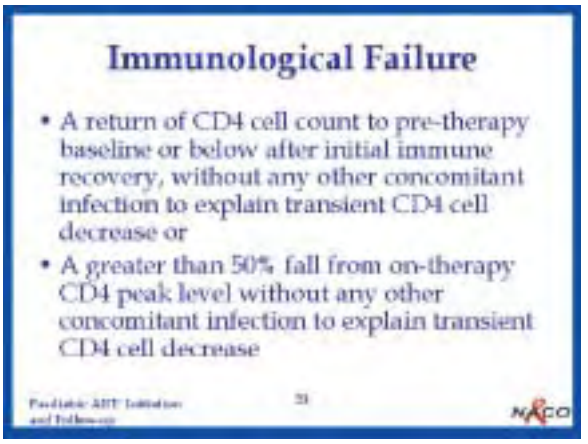
Slide 22



Reader's Notes:

- The WHO Paediatric Clinical Staging System, is suggested as a tool to support assessment of disease progression and guide decision-making in the event of treatment failure.
- Treatment failure should be considered when clinical symptoms develop in a child on therapy that are suggestive of a more severe clinical stage. However, pulmonary tuberculosis alone, although a Clinical Stage 3 condition (T3), may not be an indication of treatment failure, and thus not require consideration of second-line therapy; response to anti-tuberculosis therapy should be used to evaluate the need for switching therapy
- Treatment failure must be distinguished from immune reconstitution syndrome (IRS).

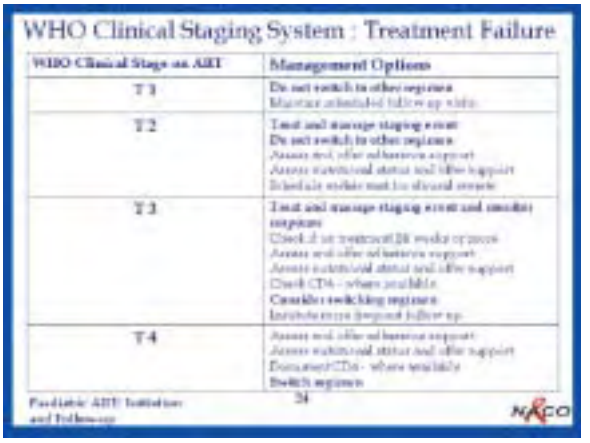
Slide 23



Reader's Notes:

- Immunological treatment failure can be differentiated as primary and secondary treatment failure.
- In primary treatment failure, children on ART may persist at or below their age-related CD4 threshold for initiation of treatment.
- Secondary failure is characterized by initial immune recovery after initiation of ART, followed by a drop of the CD4 value to values at or below their age-related CD4 threshold for initiation of treatment.

Slide 24



Reader's Notes:

- Clinical stages in this table refer to a new or recurrent stage at the time of evaluating the infant or child on ART.
- Differentiation of opportunistic infections from immune reconstitution syndrome is important.
- Pulmonary tuberculosis, a Clinical Stage 3 condition, may not be an indication of treatment failure, and thus not require consideration of second-line therapy; response to tuberculosis therapy should be used to evaluate the need for switching of therapy.

Table Notes:

a) Clinical stages in this table refer to the WHO clinical stage as per revised classification while on ART (a new or recurrent stage at the time of evaluating the infant or child on ART).

b) It needs to be ensured that the child has had at least 24 weeks of treatment trial, adherence to therapy has been assessed and considered to be adequate prior to considering switching to second-line regimen.

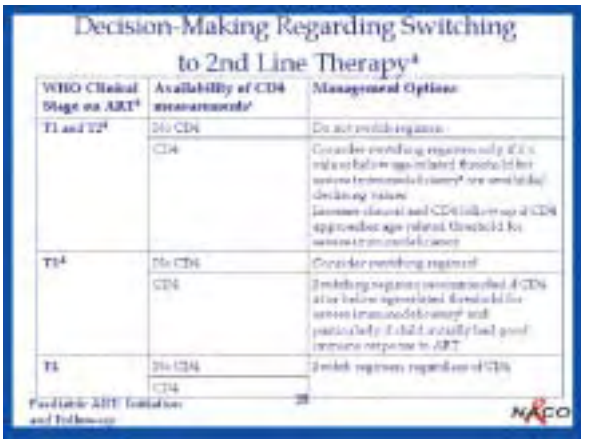
c) Differentiation of opportunistic infections from immune reconstitution syndrome is important.

d) In considering changing treatment because of growth failure, it should be ensured that the child is not failing to grow due to lack of adequate nutrition, and that any intercurrent infections have been treated and resolved.

e) Pulmonary or lymph node TB, Clinical Stage 3 conditions, may not be an indication of treatment failure, and thus not require consideration of second-line therapy; response to tuberculosis therapy should be used to evaluate the need for switching of therapy.

- Reference : Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO page 35 table 16.

Slide 25



Reader's Notes:

Notes for the superscripts mentioned in the table:

a) It needs to be ensured that the child had at least 24 weeks of treatment trial, adherence to therapy has been assessed and considered to be adequate prior to considering switching to second-line regimen. Additionally, in considering changing treatment because of growth failure, it should be ensured that the child has adequate nutrition, and that any intercurrent infections have been treated and resolved.

b) Clinical stages in this table refer to a new or recurrent stage at the time of evaluating the infant or child on ART.

c) Where CD4 cell count/% is available, at least two CD4 cell measurements should be compared.

d) Do not switch regimen if CD4 cell values are above age-related threshold for severe immunodeficiency.

e) Age-related severe immunodeficiency values; if serial CD4 cell values are available, the rate of decline should be taken into consideration. Age-related severe immunodeficiency values as defined earlier; switching should particularly be considered if the 2 values are <15% (12-35 months of age), <10% (36-59 months of age), <100 cells/mm3 (=5 years of age); % CD4 is preferred in children <5 years of age; at least two measurements should be available and the same parameter should be compared, i.e. count with count.

f) Some T3 conditions (i.e. pulmonary or lymph node tuberculosis, pneumonia, oral hairy leukoplakia, thrombocytopaenia and severe recurrent presumed bacterial pneumonia) may need to be treated and the need to switch regimens decided based on re-evaluation of the child in question.

Reference:Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO page 36 table 17.

Handout 5: Steps in Choosing 2nd Line NRTIs and PI's

Step 1: Choose 2 NRTIs

First line NRTI	Second line NRTI
AZT or d4T + 3TC	ddI + ABC
ABC + 3TC	ddI + AZT

*Continuing 3TC in a second line regimen can be considered if ddI is not available in India

Step 2: Choose 1 PI

Preferred PI	Pros	Cons
LPV/r	- Excellent efficacy especially in PI-naïve children - Have high threshold for resistance due to its high drug level from Ritonavir boosting - The only available liquid Ritonavir-boosted PI - Paediatric dosing is available at all ages	- Both liquid and gel capsule formulations require refrigeration - Gel capsule is large in size - High cost
SQV/r	- Can be used with Ritonavir boosting - Good efficacy	- Can only used in children who weigh > 25 kg and can swallow capsules - The soft gel capsule formulation is large in size and needs refrigeration - High pill load - Frequent GI side effects
Alternative PI	**Pros**	**Cons**
NFV	- Long term data showed good efficacy and safety profile - Cause less hyperlipidemia and lipodystrophy than ritonavir-boosted PI	- Data in adults shown to be inferior in efficacy compared to boosted PI and EFV - High pill burden - Frequent GI side effects

Note:

- PI components are listed in order of potency/acceptability
- LPV/r is available co-formulated as solid and liquid; requires cold chain.
- A new preparation of LPV/r (tablet) which does not require refrigeration is now available.
- SQV/r should not be used in children or adolescents weighing less than 25kg;
- Unboosted NFV may need to be used where no cold chain in place;
- For liquid LPV/r or SQV/r; it should be taken with food to improve bioavailability and high doses are needed in young children (e.g., >150 mg/kg per day).

Lopinavir/ Ritonavir Combination

- Boosted PI
- Doses:
  - 6 mo- 12 yr:
- 7- <15 kg: 12 mg/ kg lopinavir/ 3 mg/ kg ritonavir q 12 hr with food;
- 15- 40 kg: 10 mg/ kg lopinavir/ 2.5 mg/ kg ritonavir q 12 hr with food
  - > 12 yr: 400 mg lopinavir/ 100 mg ritonavir q 12 hr with food

Adverse effects: Abdominal discomfort, nausea and headache; hyperglycemia, lipid elevations and lipodystrophy.

Saquinavir/ Ritonavir

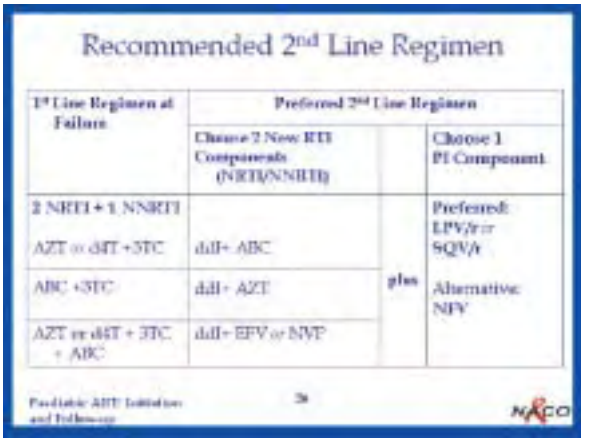
- Boosted PI
- Combination currently not available in India

Nelfinavir

- < 13 yr: 50- 55 mg/ kg q 12 hr
- > 13 yr: 1250 mg q 12 hr (max 2000 mg)

Adverse effects: Diarrhea, abdominal pain.

Slide 26



Reader's Notes:

- Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO table 18 age no.36

Handout 6: Recommended 2nd Line Regimen

Desired characteristics of a second line regimen:

- Having a high likelihood of treatment success;
- Minimizing the risk of cross- resistance, and be based upon drugs that retain activity against the patient's virus strain

In the event of treatment failure, the entire regimen should be changed from a first-line to a second-line combination.

- The new second-line regimen should preferably include at least three new drugs, one or more of them from a new class, in order to increase the likelihood of treatment success, minimize the risk of cross- resistance, and be based upon drugs that retain activity against the patient's virus strain.
- Designing potent and effective second-line regimens for infants and children is particularly difficult because of the limited formulary most resource-limited settings will maintain.
- This highlights the importance of choosing potent and effective first-line regimens and maximizing their durability and effectiveness by optimizing adherence in order to reduce the likelihood of occurrence of treatment failure and the subsequent need to switch therapy.

The goal of second line regimen is to achieve clinical and CD4 response but the response is likely less than with first line regimen due to cross resistance among ART.

- Nucleoside cross-resistance, especially in the presence of long-standing virological failure allowing accumulation of multiple drug resistance mutations, may compromise the potency of alternative dual nucleoside components. In this situation it is necessary to make empirical alternative choices with a view to providing as much antiviral activity as possible.
- Given the cross-resistance that exists between d4T and AZT, a second-line regimen for a child receiving a first-line d4T or AZT-containing regimen that might offer more activity includes ABC plus the nucleoside analogue didanosine (ddI), although high level AZT/3TC resistance can confer diminished susceptibility to ABC.
- In these guidelines, ABC plus 3TC have been introduced as nucleoside components of the first-line regimen; in this case, AZT plus ddI would be the choice for an alternative regimen.
  Administration constraints for ddI in adults (i.e. administration one hour before or two hours after meals due to reduced bioavailability of ddI with food) may not apply in paediatric patients as the systemic exposure to ddI in children is similar in the presence or absence of food

Choice of PIs

A low dose Ritonavir (RTV)-enhanced PI (PI/r) component, i.e. Lopinavir (LPV)/r, or Saquinavir (SQV)/r, is generally preferable to Nelfinavir (NFV)/r or single NFV for second-line regimens, given their potency because of the diminished potential of almost any second-line nucleoside component.

Advantages of PI-based regimens include

- Proven clinical efficacy and well-described toxicities.
- However, the use of PIs other than LPV/r (which is available in co-formulation) and NFV is more problematic in children because of
  - o A lack of suitable paediatric formulations for Indinavir (IDV) and SQV
  - o A lack of appropriate dosing information for Ritonavir-boosted PIs other than LPV/r.
  - o Other limitations related to the use of RTV-boosted PIs include the requirement for the presence of a cold chain for most products.

SQV/r can be considered as an alternative in children weighing more than 25 kg (who therefore can receive the adult dose) and who are able to swallow capsules.

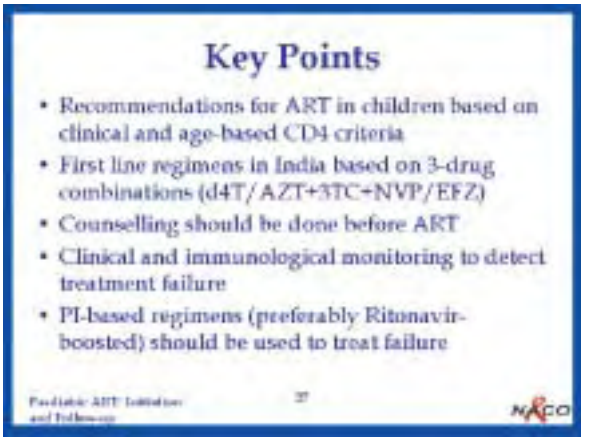
A tablet formulation of LPV/r became available in late 2005 that does not require a cold chain. These tablets have not been studied in children, but may be acceptable for use in older children for whom adult doses can be given. Therefore, in these guidelines, LPV/r remains the preferred PI for use in children if there is a secure cold chain.

PI components are listed in order of potency/acceptability.

- SQV/r should not be used in children < 25kg.
- Unboosted NFV may need to be used where no cold chain is in place;
- For liquid LPV/r or SQV/r it should be taken with food to improve bioavailability and high doses are needed in young children (e.g > 150 mg/kg/day).

Refer Handout 5: **Protease Inhibitors Formulation & Adherence Effects**

Slide 27



SESSION

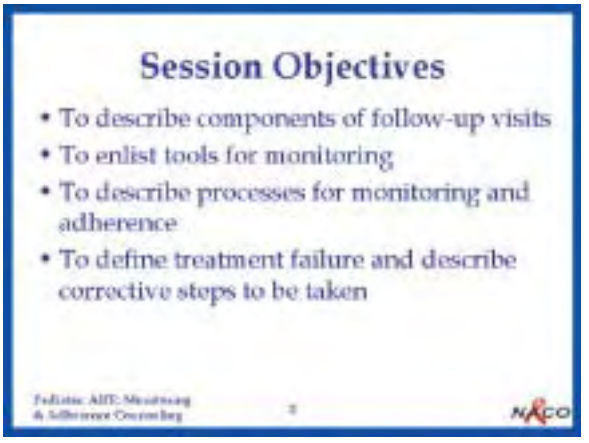
PAEDIATRIC ART: MONITORING & ADHERENCE COUNSELLING

26

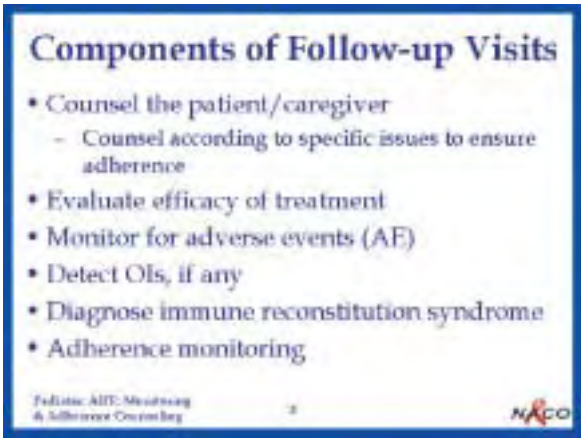
Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

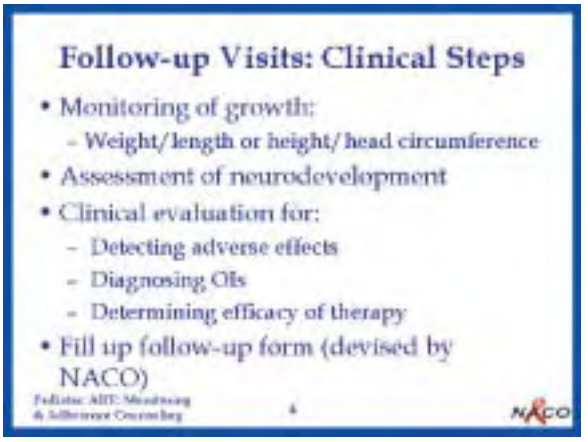
- To describe components of follow-up visits
- To enlist tools for monitoring
- To describe processes for monitoring and adherence
- To define treatment failure and describe corrective steps to be taken

Slide 1		
Slide 2		

Slide 3

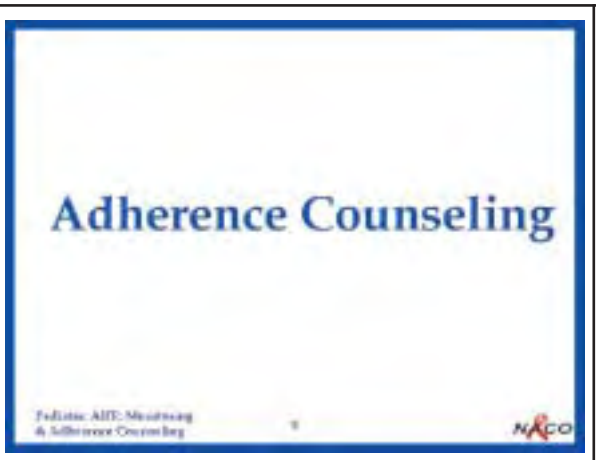
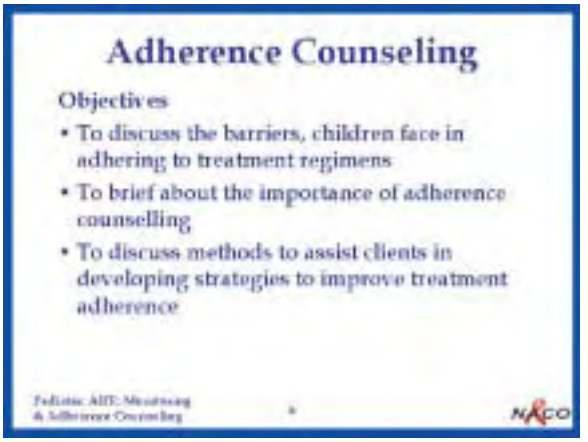
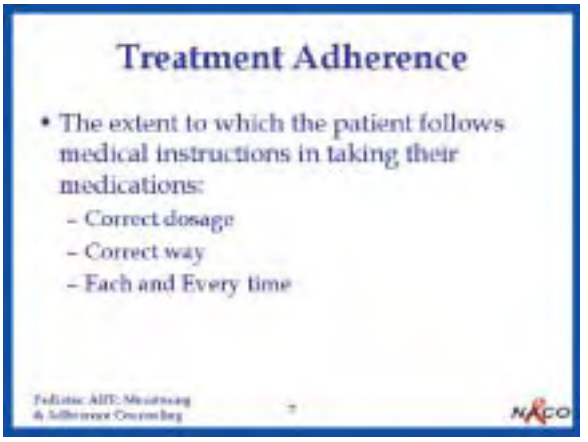


Slide 4

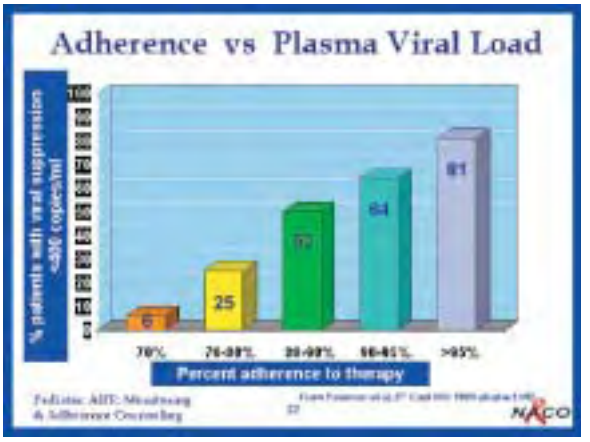
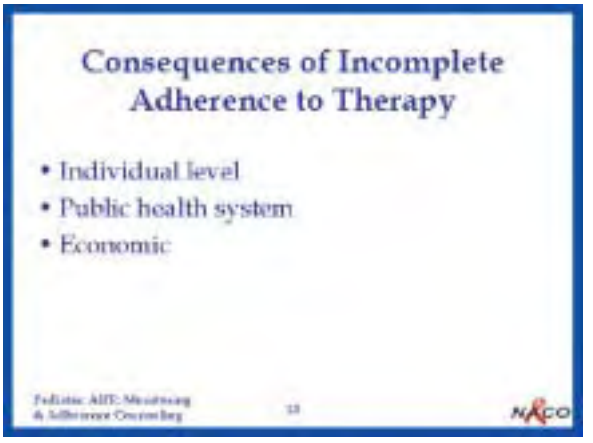


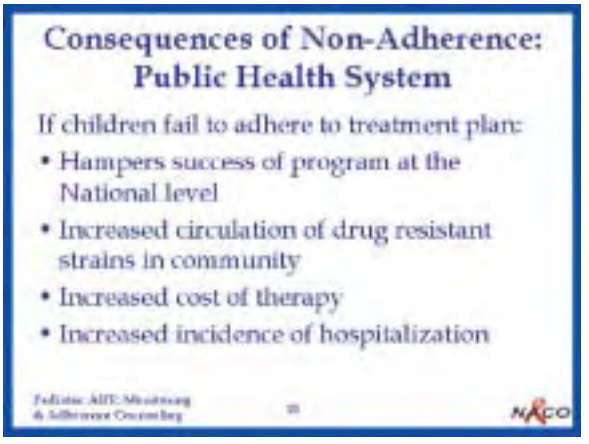
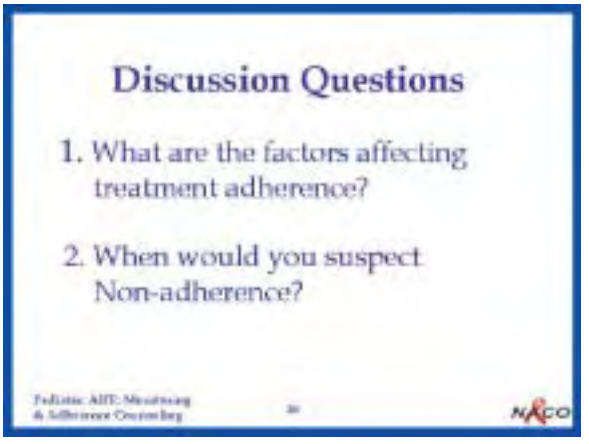
Reader's Notes:

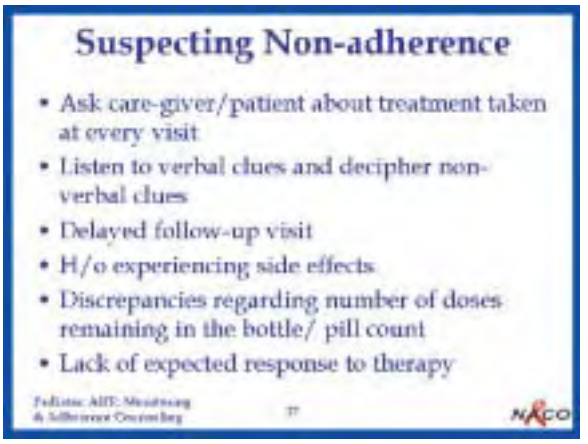
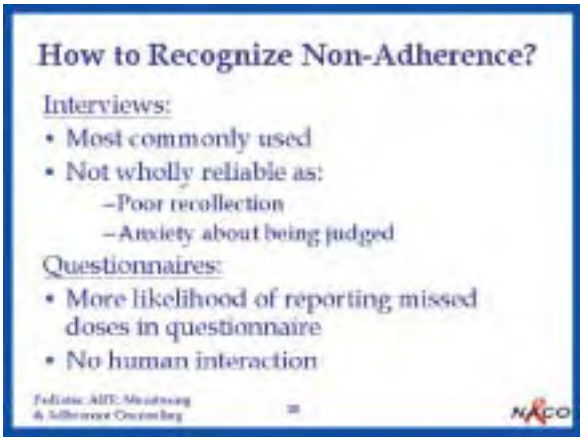
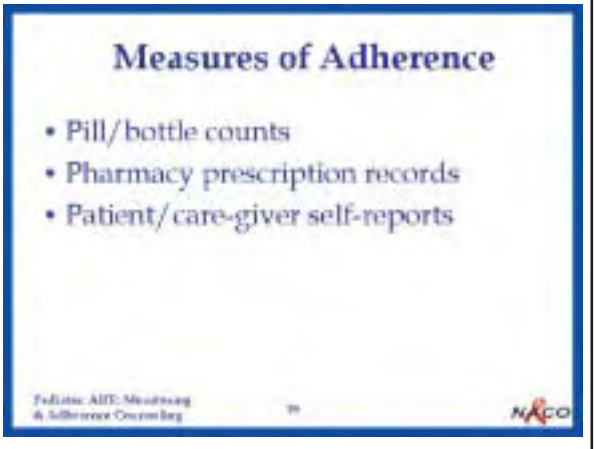
- Growth charts recommended by the Indian Academy of Paediatrics (IAP) for boys and girls (height, weight, head circumference) should be used.
- Monitoring schedule as in Page 35, section A6: 6-1; of the NACO treatment guidelines should be followed.
- Children may have rapid weight and height gain after ART, therefore recalculation of dose should be done at every visit.
- Check for concomitant drug intake and potential drug interactions
- Hb and WBC monitoring may be considered in children on AZT at 1, 2 and 3 months. Regular monitoring of liver function tests during the first 3 months of treatment may be considered for children at higher risk, e.g adolescent girls with CD4> 250, those co-infected with hepatitis B, C or other hepatic diseases.
- Pregnancy test should be done in adolescent girls especially those going to start EFV and provide family planning counselling
- If signs of clinical progression are seen, CD4 count should be done earlier. If CD4 is not available, clinical monitoring alone is used; TLC is not suitable for monitoring ART.

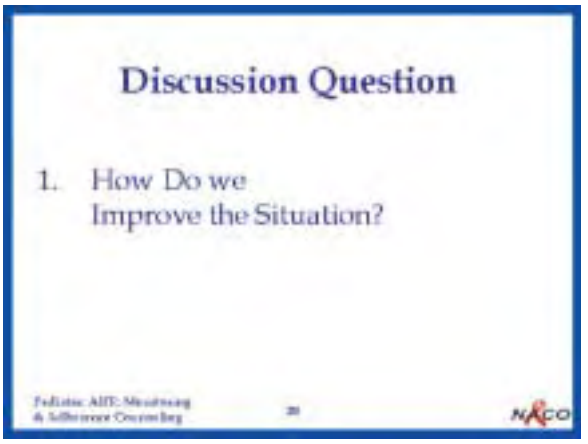
Slide 5		
Slide 6		**Reader's Notes:** • It is important for health care personnel to understand the child/caregiver's problems and provide positive reinforcement • Health care professionals should not reprimand the caregiver/child for being non-adherent but rather work with them to solve issues affecting adherence • Child-focussed counselling principles should be used.
Slide 7		**Reader's Notes:** • Patients and caregivers need to be questioned in a non-threatening way to get this information

Slide 8		
Slide 9		**Reader's Notes:** • The 3-drug FDC's recommended by NACO should be used, as they offer convenience of administration
Slide 10		

Slide 11		**Reader's Notes:** • Help patients to set their 12-hourly schedule for ART based on some activity which they do at a fixed time of the day, e.g leave home for work or watch a particular TV program.
Slide 12		
Slide 13		

Slide 14		**Reader's Notes:** • Patients beginning ART or their care givers should be explained the consequences of non-adherence, in simple language
Slide 15		
Slide 16		

Slide 17		
Slide 18		**Reader's Notes:** • Children will usually answer honestly when asked about missed doses and reasons for it. • Adolescents need a tactful approach. • Illiteracy and lack of time are factors that prevent questionnaire approach from being used routinely.
Slide 19		

Slide 20		
Slide 21		**Reader's Notes:** • It is important to find out why ARV schedule cannot be adhered to: find out the time when doses are usually missed, check reasons why they are missed and work with the family to adjust towards a suitable schedule • Find out the reasons for the child refusing to take ART: Counselling, especially peer group counselling can help reinforce adherence. If the child does not know his/her HIV status, the HCW should work with the caregiver in preparing the child for disclosure of HIV status. • Involving community and support groups and providing support outside the clinic environment such as home visits, may help.
Slide 22		

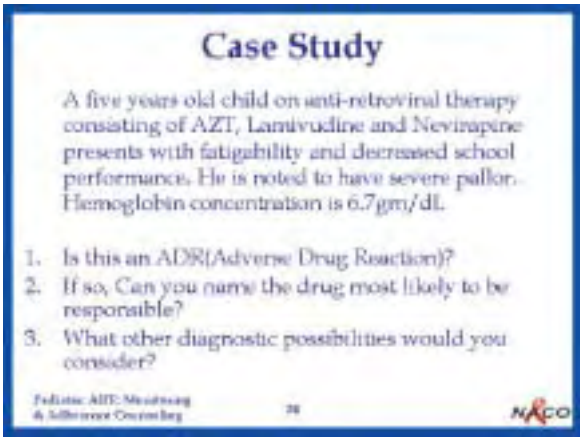
Slide 23

Step 6: Monitoring Adverse Effects and Substitution of ARVs (Slides 23-33) - 15 minutes

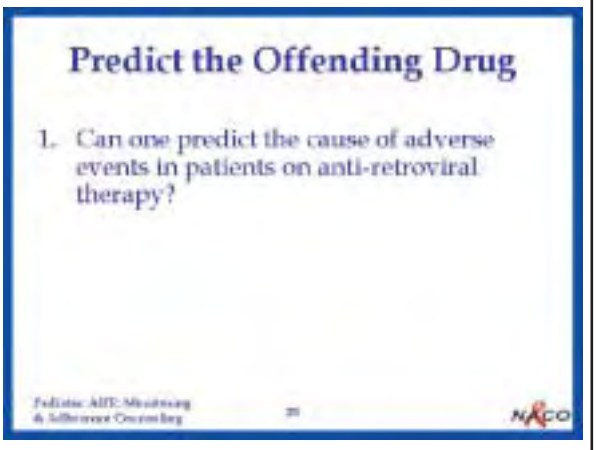
Reader's Notes:

- Determine the seriousness of the toxicity, grade it and manage it according to severity
- Evaluate the concurrent medications and determine which drug the toxicity is attributable to
- Consider other diseases, eg viral hepatitis
- Stress adherence despite toxicity for mild and moderate reactions

Slide 24

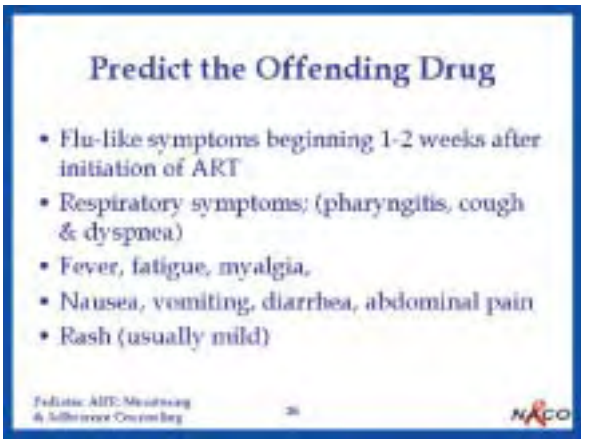
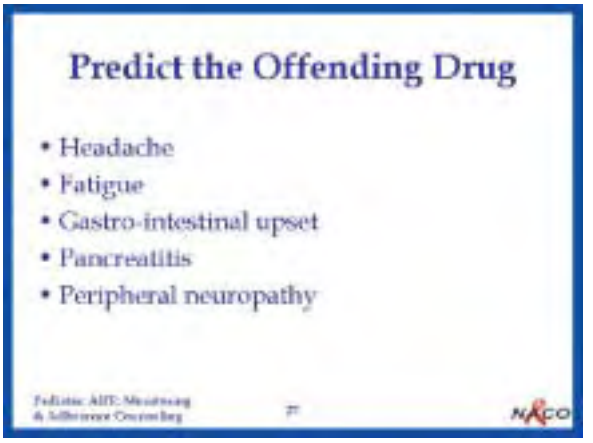
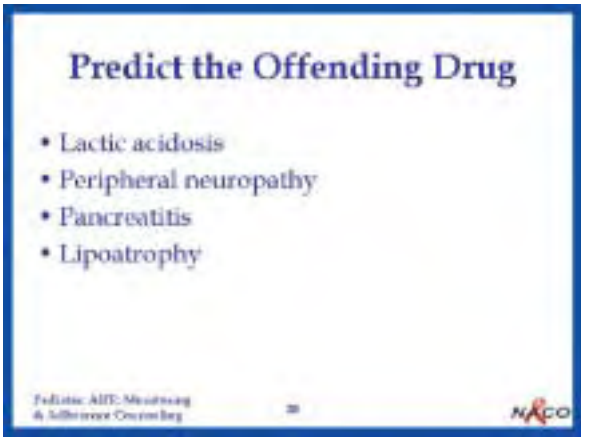


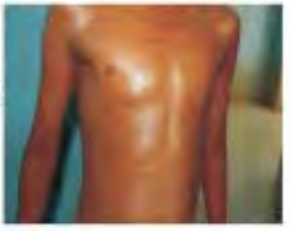
Slide 25

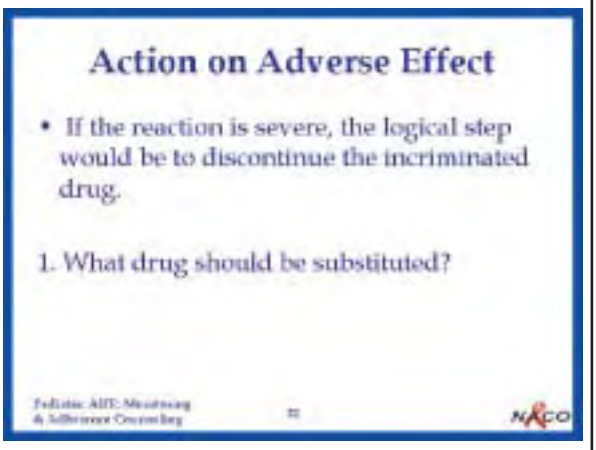
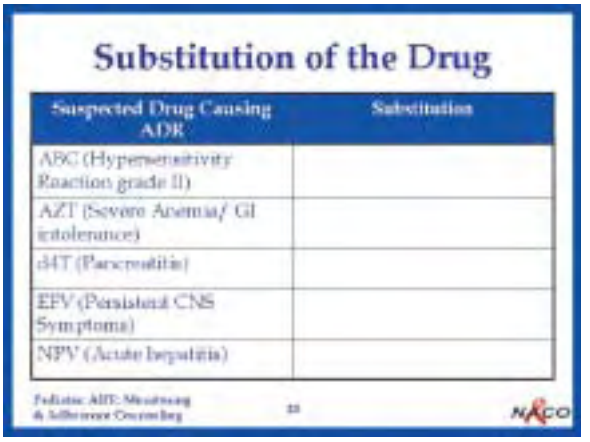


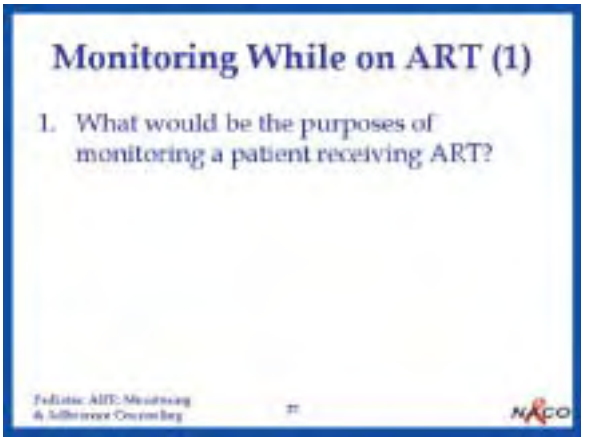
Reader's Notes:

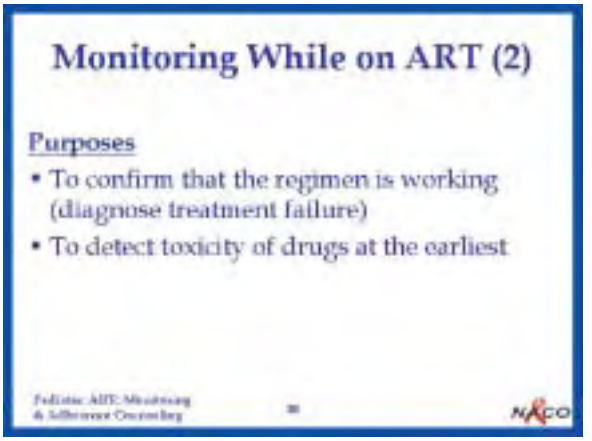
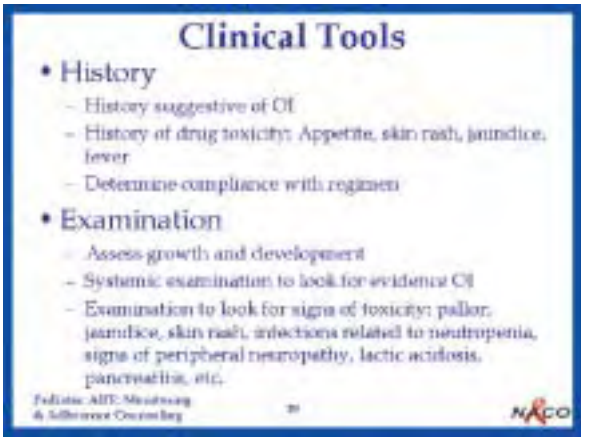
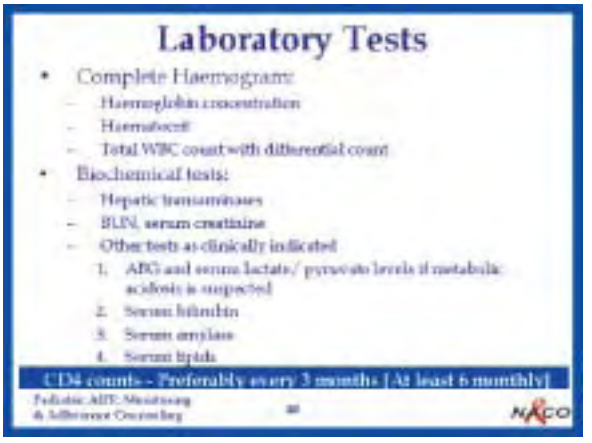
- Some adverse events are typical of certain drugs. Drugs used in ART have typical side effects and hence cause could be predicted.
- The next few slides are shown to discuss examples of predicting adverse drug reactions due to ARV drugs.

Slide 26		
Slide 27		
Slide 28		

Slide 29	**Predict the Offending Drug** • Anemia • Fatigue • Headache • Nausea • Severe neutropenia	
Slide 30	**Predict the Offending Drug** • Rash within two weeks of initiation of ART • Confusion • Agitation • Sleep disturbances • Nightmares • Hallucinations	
Slide 31	**Predict the Offending Drug** • Rash • Granulocytopenia • Hypersensitivity reaction: rash, fever, arthralgia, myalgia & lymphadenopathy • Acute symptomatic hepatitis • Renal dysfunction 	Source: GHTM HIV Fellowship Program.

Slide 32		
Slide 33		
Slide 34		**Reader's Notes:** • These points were already discussed during the previous session. • Virologic failure occurs first, followed by immunological and then clinical failure. • There may be a lag of several months between virologic failure and clinical deterioration, during this time the virus is accumulating resistance mutations

Slide 35		
Slide 36		**Reader's Notes:** • At present, second line drugs are not available in the program, so the first line regimen should be continued unless there are other options.
Slide 37		

Slide 38		**Reader's Notes:** • Clinical staging using the WHO T staging (WHO T Staging has already been discussed in the previous session) for clinical monitoring after ART initiation must be done at all visits.
Slide 39		
Slide 40		

Slide 41		

Key Messages
• Follow-up of children on ART should include clinical and laboratory monitoring as well as adherence assessment and counselling
• Doses should be frequently adjusted as weight gain can be rapid
• Monitor growth, look for opportunistic infections, adverse events and IRS
• Antiretroviral drugs have typical toxicities which should be recognized and managed

SESSION 27-30

DAY -TEN

SESSION

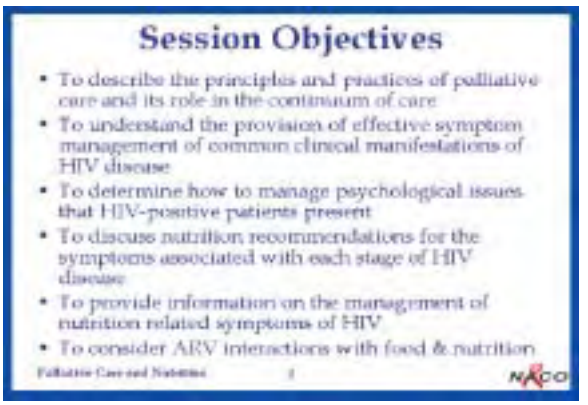
PALLIATIVE CARE AND NUTRITION

27

Total Session Time: 45 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Describe the principles and practices of palliative care and its role in the continuum of care
- Understand the provision of effective symptom management of common clinical manifestations of HIV disease
- Determine how to manage psychological issues that HIV-positive patients present
- Discuss nutrition recommendations for the symptoms associated with each stage of HIV disease
- Provide information on the management of nutrition related symptoms of HIV
- Consider ARV interactions with food & nutrition

Slide 1		
Slide 2		

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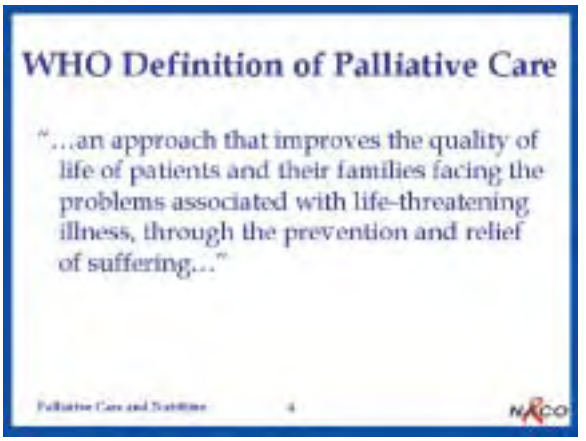
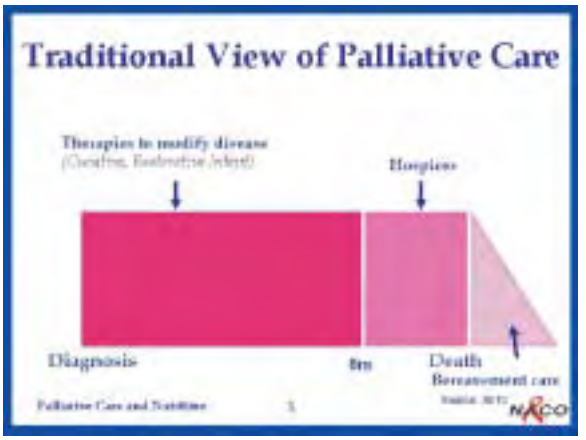


Reader's Notes:

- **Definitions of Palliative Care:**
  - Medical treatment to prevent, relieves, or reduces symptoms of a disease without effecting a cure.
  - Not intended to replace disease-modifying treatments such as antiretrovirals, but to augment the comfort and support of individuals and families who are living with life-threatening illness
- **Aspects Palliative Care:**
  - Revolves around family and patient-centered care which includes building a trusting relationship with patient, family, and friends.
  - Optimizes the quality of life by active participation, prevention and treatment of suffering.
  - It emphasizes use of an inter-disciplinary team approach throughout the continuum of illness, placing critical importance on the building of respectful and trusting relationships.
  - Palliative care addresses physical, intellectual, emotional, social and spiritual needs.
  - Mitigate side effects of treatment.
  - Provide medications to treat other conditions that impact quality of lie - fatigue, dementia, neuropathy, depression.
  - Advance care planning.

Slide 5



Reader's Notes:

- In the past, palliative care was viewed in this way. The focus was on diagnostic and preventive services. Palliative care was separate from curative care, and only happened after all treatment options had failed.
- Palliative care was considered only when the individual was near a terminal event, and there was no provision of care for the bereaved family.
- Graphic Source: Center for HIV Information, University of California at San Francisco. Northwest Center of AIDS Education and Training Centers (AETC) National Resource Center. Center for Palliative Care Education. PowerPoint presentation: Palliative Care for People with HIV/AIDS: A Curriculum and Teaching Resource for Medical Educators, 2003.

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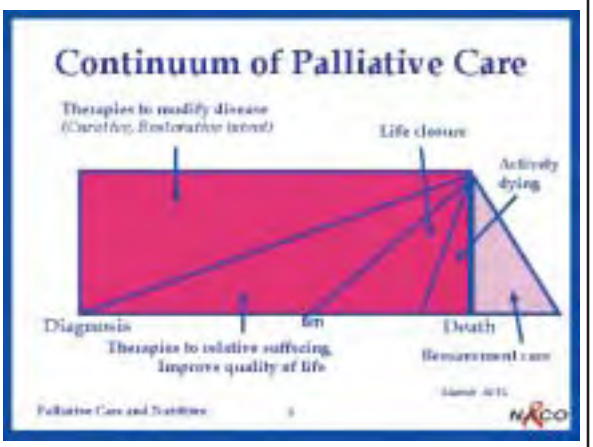

Reader's Notes:

- This chart shows the integration of palliative care early in the disease process.
- The focus still remains on preventive and curative intent early in the process.
- Palliative care should be started early and continued with increasing vigor towards the end of the patient's life. The focus is also on the care and support of the bereaved family.
- Graphic Source: Center for HIV Information, University of California at San Francisco. Northwest Center of AIDS Education and Training Centers (AETC) National Resource Center. Center for Palliative Care Education. PowerPoint presentation: Palliative Care for People with HIV/AIDS: A Curriculum and Teaching Resource for Medical Educators, 2003.

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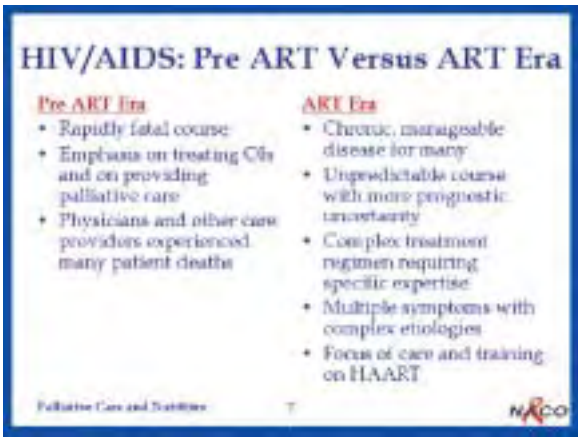
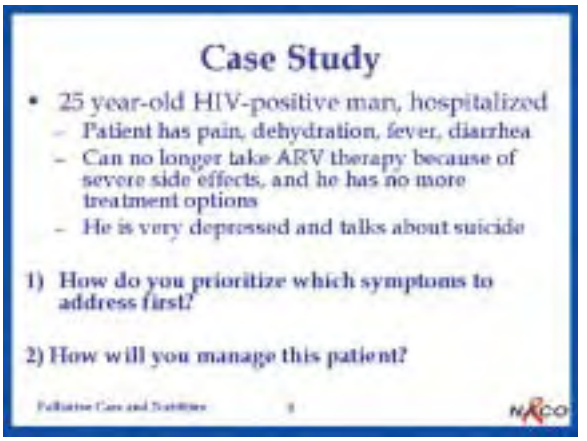


Reader's Notes:

- **In the pre ART era,** HIV was an invariably fatal disease, where the emphasis was on providing palliative care. Health providers became adept at handling patient deaths on a regular basis.
- **In the era of ART,** HIV is considered a more manageable chronic disease. However, no an individual level the course of the disease is unpredictable, and the prognosis is uncertain.
- The regimens currently available are more complex and specific expertise is required.
- Treatment of HIV is associated with complex symptoms and side effects, some of which are not easily explained.
- Recently, the focus has shifted to understanding the complexities of treating HIV and, unfortunately, palliative care has been given less attention.

Slide 8



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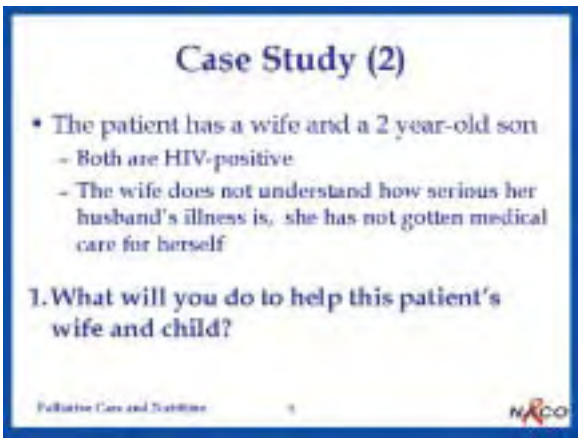

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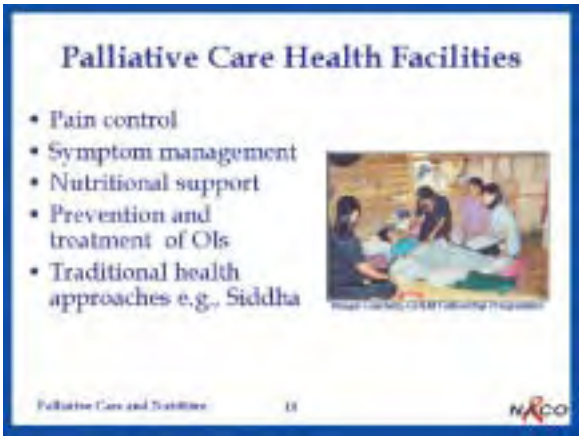


Reader's Notes:

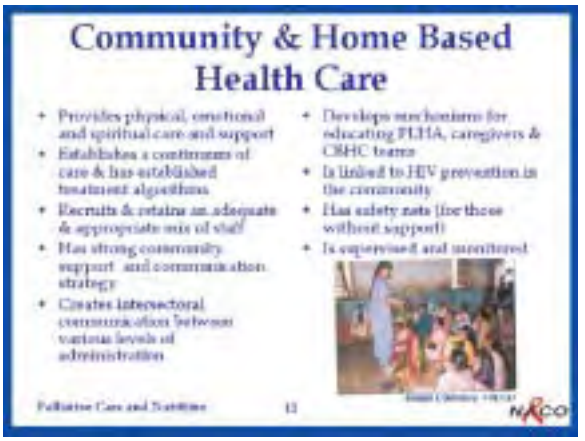
- **A community care centre for PLHA has several merits:**
  - It places the responsibility of care on the community, a more appropriate strategy with chronic symptoms that cannot be cured because specific treatment is not available, or is prohibitively expensive.
  - It provides palliative pain relief thus giving a good quality of life.
  - It promotes a community response to the consequences of HIV infection.
  - It is an affirmation that something can be done once illness has developed; and complements effective control schemes.
- **Traditional health approaches:**
  - Ayurveda and siddha products have shown encouraging results as immunomodulators and extensive studies are needed to further validate these findings. The Government Hospital of Thoracic Medicine in Tambaram, Chennai is conducting research in the siddha system of medicine and these studies are being coordinated by the Central Councils of Research on Ayurveda, Siddha and Homeopathy.

Slide 11

Reader's Notes:

- At the community level, the most effective intervention is probably home based care. This should be promoted to ensure low cost and effective care.
- Counselling and psychological support are also very important and can be done at a community level. This also can help reduce stigma.
- Care of vulnerable children and orphans should also be encouraged and numerous non governmental and faith based organizations are developing programs to address this population.
- Voluntary counselling and testing (VCT) coverage is being expanded to ensure that more people have access to testing and preventive counselling.
- Source: http://www.nacoonline.org/guidelines/guideline_6.pdf.

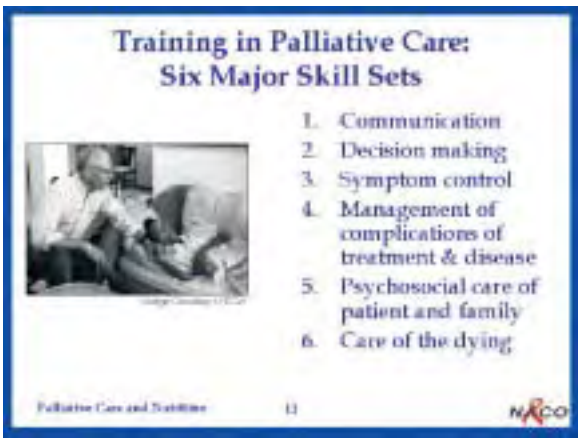
Slide 12



Reader' s Notes:

- Community care centers can be useful in the following ways:
  - It can serve as a place to counter the negative responses.
  - It can be managed as a part of an integrated cost-effective care system.
  - It can serve as an intermediatory between hospitals, home and community based care system. Promotes a community response to the constituents of HIV infection.
- As more HIV-infected persons develop into full-blown AIDS, there will be a need to develop more hospice and community based care centres. To meet that challenge, NACO has taken a decision to provide funds to establish NGOs for setting up community care centers for AIDS patients.
- Source: More information can be obtained from http://www.nacoonline.org/prog_sche_careplwha.htm.

Slide 13



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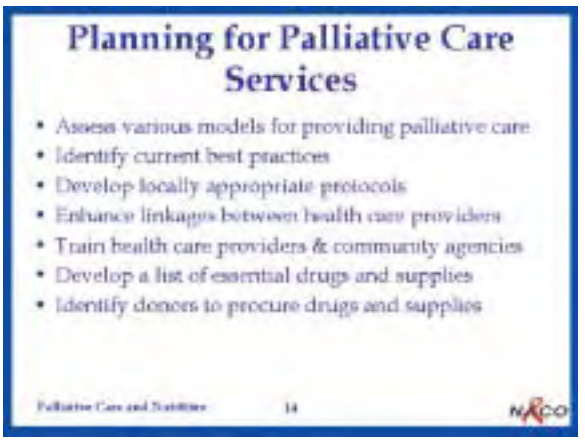

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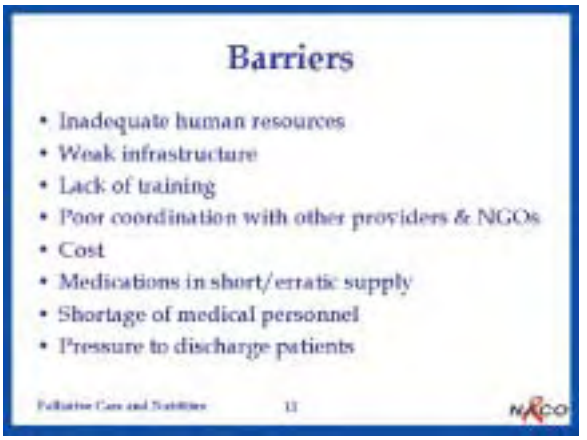

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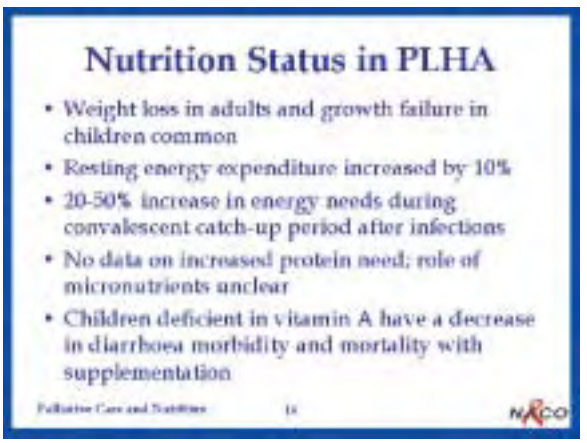
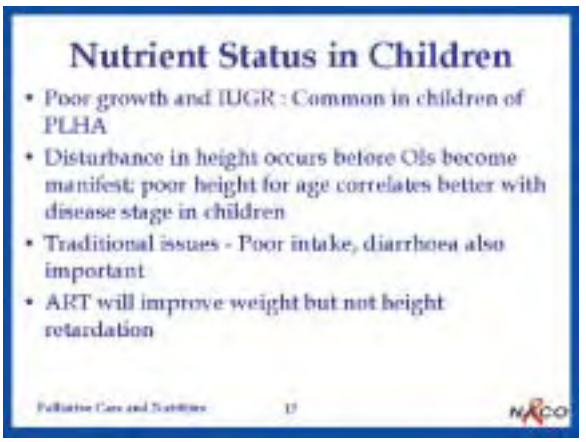
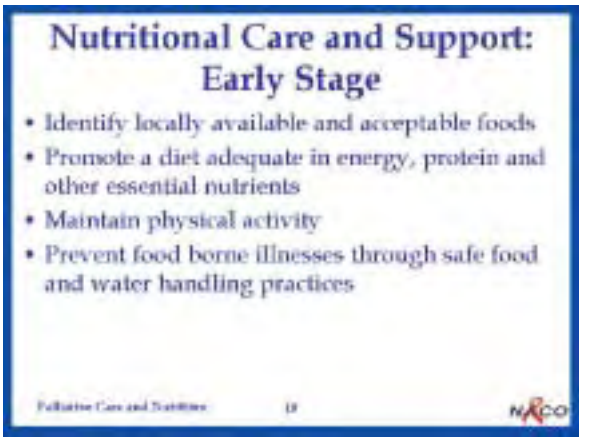


Reader's Notes:

- Data on nutritional aspects of HIV has been best studied in sub Saharan Africa, and it may be applicable to India. In the absence of adequate local data, this data can be used for guidance.
- Energy deficit is a direct result of HIV, other opportunistic infections, and reduced dietary intake as well as malabsorption, increased energy expenditure, and abnormal use of substrates like proteins.
- Apart from food insecurity, reduction of intake due to anorexia is a cause of weight loss. Malabsorption of high energy substrates, like fat, may also contribute. Anorexia generally improves once ART is started, but the role of a balanced diet and regular exercise should not be under estimated.
- Micronutrient doses have not been clearly worked out, but there is some data.

		• Vitamin A deficiency is clearly associated with diarrhoea; supplementation will bring down attributable morbidity and mortality. • Vitamin A supplementation may be associated with higher rates of HIV transmission from mother to child (in one study). In one study, supplementation of vitamin B, C and E is also associated with decreased HIV transmission from mother to child. • There is further data that suggests a daily high dose multivitamin supplementation reduces transmission of HIV from mother to child, adverse pregnancy outcomes, and also progression of HIV. • The effect on prolonging survival was not clear in the study, and data may not be applicable to non pregnant women, men and those on ART, although there appears no adverse effect with this approach. • Zinc supplementation of 20 mg per day as a part of treatment of diarrhoea can reduce severity and duration. • **Sources:** 1. Woods, M.N. "Dietary recommendations for the HIV/AIDS patient." In Miller, T.I., and S.L. Gorbach (editors), Nutritional Aspects of HIV Infection. New York, N.Y.: Oxford University Press, 199. 2. World Health Organization (WHO). Nutrient Requirements for People Living with HIV/ AIDS. Report of a technical consultation. World Health Organization, Geneva, Switzerland, 13-15 May, 2003. WHO/UNICEF/JHSPH/USAID, Implementing the new recommendations on the clinical management of diarrhoea, 2006.
Slide 17		**Reader's Notes:** • IUGR: Intra uterine growth restriction. • Poor height in children is an independent adverse prognostic factor. • Many studies have shown that children born to HIV-infected mothers are born weight and height retarded, irrespective of their HIV status. • Growth faltering continues even after birth for the HIV-infected children and can start as early as 3-4 months. • Impairments increase with age and appear to be related to level of HIV replication and chronic diarrhoea. This is also seen in HIV-negative infants born to HIV-infected mothers, but to a lesser degree.

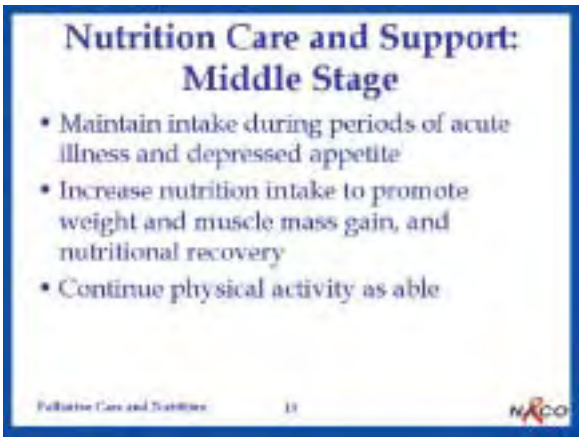
Slide 18



Reader's Notes:

- Malnutrition worsens the natural history of HIV, possibly by lowering immunity, although these effects have not been well studied.
- Even when intake is adequate, there is excessive nutrient demand for production of proteins and immunoglobulins which the body uses in fighting HIV and other infections.
- Studies have shown that changes in the intestinal epithelium occurs fairly early in HIV. This can seriously compromise the ability to absorb nutrients and the problem progressively worsens. Patients with diarrhoea not only lose water and electrolytes; they are also deprived of vital nutrients required for fighting the infection.
- PLHA also have a poor intake and this is multifactorial. Very often, the illness or the medications prevent the patient from having a good diet. Some of the drugs are known to cause nausea and vomiting; some like didanosine and indinavir need to well separated from meals to be effective; some like nelfinavir cause severe diarrhoea.
- Very often PLHA have illnesses like Candidial oesophagitis which make food intake difficult; and even if the digestive tract is structurally normal, many patients experience severe depression- this can also be due to drugs like efavirenz- which decrease intake.
- The financial burden of the problem is such that he patient spends so much on medication, there is no money for food.
- Source: http://www.fantaproject.org/downloads /pdfs/HIVAIDS_Guide02.pdf, **Recommended citation:** HIV/AIDS: A Guide For Nutritional Care and Support. 2nd Edition. Food and Nutrition Technical Assistance Project, Academy for Educational Development, Washington DC, 2004.

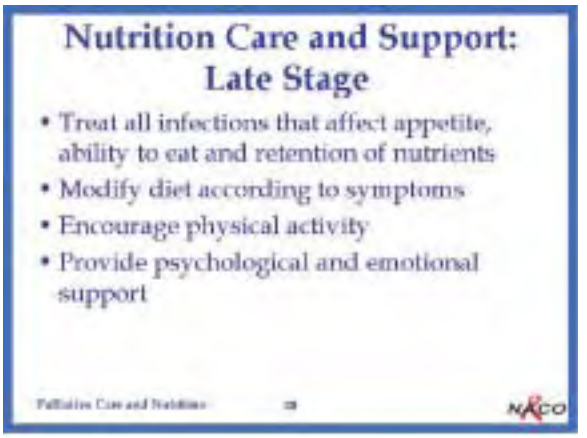
Slide 19



Reader's Notes:

- In the presence of symptoms (WHO stage 2 and above), HIV-infected persons should increase energy intake by 20 to 30 percent over the level of energy intake recommended for healthy non-HIV-infected persons of the same age, sex, and physical activity level.
- These recommendations are for HIV-infected persons, including those taking HIV-related medications such as ARVs.
- Sources:
  1. HIV/AIDS: A Guide For Nutritional Care and Support. 2nd Edition. Food and Nutrition Technical Assistance Project, Academy for Educational Development, Washington DC, 2004.
  2. World Health Organization (WHO). Nutrient Requirements for People Living with HIV/ AIDS. Report of a technical consultation. World Health Organization, Geneva, Switzerland, 13-15 May, 2003.

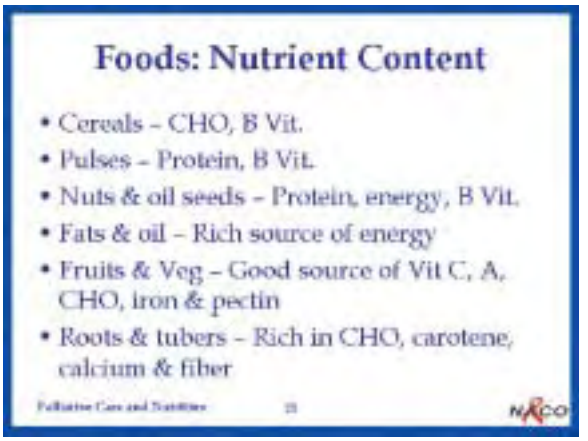
Slide 20



Reader's Notes:

- At the late stage, during palliative care:
  - Persons usually enjoy eating.
  - Caregivers can give them good meals and their favorite foods.
  - The best foods to give are easily digestible food and kept simple.

Slide 21



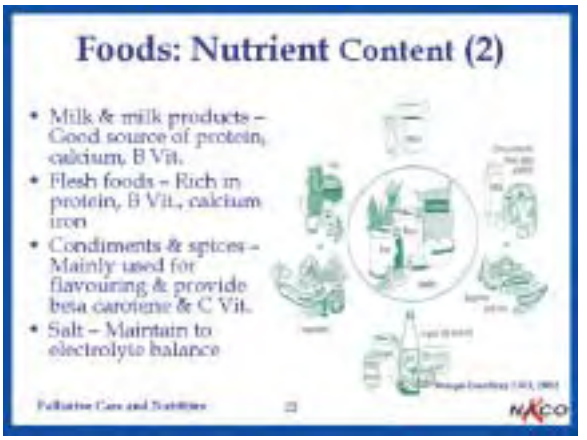
Reader's Notes:

- **PLHA should be encouraged to:**

Eat more staple foods such as rice, maize, millet, sorghum, wheat, bread, potatoes, sweet potatoes, yams and bananas.

- Increase intake of beans, soya products, lentils, peas, groundnuts, peanut butter and seeds, such as sunflower.
- Include all forms of meat, poultry, fish and eggs as often as possible. Minced meat, chicken and fish are easier to digest. Offal (such as kidney and liver) is usually the least expensive.
- Eat snacks regularly between meals. Good snacks are nuts, seeds, fruit, yoghurt, carrots, cassava crisps, crab crisps and peanut butter sandwiches.
- Slowly increase the fat content of the food by using more fats and oils, as well as eating fatty foods - oilseeds such as groundnuts, soy and sesame, avocados and fatty meat. If problems with a high fat intake are experienced (especially diarrhoea), reduce the fat intake until the symptoms are over and then gradually increase it to a level that the body can tolerate.
- Introduce more dairy products such as full-cream milk, sour milk, buttermilk, yoghurt and cheese into the diet.
- Add dry milk powder to foods such as porridge, cereals, sauces and mashed potatoes. However, do not use coffee and tea whiteners, which do not have the same nutritional benefits as milk. Note that some people may find milk difficult to digest. It should be avoided if it causes cramps, a feeling of being full or skin rashes.
- Add sugar, honey, jam, syrup and other sweet products to the food.
- Make meals as attractive as possible.

Slide 22



Reader's Notes:

- More information can be obtained from **Living well with HIV/AIDS: A manual on nutritional care and support for people living with HIV/AIDS.**
- Source: http://www.fao.org/DOCREP/005/Y4168E/Y4168E00.HTM.

Handout 1: Recommendations for Symptom-Based **Nutrition Care & Support**

Diarrhoea:

- Eat smaller meals like soft rice porridge or mashed fruits, more often.
- Eliminate milk products to see if symptoms improve.
- Avoid intake of fried and high fat foods.
- Don't eat food's fiber — take the skin off fruits & vegetables.
- Drink plenty of fluids (8-10 cups/day), and use oral rehydration solution if diarrhoea is severe.
- Avoid sweet drinks; drink diluted juice.
- Avoid very hot or cold foods (they stimulate the bowels).
- Drink plenty of fluids.
- Eat small frequent meals as tolerated.
- Add snacks between meals.

Altered Taste:

- Use a variety of herbs and spices to enhance the flavor of the food.
- Try different textures of food.
- Chew food well and move around mouth to stimulate receptors.

Constipation:

- Eat fiber rich food and sprouted food.
- Light exercise and activity.
- Water, Hot drinks.

Anaemia:

- Eat meat and fish
- Cereals — Ragi, bajra, Use variety of Green leafy vegetables - amaranth, radish, greens, mint, and cauliflower leaves (The best way for the body to utilize iron from plant sources (non-animal sources) is to combine these foods with a food rich in vitamin C — like oranges, lemons tomatoes, papaya, etc. Otherwise, these foods are not useful in boosting iron levels).
- Add jaggery, dates between meals.
- Avoid deep fried foods, unrefined cereals, turmeric & tamarind.

Loss of Appetite:

- Eat small, frequent meals (5-6meals/day).
- Eat nutritious snacks.
- Drink plenty of liquids.
- Take walks before meals-the fresh air helps to stimulate appetite.
- Have family or friends assist with food preparation.
- Light exercise and activity.
- Add Flavour.

Mouth Ulcer:

- Avoid citrus fruits, acidic & spicy foods.
- Eat foods at room temperature.
- Eat soft and moist foods.
- Avoid caffeine and alcohol.

Candidiasis:

- Eat soft, cool & bland foods (like rice porridge, oat meal, mashed vegetables, apple juice, milk).
- Add garlic; avoid sugar (glucose, cane sugar) yeast, caffeine, spicy, carbonated drinks & alcohol.

Nausea and Vomiting:

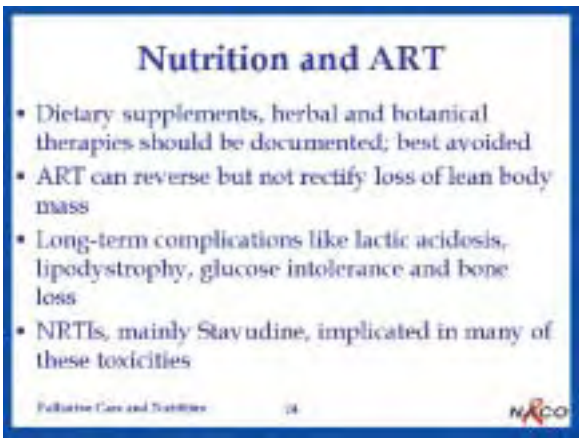
- Eat small, frequent meals.
- Avoid an empty stomach as this makes the nausea worse.
- Eat bland foods.
- Avoid foods with strong or unpleasant odors.
- Drink plenty of liquids.
- Rest and relax after and between meals.
- Avoid lying down immediately after eating.
- Avoid coffee and alcohol.

Slide 23

Reader's Notes:

- Some foods are best avoided, as these may contribute to malnutrition; however some of these same foods processed in a different way may be very nutritious.
- More information can be obtained from **Living well with HIV/AIDS: A manual on nutritional care and support for people living with HIV/AIDS.**
- Source: http://www.fao.org/DOCREP/005/Y4168E/Y4168E00.HTM.

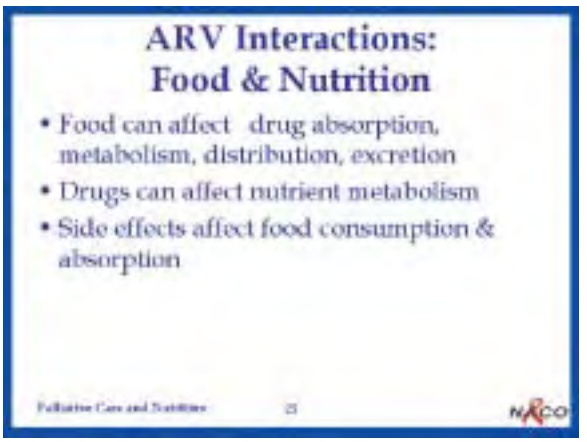
Slide 24



Reader's Notes:

- At the time of initiation of HAART, all dietary supplements, herbal and botanical therapies used by the patient should be documented.
- If possible, all non essential therapies should be avoided.
- ART has been shown to reverse the loss of lean body mass significantly but usually not completely.
- HAART therapy has been associated with significant long-term complications, some of which are listed in this slide.
- In the current program, the major offender is likely to be Stavudine.

Slide 25



Reader's Notes:

- Food has a complex relationship with retroviral therapy and some issues are highlighted on this slide. (Some of these have already been discussed in the section on ART.)
- Physicians should be vigilant in preventing or anticipating these issues in his/her patients as these may be reflective of adherence.
- Food can affect drug absorption, metabolism, distribution, excretion. For example:
  - **High fat and protein changes absorption of Indinavir.**
  - **High fat meals affect bioavailability of Tenofovir.**
- Drugs can affect nutrient metabolism. For example:
  - **Ritonavir causes changes in fat metabolism.**
- Side effects affect food consumption & absorption. For example:
  - **AZT: Anorexia, nausea, vomiting.**
- Combination of drug & certain foods: unhealthy side effects. For example:
  - **Didanosine + alcohol: Pancreatitis.**

Slide 26


Key Points
• Active disease therapies and palliative care are part of the continuum of care
• The needs of patients and availability of resources determine the balance of strategies
• Cost effective and cost beneficial strategies should be emphasized
• Donor resources should support national efforts
• Nutritional impairment is common among PLHA
• Appropriate dietary modifications and are often required

SESSION

PEDIATRIC OPPORTUNISTIC INFECTIONS: PCP, CANDIDIASIS, BACTERIAL INFECTIONS, TB AND MAC

28

Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Understand the spectrum of various OIs in children with HIV/AIDS
- Develop simplified approach for an early diagnosis
- Ensure optimum treatment to prevent re- exacerbations
- Provide primary & secondary prophylaxis when needed
- Start HAART as per guidelines to ensure early and persistent immune recovery

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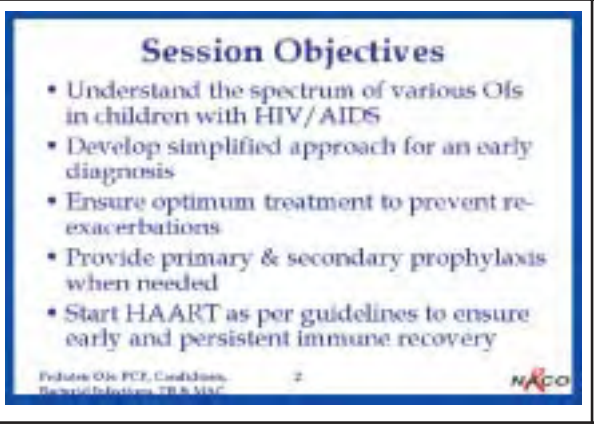
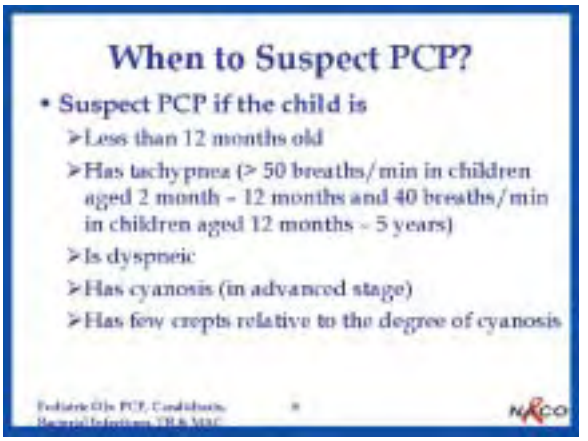
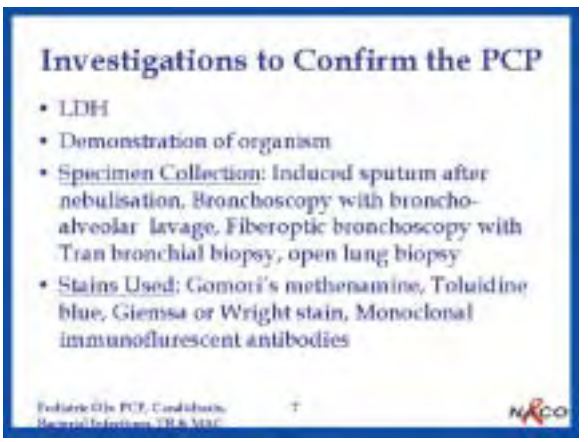
Slide 2		

Slide 3	**OIs in Pediatric HIV/AIDS** • Viral infections : - CMV - HSV - Varicella - Herpes zoster • Fungal infections: - Candidiasis - Cryptococcus - Penicillinosis • Protozoal infections: - Toxoplasmosis - Cryptosporodia - Isospora • Bacterial infections	
Slide 4	**Case Study-1** • What are the salient symptoms in this patient? • What are the possible diagnostic possibilities in this child? • How the physical examination of this child helped you in narrowing down the diagnosis? • How to investigate the child?	
Slide 5	**Interpret the X-ray?** 	

Slide 6

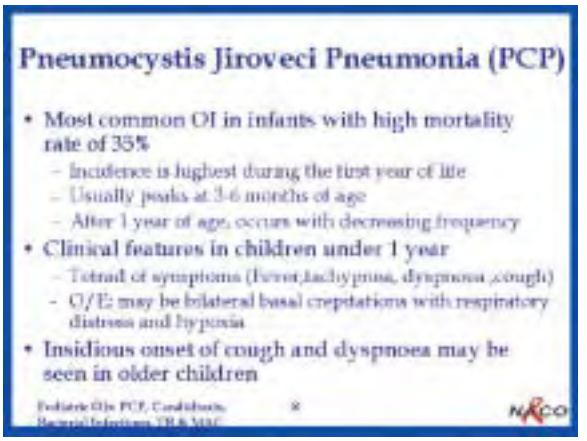


Slide 7



Reader's Notes:

- Investigations that can be done are induced sputum and bronchoalveolar lavage for PCP.
  - Stains used: Gomori's methenamine — Silver stain: Stains the cyst wall brown or black. Toluidine blue: Stains the cyst wall blue or lavender. Giemsa or Wright stain: Stains the trophozoites and intracystic sporozoites pale blue with a punctate red nucleus. Does not stain the cyst wall.
  - LDH: (LDH) is usually increased but not very specific. However it may be of utility when combined with arterial blood gas.
- In a child with respiratory distress, hypoxia and high LDH, one may strongly suspect PCP.
- Other helpful diagnostics:
  - Blood culture or elevated WBC count may help support the diagnosis of bacterial pneumonia and sepsis rather than PCP
  - Common findings on Chest x-ray:
    - Bilateral diffuse parenchymal infiltrates with "ground-glass" or reticulogranular appearance. Mild parenchymal infiltrates predominantly perihilar and progressing peripherally to reach the apical portion of the lung.
- Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Pediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO. Page number 60

Slide 8		

Pneumocystis Jiroveci Pneumonia (PCP)
• Most common OI in infants with high mortality rate of 35%
– Incidence is highest during the first year of life
– Usually peaks at 3-6 months of age
– After 1 year of age, occurs with decreasing frequency
• Clinical features in children under 1 year
– Tetrad of symptoms (Fever,tachypnea, dyspnoea ,cough)
– O/E: may be bilateral basal crepitations with respiratory distress and hypoxia
• Insidious onset of cough and dyspnoea may be seen in older children

Handout 1: Case Studies on Opportunistic Infections-1

Case Study 1

Present Medical History:
8 months old HIV positive child, presented with cough & mild fever of 10 days duration. Since the day before, the child has had difficulty in breathing and been unable to eat, drink and sleep.

Past Medical History:
At 3 months, the child was found to have failure to thrive, cervical and axillary lymphadenopathy and hepatosplenomegaly at the immunization clinic.
At 5 months, the child had bacterial pneumonia & oral thrush and was treated appropriately.
At 7 months, the child developed pneumonia & otitis media and responded adequately to antibiotics.

Family History: Both parents are living and apparently well.

Birth History: Birth weight > 2.5kg, normal delivery and breast-fed from day1.

General and Physical Examination:
- HR: 120/Min; regular.
- Respiratory rate: 60/min; regular.
- Febrile (Temp-38.5 C).
- FTT: Wt-4.3 kg (<5th percentile) Ht- 57 cm (<5th percentile).
- Ears, throat — Normal.
- O2 saturation by pulse oximeter, is 88% on room air.

Systemic Examination:
- RS: Suprasternal and subcostal retractions present, diffuse crackles and rales present.
- CVS: S1S2 normal, no murmur or cardiomegaly.
- Abdomen: Hepatosplenomegaly (4cms).
- Neuro examination : Alert, unable to sit or fix and follow.

Investigations:
- Total WBC count is 8000 cells /cu.mm.
- Differential count: P65; L26; B4; E5.
- Sputum Gram's Stain: No organisms demonstrated.
- Blood culture and Sputum culture: Negative.
- CXR-PA view is projected for interpretation.

Questions:

Question 1: ***"What are the salient symptoms in this patient?"***

Question 2: ***"What are the diagnostic possibilities in this child?"***

Question 3: ***"How the physical examination of this child helped you in narrowing down the diagnosis?"***

Question 4: ***"How to investigate the child?"***

Question 5: ***"What is the differential diagnosis?"***

Question 6: ***"When will you suspect PCP?"***

Question 7: ***"What are the investigations to confirm the diagnosis of PCP?"***

Case Study 2

Present Medical History:
8 yrs. old male HIV-positive child, presented with high grade fever, cough, vomiting, chest pain & sore neck and poor appetite of 4 days duration;

Past Medical History: Not significant.

Family History: Both parents are living and apparently well and they are HIV -positive.

Birth & Developmental History: Normal.

Immunization: Up-to-date.

Physical Findings:

- Febrile, good hydration.
- Respiratory system: Extensive crepitations over the right infra scapular, supra scapular and axillary areas. Also present over the other areas but scattered.
- The chest x-ray (1) of the child is projected for interpretation.
- The child was treated with IV antibiotics and other supportive measures. The child improved and discharged.
- The chest x-ray (2) of the child is projected for interpretation. After 2 weeks, readmitted with spiking temperature, severe breathlessness, productive cough, sputum whitish, vomiting & abdominal pain and malaise with diminished fluid intake.
- Respiratory system examination revealed tenderness over the right infra mammary, infra axillary and infra scapular areas with stony dull note and absent breath sounds in the above areas.
- The chest x-ray (3, 4, and 5) of the child is projected for interpretation.

Questions:

Question-1: "What are the Chest X-ray (1) findings?"

Question-2: "What is the interpretation of the 2nd Chest x-ray?"

Question-3: "What is the interpretation of chest x-rays 3, 4 and 5th?"

Question-4: "What are the steps in treating respiratory bacterial infections?"

Handout 2: Management and Prophylaxis for PCP

The management may be divided into 2 parts:

Supportive Therapy

(1) Provision of oxygen therapy: Give oxygen immediately for respiratory distress, even before child is fully examined
(2) Maintenance of and monitoring of hydration: IV Fluid. Once distress settles, oral feeds can be started
(3) Cover with Antibiotics for bacterial pneumonia

Specific Treatment

- Cotrimoxazole (20mg/kg/day of Trimethoprim & 75-100 mg/kg/day of Sulphamethoxazole) every 6hours IV until the acute symptoms are relieved, changing to oral drugs to complete 3 weeks if response adequate. If no IV preparation, then give same dose orally for 3 weeks.
- Prednisolone, in severe respiratory distress,
  1.5 to 2-mg/kg/day PO in twice daily for 5 days, then
  1 mg/kg/day PO for next 5 days, and then
  0.5 mg/kg/day PO for 11 - 12 days.
- Pretest counselling for HIV.

Indications for cotrimoxazole in infants and children:

(1) All HIV exposed infants from 4 weeks of age (Infants born to HIV infected mothers) till proven to be uninfected.
(2) All HIV infected asymptomatic infants till 1 year of age.
(3) All symptomatic HIV infected children (WHO Stage 2 and above).
(4) All HIV infected children with CD4 % less than 15% irrespective of symptoms.
(5) After initial treatment for PCP.

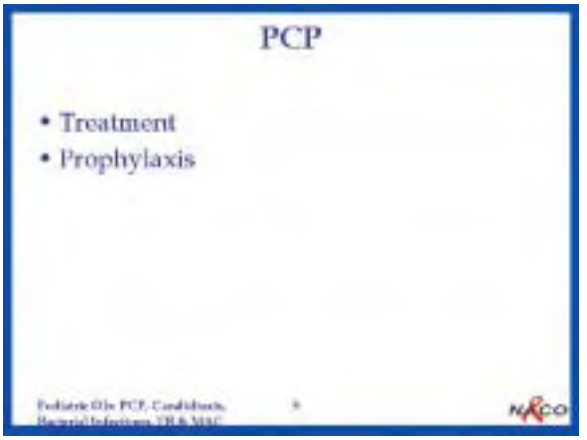
Dosage:

- Cotrimoxazole 5mg/kg/day as a single dose.
- Alternative to cotrimoxazole prophylaxis is Dapsone 2mg/kg orally daily.

Duration of prophylaxis

- In HIV exposed infants till proved to be HIV negative
- In patients on ART, if there is evidence of rise in CD4 count of > 15% on 2 occasions (at least 3 months apart), consider stopping the prophylaxis
- All HIV infected children who do not receive ART and are symptomatic — prophylaxis should be continued indefinitely.

Slide 9



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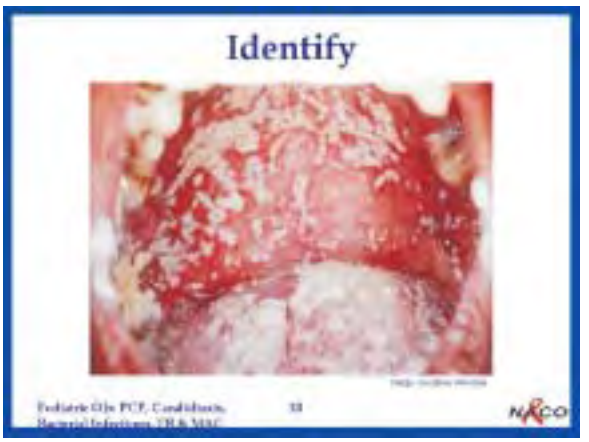

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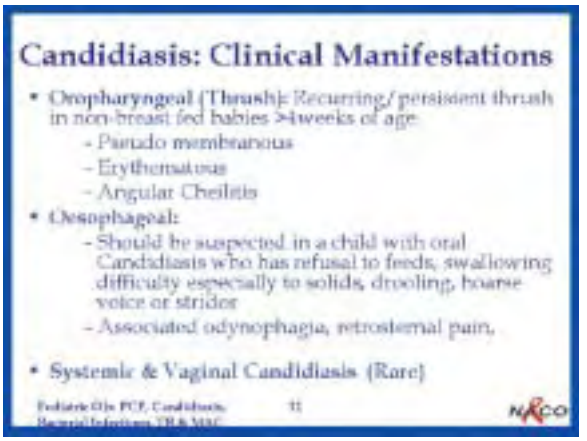
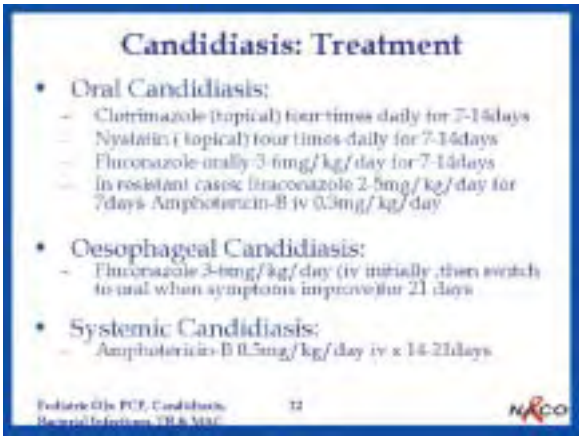


Reader's Notes:

- Candida albicans is common among fungal infections in children of which Oropharyngeal Candidiasis (thrush) is the commonest.
- Oropharyngeal Candidiasis (Oral thrush) is one of the clinical indicators of HIV infection in infants beyond 8 weeks of age. It presents as creamy white curd like patches with inflamed underlying mucosa on the oropharynx, palate & tonsils

  There are 3 main morphological presentations:
  - Pseudo membranous (hypertrophic)
  - Erythematous (atrophic)
  - Angular Cheilitis
- Esophageal Candidiasis: Is seen in patients with a low CD4 value with concomitant Oropharyngeal Candidiasis, esp. in the posterior oropharynx. It is an AIDS defining condition, presenting with odynophagia, retrosternal pain, hoarse voice & stridor,vomiting, dribbling of saliva.
- Vulvovaginal Candidiasis & Systemic Candidiasis : Endophthalomitis, hepatic, splenic & bone involvement are rare in children.

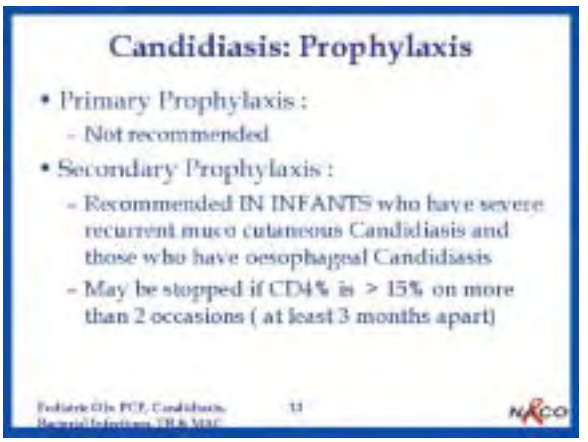
Slide 12



Reader's Notes:

- Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Pediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO. Page number 60 for the details on treatment; page 71.

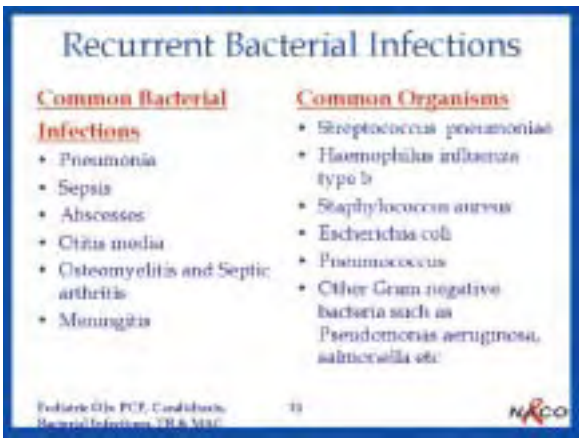
Slide 13



Reader's Notes:

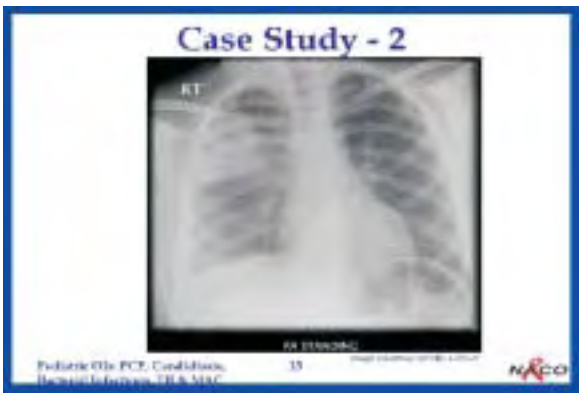
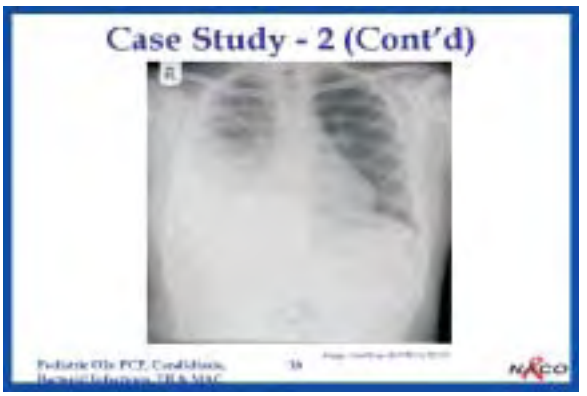
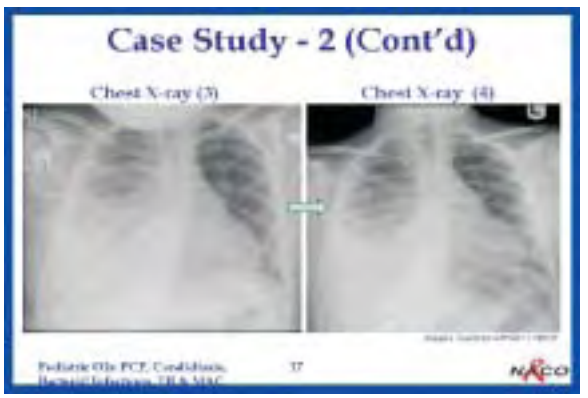
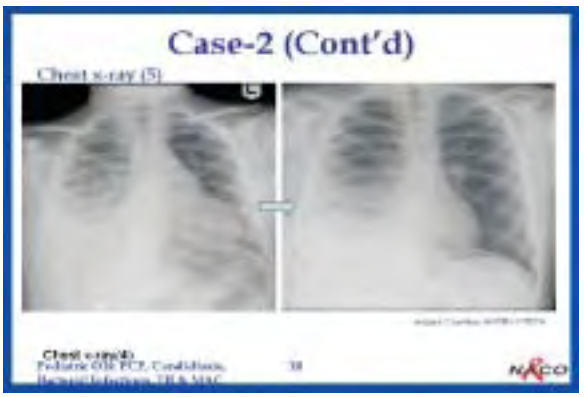
- The primary prophylaxis is **not recommended** because of
  (1) effectiveness of therapy for acute disease,
  (2) low mortality with Candidiasis,
  (3) potential for resistant Candida to develop and
  (4) possibility of drug interactions.

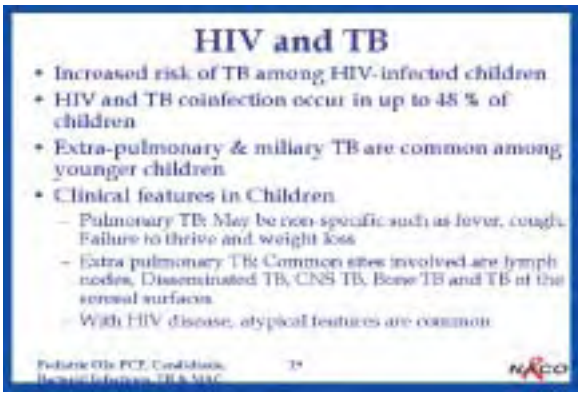
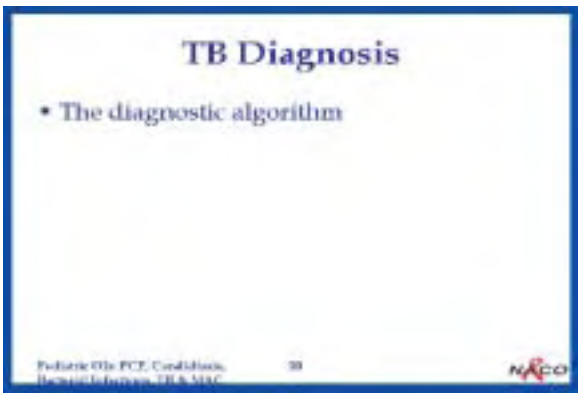
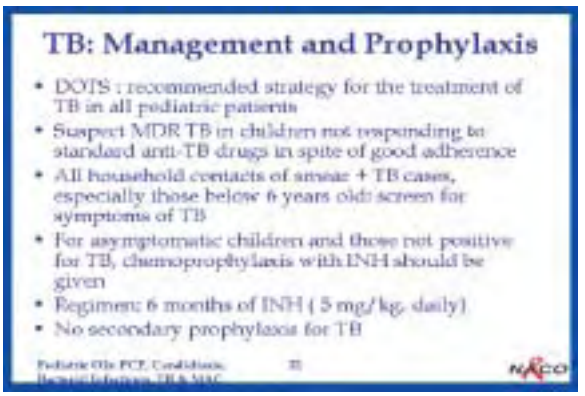
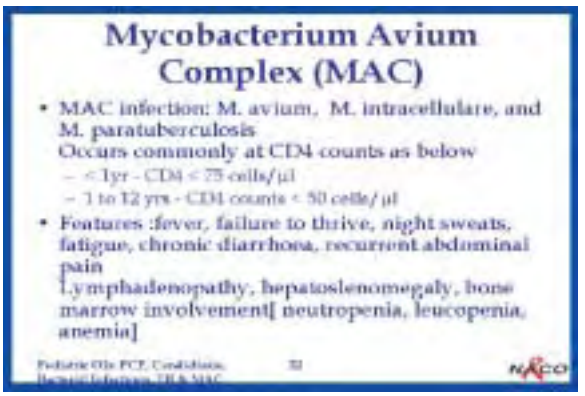
Slide 14



Reader's Notes:

- Bacterial infections are common, recurrent and serious. A child who is HIV infected is equally prone to develop bacterial infections as a child who is non-HIV infected.
- **Common bacteria causing infections are** *Strep. pneumoniae*, *H.influenzae* type b, Staphylococcus aureus, E Coli, Salmonella, Pseudomonas, Bordetella, Chlamydia, Catheter associated staphyloccous, pseudomonas, enterococcus, and Bacillus cereus.
- Diagnosis depends on the site and system involved. Infections cause severe disease. The response to standard duration of antibiotics may be poor.
- Diagnosis is by isolation of the organism by culture from tissue fluids or blood. Collecting induced sputum after nebulisation with hypertonic saline is commonly used to identify etiological agents causing pneumonias.

Slide 15		
Slide 16		
Slide 17		
Slide 18		**Reader's Notes:** • Standard guidelines are followed when antibiotics are instituted for combating bacterial infections. The same antibiotics are used as in children who are non-HIV infected. • Longer duration of therapy is generally required. • Common antibiotics for pneumonias include Cefotaxime, Ceftriaxone, and cefuroxime. Vancomycin is given for resistant staphylococcus and ceftazidime for pseudomonas infections.

Slide 19		**Reader's Notes:** • Young children present with localised pulmonary infiltrates with hilar adenopathy. 25% of children may have more than 1 lobe involved. • Middle lobe collapse and consolidation may result due to endobronchial tuberculosis. • Older children and adolescents may present with cavitary tuberculosis.
Slide 20		
Slide 21		**Reader's Notes:** • Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Pediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO. Page number 64, 65 for the details on treatment; Also the the clinical monitoring algorithm for children with TB need to be discussed, page 110; Annex 10.2, RNTCP-IAP guidelines for TB in children.
Slide 22		

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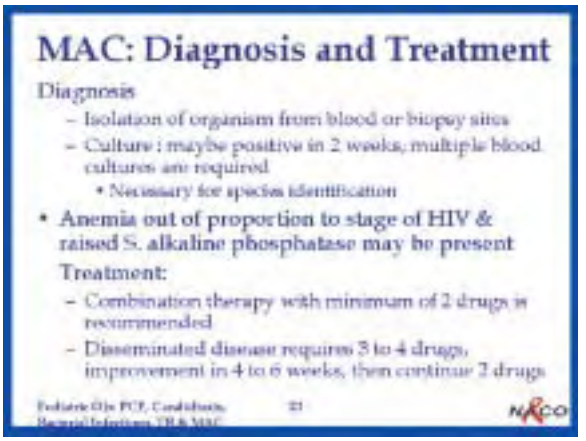
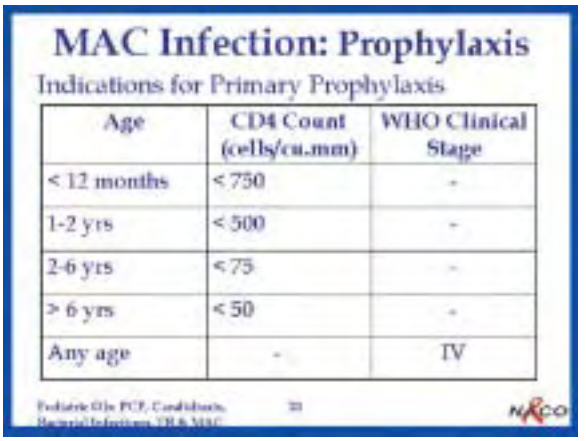


Reader's Notes:

- Organisms can be isolated from biopsy, bone marrow, lymph nodes, and other tissues. The culture takes 2 weeks and multiple blood cultures are required. BACTEC can be used for obtaining quick result. Anemia, raised alkaline phosphatase is frequently noted
- Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Pediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO. Page number 66, table 26 for the name of drugs, their dosage, route of administration, adverse effects :Treatment of Mycobacterium avium complex.

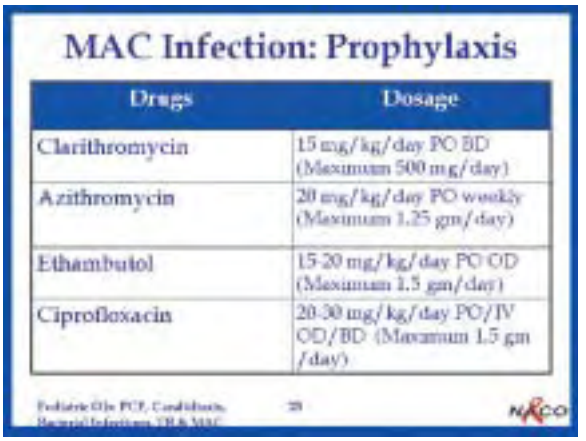
Slide 24



Reader's Notes:

- Prophylaxis may be stopped if CD4 percent is more than 15% for 6 months and ART has been continued for more than 12 months and child is asymptomatic.

Slide 25

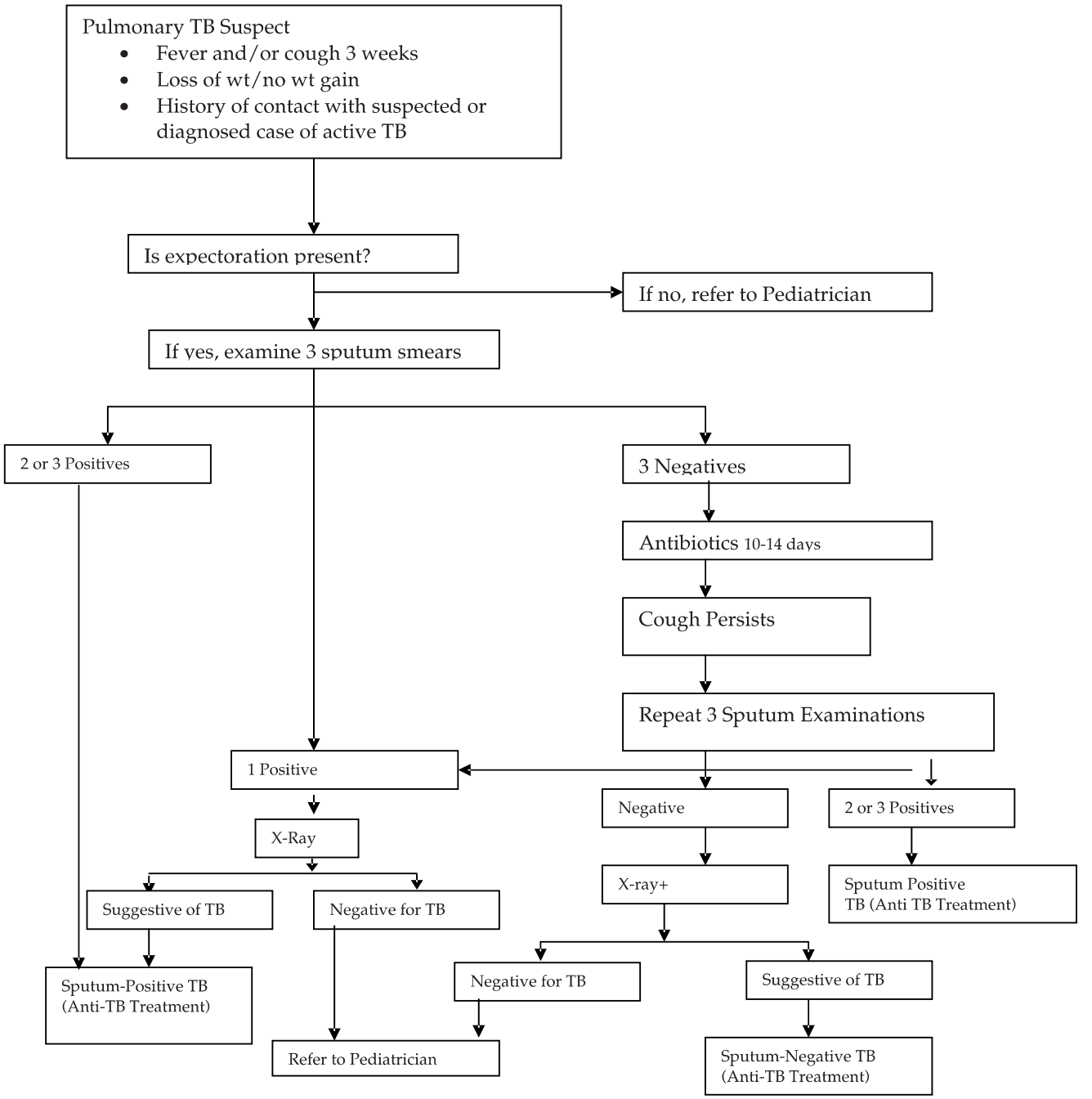


Reader's Notes:

- For primary prophylaxis, any one of the three drugs(Clarithromycin or Azithromycin or Ethambutol) is used. Secondary prophylaxis consists of Clarithromycin or Azithromycin and Ethambutol or Ciprofloxacin

Handout 3: Diagnosis of TB in children

Diagnostic Algorithm



Laboratory Investigations:

Mantoux test / MT (Tuberculin test):

Can be done from 3 months onwards using 5 TU PPD injected intradermally. Induration more than 5 mm is considered positive in HIV infected children. However, negative test may be seen in over 50% of children with tuberculosis. Thus, a negative test does not exclude TB.

Gastric lavage/ sputum examination:

Though acid fast stained sputum smears are positive in 50-70% of adults with Pulmonary TB, children with TB disease rarely produce sputum voluntarily and have a low bacterial load. Three consecutive morning gastric aspirates have a better yield than a single sample. Better diagnostic yield is seen on culture.

Other fluids and tissues for culture:

Bronchoalveolar lavage (BAL), lung biopsy, lymph node biopsy, serosal fluids and CSF. Specimens should be cultured for 2-6 weeks by radiometric culture methods (Bactec) or culture on L-J medium for 8 weeks. Antimycobacterial drug sensitivity should be done on the initial positive culture if treatment fails or relapse occurs. If no organism is isolated from the specimen of the child, drug sensitivity test can be done on the isolate from the source case.

PCR assays: These assays are not useful, as primary diagnostic tool because a negative PCR does not rule out TB and a positive result does not absolutely confirm M.tuberculosis infection. Also false positive rates are high with sensitivity ranging from 45-83%. Serological tests for TB are not very specific.

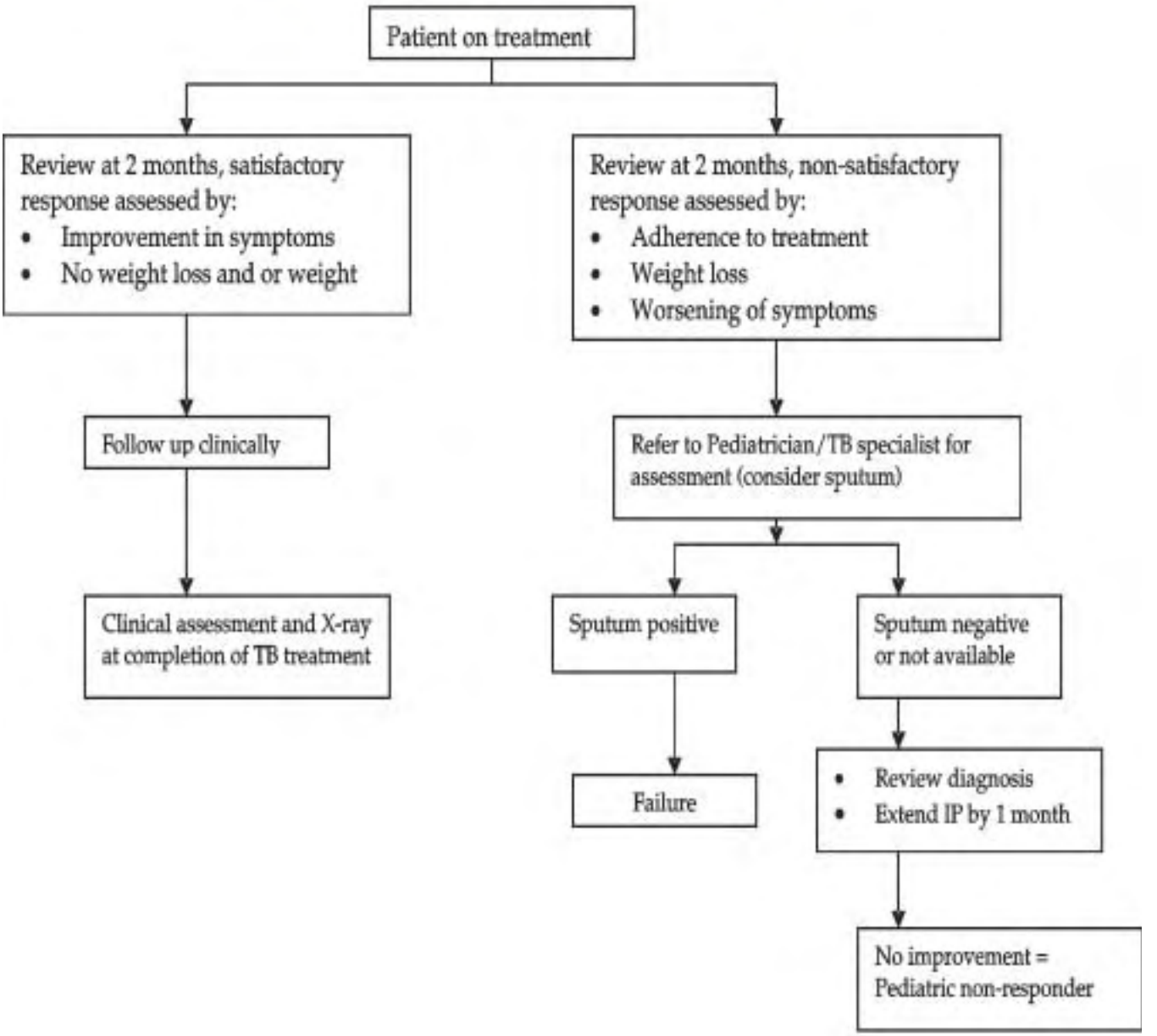
Chest X-ray:

Common Presentations in children:

- Localized pulmonary infiltrates with hilar adenopathy
- Middle lobe collapse and consolidation
- Pleural effusion
- In older children: cavitatory tuberculosis.

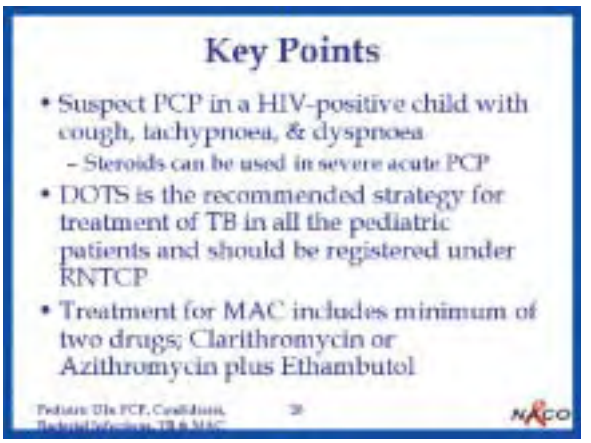
Reference: Paediatric guideline (Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO. Annex 10.1 Diagnostic algorithm.

Clinical Monitoring Algorithm for Children with TB



Source: RNTCP - IAP guidelines for TB in children.

Slide 26		


Key Points
• Suspect PCP in a HIV-positive child with cough, tachypnoea, & dyspnoea
– Steroids can be used in severe acute PCP
• DOTS is the recommended strategy for treatment of TB in all the pediatric patients and should be registered under RNTCP
• Treatment for MAC includes minimum of two drugs; Clarithromycin or Azithromycin plus Ethambutol

SESSION

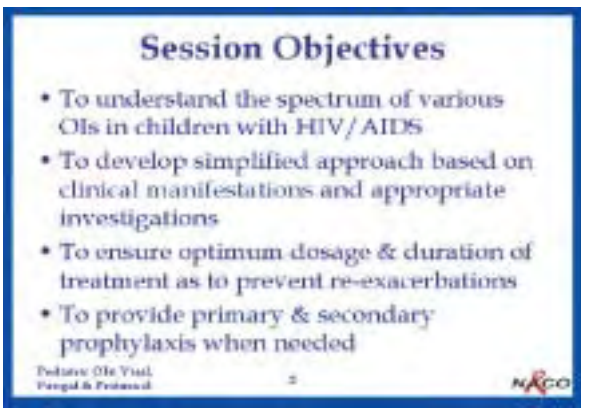
PAEDIATRIC OPPORTUNISTIC INFECTIONS: VIRAL, FUNGAL & PROTOZOAL

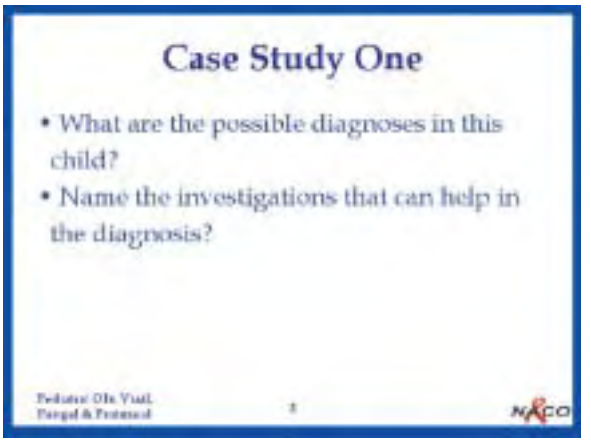
29

Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Understand the spectrum of various OIs in children with HIV/AIDS
- Develop simplified approach based on clinical manifestations and appropriate investigations
- Ensure optimum dosage & duration of treatment as to prevent re-exacerbations
- Provide primary & secondary prophylaxis when needed

Slide 1		
Slide 2		

Slide 3	 Case Study One • What are the possible diagnoses in this child? • Name the investigations that can help in the diagnosis?	

Handout 1 : Case Study One

Case Study One

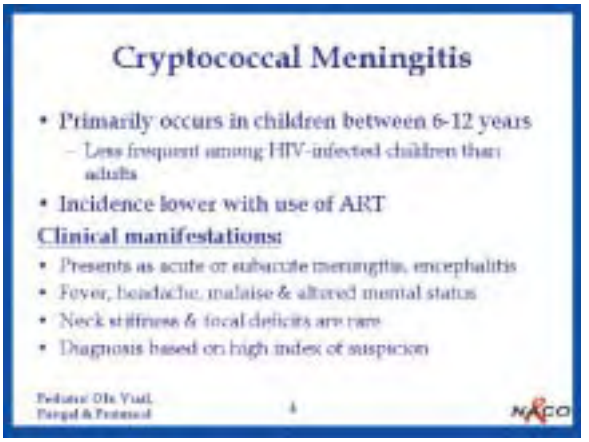
- 6 yrs. old female HIV-positive, child, presented with high grade fever, severe headache, vomiting, & malaise of 14 days duration; the child also presents with features of altered mental status.
- The child has had fever and headache on & off for the past one month but gives no history of convulsions.
- Both parents are HIV +VE and living.
    - o Her father had treatment for PCP few months ago and on Antiretroviral therapy
    - o Her mother is suffering from loose stools on and off.
- Birth & Developmental History: Normal.
- Immunization: up to date.
- Physical findings: Febrile, good hydration, no neuro cutaneous markers.
- Central Nervous System: Right handed child with confusion and mild disorientation; No focal neurological deficits; no signs of meningeal irritation; Fundus examination is normal.
- Other systems: Normal findings.

Questions:

Q.1. What are the possible diagnoses in this child?

Q.2. Name the investigations that can help in the diagnosis?

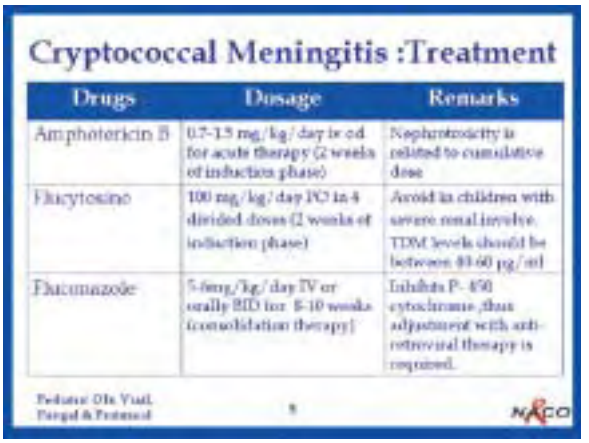
Slide 4



Reader's Notes:

- In Cryptococcal meningitis, CSF pressure should be measured as CSF cell count, glucose and protein may be virtually normal but opening pressure may be elevated.
- CSF analysis with India ink preparation is a must.
- Cryptococcal antigen on CSF should be sent in centers where facilities are available.
- SF antigen detection may be negative in culture positive Cryptococcal meningitis due to
- High titers of antigen (Prozone effect),
- Low levels of antigen or non-encapsulated organisms.
- However, Cryptococcal antigen titers in CSF is helpful in evaluation response to therapy. A CSF titer of > 1:8 after completion of therapy indicates treatment failure or relapse.
- Fungal cultures from CSF or blood may be useful especially for susceptibility testing in patients with refractory disease.

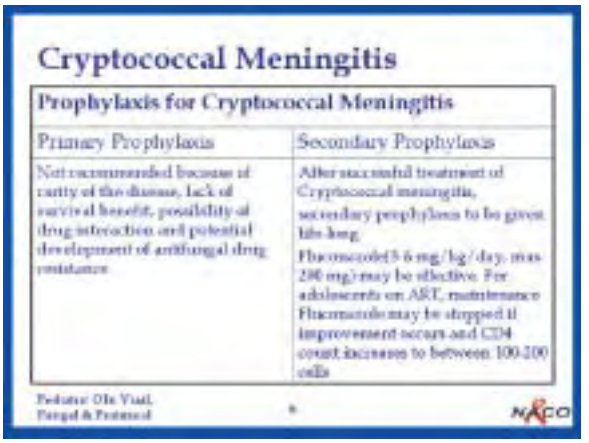
Slide 5



Reader's Notes:

- Cryptococcal meningitis is a severe infection and initial treatment consists of a combination of Amphotericin B (0.7-1.5 mg/kg/day) plus Flucytosine (100 mg/kg/day in 4 divided doses) for a minimum of 2 weeks.
- In India, Flucytosine is not available, therefore Amphotericin B alone can be used.
- Liposomal Amphotericin B (3-5 mg/kg/day) is found to be useful.
- After successful initial therapy, consolidation therapy with Fluconazole (5-6 mg/kg/do IV or orally BD) for a minimum of 8-10 weeks is recommended.
- If Fluconazole cannot be given, Itraconazole can be used as an alternative (2-5 mg/kg/dose BD).
- In refractory Cryptococcal meningitis, intrathecal or intraventricular Amphotericin B can be used.
- For elevated intracranial pressure, serial lumbar punctures to relieve CSF pressure may be required.
- Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO Page 73-74

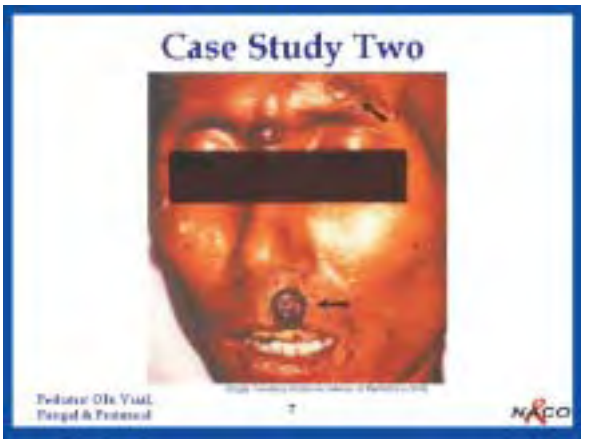
Slide 6



Reader's Notes:

- Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO Page 73-74

Slide 7



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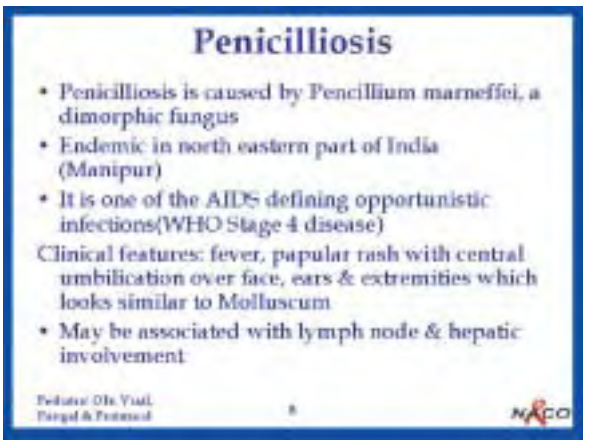
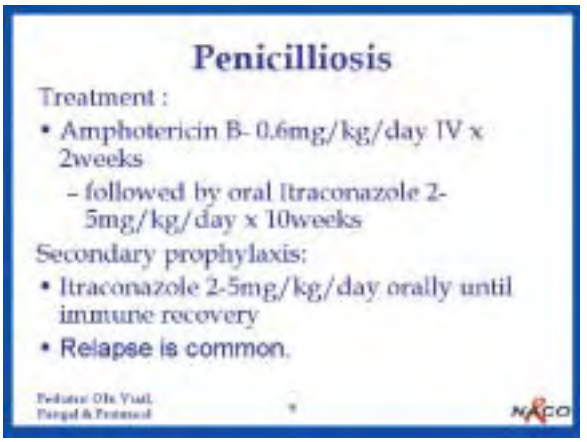
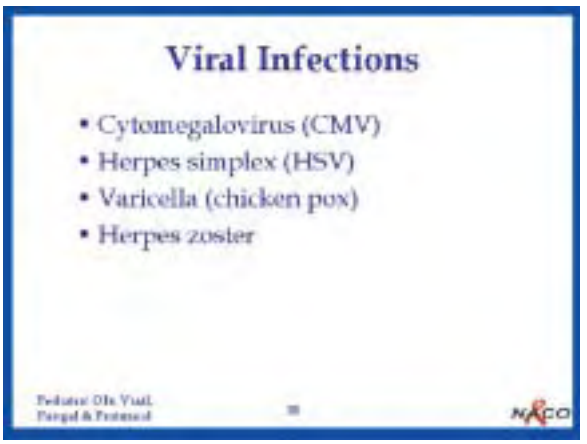


Reader's Notes:

- Penicilliosis is caused by the dimorphic fungus, *Penicillium marneffei.*
- This commonly manifests with fever, weight loss, skin lesions as well as bone marrow, lymphnode and hepatic involvement.
- Skin lesions consist of a generalized papular rash; some of the papules may have central umbilication resembling molluscum contagiosum.
- Skin lesions commonly appear on the face, ears, extremities and occasionally the genitalia. Patients with hepatic penicilliosis have fever, abdominal, pain, hepatomegaly and marked increase in serum alkaline phosphatase levels.
- Diagnosis is based on Clinical suspicion supported by
- Lab diagnosis: Wright staining of the skin scraping ,bone marrow aspirate or lymph node biopsy demonstrates organism(Many intra & extra cellular basophilic spherical, oval and elliptical yeast like organisms can be seen, some with clear central septation)

Slide 9		
Slide 10		

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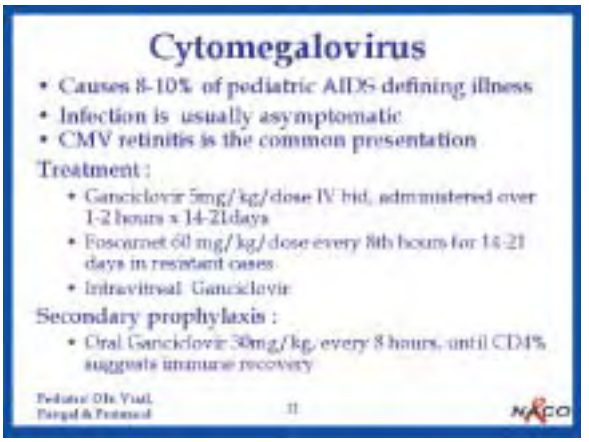
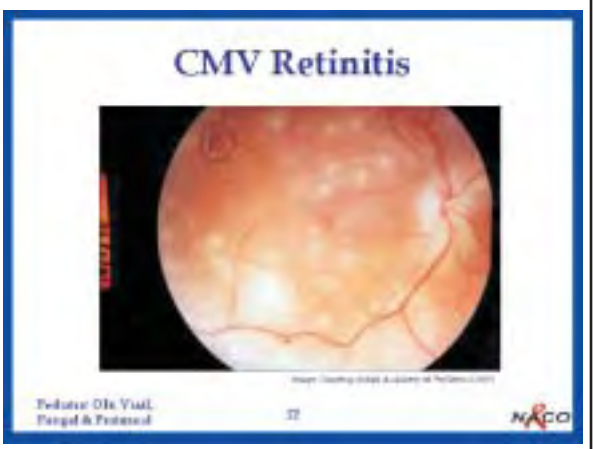


Reader's Notes:

- CMV is a Human Herpes virus type 5 .
- CMV infection in humans is common and usually asymptomatic & usually discovered on routine ophthalmic evaluation.
- CMV is usually acquired during infancy or early childhood.
- Transmission can occur congenitally or acquired post-natally through contact with saliva or urine or through transfusion, sexual contact or transplantation with infected organs. CMV can also be transmitted through breast milk.
- Systemic infections are usually rare. The other manifestation includes sensorineural hearing loss, developmental anomaly, neurological disease.
- Half yearly ophthalmologic evaluation is a must in all children
- All children with CMV infection should be treated as inpatients.
- Ganciclovir in dose of 5 mg/kg/dose IV twice daily administered over 1-2 hours for 14-21 days followed by life-long maintenance therapy is required for treatment of disseminated CMV and CMV retinitis. Intravitreal Ganciclovir not available at all referral centers.
- Alternatively, in Ganciclovir resistant CMV infections, Foscarnet may be used as 60 mg/kg/dose every 8 hours for 14-21 days followed by lifelong maintenance therapy.
- Valganciclovir is used in adults with CMV retinitis as induction dose of 900 mg PO BD for 21 days followed by 900 mg OD daily as maintenance but appropriate dose of this drug in children is not known.

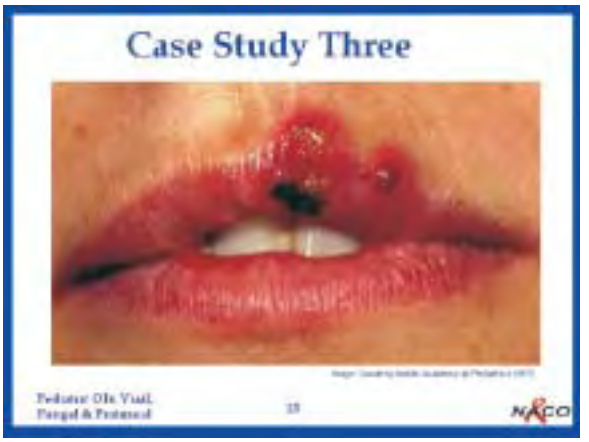
Slide 12



Reader's Notes:

- In CMV retinitis,Children present with floaters & loss of vision
- On Fundoscopy : Retinal infiltrates & hemorrhages

Slide 13		



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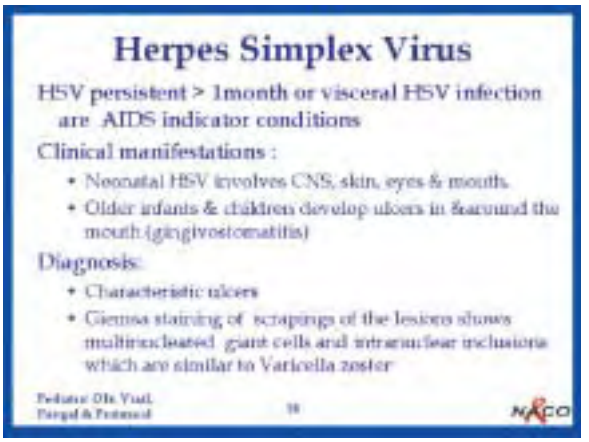
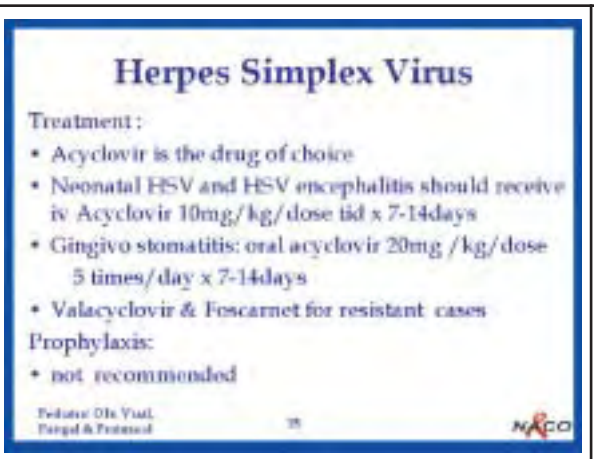
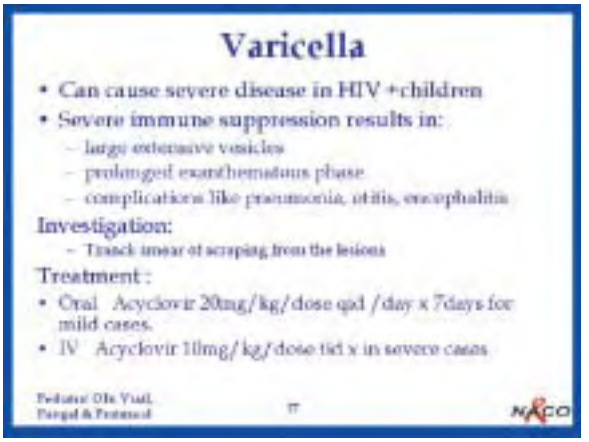


Reader's Notes:

- HSV has 2 types: HSV-1 and HSV -2
- HSV is transmitted as vertical transmission and horizontal transmission through direct contact infected oral secretions or lesions. Vertical transmission occurs predominantly intra-partum when the fetus passes through the birth canal and is exposed to genital ulcer.
- Caesarean section lowers the risk of transmission. Neonatal infections are usually caused by HSV type 2.
- Clinical features:
  - Neonatal HSV leads to CNS involvement or involves skin, eyes and mouth. Vesicular rash is seen.
  - Outside the neo-natal period,the most common manifestation is extensive ulcers in and around the mouth which are painful 4-5 mm in diameter and can be seen on tongue, lips and all mucosal surfaces (Gingivostomatitis).
  - Other sites such as esophagus, CNS, genitals and systemic disease may occur. HSV encephalitis is rare
- Diagnosis:
  - The virus can be isolated in culture and detected in tissue culture cells with 1-3 days.
  - Giemsa staining (Tzanck smear) does not differentiate HSV from varicella zoster infection and is not routinely recommended.
  - Detection of HSV 1 and 2 antigens from skin or mucosal scrapings by immuno-florescent techniques aids in diagnosis.
  - In patients with suspected HSV encephalitis, detection of HSV DNA by PCR is the diagnosis of choice.
  - Rising antibody titres of HSV 1 and 2 IgG is also useful.

Slide 15		**Reader's Notes:** • Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO page 77, table 38 for full details regarding the management.
Slide 16		

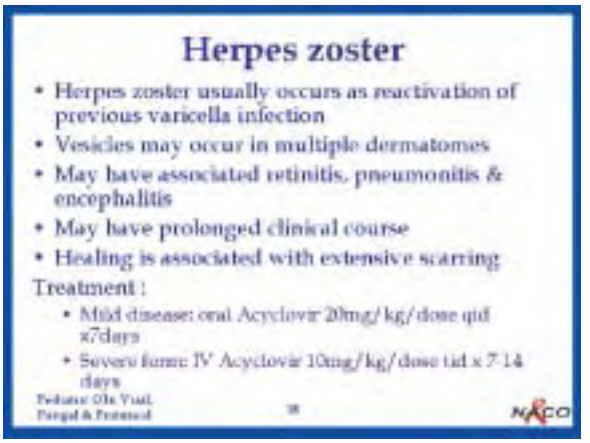
Slide 17



Reader's Notes:

- Patients present with vesicles which start as papules and eventually become crusted with distribution over face, trunks and limbs. With immunosuppression, vesicles may be large and extensive.
- New vesicles may also appear in crops over several days. Mucosal surfaces may also be involved.
- Systemic involvement in form of pneumonia, hepatitis and encephalitis may be seen with immunosuppression.
- Diagnosis: Chickenpox is a clinical diagnosis.
    - Tzanck smear of cell scrapings from lesions may show multinucleated giant cells but is non-specific.
    - Laboratory tests such as demonstration of VZV antigen in skin lesion, isolation of virus in culture from vesicle contents and a significant rise in VZV IgG antibody during convalescence of presence of VZV IgM antibody can help to confirm diagnosis.
- Management:
    - A child with chickenpox is infectious till all the lesions have crusted. Hence, they should be isolated to avoid infecting other HIV infected children or adults.
    - In the HIV-infected child with chickenpox, intravenous acyclovir (10 mg/kg/do IV tds) should be started as soon as initial lesions appear and continued till crusting of all lesions occur or till 7 days.
    - Children who continue to develop lesions or whose lesions fail to heal may have acyclovir-resistant VZV and can be treated with IV Foscarnet (120 mg/kg/day in 3 divided doses) for 7 days.

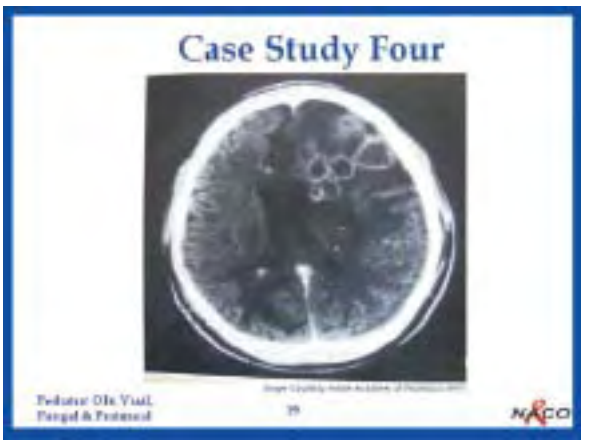
Slide 18



Reader's Notes:

- In immuno-competent adults, vesicular lesions usually occur in the region of a dermatome unilaterally and are associated with pain and fever.
    - Herpes zoster is rare in immuno-competent children and if it occurs in a child, then HIV infection should be suspected. In HIV infected children usually vesicles occur in multiple dermatomes and can occur bilaterally.
    - Patients may have associated retinitis, pneumonitis, hepatitis and even encephalitis.
- Diagnosis: Clinical presentation leads to the diagnosis.
    - Laboratory tests in form of viral isolation or detection of viral antigens in the skin lesions is confirmatory.
- Treatment:
    - IV Acyclovir may be given in children with severe immunosuppression, trigeminal nerve involvement, multi-dermatomal zoster.
    - Patients who fail to respond to Acyclovir may be treated with Foscarnet (120 mg/kg/day IV in 3 divided doses).

Slide 19



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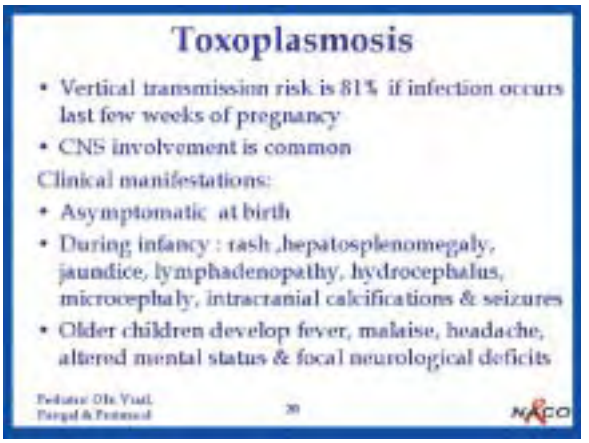
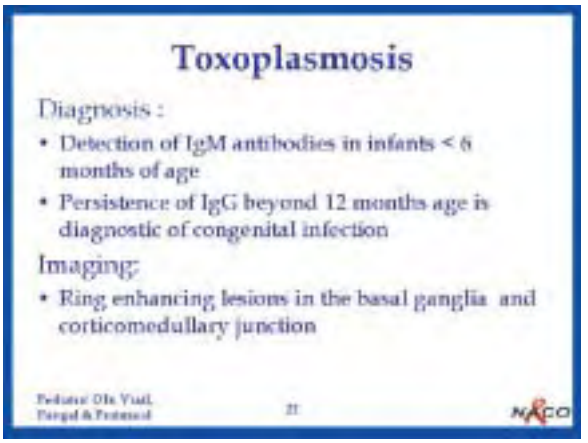


Reader's Notes:

- Very few cases of mother to infant transmission of toxoplasma in HIV infected women have been reported.
- The risk for congenital infection is low among infants born to women who became infected during first trimester(range: 2-6%) but increases sharply thereafter with a risk as high as 81% for women acquiring infection during the last few weeks of pregnancy.
- Infection of the fetus in early gestation results in more severe involvement with milder disease with infection late in gestations.
- CNS involvement with toxoplasma gondii is uncommon in HIV infected children. In most cases, Toxoplasma encephalitis is considered to be due to congenital infection.
- Rarely, it may be due to primary acquired toxoplasmosis.
- Clinical features : Most children are asymptomatic at birth.
- Late sequelae such as retinitis, visual impairment and neurological impairment may be seen after several months to years.
- Acquired Toxoplasmosis may lead to malaise, fever, sore throat, myalgia, lymphadenopathy and mononucleosis — like syndrome.
- Isolated ocular Toxoplasmosis is rare and is usually in association with CNS infection. CNS Toxoplasmosis may present as headache, fever, changes in mental status, seizures, psychosis and focal neurological deficits.

Slide 21



Reader's Notes:

- Diagnosis:
  - A presumptive diagnosis of CNS Toxoplasmosis is done with correlating clinical symptoms, presence of Toxoplasma specific IgG and presence of space occupying lesion on imaging studies of the brain especially ring-enhancing lesions in the basal ganglia and cerebral cortico-medullary junction.
  - Definitive diagnosis requires histologic or cytologic confirmation by brain biopsy.
- Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO.page 68-69, table 29 & 30 for full details regarding the management of Toxoplasmosis

Handout 2: Treatment and Prophylaxis for Toxoplasmosis

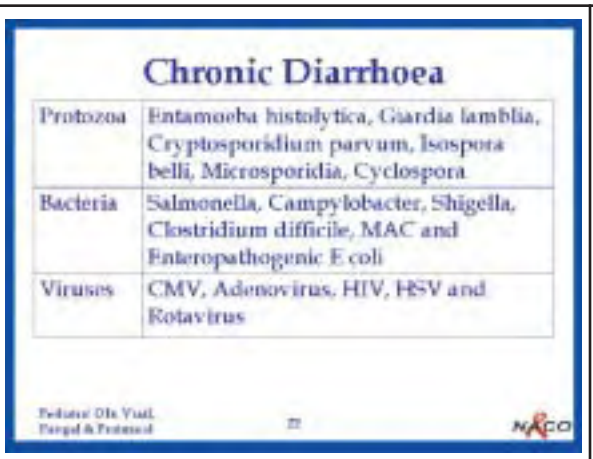
Treatment of Toxoplasmosis			
Drugs	Dosage	Adverse effects	Remarks
Pyrimethamine	***Congenital Toxoplasma*** Loading -2 mg/kg/day on Day1 & 2 Continuation-1 mg/kg/ day for 2-6 months and then 1mg/kg 3 times a week to complete 12 months ***Acquired Toxoplasma*** (CNS, ocular or systemic toxoplasmosis) Loading-2 mg/kg/day for 3 days Continuation-1 mg/kg/ day for 6 weeks	Rash (including Stevens -Johnson Syndrome) Nausea,Bone marrow suppression.	Folinic acid (10-25 mg daily) to be administered with pyrimethamine to prevent bone marrow suppression. It should be continued for 1 week after pyrimethamine has been discontinued
Sulphadiazine	Congenital Toxoplasma 50 mg/kg/dose BD for 12 months Acquired Toxoplasma 25-50 mg/ kg/dose 4 times daily	Rash (including Steven -Johnson Syndrome), fever, leukopenia, Hepatitis, GI symptoms and Crystalluria	
Alternative Drugs			
Clindamycin	5—7.5 mg/kg/dose PO 4 times daily (Max 600 mg/dose)	Fever rash, GI symptoms, Pseudomembra-nous colitis, Hepatotoxicity	In patients hypersensitive to Sulfonamide. Is given along with Pyrimethamine
Azithromycin	-	-	Used in adults with Pyrimethamine in Sulfa-allergic patients
TMP/SMX	5 mg/kg TMP + 25 mg/kg SMX IV/PO BD	-	Not used in children. Used as alternative to Pyrimethamine-Sulfadiazine in adults.
Spiramycin	1.5-3lakh units/kg/ day in divided doses.		

- Therapy should be continued for 6 weeks and longer courses may be required with extensive disease or poor response.
- For an infant born to a mother with symptomatic toxoplasma during pregnancy, empiric therapy of the newborn should be given.
- Steroids may be indicated in presence of severe chorioretinitis or CNS toxoplasmosis with mass effects. However, they should be discontinued as early as possible.

Prophylaxis for Toxoplasmosis	
Primary Prophylaxis	Secondary Prophylaxis
TMP/SMX prophylaxis also provides prophylaxis against Toxoplasmosis.	Life-long suppression is indicated after treatment for toxoplasmosis to prevent recurrence. Sulfadiazine (80—100 mg/kg/day in 2-4 divided doses) + Pyrimethamine (1 mg/kg/day PO) + Folinic Acid (5 mg PO alternate day)

- Source: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO: Page 68-69

Slide 22



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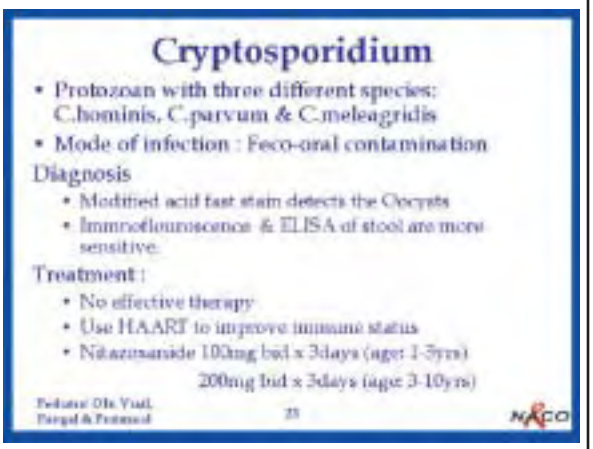
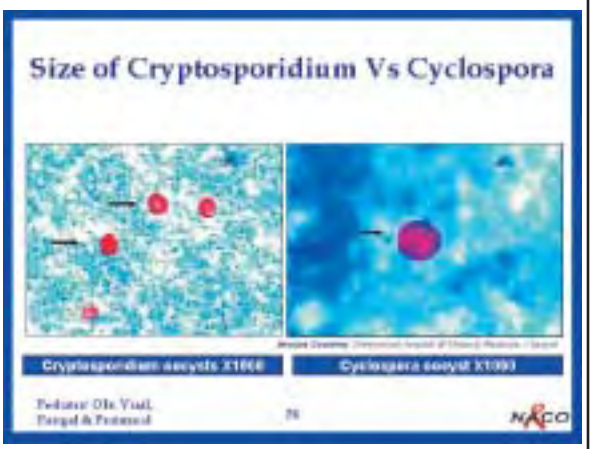


Reader's Notes:

- Cryptosporidium protozoa invade the gut mucosa causing profuse non bloody watery diarrhoea leading to dehydration and malnutrition.
- It is transmitted by ingestation of oocysts excreted in the feces of infected humans and animals.
- The parasite tends to affect the jejunum and terminal ileum.
- Cryptosporidium can migrate into the bile duct and result in inflammation of the biliary epithelium, cholecystitis and cholangitis.
- Treatment:
  - Immune restoration after HAART frequently results in clearance of Cryptosporidium.
  - No consistently effective therapy exists for cryptosporidiosis in HIV infected children.
  - Alternative: Azithromycin: 10 mg/kg on Day 1 and then 5 mg/kg PO OD for 2-10 days

Slide 24



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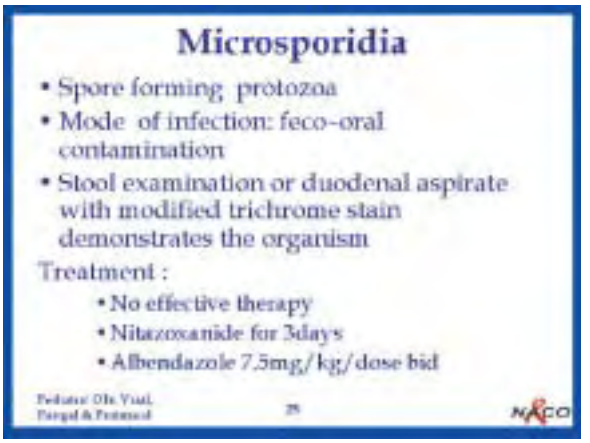
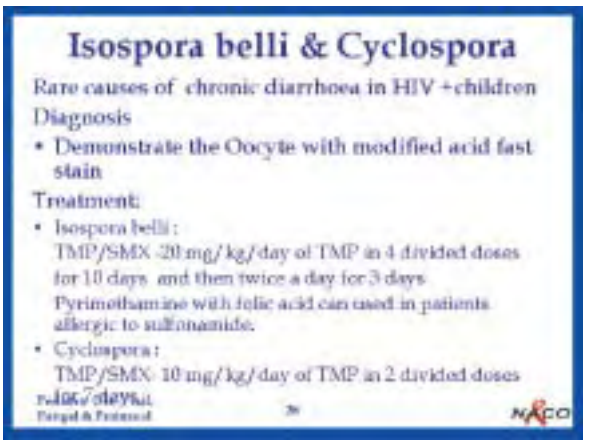


Reader's Notes:

- Microsporidia are obligate spore forming protozoa that cause moderate to severe diarrhoea with weight loss.
- They are transmitted by feco-oral route due to contamination of food or water.
- Treatment: Immune restoration after HAART frequently results in clearance of Microsporidia.
    - No consistently effective therapy exists for Microsporidia.
        - Agents used:
        - Albendazole : 7.5 mg/kg/dose BD (max dose : 400 mg BD)
        - Nitazoxanide : 1-3 years: 100 mg by mouth twice daily x 3 days; 4 - 11 years: 200 mg by mouth twice daily x 3 days.

Slide 26



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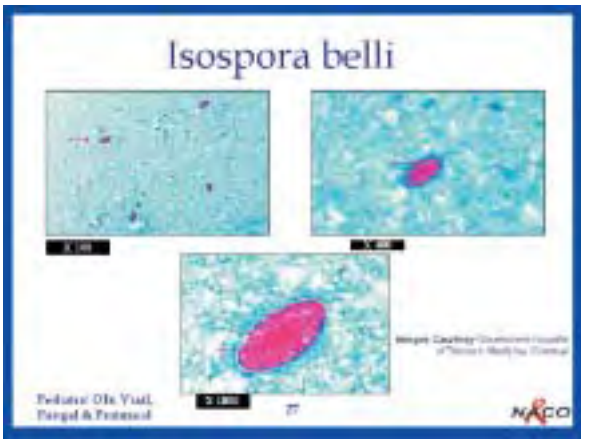

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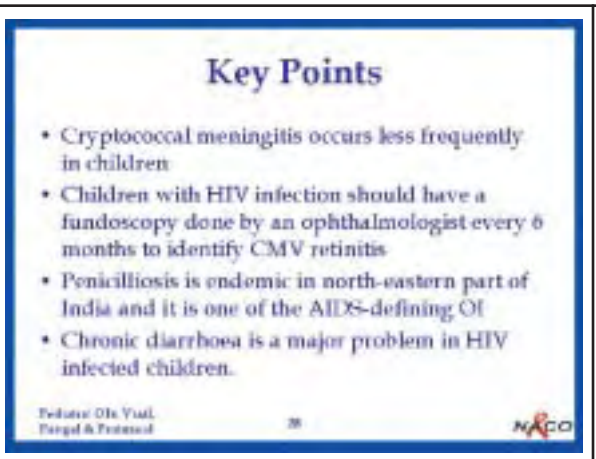

Key Points
• Cryptococcal meningitis occurs less frequently in children
• Children with HIV infection should have a fundoscopy done by an ophthalmologist every 6 months to identify CMV retinitis
• Penicilliosis is endemic in north-eastern part of India and it is one of the AIDS-defining OI
• Chronic diarrhoea is a major problem in HIV infected children.

SESSION

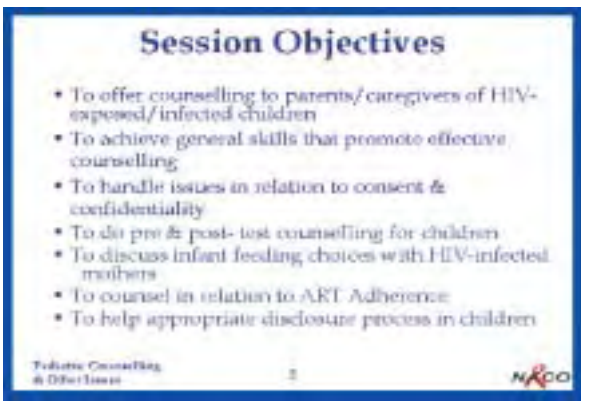
PEDIATRIC COUNSELLING AND OTHER ISSUES

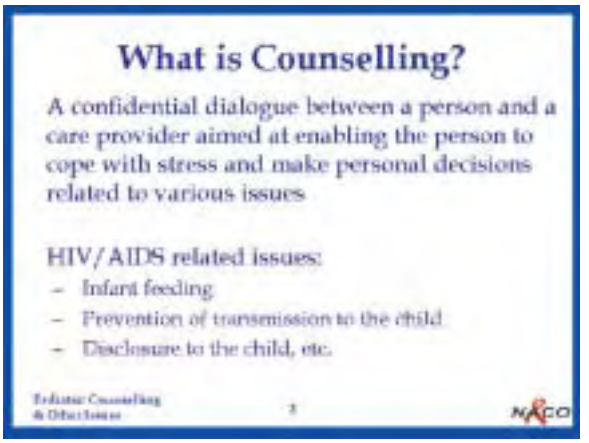
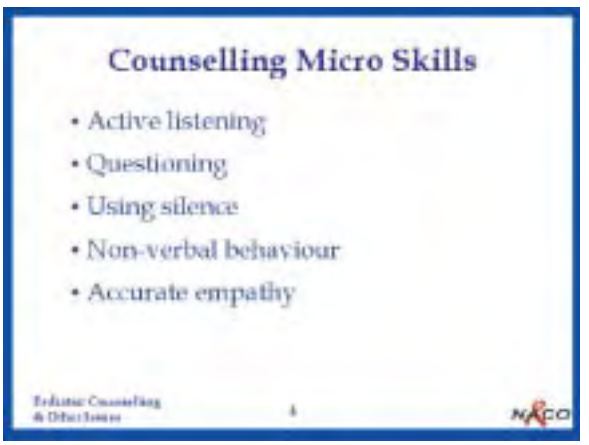
30

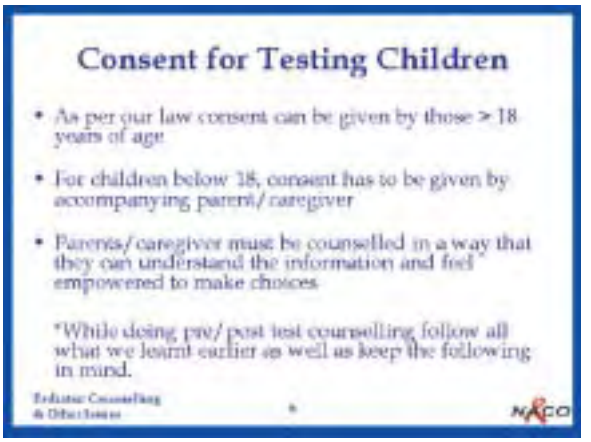
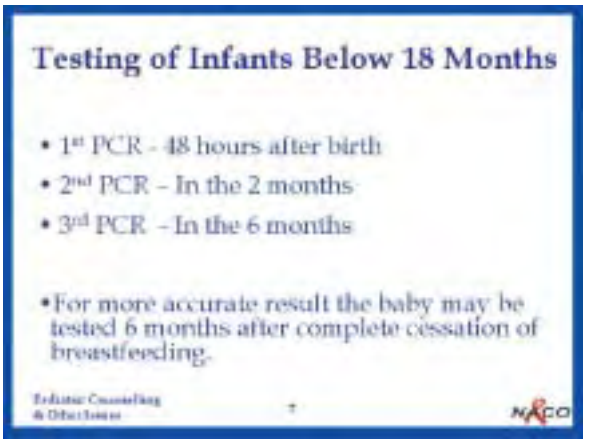
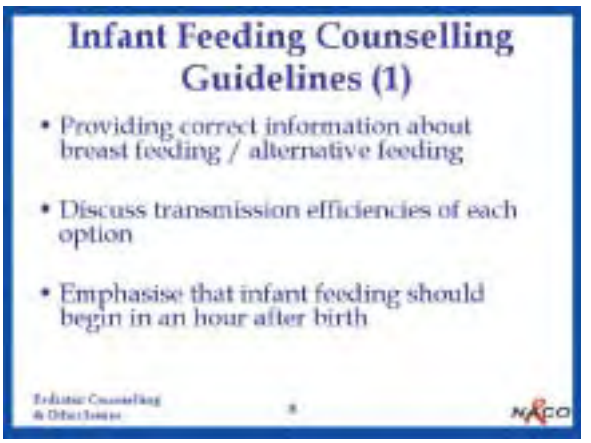
Total Session Time: 45 minutes

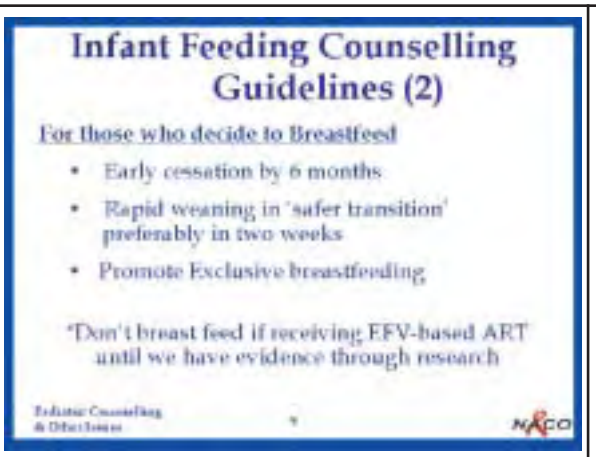
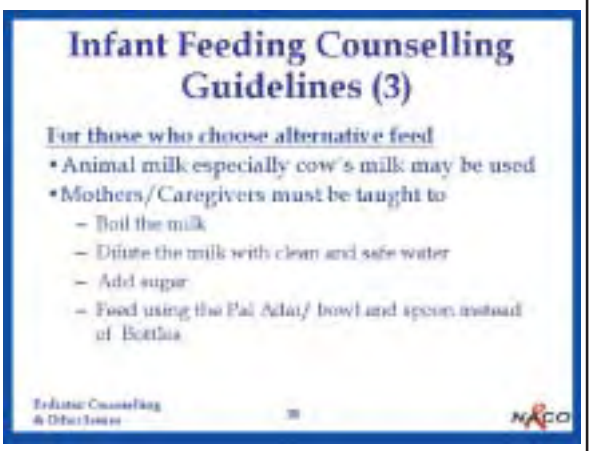
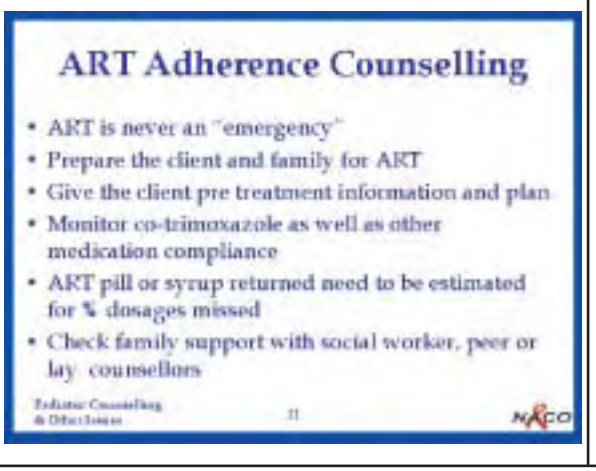
Session Objectives: At the end of the session, the participant should be able to:

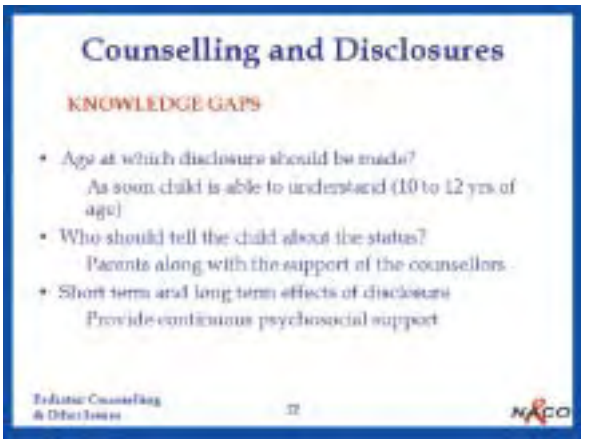
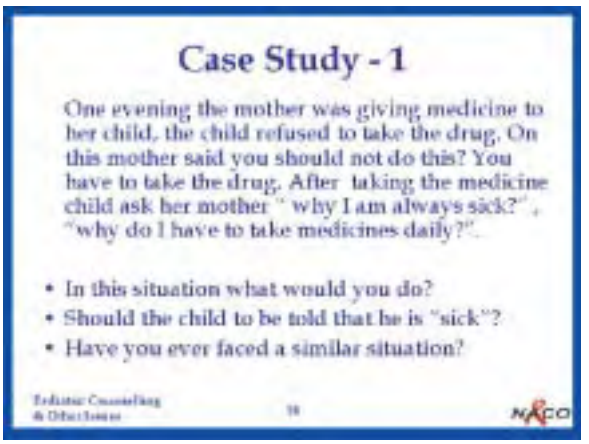
- To offer counselling to parents/caregivers of HIV-exposed/infected children
- To achieve general skills that promote effective counselling
- To handle issues in relation to consent & confidentiality
- To do pre & post- test counselling for children
- To discuss infant feeding choices with HIV-infected mothers
- To counsel in relation to ART Adherence
- To help appropriate disclosure process in children

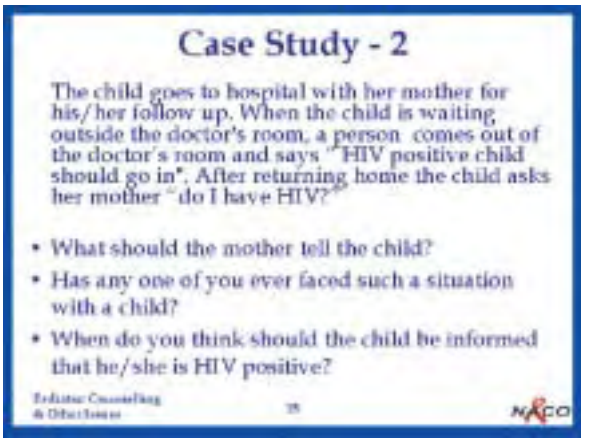
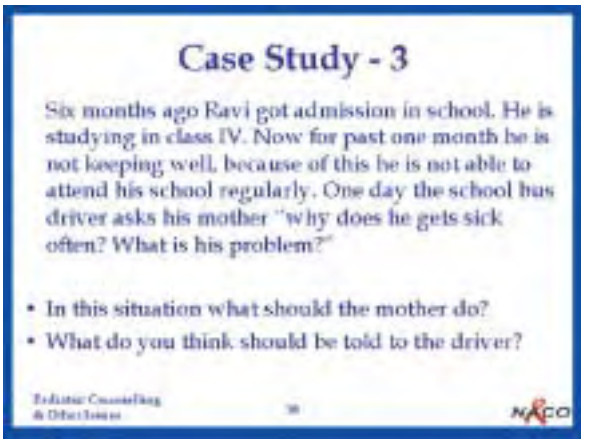
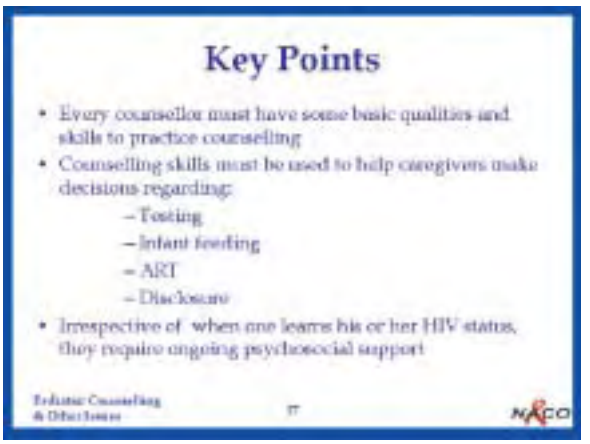
Slide 1		
Slide 2		**Reader's Notes:** • This session aims at helping paediatricians or other health care workers who may be required to take the place of a counsellor in settings where the counsellor is not available. • It is important to note that children cannot be treated as little adults and we must understand that they have issues of their own, children and their care givers must be guided in taking decisions which are informed and what is suited best for each case.

Slide 3		**Reader's Notes:** • The Counselling process is an empowering process whereby the client makes an informed decision which is best suited for him/ her. • Counselling also involves helping one cope with stress which may otherwise interfere with the client's life.
Slide 4		**Reader's Notes:** • These skills may be used in any profession; they help to build an excellent relationship with clients and are even taught in corporate and business houses as soft skills training.
Slide 5		**Reader's Notes:** • Couple or Family Counselling is very helpful in decisions that involve the spouse and sometimes other members of the family. For e.g.. Infant feeding decision - if other members of the family are also counselled, the mother or the couple will get more support from the family on whatever option they decide. • Basic essential qualities of a counsellor as discussed in the session psycho social aspects in counselling.

Slide 6		**Reader's Notes:** • Parents/ care takers may be given all the information they need to help them make the decision regarding testing. • This is a grey area as youth in today's world might not be able to get themselves tested or seek help for risky behavior even if they want to. Especially in cases, where there is sexual abuse of children, the child may learn about counselling and testing services from schools or the mass media, but cannot get tested because of this law. • All the principles of pre test counselling which was discussed before must be practiced, in addition care must be taken as the consent we are discussing now is the testing of the ward who may be children/ infants of the client. Pre-test counselling must be done very sensitively.
Slide 7		**Reader's Notes:** • The Care provider must find out where the PCR tests are done and must send the samples for the same
Slide 8		**Reader's Notes:** • The Care provider must not be biased towards any particular option, he/ she must allow the client/ mother to make a decision as to what option to choose as she is the best judge of her circumstances

Slide 9		**Reader's Notes:** • In case the mother/ family chooses to breastfeed all the necessary support must be given to the mother and the family by the health care team
Slide 10		**Reader's Notes:** • Counsellor must not forget to give complete information regarding alternate feeds, including using traditional methods of feeding babies instead of bottles which will be more difficult to sterilise.
Slide 11		**Reader's Notes:** • Every client on ART needs a lot of support and information. This can be possible only with a devoted health care team

Slide 12		**Reader's Notes:** • There is no right or wrong formula to do this, every child has a right to know his/ her HIV status. Parents are the best to break the news, counsellors could support parents and help them teach ways in which the news may be given to the child. It is important to understand that psychosocial support needs to given even much after the news is disclosed. Psychosocial support must be given in an ongoing basis.
Slide 13		
Slide 14		

Slide 15		
Slide 16		
Slide 17		

SESSION 31-33

DAY - ELEVEN

SESSION

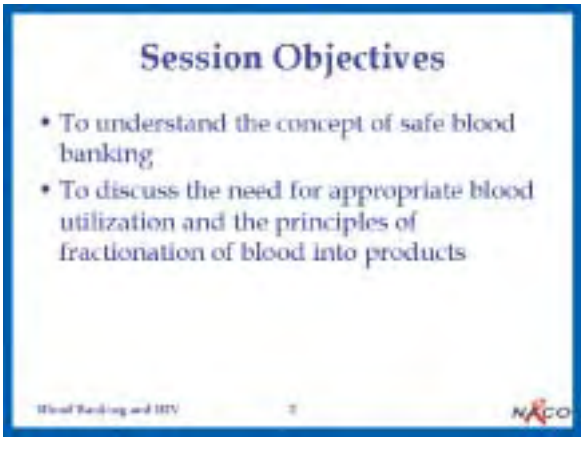
BLOOD BANKING

31

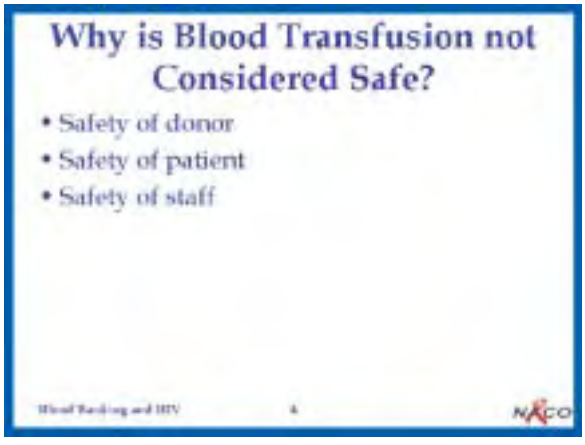
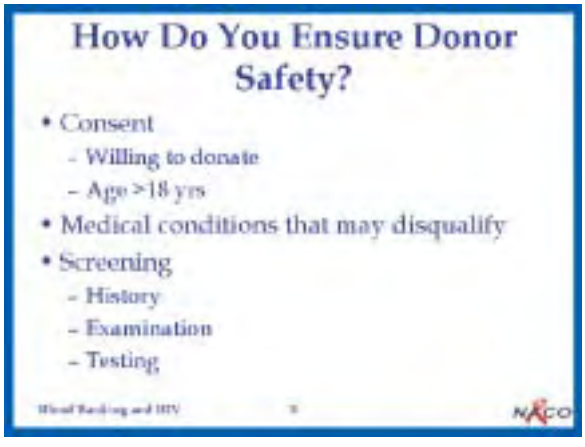
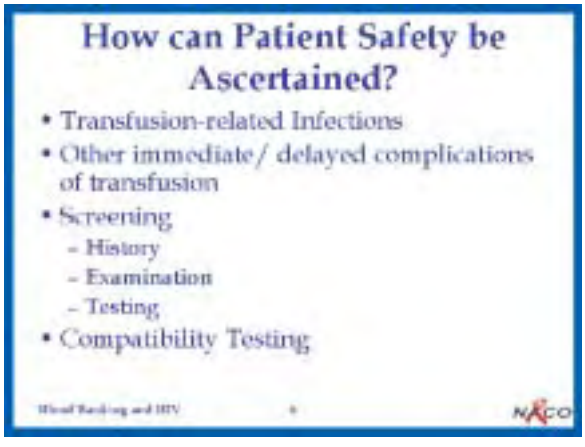
Total Session Time: 45 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Understand the concept of safe blood banking
- Discuss the need for appropriate blood utilization and the principles of fractionalization of blood into products

Slide 1		
Slide 2		

Slide 3		

Slide 4 Animation Clicks:3		
Slide 5 Animation Clicks:3		
Slide 6 Animation Clicks:4		

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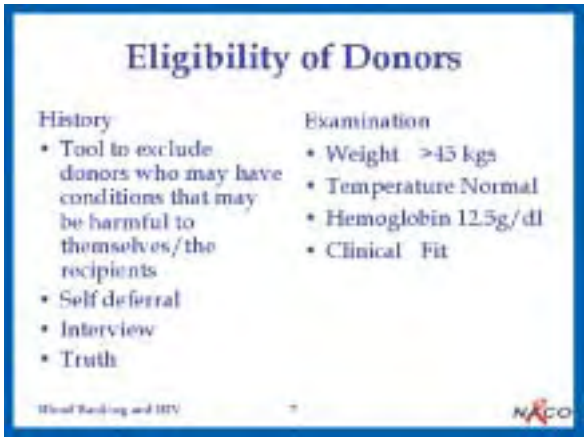
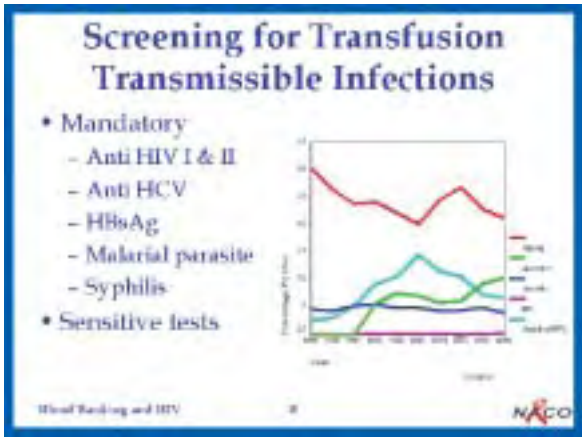


Reader's Notes:

- How can history help?
- It helps to screen donors and identify persons with conditions or behaviors that may be associated with risk to either the donor or the recipient.
- The ideal situation would be that the donor by himself defers from donating in view of the risk involved to him or the recipient.
- This rarely happens, unless the person is a voluntary donor.
- The next option is a donor interview; a check list based approach may help identifying risk factors that may help exclude donors with high risk.
- Finally, there is the concept of truth: this may be utopian and impossible t:o achieve.
- Even after careful screening, it may be impossible to ensure complete safety of the blood.

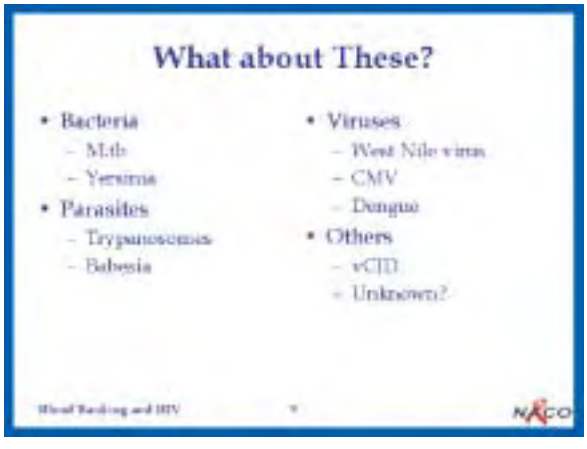
Slide 8



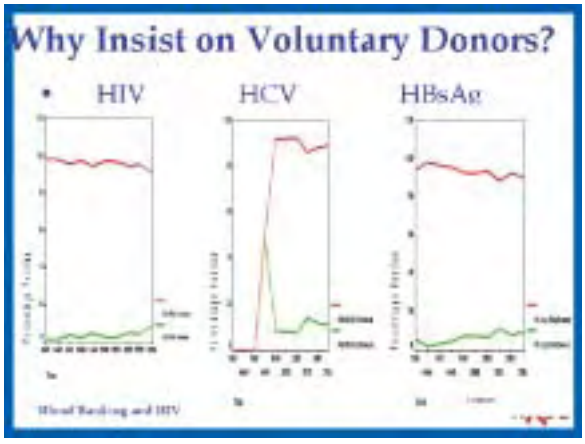
Reader 's Notes:

- Blood tests are necessarily done to rule out malaria, syphilis, hepatitis B, hepatitis C and HIV.
- Screening tests should be done using using kits with high sensitivity to detect maximum number of positives.

Slide 9



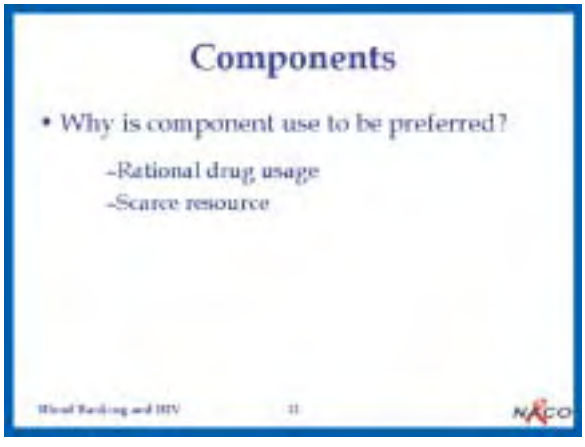
Slide 10



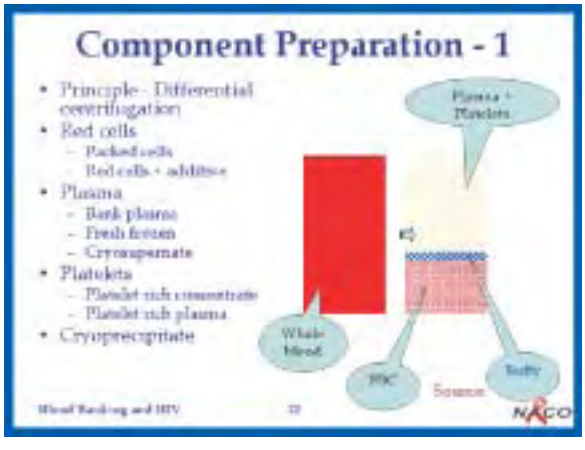
Reader's Notes:

- Data from large centers show that volunteer donors have consistently lower chances of HIV, hepatitis B and hepatitis C infection (the red line is replacement donors and the green is of voluntary donors).
- It is to be assumed that if these infections are lower in volunteer donors, it is possible that all other potentially transmissible infections are also significantly lesser.

Slide 11

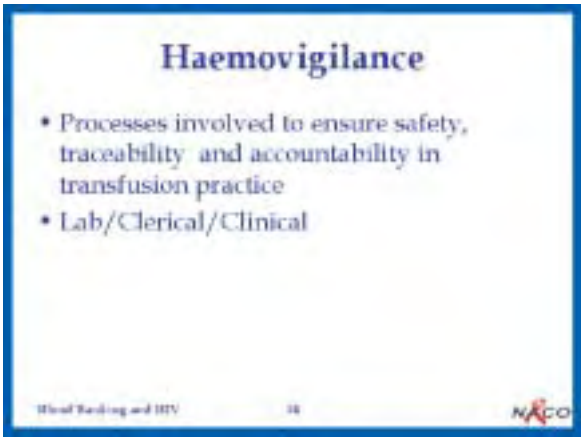


Slide 12

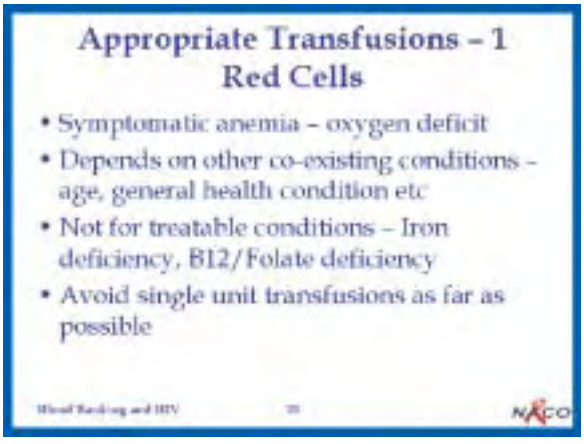


Reader's Notes:

- The principle of component preparation is that differential centrifugation will result in separation of the different components of blood.
- By this principle, blood can be separated into red cells, white cells (buffy coat) and plasma with platelets.
- The red cells are stored with additives as packed cells.
- The plasma containing platelets is used primarily as a source of platelets, which can be subsequently separated out.
- The remaining plasma can be further fractionated into cryoprecipitate, cryosupernate , fresh frozen plasma and bank plasma.
- As practicing physicians, we usually restrict our use to whole blood, packed cells, plasma and platelets.
- The other fractions are more commonly used by hematologists and in specialized set ups.

Slide 13		**Reader's Notes:** • The Government has mandated that every part of blood banking should have quality assurance. This includes the processes, the procedures and the products.
Slide 14		**Reader's Notes:** • The currently accepted term to ensure blood safety is haemovigilance. • It is a set of processes to ensure safety, traceability and accountability in transfusion practice. • This involves ensuring proper lab procedures, accurate record keeping, and following clinical practices of the highest standards.

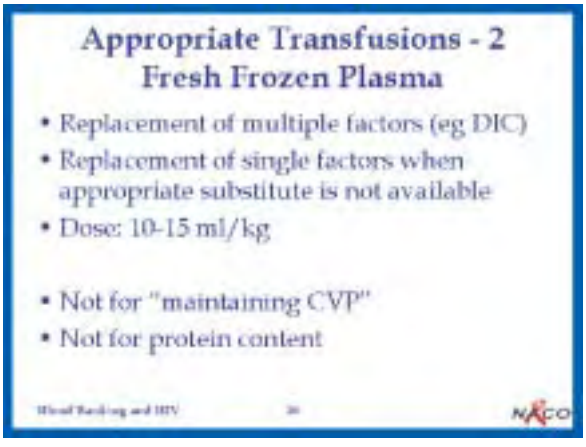
Slide 15



Reader's Notes:

- With the implementation of the Government regulations and the need for certification, there has been a drastic improvement in the safety of the blood available for transfusion.
  - Unfortunately, the clinical practices are still poor and this is a major reason for the shortage of blood availability.
- Packed red cells should always be preferred over whole blood, as this achieves the same effect, and the other components are available for use in another patient, making this the most ideal use of resources.
- The most common indication for transfusion of red cells is symptomatic anaemia, which results in oxygen deficit.
  - Its use is also dictated by the presence of other co-morbidities; the haemoglobin level at which it may be considered in a patient with heart failure is certainly higher than a normal host.
  - Red cells should never be abused- be unnecessarily used for correctable conditions like iron deficiency, vitamin (B12, folate) deficiency.
- Finally, single unit transfusions should be avoided. It is said that if only a single unit is required, it is probably true that even that unit was unnecessary. If transfusion is deemed necessary, then a minimum of two units should be considered.
- In spite of this, it is worth mentioning that 40% of all packed cells transfusions are single unit transfusions.

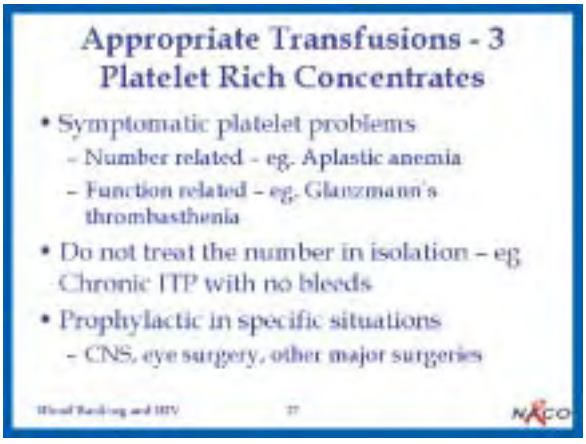
Slide 16



Reader's Notes:

- Fresh frozen plasma is another valuable resource that is misused.
- It is indicated for use in disseminated intravascular coagulation (DIC), where multiple factors are simultaneously deficient.
- It may also be used for single factor deficiency/ replacement, if the more acceptable substitute is unavailable.
- It should not be used frivolously for "maintaining central venous pressure" or fluid status.
- It is also not a protein substitute.
- It should be remembered that this is a dangerous product and possibly lethal.
- The reason for the high prevalence of HIV in haemophiliacs in the west is the use of poorly screened blood products and factors.

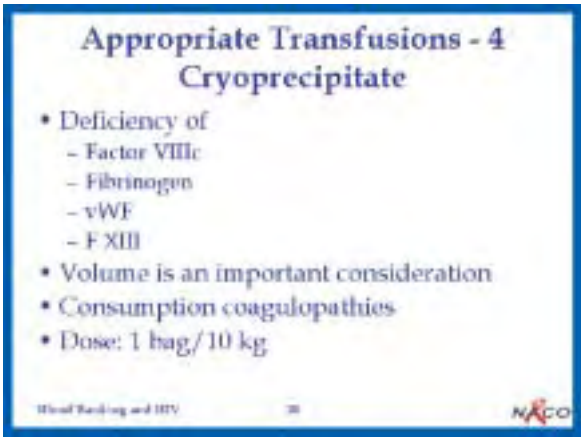
Slide 17



Reader's Notes:

- Platelets are used primarily in treatment of symptomatic platelet problem.
- As noted, the problem may be in the platelet number or function, but the treatment is only if the patient is symptomatic.
- Routine transfusion of platelets in chronic conditions that are presently asymptomatic is not only useless, but also harmful in the long run.
- Platelets are sometimes used prophylactically to reduce the risk of bleeding into closed spaces during surgery.

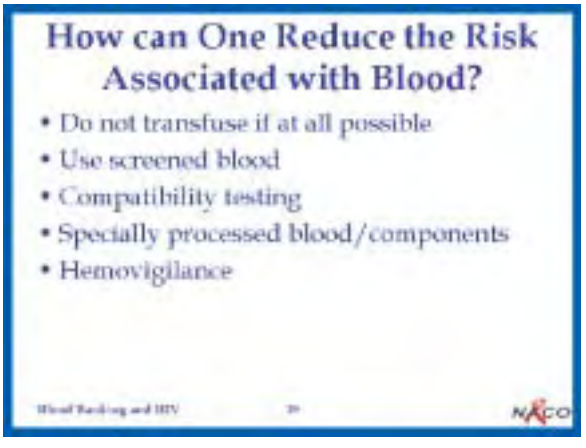
Slide 18



Reader's Notes:

- Cryoprecipitate is another precious resource that should be used judiciously.
- It contains some of the coagulation factors and is of use in DIC.

Slide 19



Reader's Notes:

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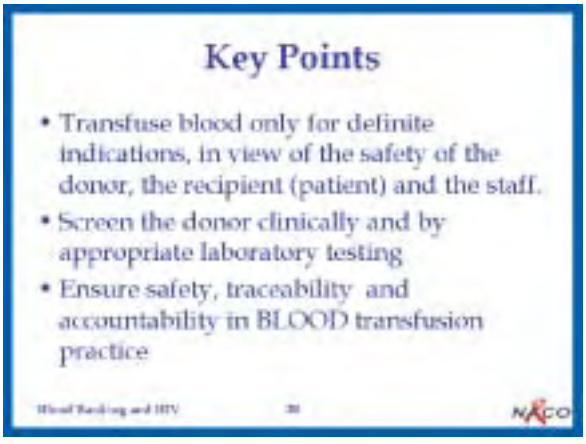
- It contains some of the coagulation factors and is of use in DIC.

Slide 20


Key Points
• Transfuse blood only for definite indications, in view of the safety of the donor, the recipient (patient) and the staff.
• Screen the donor clinically and by appropriate laboratory testing
• Ensure safety, traceability and accountability in BLOOD transfusion practice

SESSION 32

SESSION

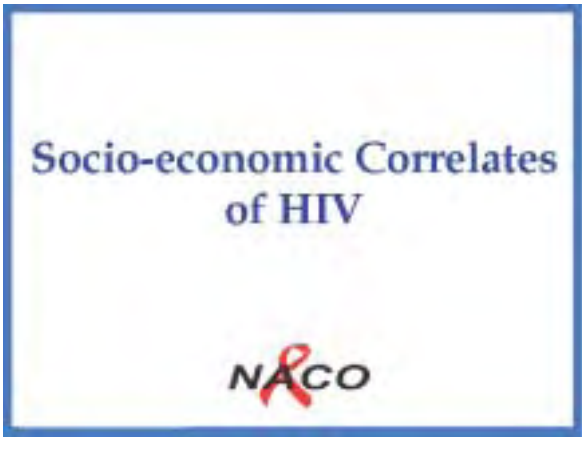
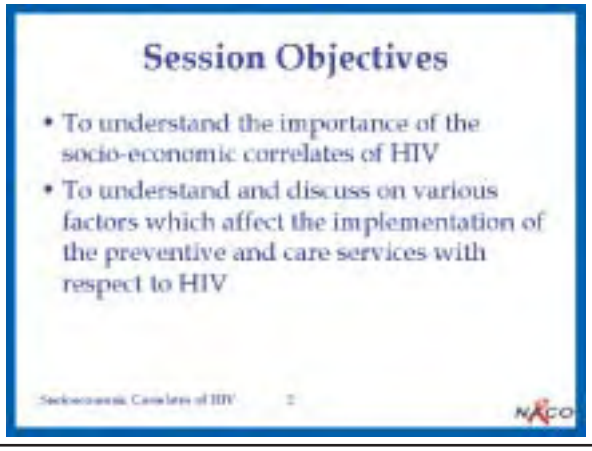
SOCIOECONOMIC CORRELATES OF HIV

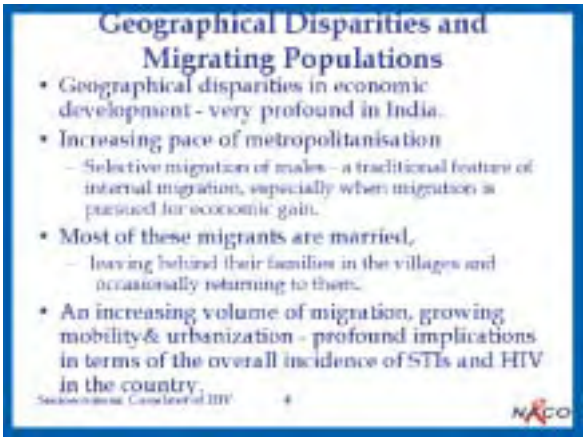
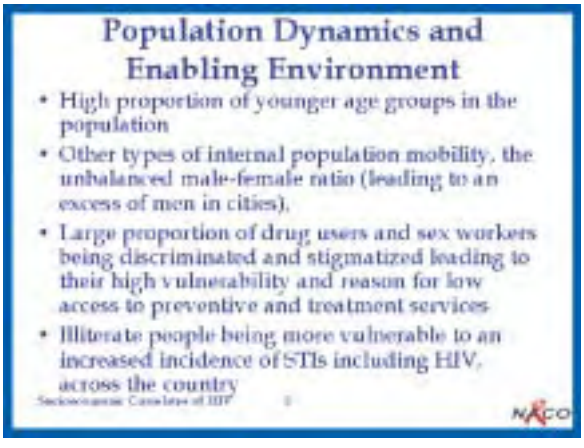
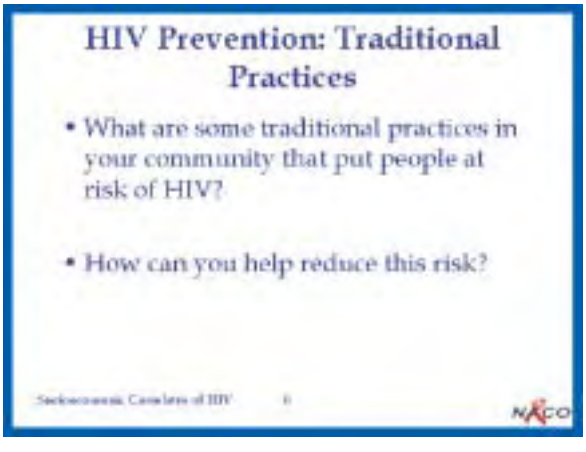
32

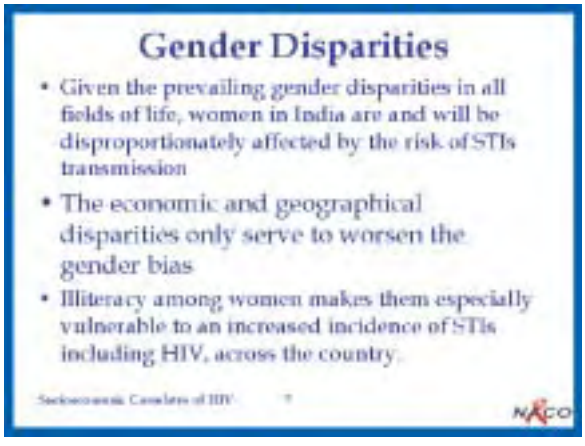
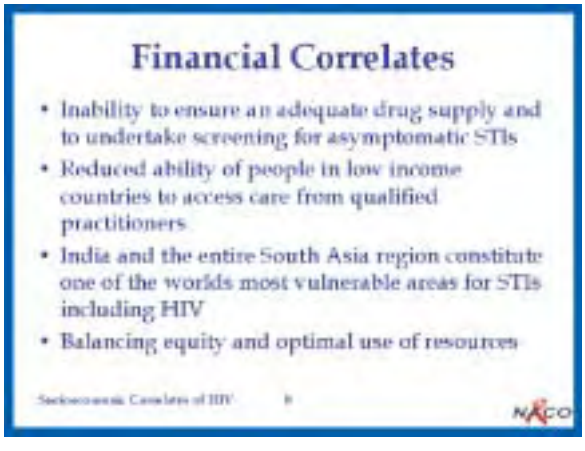
Total Session Time: 60 minutes

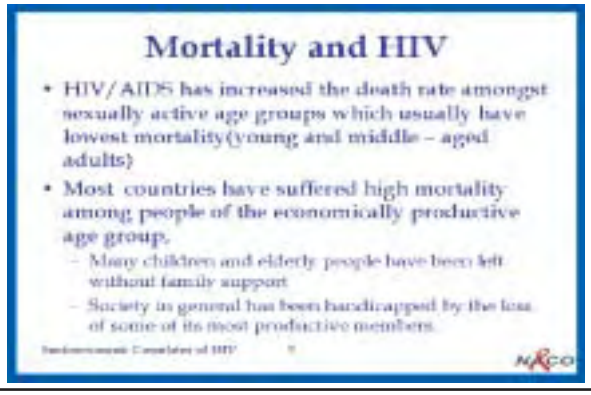
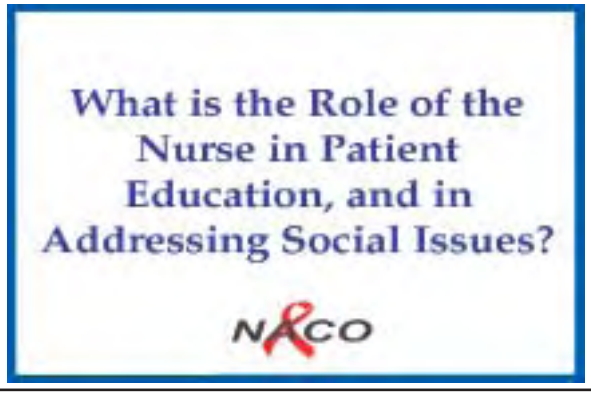
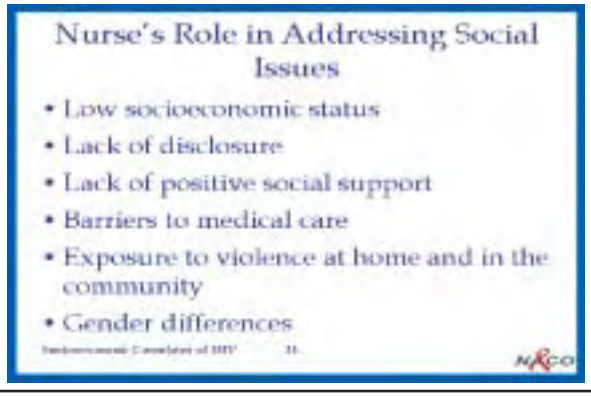
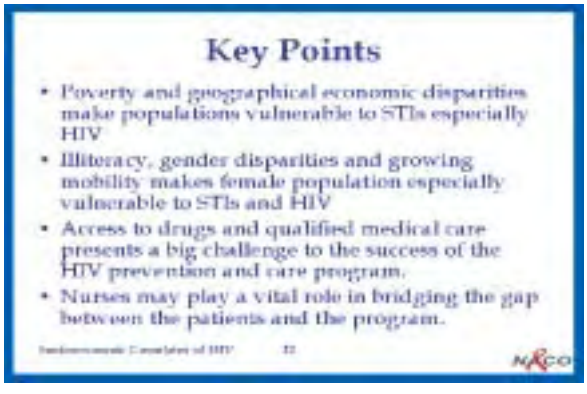
Session Objectives: At the end of the session, the participant should be able to:

- Understand the importance of socio-economic correlates of HIV
- Understand and discuss various factors which affect the implementation of HIV prevention and care services

Slide 1		
Slide 2		

Slide 3		**Reader's Notes:** • We all understand that India is still a low income country, as per the latest data. • The extent to which this improved economic performance has led to equity and social justice is disputable. • The GDP per capita is one of the highest rising in the world, but this improved economic performance has not lead to financial equity. It is of concern that more than a third of our population are still below the poverty line with meager incomes. • There is a popular misconception that HIV is prevalent only among the extremely downtrodden. • Poverty does lead to increased mobility, making them more vulnerable. • Classical examples of this are the hoards of young men arriving in big cities like Chennai,Mumbai each day in search of jobs.
Slide 4		**Reader's Notes:** • The other confounder is the differential economic development in certain parts of India. • This difference is most obvious is one were to compare Punjab or Gujarat with Bihar or Orissa. • This leads to migration to from the lesser developed areas to these areas for financial gain; sometimes the areas migrated have more than just financial opportunities • One could consider the example of married men from rural areas of Bihar coming to Mumbai to work in factories and workshops. They work for about 11 months and then return home for about a month. This large scale migration is one of the principal causes of vulnerability in the states of lower prevalence. This effect is already being seen and given the volume of such migration, it is a ticking time bomb.
Slide 5		**Reader's Notes:** • As has been noted, it is the younger age group that appears to be more affected by the problem, and this is also the economically productive group. • The trend towards going to large cities for work and the resulting formation of metropolis in many parts of the country worsens the problem. • This aggregation in large cities is selectively of males, causing an unbalanced sex ratio in these places. • Many of these people are illiterate and very vulnerable to HIV as they never get to know about the campaign on preventive measures. • Source: UNAIDS, http://www.unaids.org/en/Issues/Impact_HIV/default.asp

Slide 6		
Slide 7		**Reader's Notes:** • In our country, as we are aware, gender disparities are deeply entrenched. • Confirmation of this can be obtained by studying the sex ratio across the country. • Women are more likely to be illiterate and generally more vulnerable to STDs including HIV.
Slide 8		**Reader's Notes:** • Given the high cost involved with the disease it is very difficult to screen all the population for HIV, or for that matter, any STD. • Maintaining a good drug supply that is adequate for all people who need is a challenge by itself. • Even in the event of drugs being available, it is not always possible for the patients to find doctors qualified and experienced to the problem. • These factors make India and the entire region very vulnerable to all STDs including HIV. • Finally it should be understood that equity and optimal use of resources can never be achieved. • If the drugs were to be given only to those who cannot buy it, that would be optimal use, and would help greater numbers access care, but equitability requires all patients to be treated, irrespective of their financial background.

Slide 9		**Reader's Notes:** • Source: UNAIDS, http://www.unaids.org/en/Issues/Impact_HIV/default.asp
Slide 10		
Slide 11		
Slide 12		

SESSION 33

SESSION

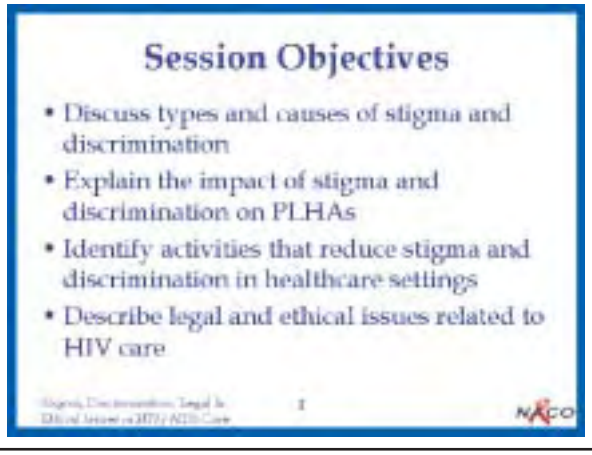
STIGMA, DISCRIMINATION, LEGAL AND ETHICAL ISSUES IN HIV/AIDS CARE

33

Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Discuss types and causes of stigma and discrimination
- Explain the impact of stigma and discrimination on PLHAs
- Identify activities that reduce stigma and discrimination in healthcare settings
- Describe legal and ethical issues related to HIV care

Slide 1		
Slide 2		

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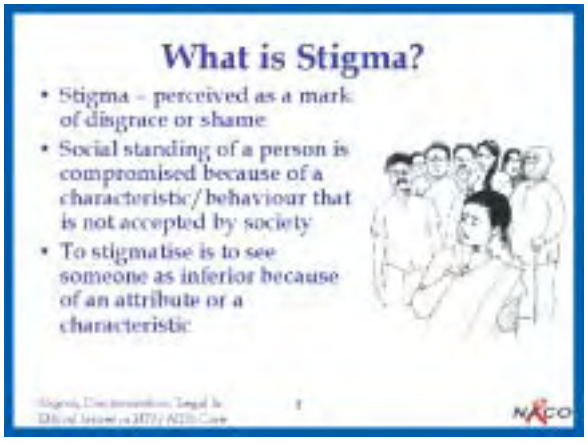
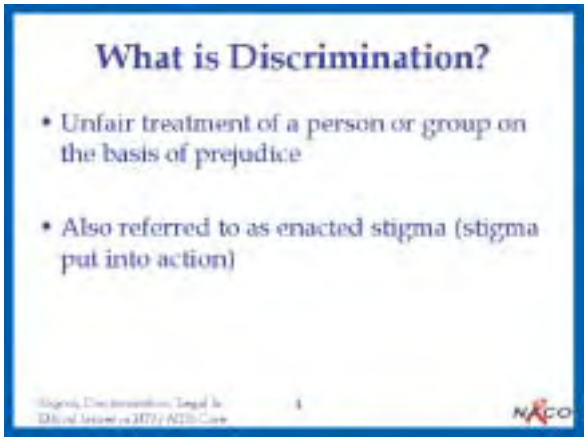


Reader's Notes:

- Stigma is defined as:
- Act of identifying, labelling or attributing undesirable qualities targeted towards those who are perceived as being "shamefully different" and deviant from the social ideal
- An attribute that is significantly discrediting used to set the affected persons or groups apart from the normalized social order (separation implying devaluation)
- HIV/AIDS stigma is often layered upon preexisting stigma concerning socially marginalized and vulnerable groups: IDU, MSM and CSW, women and children; conversely, people living with HIV/ AIDS may become implicitly associated with stigmatized behaviours, regardless of how they actually became infected
- Reference: STIGMA— DEFINITION AND CONTEXT: Dr David Miller UNAIDS, India Stigma and HIV/AIDS in Africa:Setting the operational research agenda,4 — 6 June 2001,Dar-es-Salaam, Tanzania. http://www.hdnet.org/Stigma/ Stigma_consultation_Index.htm

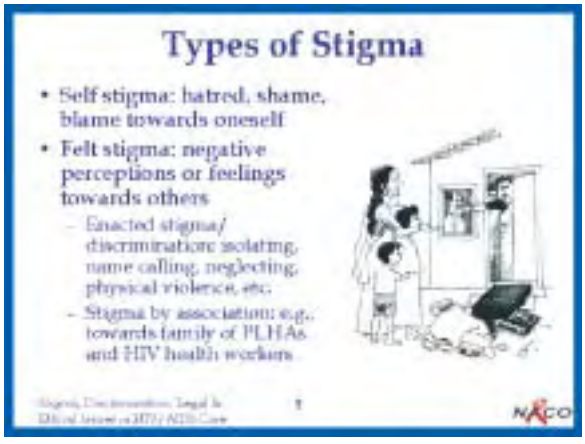
Slide 4



Reader's Notes:

- Discrimination is defined as:
  - Any distinction, exclusion, restriction or preference which is based on exclusionary perceptions or structures (e.g., re: race, beliefs, sexuality, gender) and which has the purpose or effect of nullifying or impairing the recognition, enjoyment or exercise by all person, on an equal footing, of all rights and freedoms
  - Actions or treatment based on the stigma and directed toward the stigmatized
  - Sanctions, harassment, scapegoating and violence based on infection or association with HIV/AIDS
- Reference STIGMA— DEFINITION AND CONTEXT: Dr David Miller UNAIDS, India Stigma and HIV/AIDS in Africa:Setting the operational research agenda,4 — 6 June 2001,Dar-es-Salaam, Tanzania http://www.hdnet.org/Stigma/ Stigma_consultation_Index.htm

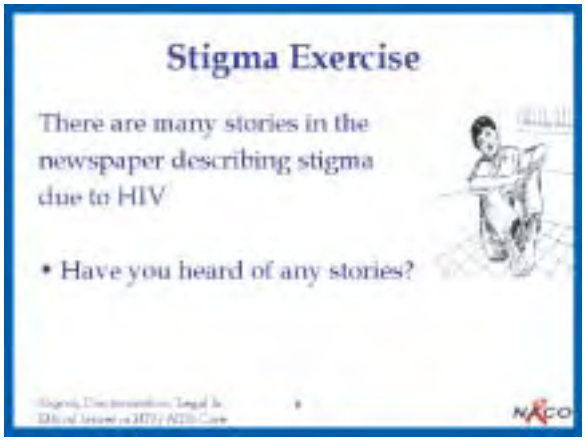
Slide 5



Reader's Notes:

- **Self or internal** stigma can be as damaging as felt **or external** stigma as it can cause PLHAs to feel bad about themselves or feel depressed when they feel they are being judged by others — whether this is really the case or not. Sometimes this leads PLHAs to isolate themselves and not access available care and support.
- **Felt or external** stigma can be because of:
- **Pre-existing stigma:** about class, gender, sexual orientation, poverty etc. Often many PLHAs come from underprivileged backgrounds (socially or economically) and may have occupations that reflect their situation (manual labourers, CSWs, migrant workers, etc.).
- **HIV-related stigma:** HIV is life threatening and incurable, visible symptoms of HIV such as skin diseases due to OIs have an exaggerated sense of danger, etc.
- **Enacted stigma** is also called **discrimination.** It is when negative feelings and thoughts are put into action and reflected in harmful behaviour towards PLHAs. It can take many forms such as those mentioned in the slide.
- **Stigma by association** –the whole family of a person with HIV is affected by stigma. HIV health workers may also be affected by association with PLHAs. Ask participants how they, as HIV health care workers, may be stigmatized.

Slide 6



Handout 1: News Article: Stigmatised Indian Woman with HIV Aborts own Baby

Stigmatised Indian Woman with HIV Aborts own Baby
Mon 4 Sep 2006; By Bappa Majumdar

KOLKATA (Reuters) - A pregnant HIV-positive woman was forced to abort her own foetus after staff in a hospital in eastern India refused to help her, officials said on Monday.

In a separate incident in the region, an infected man was stoned by people who feared he might spread the virus. He later died of his injuries.

Investigations in both cases are under way but authorities and activists said such incidents underlined how much stigma and even paranoia was attached to the disease in India. An estimated 5.7 million Indians live with HIV, more people than in any other country, according to the United Nations.

The 23-year-old woman, who recently tested HIV positive, was shunned last month by doctors and nurses in a state-run Kolkata hospital who told her they would not help her undergo an abortion.

"The hospital had no sympathy for me as I had to pull out the foetus with my hands and clean myself as health workers guided me from a distance," Roshni Mulani, a mother of a two-year-old child, told Reuters.

"They read about my HIV status from medical reports ... and threw medicines from a distance," said Mulani, who is recuperating at the house of anti-AIDS activist Ramen Pandey. "Many health workers in India still think AIDS can spread by just touching," Pandey said.

In the neighbouring state of Orissa, a 35-year-old man with full-blown AIDS died after he was pelted with stones inside a hospital compound. "He was strolling in the vicinity when some people threw stones at him last week," Alexander Pahi, a senior police official said over the phone from the coastal town of Puri.

Loknath Mishra tested positive two years ago and was ostracised by his neighbours who feared that he may spread the virus in Puri, a holy town for Hindus. The victim's brother told police that some people had threatened Mishra after they found out he had AIDS, Pahi said.

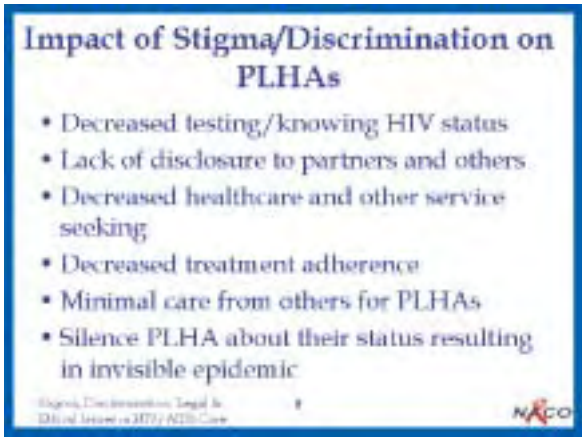
Many Indians feel that eating or touching a person with HIV could result in the virus spreading to them. In July 2003, an Indian woman was reported to have been stoned to death by panicky relatives and neighbours in the southern state of Andhra Pradesh.

Slide 7

Reader's Notes:

- People's lack of knowledge of HIV (routes of transmission, care and treatment available) is the biggest barrier for equitable treatment of PLHAs.
- No other disease currently has the degree of intensity of stigma associated with HIV disease. Stories of stigma and discrimination of PLHAs in our society are often reported by media.
- Linking the infection with moral behavior has resulted in magnification of the problem. Very often we assume that people with HIV must be injecting drug users or have multiple sex partners. We judge this behaviour as immoral and wrong.
- Fear about death and disease, or contracting HIV from an infected person, are also major causes of stigma.
- Stigma/discrimination, in many situations, is an extension of pre-existing discrimination against certain populations like sex workers, IV drug users, and transgenders. Very often, there may be social or religious disapprovals of certain behaviors or lifestyles.
- If we do not recognise that we are stigmatising or discriminating other people, we cannot correct ourselves. As Medical Officers, it is important that we recognise our own fears, thoughts and attitudes about PLHAs. If we do not address our personal reactions and emotions, we may unintentionally treat HIV patients differently than we treat other patients. Studies from health care settings in many countries have shown that myths and misconceptions are widespread even among health care professionals.

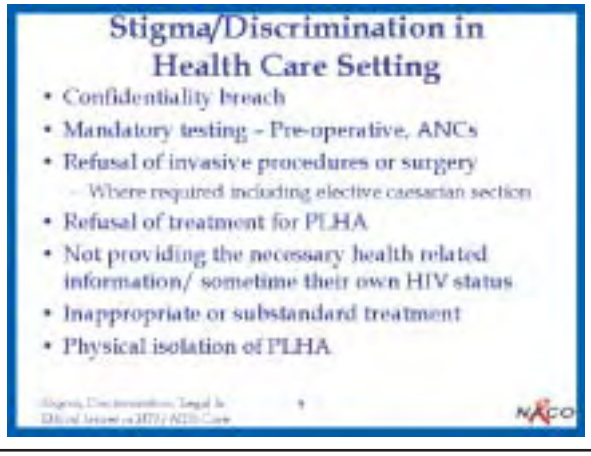
Slide 8



Reader's Notes:

- The incidence of depression is very high in PLHAs. Moreover, they become more vulnerable to infections, as they do not receive appropriate health promoting messages, they do not receive appropriate OI prophylaxis and when they fall ill, the time to treatment and recovery is substantially longer. Stigma also drives the epidemic underground, and its true magnitude is never obvious.
- Outcomes of Stigma:
  - *secrecy* about HIV/AIDS status,
  - *denial* of HIV status, individually, socially, nationally
  - *avoiding diagnosis and/or delaying* treatment support seeking,
  - *fear*, anxiety, depression, anger up to suicidal attempts and revengeful behaviour,
  - *resentment* towards HIV positive family, household or community members, and towards those free of infection
  - *disruption* of social integration processes for PLHA,
  - *marginalization* of certain groups,
  - social *invisibility* of the epidemic,
  - *resurfacing* of old prejudices or conflicts,
  - government *apathy*,
  - *polarisation and maintenance* of group concerns and interests,
  - negative effect on *economy*
  - Reference: STIGMA— DEFINITION AND CONTEXT: Dr David Miller UNAIDS, India Stigma and HIV/AIDS in Africa:Setting the operational research agenda,4 — 6 June 2001,Dar-es-Salaam, Tanzania http://www.hdnet.org/Stigma/Stigma_consultation_Index.htm

Slide 9



Reader's Notes:

- Many PLHA talk of a breach of confidentiality at while accessing health care.
- In many institutions, testing is mandatory prior to surgery and other invasive procedures. Sometimes, patients found to be reactive with one rapid test for HIV are labeled as HIV-positive and refused care.
- At times, patients are not informed of the reason for rejection from health care and even if they are informed, appropriate health information is not given.
- Counseling (both pre- and post- test) also is not provided to those patients.

Slide 10		**Reader's Notes:** • NGOs often provide proper burial services for unclaimed HIV-infected bodies.
Slide 11		

Handout 2: Steps to Reduce Stigma

All health care providers need to be trained, not only in management of PLHA, but also in sex and sexuality, and values and ethics. All hospitals and colleges should have strict written and enforced policies on confidentiality. Support units need to be created in all hospital where grievances can be addressed. Role models amongst the medical fraternity in involvement in care of PLHA will have a positive impact.

List of ways that Medical Officer's can help reduce stigma in their ART Centres

- Identify and recognise stigma
- Accept that you are responsible for challenging stigma and discrimination
- Be well informed about HIV/AIDS
- Be a role model with your own language and behaviour toward patients
- Build other's knowledge about HIV, sexuality and values/attitudes
- Encourage PLHAs and their families to use the available services
- Be a positive testimonial/ role model of a doctor who is treating PLHA

  " I treat people living with HIV, so can you…."
- Develop policies within the hospitals and medical colleges on confidentiality
- Set-up systems in ART Centres where PLHA can go when discriminated
- Encourage PLH to be positive speakers, to give visibility to the epidemic, and remove misconceptions about HIV.
- Involve PLH in training of health providers, to help them personalize the epidemic
- Create an opportunity for PLHA networks to conduct peer counseling and support PLHA and their caretakers

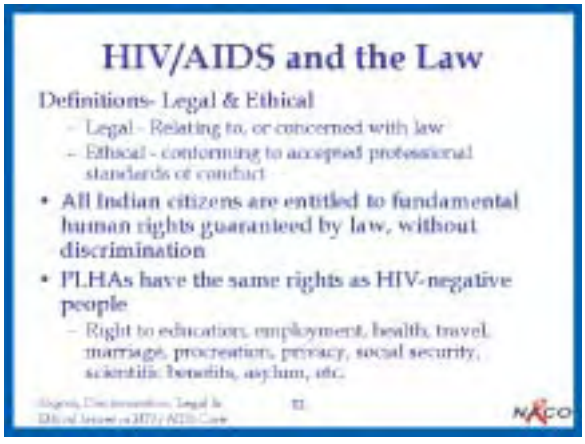
Positive people's network and support organisations:

The positive peoples' network needs to be strengthened and they should be integrated into all training programs, thereby attaching a human face to the epidemic.

The policy of GIPA (Greater Involvement of People Living with HIV/AIDS) should be followed in all the health care sittings.

PLHA should be involved as peer counselors and support network for other PLHA and their families.

Making this an official policy would be tremendously effective.

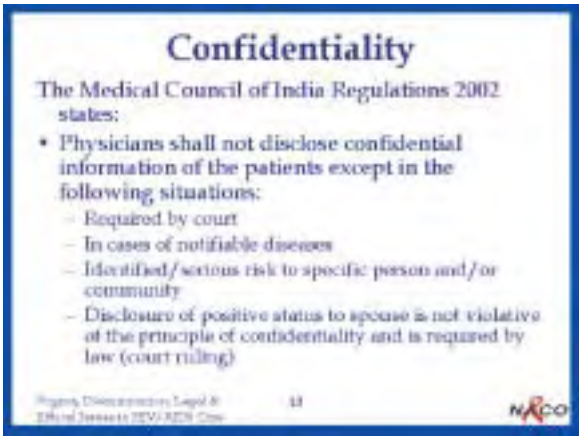
Slide 12		

Handout 3: HIV/AIDS and the Law

Some existing laws related to HIV/AIDS:

- Indian Penal code 270: Malignant act likely to spread infection of disease dangerous to Life
- Drug and Cosmetic Rule: Screening donated blood and organs for HIV
- Artificial Insemination Act: Appropriate HIV testing be done before insemination
- Bio-medical waste management regulations
- Requirements of notification to public health officials of infectious diseases

Slide 13



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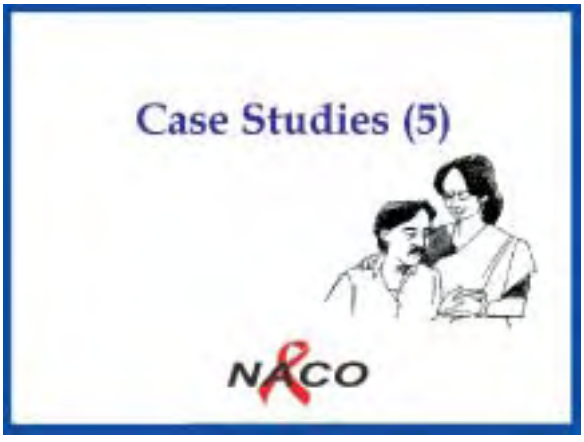


Reader's Notes

- Legal and Ethical Issues in HIV Care are concerned with:
    - HIV Screening
    - HIV Testing
    - Counselling
    - Confidentiality
    - Partner Notification
    - HIV and Pregnancy
    - Access to Healthcare and Treatment

Handout 4: Case studies

Case Study 1

Meena, who is 6 weeks pregnant, has come to the hospital for the first time. The doctor examines her and orders some tests. One of the tests is an HIV test

Questions

1. Can the doctor order for HIV test without Meena's knowledge?
2. What is essential before HIV test is done?
3. What is important when giving the test results to Meena?

Case Study 2

Ramu, suffering from TB, was admitted to the ward. Informed consent was taken and his blood was tested for HIV. Once the HIV test result came to the ward, the head nurse informed all ward staff including sanitary workers that Ramu was HIV-positive, and told them to be careful. Ramu's case sheet was marked with a red stamp saying "HIV- positive"

Questions

1. What steps were followed correctly? Give reasons for your answers
2. Which important person has not been told about the HIV test result?
3. What steps should not have occurred? Give reasons for your answers

Case Study 3

Ramu recently took an HIV test and the result was found to be positive. He was counselled to inform his wife, but he refuses to do so.

Questions

1. What must be done first?
2. Can the HIV status be disclosed to the wife by a doctor?
3. What other measures must the doctor take?

Case Study 4

Geetha and Sathish, a married couple, come and tell you that they wish to have a child. They are both HIV-positive.

Questions

1. What is the appropriate reaction of the Medical Officer in this situation?
2. What information would you give them?

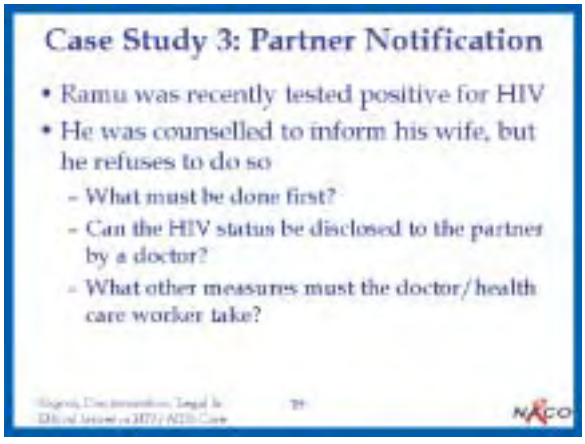
Case Study 5

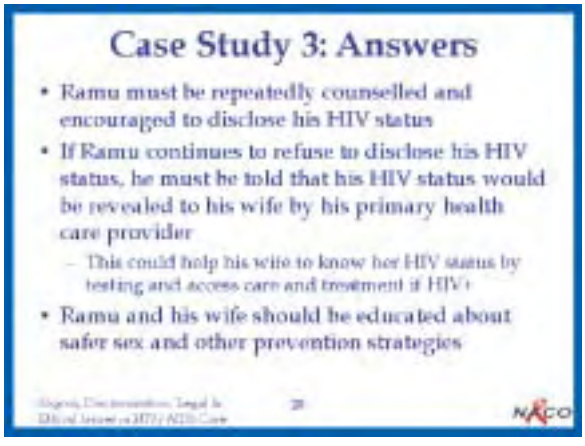
Shanthi came to the hospital with labour pains. The doctor noticed that she had severe vaginal candidiasis and ordered a rapid HIV test. The result was positive, and she was sent away with the pretense that no bed was available

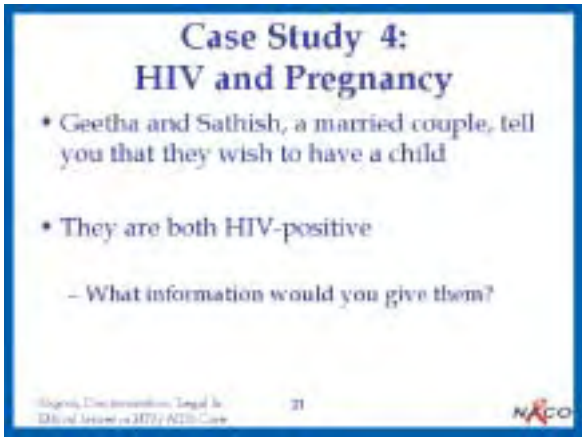
Questions

1. What are the ethical issues in this scenario?
2. What opportunity is lost here?

Slide 15	**Case Study 1: HIV Screening & Testing** • Meena, 6 weeks pregnant, has come to the hospital for the first time • The doctor examines her and orders some tests. One of the tests is for HIV status – Can the doctor order an HIV test without Meena's knowledge? – What is essential before an HIV test is done? – What is important when giving the test results to Meena?	
Slide 16	**Case study 1: Answers** • HIV test should NOT be conducted without patient's knowledge • Informed consent and pre-test counselling are a MUST before testing • Post-test counselling is essential when revealing HIV test result • Anonymous screening without consent can only be done for – Blood and organ donation – Epidemiological surveys	
Slide 17	**Case Study 2: Confidentiality** • Ramu, suffering from TB is admitted to the ward – Informed consent taken; his blood was tested for HIV – On receiving the HIV test result, the head nurse informed all ward staff including sanitary workers that Ramu was HIV-positive, and told them to be careful – Ramu's case sheet cover was marked with a red stamp saying "HIV positive" • What steps were followed correctly? • Which important person has not been informed about the HIV test result? • What steps should not have occurred?	
Slide 18	**Case Study 2: Answers** • People who give informed consent and get tested have the right to receive their results • Disclosure to health authority/referred doctor is permitted – Disclosure to health care providers not in direct care of patient is unnecessary – Identification of HIV status must be prevented on cover of the persons medical record **People have a right to confidentiality**	

Slide 19		

Slide 20		**Reader's Notes:**
		• It must be stressed that the patient's confidentiality and rights are of utmost importance and only, if after repeated counselling, he/she still does not agree to inform the sexual partner, the primary health care provider should take on the responsibility.
		• HIV test results:
		  • Inform the concerned person whom you as a healthcare provider may want to reveal their HIV status to and what the benefits of doing so will be, even if disclosure is to other health professionals.
		  • Disclosure of the HIV status to the spouse or sexual partner of the person should invariably be done by the primary health care provider such as the attending physician with proper counselling.
		  • The PLHA should also be encouraged to share this information with the family for getting proper home-based care and emotional support from the family members.

Slide 21		

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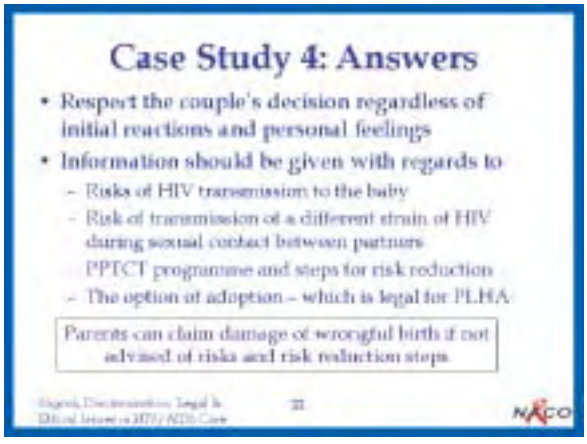
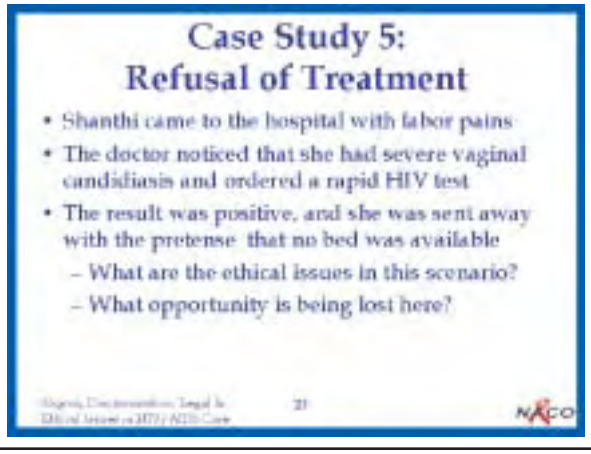


Reader's Notes:

- HIV-positive women (and couples) should have complete choice in making decisions regarding pregnancy and childbirth same as sero-negative women: keeping, abortion or adoption- in standing with the law.
- Educate on the following aspects:
  - Risks of HIV transmission to the baby
  - Preventive services available to reduce risk of transmission under the PPTCT programme (more about this will be discussed in upcoming units)
- Adoption is possible for HIV positive couples, however, they need to show availability of enough resources and support.
- Proper counselling should be given to the pregnant women and parents as they can claim damage of wrongful birth if not counselled.
- *Source: http://www.nacoonline.org/policy.htm*

Slide 23



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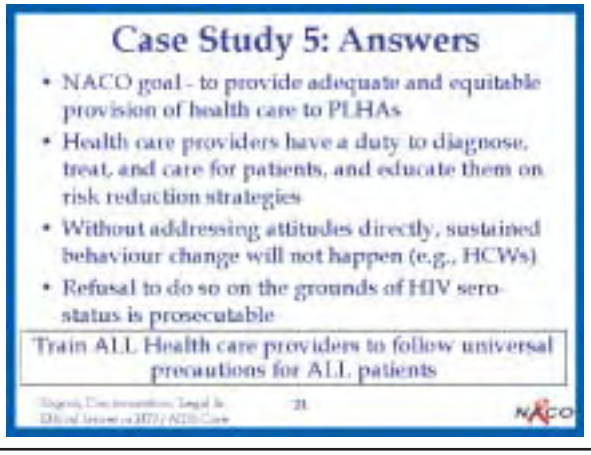

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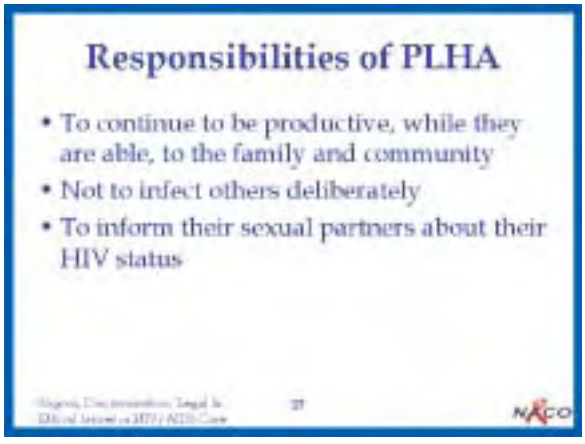
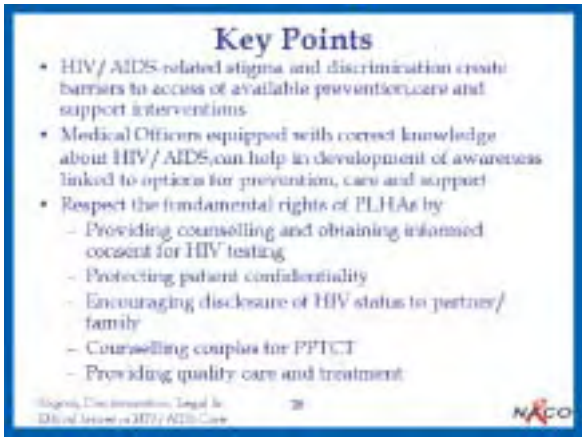


Reader's Notes:

- Being afflicted with HIV does not mean that people are helpless or need not take control over their lives and the way it impacts others. We need to think of HIV positive people as a part of the solution and not as a part of the problem.
- PLHAs along with their rights also have certain responsibilities that they need to fulfill.
- Indian Penal Code:270. Malignant act likely to spread infection of disease dangerous to life - whoever malignantly does any act which is, and which he knows or has reason to believe to be, likely to spread the infection of any disease dangerous to life, shall be punished with imprisonment of either description for a term which may extend to two years, or with fine, or with both. "

Slide 26



Reader's Notes:

References:

- *India: HIV and AIDS-related Discrimination, Stigmatization and Denial. Best Practice Collection*. UNAIDS, 2001.
- Bharat S. AIDS in the employment sector in India: A vicious cycle of silence and denial. XIII *International AIDS*
- *Conference, South Africa*, 2000, Ab TuPeD3490.
- Bharat S, Aggleton P. Facing the challenge: household responses to HIV/AIDS in Mumbai, India. AIDS Care 1999,
- 11:31-44.
- To read the Stigma-AIDS eForum archive :www.healthdev.org/eforums/stigma-aids
- For more details on India related stigma from the site: The correspondent dialogues: Issue 12 IV.
- http://data.unaids.org/Publications/IRC-pub01/jc316-uganda-india_en.pdf**:HIV and AIDS-related stigmatization, discrimination and denial:forms, contexts and determinants** Research studies from Uganda and India
- http://data.unaids.org/Publications/IRC-pub02/jc587-india_en.pdf: **India : HIV and AIDS-related Discrimination, Stigmatization and Denial**

Slide 27		


Remember...
All of you in this room can play a major role in making health care settings stigma- free for people living with HIV!

SESSION 34-36

DAY - TWELVE

SESSION 34

SESSION

CLINICAL PROBLEM SOLVING & PRESCRIPTION WRITING

34

Total Session Time: 60 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Describe the principles and practices of palliative care and its role in the continuum of care
- Understand the provision of effective symptom management of common clinical manifestations of HIV disease
- Determine how to manage psychological issues that HIV-positive patients present
- Discuss nutrition recommendations for the symptoms associated with each stage of HIV disease
- Provide information on the management of nutrition related symptoms of HIV
- Consider ARV interactions with food & nutrition

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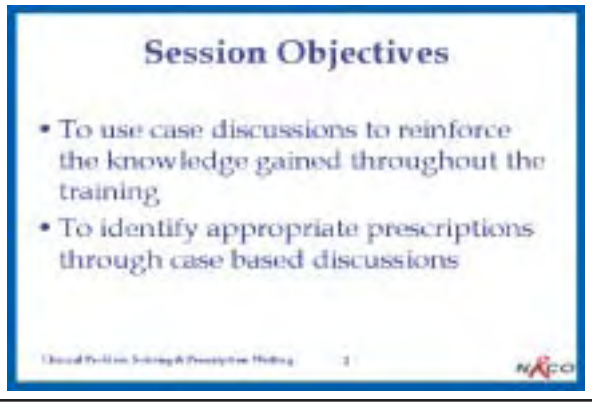
Slide 2		

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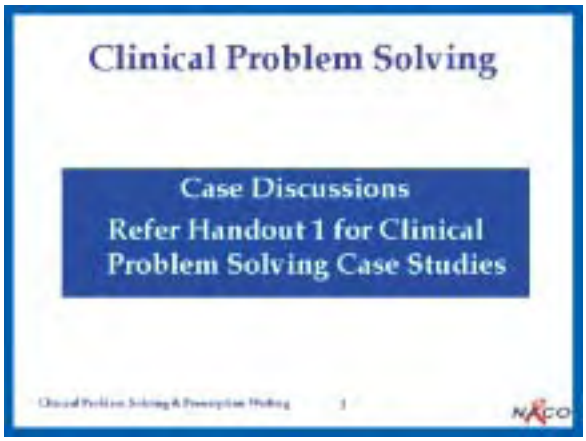


Handout 1 : Clinical Problem Solving - Case Studies

Instructions: Comment on the appropriateness of the given prescription and write down what the final revised prescription should be.

Case 1

25 year-old obese woman weighing 70 kg, known PLHA

- She is being started on ART as her CD4 count is 132 cells/cu.mm
- She is already on oral contraceptive pills and is given the following prescription:
  - Tab. Ovral 1 once daily for 21 days and restart after 7 days
  - Tab. Stavudine 30 mg twice daily
  - Tab. Lamivudine 100 mg twice daily
  - Tab. Nevirapine 200 mg twice daily

Case 2

35 year-old man, known to have fixed drug eruption in the past after taking an antimalarial

- Diagnosed HIV 2 infection after he presented with oral-oesophageal Candida
- His CD4 count is 140 cells/cu.mm and he is given the following prescription:
  - Tab. Cotrimoxazole double strength 1 daily
  - Tab. Zidovudine 100 mg five times daily
  - Tab. Lamivudine 150 mg twice daily
  - Tab. Efavirenz 600 mg twice daily

Case 3

47 year-old housewife, PLHA, diagnosed with Cryptococcal meningitis 2 weeks ago - on treatment

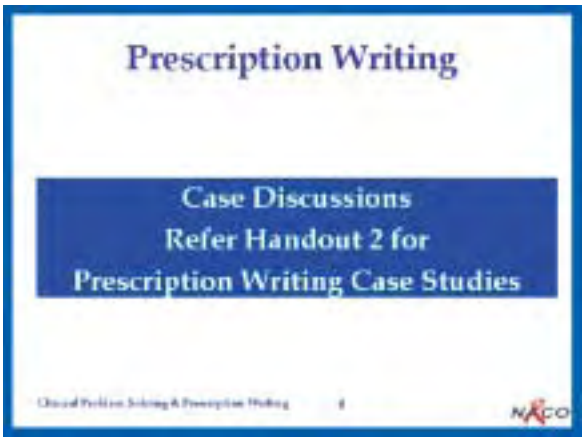
- Started on ART
- She now develops a Upper Respiratory Infection (URI) and is given the following prescription:
  - Tab. Clotrimazole double strength 1 once daily
  - Tab. Ziduvidine 300 mg twice daily
  - Tab. Lamivudine 150 mg twice daily
  - Tab. Indinavir 800 mg thrice daily with high fat meals
  - Tab. Terfenadine 60 mg once daily
  - Tab. Fluconazole 100 mg once daily

Case 4

40 year-old man, diagnosed to be HIV-positive and a known epileptic and asthmatic

- Came with a wheeze and cough with dyspnoea
- He is given the following prescription:
  - Tab. Phenytoin sodium 300 mg thrice daily
  - Tab. Deriphylline retard 300 mg thrice daily
  - Tab. Ciprofloxacin 750 mg twice daily
  - Syr. Gelusil MPS 30 ml thrice daily

Slide 4	**Clinical Problem Solving - Case 1** 25 year-old obese woman; 70 kg; known PLHA • She is being started on ART as her CD4 count is 132 cells/cu.mm • She is already on oral contraceptive pills and is given the prescription: – Tab. Ovral 1 once daily for 21 days and restart after 7 days – Tab. Stavudine 30 mg twice daily – Tab. Lamivudine 100 mg twice daily – Tab. Nevirapine 200 mg twice daily	
Slide 5	**Clinical Problem Solving - Case 2** 35 year-old man, known to have fixed drug eruption in the past after taking an antimalarial • Diagnosed HIV 2 infection after he presented with oral-oesophageal Candida • His CD4 count is 140 cells/cu.mm and he is given the following prescription: – Tab. Cotrimoxazole double strength 1 daily – Tab. Zidovudine 100 mg five times daily – Tab. Lamivudine 150 mg twice daily – Tab. Efavirenz 600 mg twice daily	
Slide 6	**Clinical Problem Solving - Case 3** 47 year-old housewife, PLHA, diagnosed with Cryptococcal meningitis 2 weeks ago - on treatment • Started on ART • She now develops a Upper Respiratory Infection and is given the following prescription: – Tab. Cotrimoxazole double strength 1 once daily – Tab. Zidovudine 300 mg twice daily – Tab. Lamivudine 150 mg twice daily – Tab. Indinavir 800 mg thrice daily with high fat meals – Tab. Terfenadine 60 mg once daily – Tab. Fluconazole 100 mg once daily	
Slide 7	**Clinical Problem Solving - Case 4** 40 year-old man, diagnosed to be HIV-positive and a known epileptic and asthmatic • Came with a wheeze and cough with dyspnoea • He is given the following prescription: – Tab. Phenytoin sodium 300 mg thrice daily – Tab. Deriphylline retard 300 mg thrice daily – Tab. Ciprofloxacin 750 mg twice daily – Syr. Gelusil MPS 30 ml thrice daily	

Slide 8		

Handout 2: Prescription Writing - Case Studies

Instructions: Comment on the appropriateness of the given prescription and a plan for managing this patient. Write down what the final revised prescription should be.

Case 1

31 year-old woman, HIV 1-positive, was started on HAART as her CD4 was 150 cells/cu.mm

- She developed a nevirapine induced rash
- She has been found to be 8 weeks pregnant

Case 2

45 year-old man, PLHA, develops tuberculosis

- He has been started on ATT (Active TB Treatment) — HREZ (H-Isoniazid, R-Rifamycin, E-Ethambutal, Z -Z-Pyrazinamide)
- 2 weeks later, he develops jaundice

Case 3

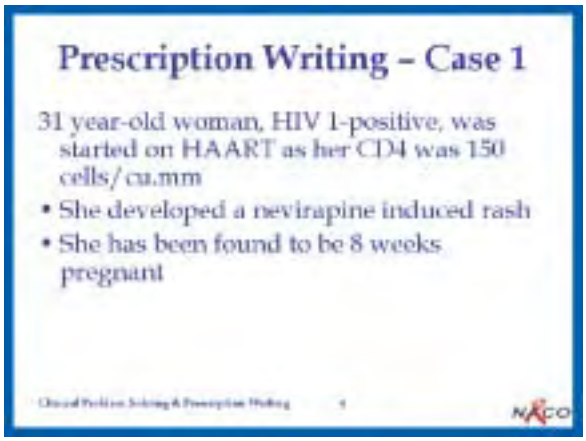
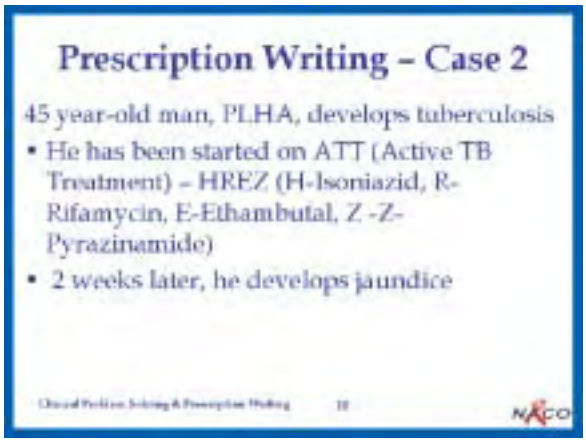
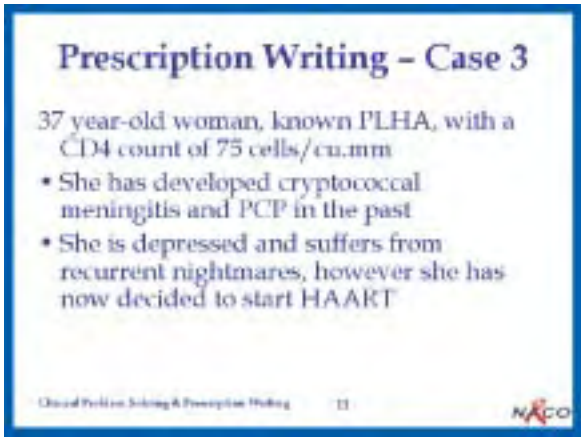
37 year-old woman, known PLHA, with a CD4 count of 75 cells/cu.mm

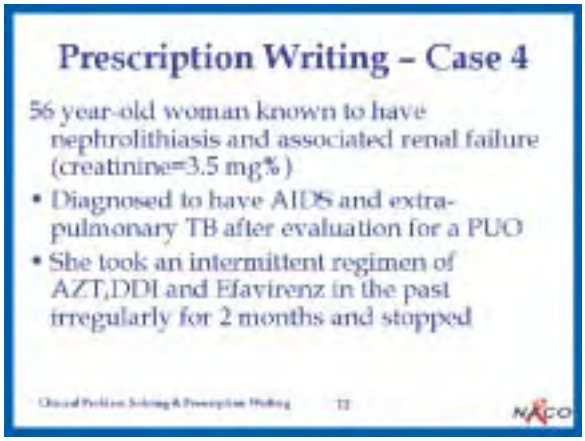
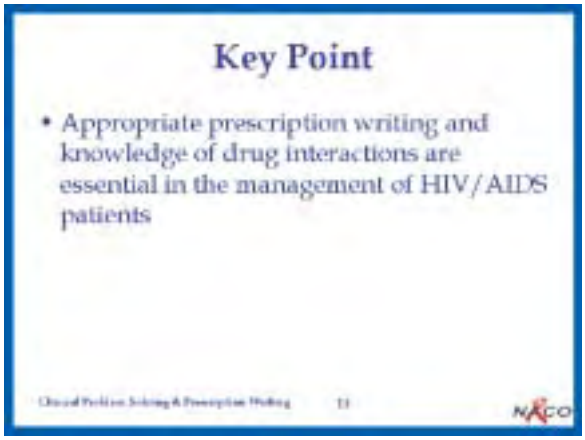
- She has developed cryptococcal meningitis and PCP in the past
- She is depressed and suffers from recurrent nightmares, however she has now decided to start HAART

Case 4

56 year-old woman known to have nephrolithiasis and associated renal failure (creatinine=3.5 mg%)

- Diagnosed to have AIDS and extra-pulmonary TB after evaluation for a PUO
- She took an intermittent regimen of AZT,DDI and Efavirenz in the past irregularly for 2 months and stopped

Slide 9		
Slide 10		
Slide 11		

Slide 12		
Slide 13		

SESSION 35

SESSION

PRESCRIPTION OF ART IN CHILDREN

35

Total Session Time: 45 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Prescribe the appropriate regimen
- Calculate the doses as per the weight bands
- Use the right formulations in children
- Modify the ART regimen in children on anti TB treatment

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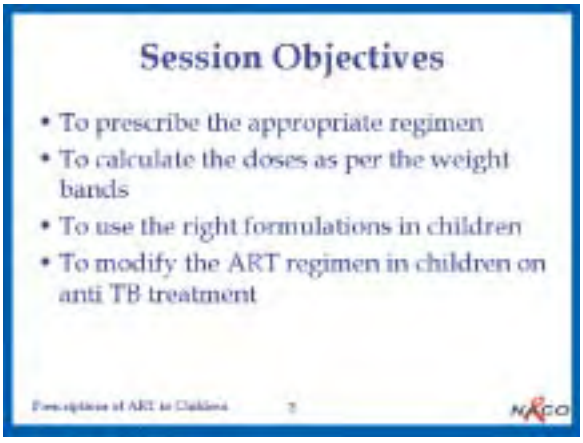
Slide 2		

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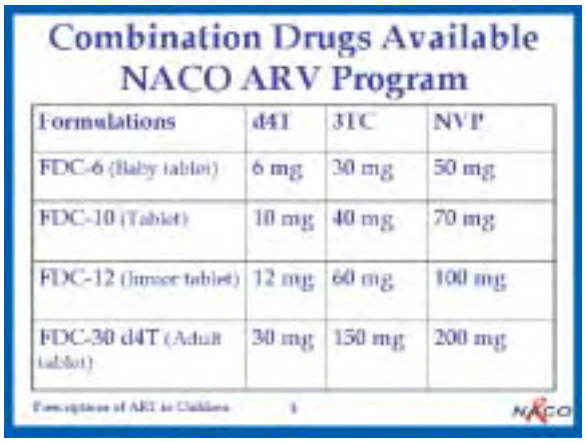
Slide 4		
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Slide 6

Reader's Notes:

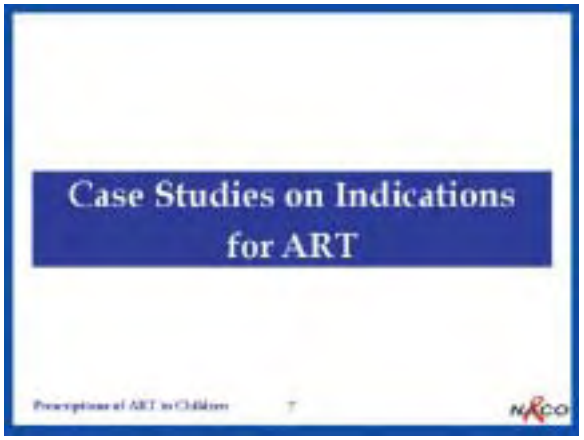
- The recommended preferred first-line ARV regimens for infants and children are:

Regimen of 2 NRTI plus 1 NNRTI
AZT* + 3TC + NVP or EFV**
D4T + 3TC + NVP or EFV**

- * AZT should not be given in combination with d4T.
- ** EFV is not currently recommended for children <3 years of age or < 10kg, and should be avoided in post-pubertal adolescent girls who are either in 1st trimester of pregnancy or are sexually active and not receiving adequate contraception.
- EFV is used to substitute NPV when anti-tuberculous treatment has to be provided concomitantly.
- However, after 2 weeks of completion of ATT, EFV should be switched back to NVP.

*** ABC+ 3TC + NVP or EFV is an alternative.However, in the national programme — ABC is not available and is still costly.

Slide 7



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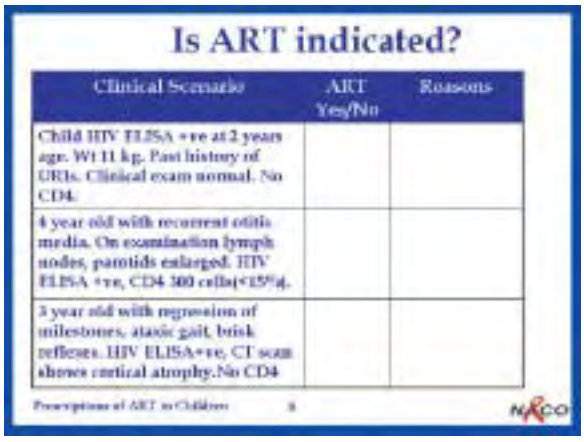

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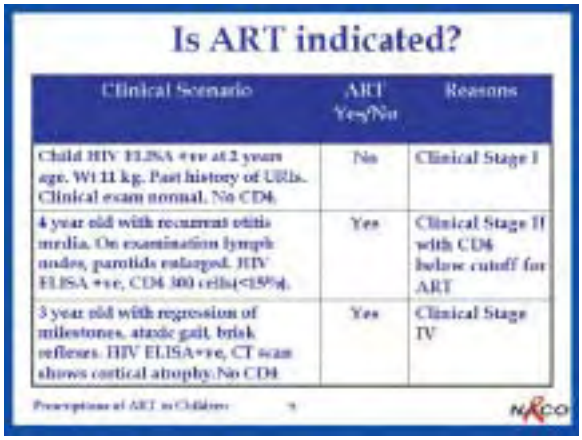

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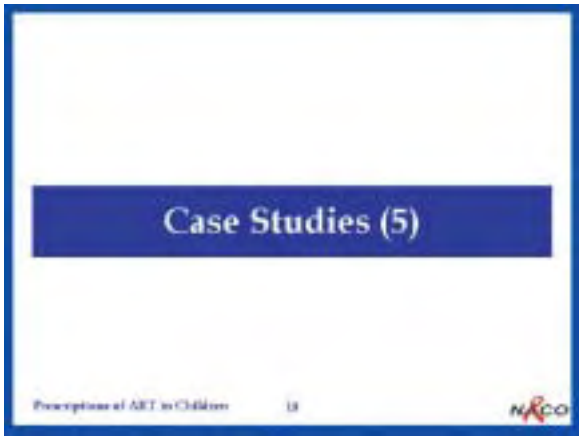

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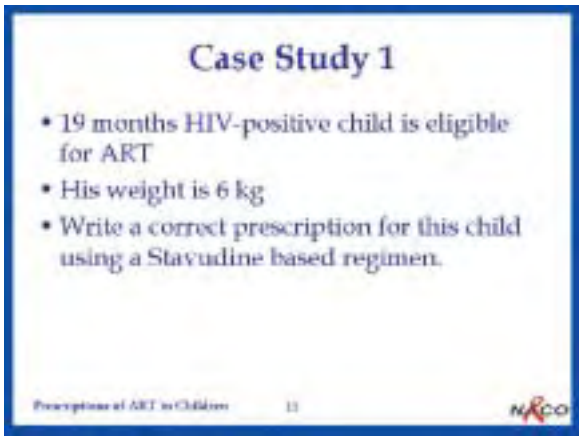

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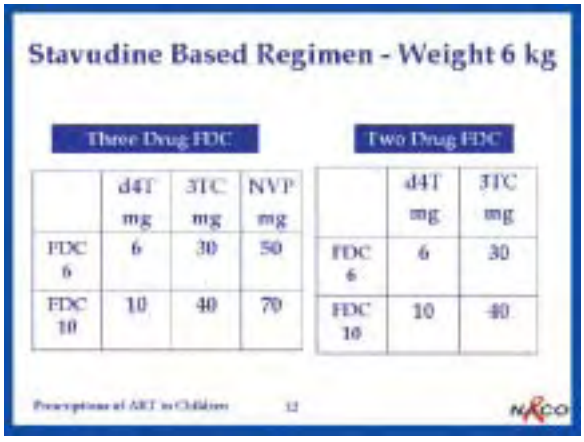
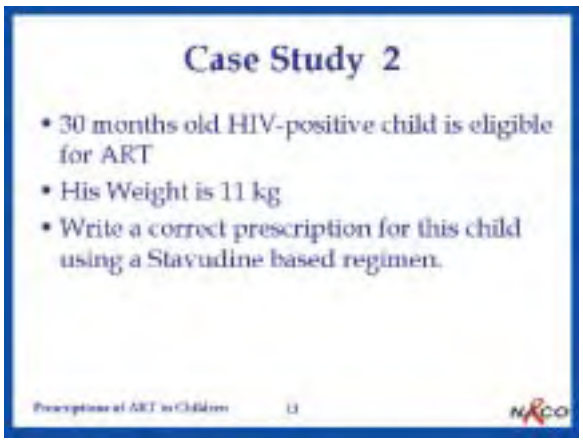


Reader's notes:

Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO. **Section A ; A5; 5.9 How much paediatric ARVs to give, Page 21 & 22**.

Slide 13



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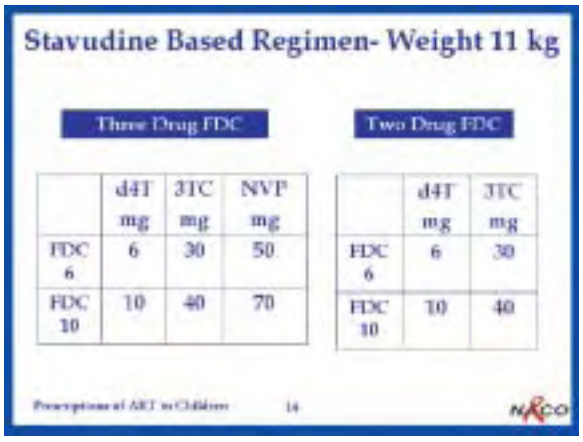

Reader's notes:

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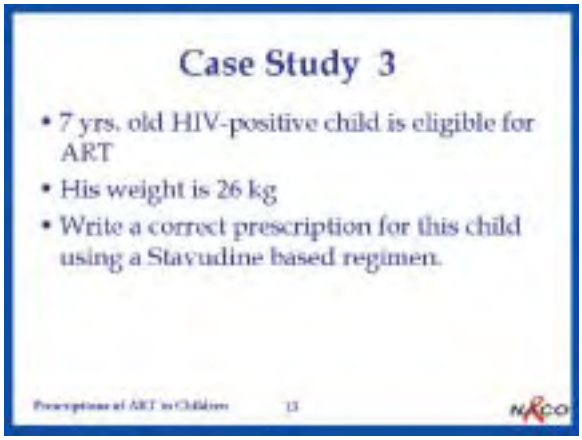

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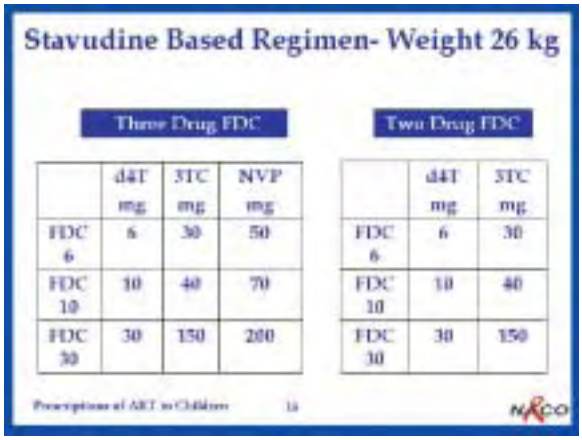

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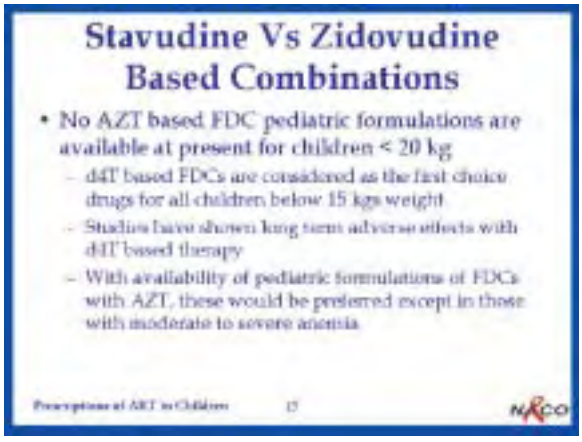
Slide 17



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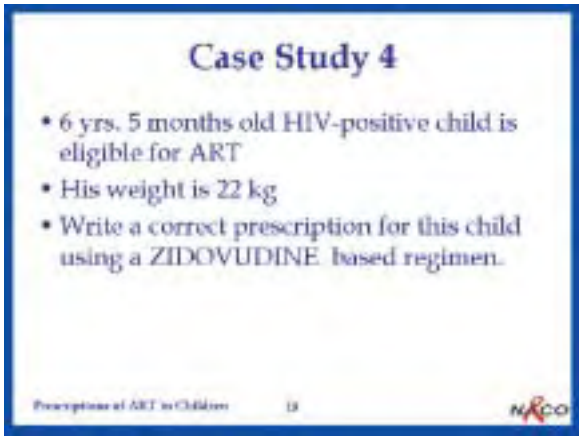

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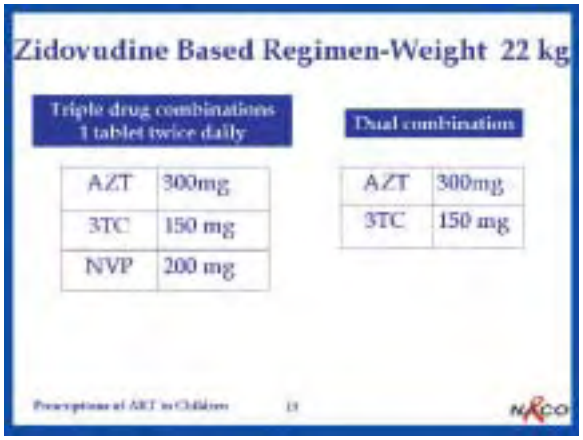

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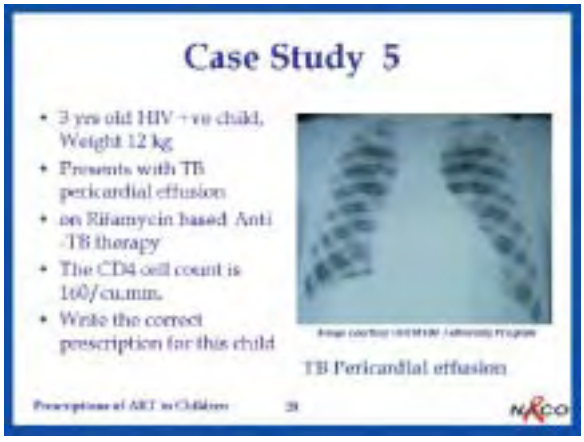
Slide 20



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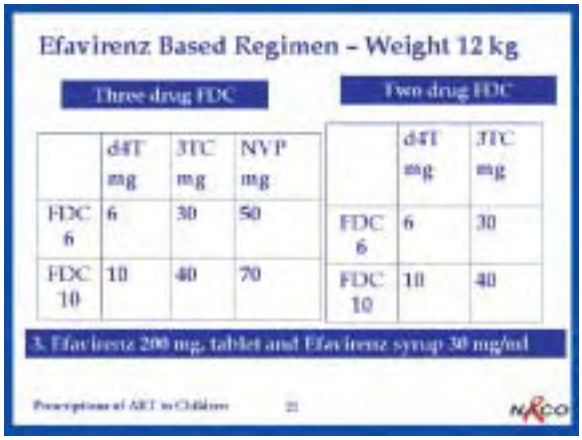

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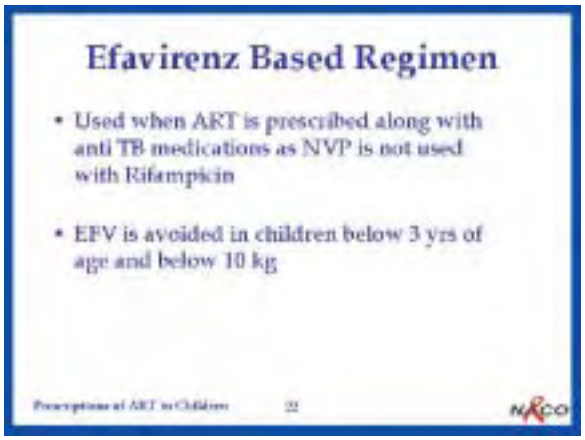
Slide 22



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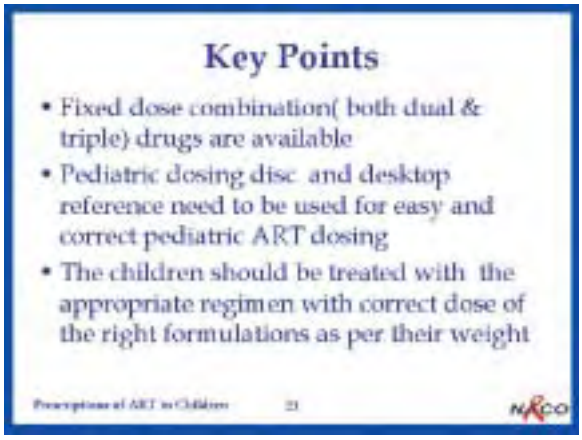


SESSION 36

SESSION

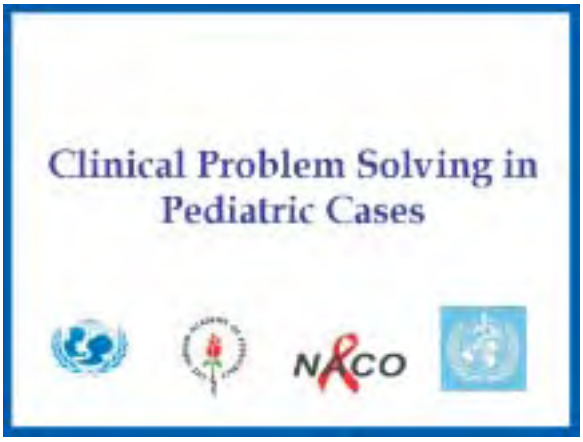
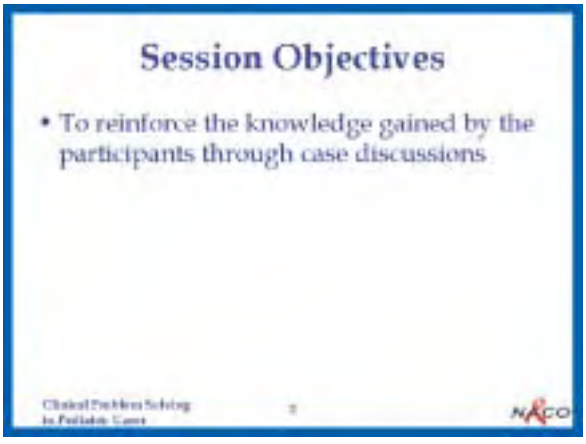
CLINICAL PROBLEM SOLVING IN PEDIATRIC CASES

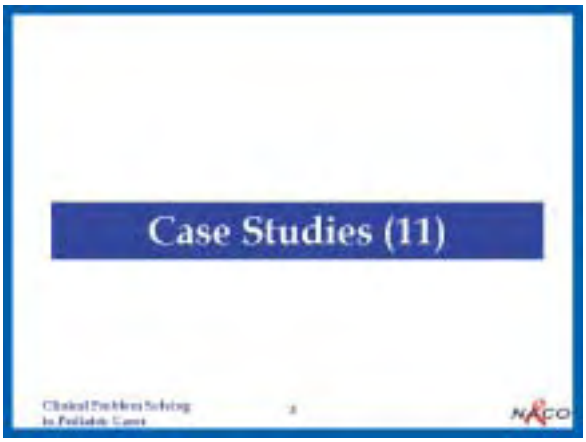
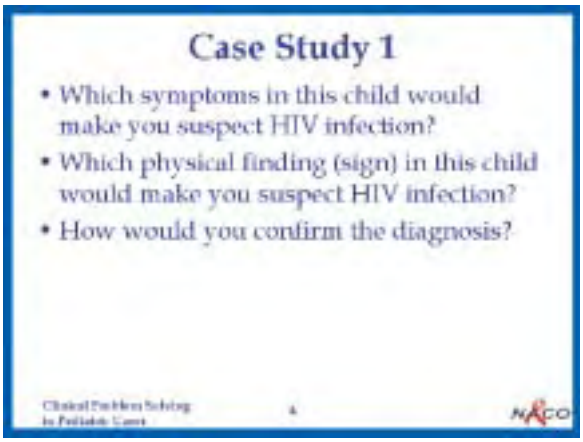
36

Total Session Time: 45 minutes

Session Objectives: At the end of the session, the participant should be able to:

- Reinforce the knowledge gained by the participants through case discussions

Slide 1		
Slide 2		

Slide 3		
Slide 4		**Reader's Notes:** ● Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO. Page 11.

Handout 1: Case Study 1

Case Study 1

4 year old Master M is brought to your outpatient clinic with complaints of recurrent episodes of purulent ear discharge and upper respiratory infections, and 1 episode of diarrhoea 3 months back that lasted for nearly 2 weeks.

He is the first-born child, born at home by normal vaginal delivery, and was breast-fed till the age of 1 year. Mother did not have any blood tests done or receive blood transfusions prior to delivery.

His father died a year ago; he was diagnosed to be HIV-infected prior to his death.

Physical examination

On examination, the child's weight is 12 kg and height 94 cm.

He has palpable cervical and axillary lymph nodes, mild pallor, no icterus or clubbing.

Abdominal examination reveals a liver palpable 3.5 cm below the right costal margin.

Questions:

Question 1: Which symptoms in a child would make you suspect HIV infection?

Question 2: What findings would you look for?

Question 3: How would you confirm the diagnosis?

Note: Refer the "The diagnostic algorithm for HIV diagnosis in children > 18 months of age; (Handout-6 of session on WHO clinical staging and Lab. testing);

Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO.) Page 11

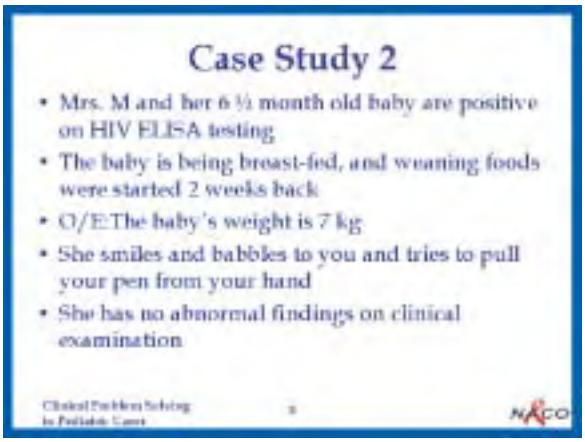
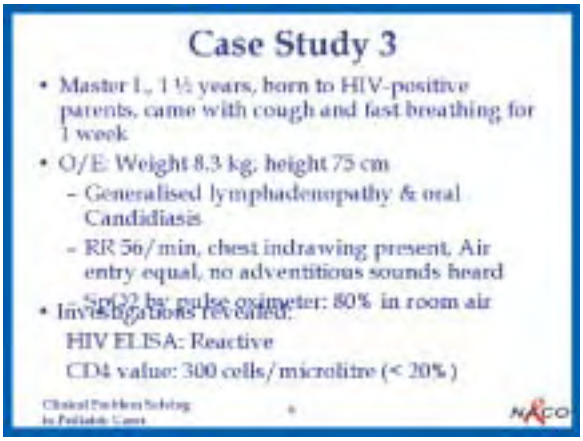
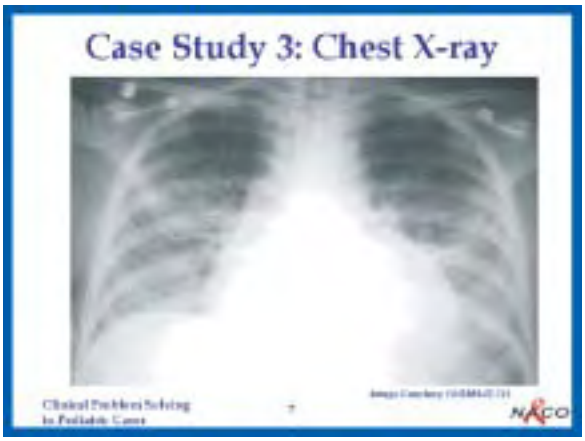
Handout 2: HIV Infection in a Child

Suspect HIV infection in any child with a history of (symptoms)

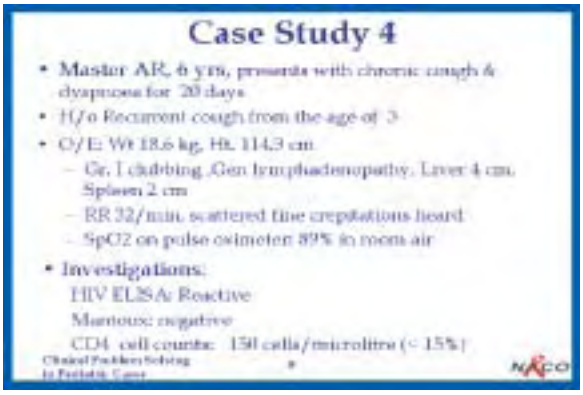
- Respiratory distress in infancy (*Pneumocystis carinii* pneumonia)
- Failure to thrive (multifactorial, associated with high HIV viral loads in infancy, poor nutrition, HIV-related diarrhoeal disease or malabsorption, or recurrent infections)
- Developmental delay, or loss of acquired developmental milestones (HIV encephalopathy, due to direct viral replication in the CNS or AIDS-related vasculitis)
- Chronic or recurrent diarrhoea (HIV-related GI inflammation or other infections)
- Recurrent sinusitis, otitis media, pneumonia, meningitis (bacterial infections)
- Recurrent oral or vaginal candidiasis (associated with immunosuppression)
- Recurrent varicella or herpes zoster (associated with immunosuppression)
- Mycobacterial infections (primary tuberculosis usually acquired through contact with a tuberculous parent, or atypical mycobacteriosis in children with advanced immunosuppression)

The commonest findings on clinical examination in children with HIV infection are(signs)

- Generalised lymphadenopathy (due to replication of HIV within lymphoid tissue)
- Unexplained hepatomegaly, splenomegaly or both (replication of HIV within the reticuloendothelial system)
- Chronic or recurrent parotid enlargement (direct HIV infection of the parotid gland and CD8 lymphocytic infiltration, sometimes bacterial parotitis)
- Bruising or petechiae (due to HIV-related thrombocytopenia)
- Oral thrush (candidiasis)
- Papular urticaria (pruritic papular eruption), recurrent scabies or other skin infections
- Unexplained chronic lung disease or clubbing (lymphoid interstitial pneumonia / LIP, or bronchiectasis following tuberculosis or repeated bacterial pneumonias)
- Hypertonia, hyperreflexia, spasticity, rigidity (with HIV encephalopathy)

Slide 5		**Reader's Notes:** ● Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO. page 3&4 for the answers related to infant feeding practices and Page 10
Slide 6		
Slide 7		**Reader's Notes:** ● Reference:Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO. Page 60-61.

Slide 8



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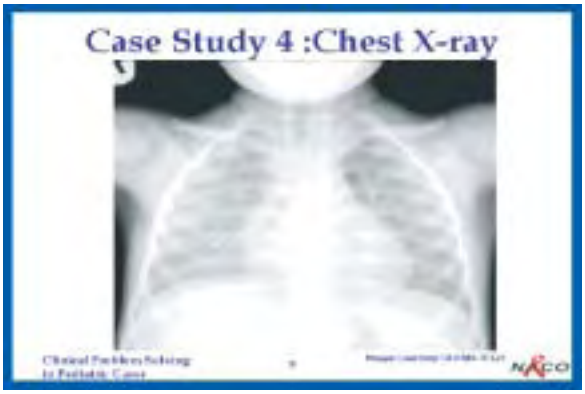

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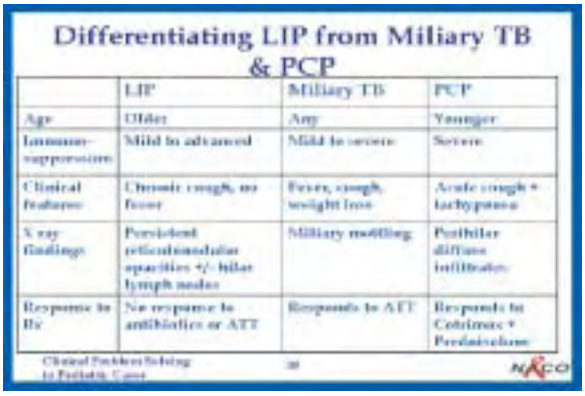
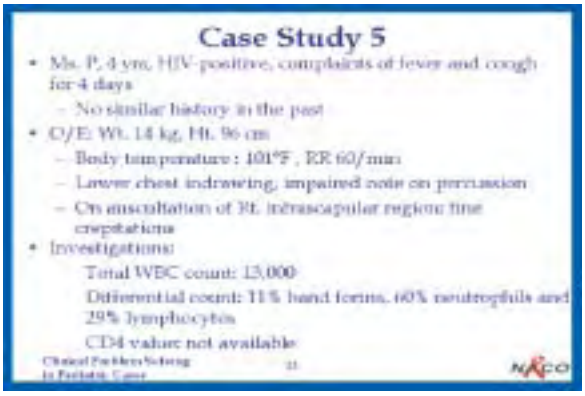
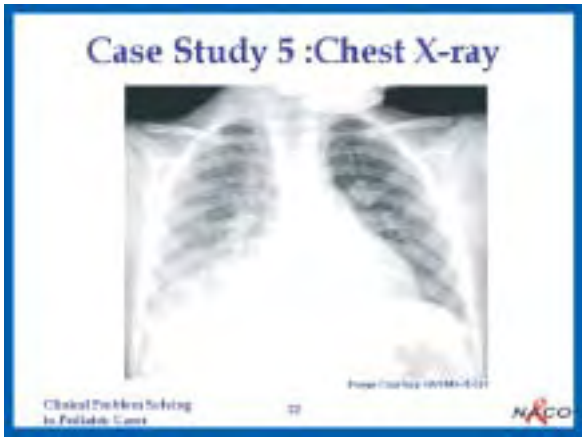
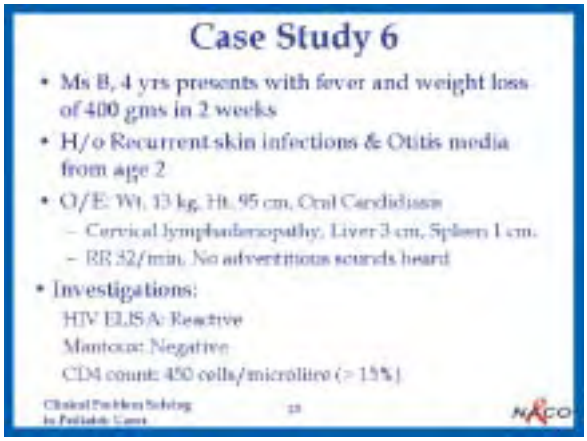
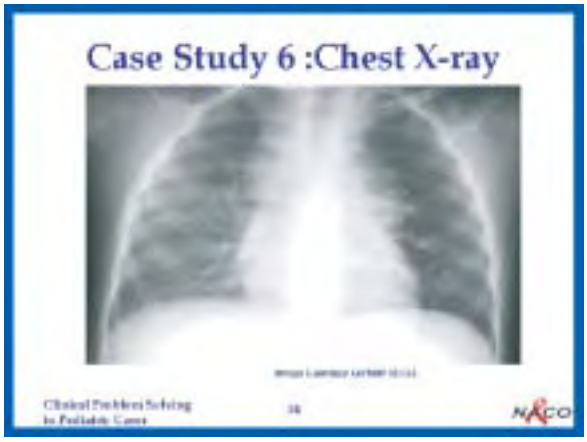


Reader's Notes:

- LIP- **Lymphocytic Interstitial Pneumonia.**

Slide 11



Slide 12		**Reader's Notes:** ● Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO. Page 62
Slide 13		
Slide 14		**Reader's Notes:** ● Reference: Guidelines for HIV care and treatment in Infants and Children, November 2006,developed by Indian Academy of Paediatrics and National AIDS Control Organization with support from Clinton Foundation, UNICEF and WHO refer page 64 and page 20, Table 13.

Handout 3: RNTCP Guidelines for Paediatric TB

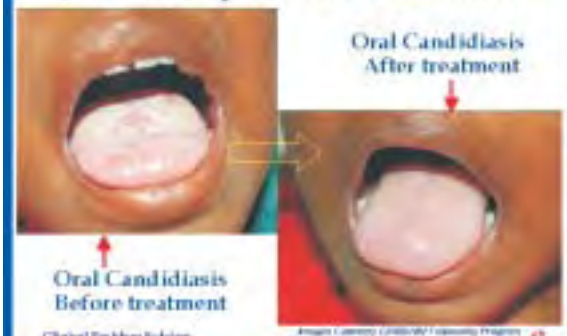
Drugs used for the treatment of Tuberculosis			
Drug	Dosage	Adverse Effects	Remarks
INH	10-15 mg/kg /day PO OD	Hepatotoxicity, peripheral neuritis, mild CNS effects Hypersensitivity reaction	Pyridoxine is recommended in children in all symptomatic HIV disease
Rifampicin	10 mg/kg/day PO OD	Stains urine, tears, sweat, contact lenses and other body fluids orange. GI upset, skin rash, hepatitis, Thrombocytopenia, cholestatic jaundice	Rifampicin accelerates clearance of PIs and NNRTIs resulting in sub therapeutic levels of the drug
Pyrazinamide	30 -35 mg/kg/ day PO OD	Hepatotoxicity, hyperuricemia, arthralgia, skin rash, GI intolerance	
Ethambutol	30 mg/kg/day PO OD	Optic neuritis, colour blindness, headache, nausea, peripheral neuropathy, rash, hyperuricemia	Monthly evaluation of vision is recommended
Streptomycin	15 mg/kg/day IM	Ototoxicity and nephrotoxicity	

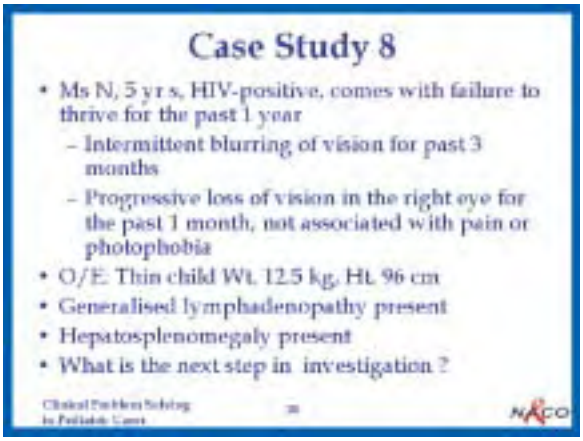
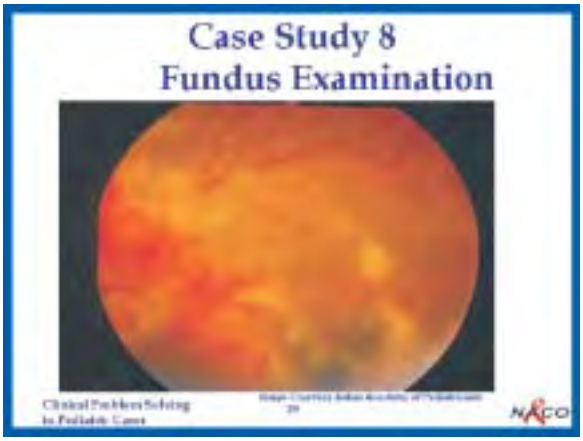
Recommended treatment regimens under RNTCP			
Category of treatment	Type of patients	Type of patients	
		Intensive Phase	Continuation Phase
Category 1	New sputum smear-positive PTB* New sputum smear- negative PTB, Seriously ill * Extra-pulmonary TB (EPTB), seriously ill	*2 $H_3R_3Z_3E_3$***	4 H_3R_3
Category 2	Sputum smear-positive relapse Sputum smear-positive treatment failure Sputum smear-positive treatment after default	2 $S_3H_3R_3Z_3E_3$ + 1 $H_3R_3Z_3E_3$	5 $H_3R_3E_3$
Category 3	New sputum smear-negative,not seriously ill ** New extra-pulmonary TB, not seriously ill **	2 $H_3R_3Z_3$	4 H_3R_3

* In seriously ill children, sputum smear negative PTB includes all forms of sputum smear-negative PTB other than primary complex. Seriously ill EPTB includes TB meningitis (TBM), disseminated TB, TB pericarditis, TB peritonitis and intestinal TB, bilateral extensive pleurisy, spinal TB with or without neurological complications, genitor-urinary TB, and bone and joint TB.

** Not seriously ill sputum smear-negative PTB includes primary complex. Not seriously ill EPTB includes lymph node TB and unilateral pleural effusion.

***The number before the letters refers to the number of months of treatment (prefix). The subscript after the letters refers to the number of doses per week.
In patients with TB on Category 1 treatment, 4 drugs used during the intensive phase should be HRZS (instead of HRZE). Continuation phase of treatment in TBM and spinal TB with neurological complications should be given for 6-7 months, thus extending the total duration to 8-9 months. Steroids should be used initially in hospitalized cases of TBM and TB pericarditis and reduced gradually over 6 -8 weeks.

Slide 15	**Case Study 7** • Master C, 4 years, presents with – Failure to thrive for past 2 years – difficulty in eating for the past 2 weeks – Retrosternal pain on swallowing food or fluids • O/E Wt. 7.8 kg, Ht. 85 cm – Oral Candidiasis, small cervical lymph nodes, liver palpable 3 cm below the costal margin	
Slide 16	**Case Study 7** Investigations: • WBC total count: 5000 cells/cu.mm • HIV Elisa:Reactive • CD4 value not available What is your diagnosis in this child? 	
Slide 17	**Case Study 7: Post Treatment**  	

Slide 18		
Slide 19		**Reader's Notes:** ● Picture showing white and yellow retinal infiltrates and retinal hemorrhages, probably due to CMV Retinitis.
Slide 20		

Handout 4: Case Study 9

Case Study 9

6-year-old Master G comes with history of moderate fever and malaise for 2 days, after which he has developed itchy skin lesions, initially on the trunk then appearing on the limbs and face.

Physical examination

Patient presented with papules, which turned into vesicles. The vesicles are relatively large and extensive. Mucosal surfaces are also involved.

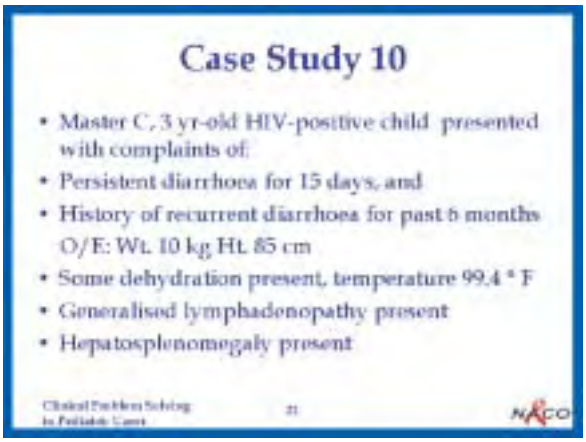
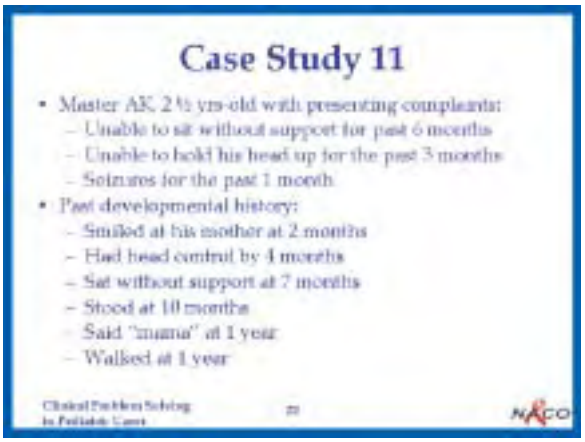
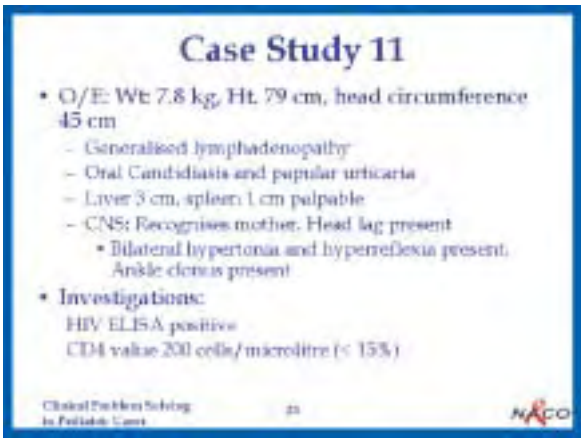
Questions:

Question 1:What is your clinical diagnosis?

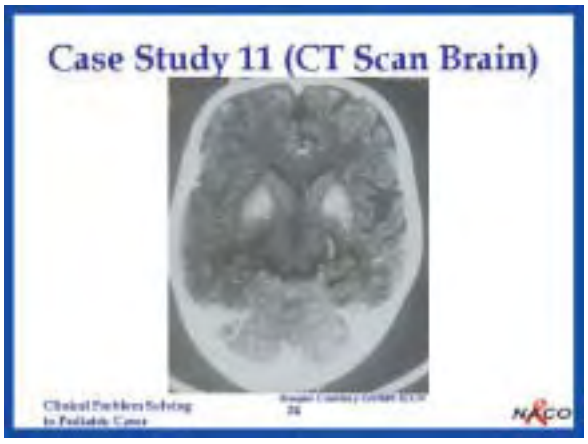
Question 2: What are the differential diagnoses?

Question 3: What are the complications that are likely to occur in an immuno compromised child?

Question 4: How would you treat this child?

Slide 21		
Slide 22		
Slide 23		

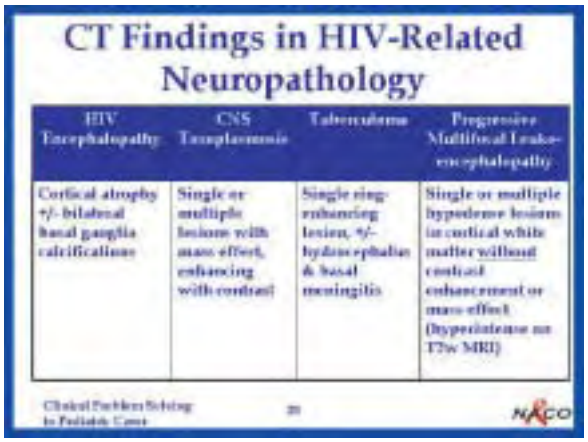
Slide 24



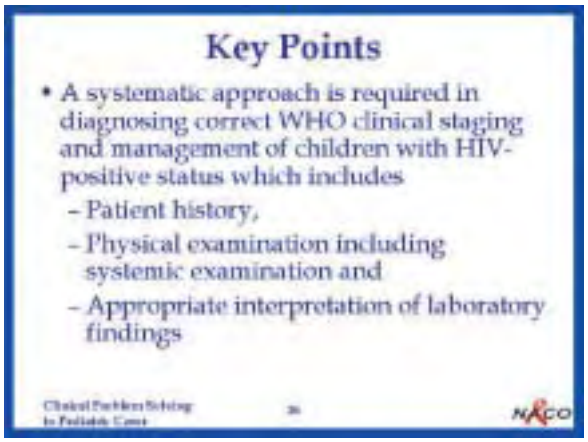
Reader's Notes:

- CT showing cortical atrophy and bilateral basal ganglia calcifications

Slide 25



Slide 26



SESSION 37

SESSION

OI VIDEO CASE STUDY REVIEW GUIDE

37

Total Session Time: 45 minutes

Each video case study depicts a physician examining a patient with at least one Opportunistic Infection (OI). The signs are presented first during the examination. In most cases, the summary of signs and symptoms is followed by the diagnosis and treatment.

The following Opportunistic Infections video cases are included in this session.

1. PCP
2. Candidiasis
3. Herpes Simplex Stomatitis
4. Herpes Zoster Virus
5. Molluscum Contagiosum

Case 1: PCP

Video Case Study Context:

A 30 year-old man diagnosed with HIV three months ago. He presents with the following signs: acute breathlessness of ten days duration, pain in the chest, and phlegm collection at back of throat.

Questions:

Q.1. What is the differential diagnosis for this patient?

Q.2. If the patient is HIV positive what should be your first presumptive diagnosis?

Q.3. What investigations will you conduct to determine the diagnosis?

Q.4. How do you treat PCP? What are the possible outcomes of treatment?

Q.5. What are the possible complications of PCP drug therapy? What are some alternative treatments?

Case 2: Candidiasis:

Video Case Study Context:

An adult male with the following signs: oral ulcers; difficulty in mastication, swallowing; bleeding from the gum, oral cavity; white patches inside oral cavity; absence of taste, loss of appetite.

Questions:

Q.1. What is the clinical condition of these patients?

Q.2. How would you treat this patient?

Q.3. What other drugs might you use if the patient is resistant to the recommended treatment?

Q.4. How do you decide when to use topical vs. oral vs. intravenous treatment?

Case 3: Herpes Simplex Stomatitis Two Cases

1st Video Case Study Context:

An HIV-positive adult female presenting with the following signs: ulcers in the lip for past month, painful deglutition for past fifteen days.

Questions:

Q.1. What are the common causes of oral ulcers in patients with HIV?

Q.2. What is the diagnosis in this case?

Q.3. What is the drug of choice in treating herpes simplex stomatitis?

Another Case of Herpes Simplex

2nd Video Case Study Context:

A 45 year-old HIV-positive male presenting with the following signs: painful ulcers in glans penis, base of the scrotum, and in the upper medial aspect of the right thigh.

Questions:

Q.4. How will you differentiate this from Herpes Zoster?

Q.5. How will you manage this patient?

Case 4: Herpes Zoster

Video Case Study Context:

An HIV-positive adult female with the following signs: low-grade fever for one week, pain in the left loin for five days, vesicles on the left side.

Questions:

Q.1. What is your diagnosis for this patient? What is your diagnosis based on?

Q.2. How do you treat herpes zoster?

Q.3. What are possible post-treatment complications, and how do you treat them?

Case 5: Molluscum Contagiosum

Video Case Study Context:

An adult male with a history of typhoid and Tuberculosis, presenting with the following signs: papular lesions over face, papules of 5-10 mm with pearly white central umbilication.

Questions:

Q.1. What are the differential diagnoses for this patient?

Q.2. What investigations would you do in order to make the diagnosis?

Q.3. How would you treat this patient?

Q.4. How do you prevent the further spread of infection?