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WORLD HEALTH ORGANIZATION

Department of Communicable Disease Control, Prevention and Eradication

Contents

Acronyms

9GPW	WHO Ninth General Programme of Work, 1996-2001
AFP	Acute flaccid paralysis
AFRO	WHO Regional Office for the African Region
Ag	Antigen
AIDS	Acquired immunodeficiency syndrome
AMRO	WHO Regional Office for the Americas
aP	Acellular vaccines (pertussis)
APOC	African Programme for Onchocerciasis Control
ARI	Acute respiratory tract infections
BSE	Bovine spongiform encephalopathy
CD4	T4 lymphocyte population
CDC	Centers for Disease Control and Prevention, USA
CJD	Creutzfeldt-Jakob Disease
CRS	Congenital rubella syndrome
CSF	Cerebrospinal fluid
DAT	Direct agglutination test
DHF	Dengue haemorrhagic fever
DSS	Dengue shock syndrome
DT	Diphtheria, tetanus vaccine
DTP	Diphtheria, tetanus, pertussis vaccine
ELISA	Enzyme-linked immunosorbent assay
EMRO	WHO Regional Office for the Eastern Mediterranean
EURO	WHO Regional Office for Europe
FluNet	Influenza network
FTA	Fluorescent treponemal antibody-absorption test
GIS	Geographic Information System
GPS	Global Positioning System
HAV	Hepatitis A virus
HBcAg	Hepatitis B core antigen
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HDCV	Human diploid cell vaccine (rabies)
HDV	Hepatitis D virus
HepB	Hepatitis B vaccine
HEV	Hepatitis E virus
Hib	*Haemophilus influenzae* type b
HIV	Human immunodeficiency virus
IARC	International Agency for Research in Cancer, WHO
ICD-10	International Classification of Diseases, 10th revision, WHO
IgG	Immunoglobulin G
IPV	Inactivated polio-virus vaccine
IUATLD	International Union against Tuberculosis and Lung Diseases
IHR	International Health Regulations
MDT	Multidrug therapy
MoH	Ministry of Health
NGO	Nongovernmental organization
OPV	Oral poliovirus vaccine
PAB	Protected at birth
PAHO	Pan-American Health Organization
PCECV	Purified chick embryo cell vaccine (rabies)
PCR	Polymerase chain reaction
PVRV	Purified vero cell vaccin (rabies)
PDEV	Purified duck embryo vaccine (rabies)
REMO	Rapid epidemiological mapping of onchocerciasis
SEARO	WHO Regional Office for South-East Asia
STI	Sexually transmitted infection
Td	Tetanus-diphtheria [toxoid]
TST	Time, Steam and Temperature indicator
TT	Tetanus toxoid
UNAIDS	Joint United Nations Programme on HIV/AIDS
VDRL	Venereal Disease Research Laboratory
WHA	World Health Assembly
WHO	World Health Organization
WPRO	WHO Regional Office for the Western Pacific

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WHO is grateful to the staff at the Centers for Disease Control and Prevention, Atlanta, GA, USA, for their careful review and useful contributions to the document in draft form.

Introduction

Communicable diseases are a major cause of suffering, disability and death in the world. The World Health Organization's Programme on Communicable Diseases provides technical guidance and support to national governments to organize and implement programmes aimed at setting up or strengthening ongoing control of common diseases, reducing transmission, mortality, morbidity and human suffering, and gradually eliminating these diseases so that they cease to be a public health problem. In some cases, the aim may also be to eradicate selected communicable diseases.

WHO technical programmes dealing with specific communicable diseases have issued a variety of guidelines on interventions and programme organization. WHO supports countries in adapting these guidelines to national conditions and resources. However, there is at the moment no document summarizing the main prevention and control strategies and interventions that could facilitate planning of coordinated activities at national, state and district level.

The present document has been produced jointly by technical units in WHO and UNAIDS. It is a catalogue of key public health interventions against communicable diseases and aims to complement the *WHO Recommended Surveillance Standards* (WHO/CDS/CSR/ISR/99.2, 2d ed., revised October 1999). The document reviews the main strategies for disease control activities, in order to facilitate coordination of programmes at country level and in external institutions, and in order that these programmes and activities become integrated as soon as possible within primary health care delivery.

The document is not meant to replace existing technical guidelines or be an exhaustive description of control methods for communicable diseases. It should be of particular use at the Ministry of Health level in Member States in approaching communicable diseases, and at district or province level in implementing coordinated activities. In so doing it will serve as a guide to good practice in order to harmonize control activities, and as handy reference for key elements and contact information for communicable diseases covered by WHO programmes. The main criteria for inclusion of a disease have been the availability of a control, elimination or eradication strategy together with the feasibility and affordability of the interventions identified within the strategy.

A chapter on the general organization of control activities, followed by brief overviews of the main control methods – cross-referenced to diseases or disease groups – precedes disease-specific items. The diseases addressed are listed alphabetically, with ICD-10 codes to facilitate reporting and data exchange. Each disease item normally includes a general introduction on the rationale for control, a summary of etiology and main modes of transmission, a clinical description and case definition, a list of recommended control interventions, together with other specific aspects and indicators of control. Each item ends with a list of the relevant contact(s) in WHO/UNAIDS and a selection of references, as appropriate (see model at the beginning of the section in diseases).

In view of the changing nature of prevention and control strategies and methods for infectious diseases, the document will be updated regularly and will be made available on the Web. Feedback from readers will be appreciated as a means to help improve its usefulness.[1]

[1] For further information, comments and suggestions, please contact the relevant WHO Regional Office or:
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1. NATIONAL COORDINATION OF COMMUNICABLE DISEASE PREVENTION AND CONTROL

Developing and strengthening communicable disease control in endemic countries at national level requires a substantial and long-term commitment of human and material resources. This usually begins with a systematic assessment of national priorities as regards disease burden, and leads eventually to national strategies and plans for the prevention and control of communicable diseases. Endemic countries have implemented prevention and control strategies for relevant communicable diseases with a high burden and periodically elaborate responses to specific short-term needs to tackle other diseases of lesser importance or visibility. The prevention and control of communicable diseases is essentially a national function and responsibility; it and is carried out largely by national authorities in concert with other key stakeholders in health.

1.1 What is meant by a "multidisease approach to prevention and control"?

Activities related to prevention and control may be carried out independently (as is the case for instance in epidemics such as plague or viral haemorrhagic fevers, which may require special short-term efforts) or may be integrated with overall public health activities. Whenever possible, activities in personal prevention or in care that are related to endemic problems should become part of standard health care delivery. This helps ensure sustainability, accessibility and reductions in costs. Such may easily be the case, for instance, in the prevention and control of intestinal helminths and of lymphatic filariasis, in immunization, and in the management of acute respiratory infections. For others, a more combined approach is required: HIV/AIDS control implies multifaceted health care plus a multisectoral approach dealing mainly with education for behavioural change; the prevention and control of malaria require a combination of case management and vector control, with intersectoral partnerships.

In many countries some disease prevention and control activities are managed through vertical disease prevention and control programmes using dedicated staff to provide specific services. This approach facilitates training and management but it is expensive and difficult to sustain and reduces community involvement. The current trend is to move towards activities that maintain essential resources, planning, monitoring and evaluation, so as to monitor the quality of prevention and control activities and assess their impact on the disease(s) concerned.

The blending of various disease-specific prevention and control programmes into primary health care requires a careful balance to avoid creating a situation where several complex systems resort to a multiplicity of methods, terminologies, reporting forms or schedules, and evaluation methods – thus leading to extra costs and training requirements, and often to work overload and lack of motivation among health workers. The degree of specialization for staff undertaking prevention and control tasks will vary according to their administrative level in the same way that this varies in clinical practice according to the level of care:

- At *primary* or *peripheral* level, generalists (often paramedical) usually manage all diseases, while at tertiary level health care specialists may be required for more elaborate procedures. Similarly, in public health management, one person often collects and reports all data at the peripheral level, together with a preliminary analysis (as part of *surveillance*), and is responsible for the local implementation of standard prevention and control activities/programmes; in some cases, that person may also initiate implementation. The peripheral level also undertakes *monitoring* of the activities and of the impact on disease occurrence and on disease-specific mortality/disability.
- *Training*, *funding*, ordering and management of *supplies* and *equipment*, on the other hand, tend to be undertaken at the intermediate (state/district) or central level.
- In addition to the above-mentioned tasks, intermediate level teams must ensure the minimum essential information required for the analysis and management of priority diseases, and consolidate training, data collection and supervision as far as possible. Individual staff members may be responsible for one or more diseases according to workload, with the larger team working in close coordination.
- At national level, specialized disease prevention and control teams or professionals provide technical guidance, programme and disease monitoring, and ensure the availability of resources. They act as technical advisers and ensure the availability of additional resources (e.g. vaccines, essential drugs, specific training).

In practice, coordination occurs without too many problems at the peripheral level, since:

- The tasks identified for prevention and control can often be grouped into sets that require similar basic operational skills.
- The resources available can easily be pooled.
- The persons responsible for the coordination and implementation of the various disease programmes are often one and the same.

At the intermediate and central levels, it is important to avoid the impression that disease prevention and control are fragmented among distinct and circumscribed areas. One way to achieve this is to set up a *central unit for disease prevention and control* that provides standard procedures for logistics and supplies, models of training manuals and supervision procedures, models for activity monitoring and for impact assessment.

Financial resources are another area where it is important to promote synergistic activities – even though this is not often practised. The type of central unit mentioned earlier may assist by setting up monitoring tools to assess the amount and proportion of resources devoted to the prevention and control of individual diseases and the amounts to be requested from donors, as part of a general policy decision at the level of the Ministry of Health or of the Council of Ministers. The *management* of these resources may occur at various levels aside from the central authorities (e.g. drugs and vaccines may be bought by the prevention and control programme, by the essential drugs programme, by the health services – hospitals, districts – or even by the patients themselves).

1.2 Setting priorities

It is thus possible to approach development and strengthening of the disease prevention and control system as a whole in a coordinated way. The challenge is to identify where synergy between programmes is possible, while recognizing the special needs of some programmes.

The core functions in the prevention and control of disease are:

- Setting priorities (a fundamental step in selecting diseases for prevention and control).
- Detecting and reporting cases.
- Investigating outbreaks and if necessary confirming their existence (these 3 items are part of surveillance and overlap with control as regards analysis and interpretation of information).
- Choosing a control strategy.
- Undertaking action (control/response; policy; feedback).
- Assessing the results of action.

The level of coordination in a prevention and control programme can affect:

- Performance.
- Cost (through the avoidance of duplicate efforts).
- Accessibility.
- Sustainability (insofar as it reduces the ongoing workload).

The following support activities improve core surveillance and control functions:

- Setting up monitoring/evaluation criteria and methods.
- Setting standards (e.g. case definitions).
- Setting up laboratory support.
- Setting up communications.
- Managing resources.
- Supervision and training.

The latter are particularly important not only in technical matters but also for the development of operational and managerial skills for health workers in the field of communicable disease prevention and control.

One of the important components of a national prevention and control plan is a list of those national priority problems (e.g. infant or maternal mortality) that require action. This list, which must be kept as short as possible, must be established by the national health authorities, preferably with the consent of the community and its leaders (academics, medical societies, nongovernmental organizations, etc), and with reference to current international guidelines if available.

In addition to specific diseases, certain syndromes (e.g. haemorrhagic fever syndrome) as well as some specific public health issues (e.g. antibiotic sensitivity of some infectious agents) may be considered for surveillance or control. Communicable diseases should be prioritized using the criteria listed hereafter (see box), not only from the national perspective but also from a regional and an international viewpoint – diseases may present different epidemiological characteristics within a country and may also spread rapidly across national boundaries:

1. Impact *Does the disease have much impact on health (morbidity, disability, mortality), as is the case for tuberculosis, diarrhoea or pneumonia?*
2. Epidemic potential *Does the disease have significant epidemic potential, and has its prevalence changed significantly in recent times (cholera, meningitis, measles, etc.)?*
3. Potential for prevention and control *Can available tools and resources effectively control the disease?* *Can the information that is collected lead to significant public health action?*
4. International importance *Is the disease a specific target of an international control, elimination or eradication programme (such as in the Ninth Global Programme of Work – 9GPW), or is it included in a WHO Regional Plan, or is it a notifiable disease according to WHO International Health Regulations or other WHO international or regional prevention and control programmes?*

1.3 Implementation

Following, or if possible preceding, the setting up of a list of priority diseases/syndromes, an inventory of existing prevention and control activities must be carried out (routine information available at national level in this regard may have to be complemented through site visits). A review of key components of the health system, including both public and private stakeholders where appropriate, as well as nongovernmental organizations involved in long-term health activities in the country, will help identify resources.[2]

The following elements must be addressed for each disease or syndrome for which a prevention and control programme is envisaged:

- Is the case definition:
  - Clear?
  - Appropriate?
  - Consistent throughout the system?

The case definitions in this document are in most cases those already identified for the purposes of epidemiological surveillance, with the inclusion in many cases of "suspected" or "clinical" case definitions. Some diseases/syndromes (e.g. malaria) do not yet have case definitions that answer those criteria; nevertheless, they are included pending local agreement on such definitions.

- Is the reporting mechanism:
  - Clear?
  - Efficient?
  - Of appropriate reporting periodicity?
  - Available to all relevant persons and institutions?
- Is the analysis of data:
  - Done at the appropriate level for decision-making?
  - Appropriate?
  - Susceptible to proper presentation?
  - Used for decision-making?
- Do the personnel involved:
  - Have a good understanding of the value of control for the disease or syndrome?
  - Understand, show interest in, and support, their own prevention and control tasks?
  - Have enough appropriate human and material resources?
- Do the personnel involved receive appropriate:
  - Training?
  - Supervision?
- Is the feedback from intermediate and central levels:
  - Appropriate?
  - Sufficient?

[2] Several WHO programmes have produced guidelines to evaluate their specific areas of interest. These are mentioned as *References* under individual disease entries.

Some diseases or syndromes may already be the object of prevention and control programmes, or there may be contingency plans for prevention and control if a given disease is identified. This is especially true for diseases that may lead to epidemics. Once priority diseases have been selected, an approach that aims to *coordinate and streamline prevention and control activities is advisable*. To this end a central body, which may be based in the Ministry of Health, must coordinate prevention and control activities. The key decisions in disease prevention and control are those relating to the choice and implementation of method(s).

Prevention and control strategies must be appropriate not only to the disease epidemiology, but also to the infrastructure and resources of each country. National prevention and control systems should fit global goals for communicable disease prevention and control and also fit regional plans as defined by WHO Regional Offices. Feedback loops must be built into the system (for instance a regular epidemiological bulletin with tables and graphs showing progress towards targets and reports on the investigation and control of outbreaks). Personnel involved in prevention and control activities must be trained for their tasks, with ongoing in-service training at all levels, e.g. through workshops followed by close supervision in the field.

1.3.1 Levels of intervention

The following paragraphs attempt to break down prevention and control activities according to functional levels, concentrating on the various activities that would usually be carried out at each level of a country (peripheral, intermediate, central). This represents only a prototype that must be adapted to reflect the structure and level of sophistication of current health services. No matter what structure is decided upon, each level must have adequate resources and receive/provide appropriate training.

Most disease prevention and control programmes are mainly based on activities of the public health sector. In developing countries particularly, private practitioners (physicians, laboratories and pharmacies) often do not report communicable diseases despite legal requirements that they should do so, and often do not keep adequate records. They rarely receive updated information regarding public health interventions. However, more than half the contacts of patients for diagnosis are with the private sector, and for many diseases where the control intervention is case management, the provision of treatment by the private sector is important. For each prevention and control programme it is essential to evaluate the role of private practice, the extent to which private practitioners can be involved and the methods that can be used for this purpose. Examples include programmes such as the control of acute respiratory infections and of diarrhoeal diseases in children. In most cases the public programme must be organized first, if only because it is a direct government responsibility. A major factor for success is the quality and appropriateness of the formal education received by the practitioners in the public health aspects of health care.

1.3.1.1 The peripheral level

This is the first point of contact of an ill person with the health services. A primary care health worker usually sees the patient. It is normally at this level that the first opportunity for epidemiological surveillance occurs and that the need for prevention and control activities may first be noted. The staff at this level are unlikely to have much epidemiological training and may not be prepared to identify situations that require consideration of prevention and control activities. The situation is made worse by the lack of clear instructions on how to proceed in cases of outbreaks or emergencies. In order to be successful, these instructions must be simple and adapted to local conditions, and deal with a limited number of easily recognizable diseases or syndromes.

The sections on specific prevention and control methods, given below, provide details on the types of activities that can be undertaken at this level. Once a disease or syndrome has been identified, appropriate prevention and control procedure(s) must be selected and those elements that can be undertaken at the peripheral level must be implemented as early and as completely as possible. The first thing to do (and this applies to all the elements listed hereafter) is *to inform the community and mobilize their support*.

In order to motivate participants in their implementation of prevention and control measures and encourage appropriate initiative, it is also essential to provide regular feedback to:

- The members of the community.
- The staff working at more peripheral levels (in the community or, in the case of feedback from the central level, in the district or province teams).

Some prevention and control tasks at the peripheral level:

- ***Immunization*** (see also *Overview of Main Strategies*, page 17)
  - Organize immunization sessions as part of general care.
  - Set up a timetable for special immunization sessions if appropriate.
  - Identify locations and times for outreach sessions.
  - Assess the numbers to be immunized.
  - Identify requirements in material and vaccines.
  - Request material and vaccines.
  - Ensure adequate sterilization facilities.
  - Ensure that the cold chain is functioning properly.
  - Undertake immunization or assist in special immunization activities.

- ***Mass chemoprophylaxis/chemotherapy*** (see also *Overview of Main Strategies*, page 24)
  - Set out procedures for mass drug administration.
  - Assess the need for outreach distribution.
  - Set up locations and times for outreach sessions.
  - Assess numbers of individuals to be provided with drugs.
  - Identify requirements (drugs, and material if needed).
  - Request drugs and material as the case may be.
  - Ensure storage.
  - Undertake the administration of drugs.
  - Report on drug administration (amounts, estimated coverage, need for repeat action).
- ***Safe water supply and sanitation*** (see also *Overview of Main Strategies*, page 29)
  - Identify sources of potential or actual contamination of the water supply.
  - Select prevention measures (interim or permanent) to be undertaken by the community (boiling, chlorination, other).
  - Identify sources of potential or actual contamination by wastage/faecal matter.
  - Select prevention measures (interim or permanent) for the improvement of sanitation to be undertaken by the community (trench pits, fly-proofing or other improvement to latrines, rubbish disposal, hand-washing).
  - Implement health education and training activities towards the selected prevention measure(s).
  - Identify negative and positive elements towards implementation of the measure(s).
  - Identify help to be requested from specialized services in the community or at more central levels.
  - Undertake action to obtain such help and mobilize the assistance of the community.
- ***Food safety*** (see also *Overview of Main Strategies*, page 28)
  - Inform the community (particularly food-handlers and vendors) and enlist their support.
  - Identify sources of potential or actual contamination of food supplies.
  - Select prevention measures to be undertaken within the community (hand-washing, proper cooking and conservation of foods).
  - Implement health education and training activities towards the selected measure(s).
  - Identify negative and positive elements towards the implementation of these measure(s).
  - Identify help to be requested from specialized services in the community or at more central levels.
  - Undertake action to obtain such help and mobilize the assistance of the community in implementing the solutions.
- ***Injection safety/sterilization*** (see also *Overview of Main Strategies*, page 31)
  - Apply the rules of injection safety and sterilization.
- ***Vector control*** (see also *Overview of Main Strategies*, page 37)
  - Identify vector sources of potential or actual infection.
  - Identify help/advice to be requested from specialized services in the community or at more central levels.
  - Undertake action to obtain such help and mobilize the assistance of the community in implementing the solutions.
- ***Case management*** (including transfer to the next level facility if appropriate) – this involves not only implementation but also training activities in order to:
  - Ensure diagnosis (or recognition of syndrome), including clinical interpretation and complementary examinations.
  - Detect cases for specific diseases, such as pulmonary infectious tuberculosis (in adults attending with cough of long duration) and leprosy (in individuals with skin lesions) even if the patient has attended for other reasons; this also applies to family contacts (diagnosis and chemoprophylaxis of tuberculosis in child contacts of infectious cases).
  - Inform/counsel the patient on the expected outcome and alternatives.
  - Manage or transfer the case, according to local capacities for providing care.
  - Set up treatment (for some diseases, provide treatment free of charge).
  - Educate the patient regarding treatment.
  - Follow-up:
    - For most problems and specially in the private sector, the patient is expected to be responsible for obtaining and taking the medicines, and for returning for follow-up;
    - For some diseases of public health importance, where patients may represent a risk for the community (e.g. tuberculosis), public health facilities are responsible for facilitating and monitoring the intake of drugs and the outcome of treatment.
  - Reporting, with different characteristics according to the disease and the risk to the community.

In all of the above areas, an essential task of health staff at peripheral level is to increase the awareness of community members and mobilize their support

At the peripheral level also, the role of *nongovernmental organizations (NGOs)* working in the field, including mission health facilities, as well as the role of the private sector, has become increasingly important in disease prevention and control. These partners must be considered in the preparation and implementation of prevention and control activities at local and other levels where possible.

1.3.1.2 The intermediate level collects and analyses data, prepares activities and implements them or organizes their implementation throughout the district or province. Its main function from the perspective of communicable disease prevention and control is the ongoing analysis of data from the periphery in order to identify changes in disease trends and undertake responses such as investigation and intervention, including ongoing training of staff. The effectiveness of interventions can be monitored using the same data sources. Some countries may have 2 intermediate levels (e.g. district and region) – this will depend on the size of the country and on the structure and level of development of the health services. In many cases the professionals at this level will have other tasks in the area of programme management – tasks must be manageable so that prevention and control activities are perceived as of immediate relevance. Although it may be appropriate for the central level to undertake outbreak investigations, it is generally preferable that the intermediate level ensure subsequent prevention and control activities where this is technically feasible.

- ***Some prevention and control tasks at the intermediate level:***
  - Analyse data from the peripheral level (epidemiological links, trends, achievement of targets for prevention and control).
  - Investigate and follow up suspected outbreaks.
  - Feed information back to the peripheral level.
  - Provide material and technical support (including training and supervision) to the peripheral level.
  - Implement prevention and control activities through the peripheral level if appropriate.
  - Report to the central level on:
    - Suspected/confirmed outbreaks
    - Surveillance of endemic diseases
    - Achievement of prevention and control interventions.
  - Identify resources needed (technical, human, financial).
  - Provide resources or request them from the central level.
  - Organize those aspects of case management that cannot be undertaken at the peripheral level.

1.3.1.3 The central level is usually also at the national level where policies on infectious disease are set and where resource allocation most often occurs. The central level in some large countries may actually be at a federal level. The central level plays a key role in supporting the intermediate levels by providing services that are not available elsewhere, such as high-level epidemiological skills, laboratory facilities or tertiary health care facilities. The central level must be able to deal with outbreaks of national importance in a coordinated fashion. It must also liaise with other countries and international agencies in the response to outbreaks of international significance and in the management of diseases that are subject to the *International Health Regulations* or that are internationally agreed targets for control or elimination. It may have access to alternative data sources such as national reference laboratories where the identification of unusual organisms should trigger a response.

- ***Some prevention and control tasks at the central level:***
  - Coordinate national prevention and control activities, and provide overall support to these activities.
  - Provide laboratory diagnosis data not available at the intermediate level (use regional or international reference laboratories if required).
  - Analyse data from the intermediate level (epidemiological links, trends, achievement of prevention and control targets).
  - Support the intermediate level for outbreak prevention and control (case management, laboratory, epidemiology, training, logistics).
  - Provide feedback to the intermediate level and, as appropriate, to the peripheral level.
  - Report to WHO as required (*International Health Regulations*, specific needs of prevention and control programmes).
  - Identify requirements and, if necessary, obtain assistance from international or bilateral sources.

At all levels, *collaboration with non-medical sectors* such as education, agriculture, veterinary medicine and environment must be considered where appropriate (e.g. water or food-borne diseases, vector-borne diseases, anthropozoonoses, mass drug administration).

2. OVERVIEW OF MAIN CONTROL STRATEGIES*

** Excluding case management, which is dealt with individually for each disease/syndrome*

2.1 Immunization

WHO recommends *routine immunization* of all children for the following diseases:

Disease	Comments
Diphtheria, hepatitis B, measles, pertussis, poliomyelitis, maternal/neonatal tetanus	
Haemophilus influenzae type b	Subject to resources
Yellow fever	Endemic countries
Tuberculosis	High-incidence areas

Other situations for possible recourse to immunization include:

Disease	Relevant situations
Cholera	Refugee camps
Japanese encephalitis	High-risk populations in certain endemic areas
Influenza	Persons at risk of severe disease. e.g. aged >50
Meningococcal meningitis (A & C)	During outbreaks; epidemic areas (meningitis belt)
Plague	Exceptionally during epidemics
Rabies	Post exposure; high-risk individuals
Typhoid fever	Susceptible subjects exposed to risk
Rubella	Girls or total population

NOTE: Immunization against anthrax may exceptionally be considered among high-risk occupational groups.

2.1.1 Circumstances and groups requiring routine immunization

Infants and children.

Pregnant women (prevention of maternal and neonatal tetanus).

Adults and those aged 50 and over (boosters, especially tetanus).

- **Immunization for high-risk groups**
  - Occupational high-risk groups (anthrax, plague, leptospirosis).
  - Others (refugees and internally displaced persons; hospital settings, etc.).
  - Special public health strategies for control or eradication.
- **Outbreak response immunization, for instance:**
  - Measles in refugee situations (refugee populations).
  - Cerebrospinal (meningococcal) meningitis outbreak (immunization of total population).
  - On detection of confirmed poliomyelitis (immunize under-5s in appropriate geographic areas).
  - In some cases, on detection of 1 case of clinical diphtheria (immunization of contacts).

2.1.2 Getting vaccines to those who need them

- **Use of routine clinics** (MCH, other)
  - Special vaccination sessions at routine clinics.
  - Outreach vaccination stations (and "mobile clinics").
  - Clinics serving large populations should preferably organize immunization sessions daily.
  - Clinics serving smaller populations (< 40 000) may wish to calculate a required number of sessions per month. This will depend on the size of the target population (if unknown, this can be assumed to be 3% of the total); number of contacts required for a child to be fully immunized; average number of contacts per month; number of children that can be served by the health centre staff in one session. It is advisable for each centre to hold one session per week at least, on the same day.

It is important to come to an agreement with the community about the days on which immunization sessions will be held.

- **Supplemental immunizations**
  - Special vaccination sessions at routine clinics.
  - Outreach vaccination stations (and "mobile clinics") – these should be held:
    - at regular fixed intervals (1 to 6 months)
    - preferably in the same place on each occasion, in order to facilitate attendance.

Some mobile clinics may be held "as needed". Discuss with community leaders and agree on suitable days, time and place for both outreach and mobile clinics.

2.1.3 Immunization schedules

Schedules for routine immunization are normally determined by the national health authority. Schedules for other immunizations (e.g. meningococcal meningitis) depend on local circumstances. For the following vaccines, one dose is sufficient:

- BCG.
- Yellow fever.
- All booster doses.

Measles and rubella vaccines need one dose plus a second opportunity for a dose.

The following vaccines normally require more than 1 dose to complete the initial course:

- Diphtheria, tetanus, pertussis, poliomyelitis, Hib, hepatitis B (as mono-doses or as combination vaccines).

2.1.4 Stock management

- **How many doses should be ordered?**

  The frequency and amount of orders will depend on:
  - Distance from supplies
  - Storage capacity of the cold chain at local level
  - Local administrative regulations.

ROUTINE IMMUNIZATION: The amount to be ordered for each quarter or each month is a *pro rata* of the yearly requirements, which is estimated from:
  - The size of the birth cohort
  - The coverage rate expected
  - The number of doses expected for one full immunization schedule
  - A correction factor for wastage or unused vaccines.

AD HOC IMMUNIZATION: The number of vaccine doses to be ordered at a time is estimated from:
  - The size of the population to be immunized
  - The coverage rate expected (usually 100% of the population to be immunized)
  - The number of doses expected for one full immunization schedule.

- **Where to obtain vaccines**

In most countries, vaccines will be obtained through the central Ministry of Health. In the case of emergency *ad hoc* immunization, vaccines may be delivered through nongovernmental or intergovernmental organizations such as WHO.

2.1.5 Managing vaccines during transport and maintaining stocks

The cold chain must never be broken.
Any vaccine may be damaged by heat.
Some vaccines are damaged by freezing.

In order to maintain the cold chain that protects the vaccines between manufacture and point of use, vaccines must be:

- Collected from the airport immediately on arrival.
- Transported and stored at correct temperature (central/regional/district stores and health centres).
- Transported at correct temperature to outreach sites.
- Kept cold during immunization sessions.

Refrigerators (powered by gas, kerosene, solar energy, or electricity – the latter are the least costly to run and the easiest to maintain) must be large enough to hold:

- A 1-month supply of vaccines, **and**
- A 1-week to 2-week reserve stock of vaccines (25-50% of 1-month supply), **and**
- Frozen ice packs/water bottles in bottom of refrigerator to keep it cool if power fails.

Leave the refrigerator half-empty (to allow air to circulate).

Cold boxes (insulated container lined with frozen ice packs) are also needed to transport vaccines and to store them when the refrigerator is out of order. Health centres require enough cold boxes to hold:

- A 1-month supply of vaccines, **plus**
- A 1-week to 2-week reserve stock of vaccines.

Vaccine carriers (small, insulated containers that can be lined with frozen ice packs to keep vaccines and diluents cold) are used for transport to outreach centres and for temporary storage during immunization sessions. They keep the temperature low for 24 to 72 hours.

Ice packs (square plastic bottles filled with frozen water) are used inside cold boxes and vaccine carriers. It takes 48 hours to freeze an ice pack completely; 2 sets are needed, one set being frozen while the other set is in use.

Cold-chain monitoring equipment (thermometers, cold-chain monitoring cards, freeze-watch indicators and vaccine vial monitors) are needed to keep track of the temperatures to which vaccines and diluents are exposed.

Storage temperatures for vaccines normally are **+2°C to 8°C.** The following vaccines must never be frozen: DTP, DT, Td, TT, hepatitis B, Hib, meningococcal meningitis. If you suspect the product has been frozen:

- Shake the vial and examine it after 30 minutes.
- If there is heavy sedimentation and clear or a nearly clear supernatant fluid, freezing has occurred and the vaccine must not be used.

The following vaccines are not damaged by freezing: *BCG, OPV, measles, yellow fever.*

DILUENTS

Only use diluents supplied by the manufacturers and specific for the vaccine.
Diluents must be shipped together with the vaccine they will be used for. Before reconstitution, diluents must be cooled to below +8°C in order to avoid heat damage to the vaccine.
Reconstituted BCG, measles, yellow fever and combination vaccines must be kept cooled and be discarded within 6 hours of reconstitution.
Freeze-dried vaccines need not be kept at –20°C but may be kept at +2°C to +8°C until reconstituted.

Before introducing new vaccines or implementing routine or mass immunizations:

- Assess cold chain storage capacity and cold chain procedures at all administrative levels.
- Develop and implement plans to modify cold chain storage capacity or adjust the supply period and procedures if needed.

Storage volumes (vial plus packaging) range from 20 to 95 cubic centimetres per dose for single-dose vaccines and from 2.5 to 5 cubic centimetres per dose for multiple doses, according to the vaccine. Diluent for freeze-dried vaccines double the amount of storage space needed.

2.1.6 Monitoring and reducing vaccine wastage

Monitoring vaccine wastage becomes increasingly important as the costs of the vaccine rise. Monitoring increases ordering accuracy and reduces wastage by providing reliable data for estimating the number and size of vials to be ordered. It also serves as a tool for improving the practices of health centres when wastage rates are found to be unacceptably high.

Strategies to reduce vaccine wastage include the following:

- Careful planning of vaccine ordering and distribution.
- Use of both single-dose and multi-dose vials.
- Careful maintenance of the cold chain.
- Implementation of WHO's multi-dose vial policy, when appropriate.

2.1.7 Immunization safety (See also *Injection safety*, page 31).

- **Injection equipment (types, disposal)**

TYPES OF INJECTION EQUIPMENT

- *"Autodisable"* syringes, designed so that it is impossible to use them more than once, present the lowest risk of person-to-person transmission and are the preferred type of equipment, particularly for mass immunization programmes.
- As regards *standard disposable* syringes, WHO and UNICEF have issued a joint statement that these will not be acceptable after the end of 2001 (see box).
- *Sterilizable* or *reusable* syringes and needles are neither practical nor economical for mass immunization sessions and must not be used for this purpose, although they can be used for individual use.

Different sizes of syringes and needles are needed for different uses.

NOTE: *Prefilled single-use* syringes – not in general use – are occasionally used for hepatitis B or tetanus toxoid.

WHO, UNICEF and UNFPA urge that by the end of 2001 all countries use only "autodisable" syringes or syringes designed to be sterilized, Standard disposable syringes should no longer be used for immunization. By the end of 2003, all countries should use only "autodisable" syringes for immunization.
All partners of immunization services are requested to support not only the purchase but also the safe administration of vaccines, "autodisable" syringes and safe management of waste.
WHO and UNICEF recommend that countries exert maximum effort to ensure that procedures for injection safety are rigorous – including routine use and monitoring of indicators of sterilization while sterilizable equipment is still used. Partner agencies involved in immunization programmes at country level should provide maximum support for the strengthening of safe injection practices.

DISPOSABLE OR REUSABLE?

- Disposable/single-use syringes and needles:
  - Use once, collect in a disposal box, burn and bury.
- Reusable syringes and needles (**not advisable for mass immunization**):
  - Flush, soak, clean.
  - Sterilize.
  - When they can no longer be used, collect in a disposal box, burn and bury.

CONTROLLING THE SAFETY OF INJECTIONS
Rigorously adhere to sterilization procedures.
Do not recap syringes.
Immediately discard in a "sharps" box to prevent needlestick injury.
Dispose of by incineration and burial.

- **Sterilization equipment:**

Each immunization centre needs:

  - 1 washbasin
  - 2 forceps
  - 1 steam sterilizer (single rack up to 40 syringes, or double rack)
  - 1 indicator for Time, Steam and Temperature (enough for 1 month)
  - 1 hard water pad (optional)
  - 1 timer (20 minutes)
  - 1 stove, fuel, and matches.

2.1.8 Information

Local government officials and community leaders can help in deciding when and where to hold immunization and outreach sessions, and can recommend contacts to mobilize the community. Health personnel should train local people to help with:

- Patient flow
- Completion of immunization card
- OPV administration
- Health education and other tasks.

If the client has come to the health centre (or outreach site) for some reason other than immunization, respond to his/her needs first.

Inform the client about immunization. The 5 essential messages are:

Date and time of next immunization session.
Place of next immunization session (preferably this should always be the same).
Number of visits still needed for full immunization.
Side-effects that can occur.
Treatment of side-effects.

2.1.9 Assessment of immunization activities

- *Set targets* for immunization; these are usually defined at national level by the national authorities and must be referred to at regional and district levels.
- *Record immunizations* when they are given:
  - On the child's immunization card
  - On a tally sheet (for child immunizations, women of childbearing age, and children protected at birth (PAB) against tetanus).

List types and number of vaccines given at the end of each immunization session.

- *Report numbers of immunizations* given each month, by vaccine and by dose for the following groups:
  - Infants
  - Children aged 1-5 years
  - Pregnant women
  - Non-pregnant women of childbearing age.
- *Assess* immunization coverage, using an immunization monitoring chart.
- *Compare cumulative monthly totals* to the targets set for immunization.
- *Assess outcome*: trends in incidence, surveillance of target diseases.

2.1.10 Adverse events following immunization

Programme managers and vaccinators need to know what is normal – what reactions are to be expected, and how often? Without this background information, it is impossible to know whether or not these adverse events are occurring more frequently than expected. Most vaccine reactions are mild, settle with little or no treatment and have no long-term consequences. More serious reactions are rare.

Summary of common minor vaccine reactions

Vaccine	Local reaction (pain, swelling, redness)	Fever	Irritability, malaise, non-specific symptoms
BCG	Common	-	-
Hib	5–15%	2–10%	-
Hepatitis B	Adults up to 30% Children up to 5%	1–6%	-
Measles/MMR	Up to10%	Up to 5%	Up to 5%
Oral polio (OPV)	None	Less than1%	Less than 1% [a]
Tetanus/DT	Up to 10% [b]	Up to 10%	Up to 25%
DTP [c]	Up to 50%	Up to 50%	Up to 60%

[a] Diarrhoea, headache and/or muscle pains.

[b] Rates of local reactions are likely to increase with booster doses.

[c] Whole-cell pertussis vaccine (rates are lower for acellular pertussis vaccine).

Summary of rare, serious vaccine reactions, onset interval and rates

Vaccine	Reaction	Onset interval	Reactions per million doses
BCG	Suppurative lymphadenitis	2–6 months	100–1000
	BCG osteitis	1–12 months	0.01–300
	Disseminated BCG-itis	1–12 months	0.19–1.56
Hib	Not reported		
Hepatitis B	Anaphylaxis	0–1 hour	1–2
Measles/MMR [a]	Febrile seizures	5–12 days	330
	Thrombocytopaenia (low platelets)	15–35 days	30
	Anaphylaxis	0–1 hour	about 1
Oral polio (OPV)	Vaccine-associated paralytic poliomyelitis	4–30 days	0.4 [b]
Tetanus	Brachial neuritis	2–28 days	5–10
	Anaphylaxis	0–1 hour	0.4–10
Tetanus–diphtheria	None, other than those attributable to tetanus reactions		
DTP	Persistent (>3 hrs) inconsolable screaming	0–24 hours	up to 60 000 (0.1–6%)
	Seizures	0–3 days	80–570 [c]
	Hypotonic, hyporesponsive episode	0–24 hours	30–990
	Anaphylaxis/shock	0–1 hour	20
	Encephalopathy (risk may be zero)	0–3 days	0–1

[a] Reactions (except anaphylaxis) do not occur if already immune (~90% of those receiving a second dose); children >6 years unlikely to have febrile seizures.

[b] Risk higher for first dose.

[c] Seizures are mostly febrile; rate depends on past history, family history and age, with lower risk in infants

(After*: Immunization Safety Surveillance*. WPRO/EPI/99 Manila: WPRO, 1999)

The information in the above Tables can be used to:

- Anticipate reactions for a specific immunization programme (type and number).
- Identify events that are unrelated to immunization (e.g. when outside the time window).
- Compare reported with expected rates of reactions (the efficiency of reporting).
- Trigger an investigation if the reported rate appears excessive.

As vaccine-preventable diseases continue to decline, there are increasing concerns about the risks associated with vaccines. Damaging statements regarding vaccine-related adverse effects, if not rapidly and effectively dealt with, can undermine confidence and ultimately have dramatic consequences for immunization coverage and disease incidence. In order to avoid poorly informed and hasty decisions regarding immunization and consequent potential damage to public health in the long term, WHO has established a Global Advisory Committee on Vaccine Safety. This will provide an independent scientific assessment of vaccine safety issues and develop a network of collaborating centres to carry out this work on a global basis.

2.1.11 Recommended reading before setting up or reviewing an immunization programme

WHO. *Immunization in practice*. WHO/EPI/TRAM/98.01 to WHO/EPI/TRAM/98.11(1998)

Module 1 WHO/EPI/TRAM/98.01: Target diseases
Module 2 WHO/EPI/TRAM/98.02: EPI vaccines
Module 3 WHO/EPI/TRAM/98.03: The cold chain
Module 4 WHO/EPI/TRAM/98.04: Ensuring safe injections
Module 5 WHO/EPI/TRAM/98.05: Organizing immunization sessions
Module 6 WHO/EPI/TRAM/98.06: During a session: registering and assessing clients
Module 7 WHO/EPI/TRAM/98.07: During a session: preparing vaccines
Module 8 WHO/EPI/TRAM/98.08: During a session: giving immunizations
Module 9 WHO/EPI/TRAM/98.09: After a session
Module 10 WHO/EPI/TRAM/98.10: Communicating with parents and involving communities
Module 11 WHO/EPI/TRAM/98.11: Monitoring immunization coverage

(V&B documentation centre: E-mail: vaccines@who.int; Fax: 0041 22 791 4227)

WHO. *Immunization Safety Surveillance – guidelines for managers of immunization programmes on reporting and investigating adverse events following immunization.* Manila: WHO Regional Office for the Western Pacific, 1999. WPRO/EPI/99.01

WHO. *Surveillance of adverse effects following immunization: field guide for managers of immunization programmes.* Geneva: WHO, 1993. WHO/EPI/TRAM/93.02 Rev.1 http://www.who.int/gpv-documents/DocsPDF/www9541.pdf

2.2 Mass drug distribution (chemoprophylaxis/chemotherapy)

Mass chemoprophylaxis or chemotherapy campaigns are not related to individual case management. They deal with the community rather than the individual and are not necessarily dependent on the effective presence of signs or symptoms. Their purpose is to ensure the protection of a community against infection or to treat members of the community where the disease is highly prevalent, without submitting individuals to a preliminary clinical or parasitological investigation. The strategic aspects of mass drug distribution are usually decided at national level and will not be discussed here. The following points must be considered when implementing a mass chemoprophylaxis or chemotherapy campaign.

2.2.1 Analysing the situation

- Collect existing information on the distribution of infection and disease in your area.
- Identify characteristics of your area that put people at risk of the disease and collect information on what happens in other areas similarly at risk, in order to propose action without having to resort to surveys or other additional investigations.
- Review resources, experiences and linkages to other programmes:
  - Within the health sector (Ministry of Health and private health sector) to identify the responsibilities that can be assigned to them.
  - Within other sectors (government and nongovernmental organizations, private sector) in order to identify:
    - ◊ resources for drug distribution, information campaigns, etc. (e.g. teachers and other staff, transport, information, equipment).
    - ◊ populations that can be reached through these resources (e.g. employees, schoolchildren).

2.2.2 Choosing a mass drug administration strategy (if not already done)

Systematic or community-wide distribution

Disease	Drug	Amount	Target	Periodicity
Filariasis	Albendazole +	400 mg	Community > 2 yrs	Once a year
	DEC	(6 mg/kg)		
(if onchocerciasis co-endemic)	Albendazole +	400 mg	Individuals > 5 years or 15 kg (in practice, individuals taller than 90 cm)	Once a year
	Ivermectin	150 microg/kg administered according to height		
Soil-transmitted Intestinal helminths	Albendazole	400 mg	School-age children	3 times a year
	or Levamisole	40 mg tablets	Pre-school age	Twice a year
	or Mebendazole	500 mg	Pregnant women	Once a year (2d/3d trim.)
Onchocerciasis	Ivermectin	150 microg/kg administered according to height	Individuals > 5 years or 15 kg (in practice, individuals taller than 90 cm)	Once a year (twice a year in some areas)
Schistosomiasis (> 20% haematuria)	Praziquantel	40 mg/kg	School-age children	Once a year
Non-venereal treponematoses	Benzathine penicillin	600 000/1 200 000 units IM	Community-wide	Once a year

Selective distribution

Disease	Drug	Amount	Target	Periodicity
Measles	Vitamin A	Capsules 200 000 IU Oily solution 100 000 IU/ml	Children 2 to 5 yrs Children < 2 yrs	Once a year Twice a year
Meningococcal meningitis *(chemotherapy)*	Chloramphenicol	Oily suspension IM Vials 0.5 g per 2 ml Dosage: see meningococcal disease	All patients	Once when needed

NOTE: In epidemic-prone regions, mass administration of a locally effective antimalarial treatment to the whole population at risk or for fever cases only (depending on epidemiology and available logistic support) may help control malaria epidemics at an early stage. Mass drug administration should always be combined with transmission control. In rare circumstances, appropriately timed mass antirelapse treatment with primaquine may help prevent seasonal *P. vivax* epidemics. Antimalarial drugs should be used according to the country's preparedness plan of action.

- **Periodicity of administration**

Drug administration can occur on a given day or week at district or national level, or can be staggered over several days or weeks throughout the country.

- **Mechanisms of administration**
  - House-to house: ensures full coverage but is labour-intensive especially in sparsely populated areas.
  - Booths: distribution booths set up at sites selected to be accessible to the community (suitable in urban/semi-urban populations but depends on motivation of beneficiaries).
  - Meeting places: markets, bus/railway stations, other gatherings.
  - Private clinics/ pharmacies.
  - Workplace distribution.
  - Special groups: e.g. schoolchildren for schistosomiasis; camps (displaced persons); army and prison health services, etc.
  - Elements such as fortified salt, condoms, etc. often require a recourse to the techniques of marketing and distribution, which can be handled by specialized marketing agencies.

Decisions on timing and mechanism of administration must be taken in close cooperation with the community and its representatives.

2.2.3 Estimating drug requirements

Population-wide chemotherapy/prophylaxis in a population of 100 000:

- **Filariasis**

Albendazole	100 000 tablets @ 400 mg
Ivermectin	300 000 tablets @ 3 mg
Diethylcarbamazine	275 000 tablets @ 100 mg 500 000 tablets @ 50 mg

- **Intestinal helminths (100 000 children)**

Albendazole	100 000 tablets @ 400 mg
Levamisole	200 000 tablets @ 40 mg
Mebendazole	100 000 tablets @ 500 mg

- **Onchocerciasis**

Ivermectin	300 000 tablets @ 3 mg

- **Schistosomiasis**

Praziquantel	250 000 tablets @ 600 mg

- **Non-venereal treponematoses**

Benzathine benzylpenicillin	450 000 vials of 5 ml (2 400 000 units):

NOTE: It is advisable to add 5% to 10% contingency after calculating requirements, allowing for losses, pilferage, etc.

Chemotherapy/prophylaxis for part of the population (per 1000 persons to be reached)

- **Measles:**

Vitamin A	800 capsules @ 200 000 units 200 ml oral oily solution @ 100 000 units/ml

- **Meningococcal meningitis (mass chemotherapy)**

Chloramphenicol	2000 to 3000 2-ml vials of 1M oily suspension

Purchases should, whenever feasible and appropriate, be undertaken by the Ministry of Health through the Procurement Office of WHO or UNICEF with the assistance of their representatives.

2.2.4 Storage requirements

To give an idea of what is required, the storage space for 100 000 tablets of albendazole is about 0.6 cubic metres; requirements for other drugs in tablet form are of the same order of magnitude.

The drugs need to be kept dry and secure, with a good stocks recording system. Tablets can be kept in non air-conditioned stores – efforts must, however, be made to keep the room temperature below 30°C (86°F).

Special bulk transport may have to be arranged if the unit deals with a large population.

2.2.5 Resources

- ***Training and capacity-building*** Staff must be trained in the techniques of distribution before mass distribution programmes are initiated. Distributing agents can be:
  - Members of the regular health staff.
  - Non-medical organized personnel, for instance teachers – it is important to clarify the roles and responsibilities of this category of staff and to provide special training and incentives (not necessarily monetary) for these latter groups. Group training sessions often also provide an efficient way of distributing drugs if the participants take their drugs back with them.
- ***Preparing budget and resource requirements*** In addition to drugs, the following supplies and resources must be prepared:
  - Recording forms and material
  - Transport
  - Training
  - Supervision
  - Equipment (portable scales, tumblers, water bottles, spoons … as appropriate).

As an example, one budget for the first year of a helminth control programme in Africa (excluding baseline data collection) amounted to about US$ 40 000 for 100 000 school-age children (Drugs, 64%; Supervision and outreach, 23%; Training, 12%, Sundries, 1%).

2.2.6 Implementation (including supervision, monitoring and evaluation)

Populations eligible for community-wide treatment or prophylaxis must include everyone, with the following exceptions (unless otherwise decided):

- Very sick people
- Children under 2 years (in some circumstances, under 5 years)
- Pregnant women.

Ingestion of drugs must always be supervised by the person giving the drug.

Supervision, monitoring and evaluation

Monitoring approaches must be adapted to the size and resources of the programme itself. Monitoring indicators include:

- *Process/output* indicators such as:
  - Number of persons treated (calculate rates using as denominator the number of targeted or eligible persons, or the total population).
  - Availability of supplies.
  - Availability of staff resources (including training).
  - Drug coverage:
    - Each peripheral unit/drug distributor must report on the number of individuals receiving the drug and on the coverage rate in each geographical unit
    - Supervisors must check the reported coverage rates through surveys in sentinel and spot-check sites.
- *Outcome* indicators (e.g. changes in the prevalence or incidence of parasite infections).
- *Impact* indicators (e.g. proportion of children who present specific signs or symptoms – these must be determined in advance).

Some mass chemotherapy/chemoprophylaxis programmes (e.g. filariasis, onchocerciasis, non-venereal treponematoses) will be evaluated externally (implementation and impact) at intervals of 2 to 3 years. The findings of the evaluation must be used to strengthen or revise programme strategies.

2.2.7 Adverse effects

- Inform the community in advance that adverse effects, although rare, can occur and list the main possible adverse effects.
- Ensure provision of, and access to, appropriate attention for all those who present adverse effects.
- Advise community leaders of places where help is available for the management of adverse effects.
- All serious adverse effects (fatal, life-threatening or disabling, or resulting in prolonged hospitalization) must be reported to the manager of the National Control Programme.

2.2.8 References and further reading

WHO. *Preparing and implementing a national plan to eliminate lymphatic filariasis (in countries where onchocerciasis is not co-endemic).* WHO: Geneva. WHO/CDS/CEE/2000.15.

WHO. *The programme to eliminate lymphatic filariasis – essential elements for medical personnel in onchocerciasis co-endemic countries.* WHO: Geneva. WHO/CDS/CEE/2000.13.

WHO. *Helminth control in school-age children.* WHO: Geneva. WHO/CDS/CPE (in preparation).

APOC/WHO. *Community-directed treatment with ivermectin (CDTI).* BP 549 Ouagadougou, Burkina Faso.

2.3 Five keys to food safety

2.3.1 Keep clean

Why? While most microorganisms do not cause disease, dangerous microorganisms are found in soil, water, animals and people. These are carried on hands, wiping cloths and utensils, especially cutting boards; contact can transfer them to food and cause foodborne diseases.

How?

- Wash your hands before handling food and often during food preparation.
- Wash your hands after going to the toilet.
- Wash and sanitize all food contact surfaces and equipment.
- Protect kitchen areas and food from insects, pests and other animals.

2.3.2 Separate raw and cooked food

Why? Raw food, especially meat, poultry and seafood, and their juices, can contain dangerous microorganisms that may be transferred during food preparation and storage.

How?

- Separate raw meat, poultry and seafood from other foods.
- Use separate equipment and utensils such as knives and cutting boards for handling raw foods.
- Store food in containers to avoid contact between raw food and prepared food.

2.3.3 Cook thoroughly

Why? Proper cooking kills almost all dangerous microorganisms. Studies show that cooking food to a temperature of 70ºC can help ensure the food is safe for consumption. Foods that require special attention include minced meats, rolled roasts, large joints of meat and whole poultry.

How?

- Cook food thoroughly, especially meat, poultry, eggs and seafood.
- Bring foods like soups and stews to boiling to make sure that they have reached 70º C. For meat and poultry, make sure juices are clear, not pink.
- Reheat cooked food thoroughly.

2.3.4 Keep food at safe temperatures

Why? Food microorganisms can multiply very quickly if food is stored at room temperature. By holding at temperatures below 5ºC or above 60ºC, the growth of microorganisms is slowed down or stopped. Some dangerous microorganisms still grow below 5ºC.

How?

- Do not leave cooked food at room temperature for more than 2 hours.
- Refrigerate promptly all cooked and perishable food (preferably below 5ºC).
- Keep cooked food piping hot (more than 60ºC) prior to serving.
- Do not store food too long even in the refrigerator.
- Do not thaw frozen food at room temperature.

2.3.5 Use safe water and raw materials

Why? Raw materials, including water and ice, may be contaminated with dangerous microorganisms and chemicals. Toxic chemicals may occur in damaged and mouldy foods. Care in selection of raw materials and simple measures such as washing and peeling may reduce the risk.

How?

- Use safe water or treat the water to make it safe.
- Select fresh and wholesome foods.
- Choose foods processed for safety, such as pasteurized milk.
- Wash fruits and vegetables, especially if eaten raw.
- Do not use food beyond its expiry date.

More information at: www.who.int/fsf

2.4 Safe water and sanitation

Even today, approximately 1 person in 4 worldwide remains without proper access to safe water and 1 in 3 has no access to appropriate sanitation. This leads to high morbidity and mortality from water-related diseases.

2.4.1 Safe water

Each person should ideally have at least 20 litres of water a day for drinking, cooking and washing. Health facilities need 40-60 litres of water a day to maintain adequate levels of hygiene. Every family must know how to treat water so that it will be safe for drinking.

Simple inexpensive measures will provide clean water for individuals in developing countries without having to wait for years until the required infrastructure investments are put into place. Piped water, or water that is delivered in trucks or drums, must be adequately chlorinated. Other sources of water are usually contaminated (e.g. rivers, shallow well). Relevant measures may include closing the water source or providing another source of safe water. If that is not possible, people using the water must be informed how to make the water safe:

1. ***Boiling*** water is the most commonly used way of making water safe for drinking, but it requires fuel that may be too scarce or too expensive.
2. Where fuel is scarce, ***chlorination*** is less expensive than boiling water. Even in conditions of poor sanitation and hygiene, if the water collected for household water supply – however tainted – is chlorinated appropriately, there is a decrease in diarrhoeal diseases. The stock solution of chlorine must be stored in a closed container, in a cool dark place and used within 1 month; add to water as follows:

Stock solution[3]	Added volume of water
0.6 ml or 3 drops	1 litre
6 ml	10 litres
60 ml	100 litres

   Chlorinated water must stand for 30 minutes before use. If the water is cloudy or turbid, it must be either:

   - Filtered before chlorination, or
   - Boiled vigorously rather than chlorinated.

3. Another small-scale and cost-effective immediate technique is ***solar water disinfection*** (SODIS) by which transparent plastic bottles filled with water are placed horizontally on a flat surface and exposed to solar light for about 5 hours in order to let the ultraviolet light in solar irradiation kill the pathogens. The effect of solar irradiation can be enhanced by painting the bottom half of the bottled black or placing them on a black background.

[3] **Stock solution of chlorine:** The most common solution is household Clorox or Javel; the solution can be prepared by adding the listed amount of any one of the following products to 1 litre of water:

Product (% indicates concentration by weight of available chlorine)	**Amount for 1 litre**
Calcium hypochlorite powder (70%)	15 grams
Bleaching powder/Chlorinated lime (30%)	33 grams
Sodium hypochlorite solution (3.5%)	350 millilitres
Sodium hypochlorite solution (5%)	250 millilitres
Sodium hypochlorite solution (10%)	110 millilitres

Environmental health experts can test water using DPD (diethyl-p-phenylenediamine) kits to see if the levels of residual chlorine are high enough so that the water is safe for drinking. The recommended levels of residual chlorine for an area where there is an epidemic of diarrhoeal disease are:

- All sampling points in a piped water system 0.5 mg/litre
- Standposts (where applicable) 1.0 mg/litre
- Tanker trucks, at filling 2.0 mg/litre
- Water-treated with stock solution of chlorine 0.2-0.5 mg/litre

Storing and using water safely

Once water has been made safe, it must be stored and used safely, or it can become contaminated again. The following steps can prevent recontamination.

- *Store water for laundry use in a **narrow-mouthed** container with a cover.* The opening must be so small that a hand cannot fit in. If possible, store drinking-water apart from water for other uses. Do not let young children or animals have access to the family's drinking water.
- *Pour water **from** the container.* If that is not possible, a long-handled dipper, which is not used for anything else, must be used to take water from the container. The container must be cleaned every day with soap and water or with chlorine stock solution.

2.4.2 Hand-washing

Studies of diarrhoea show that washing one's hands with soap and water (where soap is not available one may use ash) reduces the incidence of diarrhoea by up to 35%. Hands must be washed:

- After defecation
- After any direct or indirect contact with stools
- Before preparing food
- Before eating
- Before feeding children.

2.4.3 Sanitation

Improvements in water supply and environmental sanitation will reduce the incidence of diarrhoeal diseases in the long run. Even where sanitation is poor, simple measures help ensure the safe disposal of stools and must be followed – particularly in the case of outbreaks of diarrhoeal diseases:

- No defecation on the ground – cover stools with earth (or use trench latrines that are regularly covered).
- No defecation near a water supply.
- Disposal of children's stools in toilets or latrines or buried in the ground.
- Washing hands with soap (or ash) after any contact with stools.
- Build and use latrines – a pit latrine 2 metres deep with an opening of 1 metre by 1 metre can be used by a family of 5 persons for a period of 2 to 4 years. Latrines must be sited downhill and away from sources of drinking-water (at least 30 metres), washed daily and regularly disinfected with cresol or bleaching powder.

2.4.4 References

WHO. *Epidemic Diarrhoeal Disease Preparedness and Response.* WHO/EMC/DIS/97.3

Franceys R, Pickford J, Reed R. *A Guide to the Development of On-site Sanitation.* Geneva: World Health Organization, 1992. ISBN 92 4 154443 0.

WHO: *Cholera and Other Epidemic Diarrhoeal Diseases Control – Fact Sheets on Environmental Sanitation.* WHO/EOS/96.4

http:// www.worldwaterday.org

2.5 Injection safety and sterilization

Worldwide, unsafe injection practices and the overuse of injections combine to cause an estimated 8 to 16 million hepatitis B infections, 2.3 to 4.7 million hepatitis C infections and 80 000 to 160 000 HIV infections each year.

Sterilizable injection equipment has been used in many countries for many years, notably in the context of the Expanded Programme of Immunization (EPI). To ensure that injections administered with sterilizable equipment do not harm the recipient or the provider, strict procedures must be followed and quality assurance must be implemented, including use of Time Steam Temperature (TST) spot indicators. Evaluation of the safety of injections administered in settings where sterilizable injection equipment is used has shown that system breakdowns make it impossible to guarantee the quality of sterilization procedures and that injections given with sterilizable equipment are on the whole unsafe.

In 2000, WHO, UNICEF, UNPFA, and the International Federation of Red Cross and Red Crescent Societies issued a joint policy statement calling for the exclusive use of "autodisable" injection equipment (i.e. equipment that it is impossible to re-use) in EPI programmes by the year 2003.

Evidence-based best injection practices recently formulated by WHO recommend against the use of sterilizable injection equipment. Thus, unless the quality of sterilization can be formally ensured with TST spot indicators, sterilizable injection equipment should be phased out in favour of the exclusive use of disposable injection equipment, including "autodisable" equipment for immunization services.

2.5.1 Key elements

It is the responsibility of governments to ensure the safe and appropriate use of injections. The achievement of this goal requires the establishment of a national multidisciplinary coalition involving different departments of the Ministry of Health and other stakeholders, such as nongovernmental organizations and associations, and private health care providers. The coalition should be coordinated by a Ministry of Health team and should receive political support, adequate funding and trained staff. Important activities include:

- Initial assessment (including behavioural and systems analyses) of injection frequency, of occasions when injection safety was not respected, and of adverse events associated with injections.
- Establishment of an injection safety unit to coordinate departments of the Ministry of Health, covering health promotion, immunization, family planing, essential drugs programmes, health care service delivery, nosocomial infections, blood transfusion service and waste management.
- Establishment of a national coalition, including UN agencies such as WHO, UNICEF and UNFPA, universities, nongovernmental organizations, specialists in behaviour change and associations (e.g. consumers, public and private health care workers, traditional practitioners).

2.5.2 National policy on the safe and appropriate use of injections

- Development by the national coalition of a national policy and plan (including costing, budgeting, and financing) to be included within the Ministry of Health's overall plan of action.
- Prevention through behaviour change activities (to reduce injection overuse and achieve injection safety); provision of sufficient quantities of injection equipment and infection control supplies; and management of "sharps" waste.
- Monitoring of the impact through process indicators (injection frequency and injection safety) and outcome indicators (incidence of injection-associated infections, rational use of injections).

2.5.3 Behaviour change

The basis for the safe and appropriate use of injections is a behaviour-change strategy targeting consumers as well as public, private and lay health care workers. Important activities include:

- Development of a national communication and behaviour-change strategy on the basis of behaviour and systems analyses.
- Definition of national standards for safe injection practices.
- Incorporation of injection safety into minimum standards of care.
- Promotion of safe techniques.
- Promotion of the rational use of injections within essential drug programmes (e.g. restriction of unnecessary injectable drugs) and with the private sector.
- Addressing issues that may lead to poor injection practices, including attitudes, emotions, incentives, beliefs, power relationship, norms and systems.

2.5.4 Equipment and supplies

Eradication of the re-use of syringes and needles without sterilization requires the continuous and sufficient availability of injection equipment and infection control supplies in all health care facilities. Important activities include:

- Adoption of "autodisable" syringes for immunization.
- Selection of appropriate types of syringes and needles (sterilizable, disposable or "autodisable" for curative care.
- Enforcement of international norms and standards by the national regulatory authority.
- Central bulk procurement of injection equipment and infection control supplies, including safety boxes.
- Central management of storage.
- An efficient distribution system to ensure continuous and sufficient availability in all health care facilities nationally.

2.5.5 Management of "sharps" waste

Skin punctures with contaminated needles or "sharps" represent a major hazard in health care settings. Puncture-resistant disposal containers must be readily available for the disposal of "sharps" – they can if necessary be made from easily available objects (tin with lid, heavy plastic bottle, heavy plastic or cardboard box). "Sharps" containers must be burnt or buried in a designated place after use when three-quarters full. Recapping needles is to be avoided in so far as possible.[4]

The efficient, safe and environmentally-friendly management of "sharps" waste is the only means of ensuring that disposable syringes and needles are not re-used and do not lead to accidental needlestick injuries. Important activities include:

- Formulation of a policy stating that disposal is part of the life-cycle of a syringe and that health care services have a duty to manage "sharps" waste.
- Assessment of the waste management system, including expressed and real needs.
- Selection of appropriate waste disposal systems for all levels of health care facilities.
- Implementation of a regulatory framework.
- Identification of the human and financial resources required.
- Implementation of a waste management system.
- Training and supervision.

Ten actions that will improve injection safety	
Patients	▪ State a preference for oral medications when visiting health care facilities ▪ Demand a sterile syringe for every injection
Health workers	▪ Avoid prescribing injectable medication whenever possible ▪ Use a sterile syringe for every injection and dispose of it properly
Immunization services	▪ Deliver vaccines with matching quantities of "autodisable" syringes and "sharps" boxes ▪ Make sterile syringes and "sharps" boxes available in every health care facility
Essential drugs	▪ Include awareness of risks for unsafe injection in all education and behaviour-change activities
HIV/AIDS prevention	▪ Ensure "sharps" disposal management as part of the system's duty of care
Health care system	▪ Monitor safety of injections as a critical quality indicator for health care delivery
Ministry of Health	▪ Coordinate safe and appropriate national policies with appropriate costing, budgeting and financing

CONTROLLING SAFETY OF INJECTIONS

Rigorously adhere to sterilization procedures.

Do not recap syringes.

Immediately discard in a "sharps" box to prevent needlestick injury.

Dispose of by incineration and burial.

[4] If recapping is absolutely unavoidable, place the needle cap on a hard flat surface and remove your hand. With one hand hold the *syringe* and use the *needle* to scoop up the cap. When the cap completely covers the needle, use the other hand to fix the cap firmly on the hub of the needle.

2.5.6 Sterilization

The term sterilization describes the procedures aimed at the complete elimination of any microbial life, including spores. The methods used for sterilization include:

- Heat
- Ionizing radiation (X-rays and gamma rays)
- Chemical means (mainly formaldehyde).

Only heat-related procedures will be covered here because ionizing radiation and chemical sterilization procedures require means that are not always available.

Cleanliness is the essential preliminary step required to guarantee proper sterilization. More than 90% of microorganisms are physically removed from a surface by simply washing it with water and a common detergent. Equipment must be cleaned as soon as possible after use in order to avoid the formation of blood clots, which would allow microorganisms to survive. It is essential to store drums containing sterilized material properly in order to avoid contamination. Drums and other containers must be hermetically sealed and stored away from dust and mould. Separate paths must be set up for the sterilization working procedures in order to avoid contamination between sterilized and non-sterilized items. The elaboration and use of written working procedures is highly recommended.

2.5.6.1 Sterilization procedures using a dry heater or an autoclave

Dry heaters destroy microorganisms by using hot air at atmospheric pressure. There are different recommended schedules: 160°C for 2 hours; or 170°C for 1 hour; or 180°C for 45 minutes. Because of the high temperatures involved, thermolabile items such as latex gloves or fabrics cannot be sterilized using dry heat.

The autoclave (steamer) produces high-pressure saturated steam, which is more effective in destroying microorganisms than dry heat. For this reason, less time is required and lower temperatures can be used than in dry sterilization. The most common time and temperature schedules are 121°C for 20 minutes or 138°C for 5 minutes. The pressure in an autoclave adapts automatically to the temperature. The autoclave can be used to sterilize tools such as surgical instruments, glassware, latex gloves, plastic pipes and various fabrics (i.e. white clothes, surgical clothes, etc.). The disadvantages of the autoclave are relative complexity of use and the need for proper maintenance.

The need to respect schedules must be stressed both for the autoclave and for the dry heater. In particular, times must be calculated from the moment the required temperature has been reached and not from the time the machine has been switched on. The thermometer must be well maintained. It is recommended to use the Time, Steam and Temperature (TST) indicator at every cycle – this is an adhesive indicator that turns a certain colour when conditions inside the machine become effective for sterilizing. The indicator is inexpensive and is essential in ascertaining the success of the procedure. However, it works only for autoclaves, not for dry heaters.

Sterilization of syringes and needles must be avoided, but this is not always possible in resource-poor settings. The sterilization of syringes and needles is a very delicate procedure because of the high risk of infection:

- For the health workers (incidental needle-prick), and
- For the patients (ineffective sterilization).

The high risk of contamination of syringes and needles (blood) renders adequate sterilization essential; their conformation (in particular the presence of a needle hole) makes this sterilization difficult to achieve. The following rules must be adhered to:

- Only appropriate re-usable needles and glass syringes should be used; disposable needles and plastic syringes *MUST* be discarded after one use and should *never* be re-sterilized.
- Thorough pre-sterilization cleaning of syringes and needles is a key point, in particular the removal of clot obstructions inside the needles – for health workers this is the most dangerous phase of the process.
- Re-usable needles and glass syringes must be put inside autoclaves or dry heaters in special drums with an appropriate stand for the components of needles and syringes; other types of containers are best avoided.

2.5.6.2 Sterilization procedures when an autoclave or a dry heater is not available

In peripheral health units, several instruments (scissors, forceps, vaginal speculum, etc.) have to be sterilized even though an autoclave or a dry heater is not always available.

The steam sterilizer (a type of pressure cooker) is commonly used in peripheral health units. The sterilization principles are similar to those of a steam autoclave. Most pressure cookers usually work at 125°C and the adequate duration for sterilization is 20 minutes from the moment this temperature is reached. This schedule can vary among the different types of steam sterilizers, and it is important to read and apply the manufacturer's instructions. The use of a TST indicator is recommended at each cycle. If syringes and needles are sterilized using this instrument, the rules mentioned above must be followed. Sterilization using the steam sterilizer is shorter and more effective than using boiling water, but some points must be remembered:

- The procedure is ineffective if the water level is not correct (either too much or too little water).
- The pressure cooker must be in good working order to ensure proper sterilization (if the rubber seal or the closing mechanism is not perfect, the pressure is not maintained and the water boils at 100°C as in a normal pot).
- The pressure cooker must be in good working order for safety reasons (a clogged or damaged valve can trigger an explosion).

Boiling water is *not a recommended sterilization method* because the temperature reached (100°C at sea level) does not necessarily ensure that all microorganisms (in particular spores and the virus of hepatitis B) are eliminated. Boiling water provides high-level disinfection, not sterilization. If it is the only procedure available, some rules have to be followed in order to obtain the best results possible:

- Items must be carefully washed prior to boiling.
- Only "large" instruments should be boiled – the more there are areas in which organic material or dirt can hide, the less effective the boiling procedure.
- Instruments must soak in direct contact with the boiling water throughout the procedure.
- Boiling time should be at least 2 hours.
- Boiling time must increase with altitude because water boils at a lower temperature.
- Syringes, needles, blood bags and perfusion sets must never be sterilized using the boiling water procedure, even in very resource-poor settings.
- The water must be changed at every cycle.

2.5.7 Contacts and references

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2.6 Blood safety

A well-organized blood transfusion service (BTS) is a prerequisite for the safe and effective use of blood and blood products. The HIV/AIDS pandemic has focused particular attention on the importance of preventing transfusion-transmitted infections (TTIs). Between 5% and 10% of HIV infections worldwide are transmitted through the transfusion of contaminated blood and blood products. Many more recipients of blood products are infected by hepatitis B and hepatitis C viruses, syphilis and other infectious agents, e.g. *Trypanosoma cruzi*.

Transfusion-transmitted infections can be eliminated or substantially reduced through a strategy for blood safety. It is the responsibility of governments to ensure a safe and adequate supply of blood. This responsibility may be delegated to a non-profit nongovernmental organization, but the blood transfusion service should be developed within the framework of the country's health care infrastructure. A blood transfusion service requires government commitment and support and must be recognized as a separate unit with an adequate budget, a management team and trained staff.

Important strategies in establishing a blood transfusion service include:

- Collect blood only from voluntary non-remunerated blood donors from low-risk populations.
- Screen all donated blood for transfusion-transmissible infections, including HIV, hepatitis viruses, syphilis and other infectious agents.
- Reduce unnecessary transfusions through the effective clinical use of blood, including the use of simple alternatives to transfusion wherever possible.

2.6.1 Establishing a blood transfusion service

- At the central level:
  - Secure government commitment and support for the national blood programme.
  - Formulate a national blood policy/plan.
  - Establish the blood transfusion service as a separate unit with responsibility and authority.
  - Provide a budget and finance system for a sustainable programme through cost recovery and/or annual budget allocation.
  - Ensure a national quality system, including guidelines, standard operating procedures, accurate records, monitoring and evaluation.
  - Set up appropriate legislation/regulation.
  - Set up a quality system for the blood transfusion service.
- At the peripheral level: Implement the above.

Collect blood only from voluntary non-remunerated blood donors among low-risk populations.

High priority must be given to the elimination of systems, such as family/replacement and paid blood donors, that are associated with a significantly higher prevalence of transfusion-transmitted infections. Voluntary non-remunerated blood donors from low-risk populations who give blood regularly are the foundation of a safe and adequate blood supply. Important activities include:

- At the central level:
  - Establish a blood transfusion service unit responsible for donor education, motivation, recruitment and retention.
  - Prepare standard operating procedures in accordance with blood transfusion service guidelines.
  - Develop educational materials (may be done at both central and peripheral level).
- At the peripheral level, implementation of the above, plus:
  - Identify low-risk donor populations.
  - Educate, motivate, recruit and retain voluntary non-remunerated blood donors from low-risk populations.
  - Ensure donor selection, referral, care and confidentiality.
  - Ensure that any blood testing positive is removed from the supply and not transfused.
  - Apply standard operating procedures.
  - Train staff in blood donor units.
  - Develop educational materials (may also be done at the central level).
  - Develop and maintain a register of voluntary non-remunerated blood donors.
  - Monitor the occurrence of transfusion-transmitted infections (TTIs).
  - Screen all donated blood for HIV and other transfusion-transmissible infections.

The blood transfusion service must develop and maintain a national strategy for the screening of donated blood and blood products for TTIs, using the most appropriate and effective tests, and for good laboratory practice in areas of blood grouping, compatibility testing, component preparation, storage and transportation of blood products. Important activities include:

- At the central level:
  - Develop protocols for the testing, selection and evaluation of appropriate screening assays to be used at each site.
  - Train laboratory technical staff (can be done at peripheral or central level).
  - Ensure procurement, supply, central storage and distribution of reagents and materials to ensure continuity in screening at all sites.
- At the peripheral level, implementation of the above, plus:
  - Maintain an effective blood cold chain for storage/transportation of blood/blood products.

Reduce unnecessary transfusions through the effective clinical use of blood, including alternatives to transfusion. The risks associated with transfusion can be reduced by avoiding unnecessary transfusions through the effective clinical use of blood and blood products and the appropriate use of simple alternatives to transfusion that are safer and more cost-effective. Important strategies/activities at the central level include:

- Developing a national policy and guidelines on the clinical use of blood:
  - Providing training in the safe provision and clinical use of blood for staff involved in the transfusion process.
  - Implementing the prevention, early diagnosis and treatment of conditions that could result in the need for transfusion (obstetrical complications, trauma, other causes of anaemia).
  - Ensuring availability of intravenous replacement fluids (crystalloids and colloids) for the correction of hypovolaemia, and pharmaceuticals and devices to minimize the need for blood.
  - Undertaking monitoring and evaluation.

2.6.2 Contacts and References

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2.7 Vector control

The main current options for vector control include:

- Larval control
- Control of adult vectors
- Limitation of contact between vectors and humans (*personal protection measures*).

The ecology and behaviour of the target vector(s) largely determine the choice of control method or combination of methods. Methods of control may include recourse to environmental modifications (e.g. drainage), to mechanical control (mosquito-proofing, screening), to chemicals (insecticides or larvicides) or to combinations thereof (insecticide-treated bednets and traps). However, biological control and environmental management have limited applications and chemical control is still considered to be an important element in the control of vectors and pests of public health importance. The following comments, while pertaining specifically to mosquito vectors, are also relevant to the other main categories of vectors.

2.7.1 Larval control

Larval control is only relevant as a method of vector control if breeding places are limited in number and if a high proportion of them:

- Are accessible and of manageable size.
- Can be located within the vector's flight range of the community to be protected.

Many larval habitats are man-made (unprotected receptacles such as pots and tyres, as well as leaks, borrow-pits, etc.) and it is probably preferable to avoid creating such sites rather than having to resort to larviciding later. Environmental changes created during development activities can increase the risk of malaria and other vector-borne diseases. Borrow pits, for instance, are potential mosquito breeding sites. Policies and legislation to reduce the negative impact of development activities may be required.

Methods to control larvae include:

- Physically changing or eliminating the breeding place:
  - Removal of small containers.
  - Filling of the smaller sites.
  - Drainage.
  - Flushing (e.g. periodic flushing by small dams with siphons and sluice gates).
  - Clearing of vegetation (effective for vectors of lymphatic filariasis in parts of south-east Asia).
  - Other (in Indonesia, changing the salinity of breeding sites has been used as an environmental management approach).
- Making the breeding place inaccessible to adult mosquitoes (for small enclosed habitats such as wells or latrines, through mechanical mosquito-proofing).
- Releasing fish or other predators that feed on larvae. The introduction of larvivorous fish, whether in clean water (*Gambusia*) or in organically polluted water (*Poecilia*) must be carefully considered in order not to induce imbalance in the local ecology; imported fish should only be used, if at all, in man-made breeding habitats giving no access to the natural environment. Rearing larvivorous fish and edible fish together reduces the larval population and provides income-generating opportunities. Predatory copepods have been used with some success to control *Aedes aegypti* in water storage containers and storm drains.
- Applying a film of oil or other material to water surfaces in order to kill larvae by suffocation. Commercial oils and surfactants designed for mosquito larviciding are effective for short periods of time in certain habitats, but consideration must be given to their effect on other surface-breathing aquatic insects. Floating layers of expanded polystyrene beads prevent mosquito breeding for long periods when used in confined sites such as cesspits and water tanks. They may be used effectively against *Anopheles stephensi*, *Aedes aegypti* and *Culex quinquefasciatus.*
- Applying chemical or bacterial larvicides, or insect growth regulators (e.g. methoprene) to aquatic environments. The toxicity of these products and their potential for killing non-target organisms including crustaceans, fish and arthropod predators of vector species must be taken into consideration. Insect growth regulators are most widely used against mosquito larvae. The bacterial larvicides, such as those produced by *Bacillus thuringiensis* serotype H-14 and *Bacillus sphaericus* are used for the control of mosquito and blackfly larvae.

2.7.2 Control of adult vectors

- ADULTICIDES: INDOOR RESIDUAL SPRAYING Indoor residual spraying with long-acting insecticides remains an important malaria control method in many affected tropical countries, although problems of resistance have arisen in some areas. It may be considered an appropriate method for vector control when *all* the following conditions are met:
  - The majority of the vector population is *endophilic*, i.e. the vector rests indoors.
  - The vector is *susceptible* to the insecticide in use.
  - A high percentage of the structures in the area have *adequate sprayable surfaces* and can be well sprayed. Where studies of vector resting behaviour so indicate, spraying may be confined to selected surfaces within houses, such as thatched roofs, the upper parts of walls and the eaves. Residual indoor spraying may be restricted to selected houses where the risk of transmission is highest.

Indoor residual spraying is the preferred method of prevention and control against Chagas disease in endemic areas. Although it is effective against indoor resting sandflies, few leishmaniasis prevention and control programmes use it. It is not recommended for the control of:

- *Aedes* vectors of dengue or *Culex* vectors of lymphatic filariasis (which frequently rest on hanging fabrics rather than walls).
- *Culex* vectors of Japanese encephalitis (outdoor biting and resting species).

Where indoor residual spraying is to be carried out, the delineation of areas to be covered and the frequencies and times of applications must be determined. Once spraying has begun, clear criteria must be used to:

- Extend spraying into new areas.
- Discontinue current spraying.
- Maintain spraying beyond an initial set time period.

ADULTICIDES: SPACE SPRAYS Space sprays are mainly used to control outbreaks of arboviral diseases but the insecticidal effects are transient and larvae and pupae are unaffected. Such methods may (rarely) be used to control exophilic and exophagic vectors.

2.7.3 Assessment

- The following points must be carefully considered in spraying or larviciding programmes:
  - Timing
  - Equipment
  - Cost
  - Possibility of recourse to alternative methods
  - Choice, formulation and dosage of insecticide, spraying technique, precautions.
- The following elements can be used as process or outcome indicators:
  - Coverage (proportion of areas effectively treated)
  - Acceptance by the community
  - Expectations of the community
  - Entomological indicators.

2.7.4 Personal protection measures

- **Household insecticides and repellents**

Household insecticides and repellents for the control of insect pests in the home and for personal protection are widely available from retail outlets. They include aerosol sprays, mosquito coils, vapourisers and fumigants. Their effectiveness in reducing human-vector contact is well documented but there is little evidence that they reduce the incidence of vector-borne diseases.

- **Insecticide-treated materials**

Insecticide-treated mosquito nets, curtains, hammocks, eaves strips, papyrus mats, and cloth are used as barriers or repellents to reduce human-vector contact (and, in the case of *Glossina*, to attract and kill adults as a method of control). So far only selected pyrethroid insecticides have been extensively tested for treatment of bednets or curtains as they are considered safe for humans. The insecticide treatment of materials, e.g. for bednets, can be accommodated within the primary health care system and carried out under the guidance of trained community health workers.

- **Insect-proofing of households**

Methods include design of houses, screening eaves, doors and windows. Location of settlements and quality of housing affect mosquito entry, resting habits and human-vector contact. Communities must be made aware of conditions that increase the risk of exposure to mosquitoes.

- **Operational considerations for insecticide-treated bednets and curtains**

These include:

- Dosage of insecticide
- Coverage/usage
- Percentage of households and of people in each house that use the nets every night
- Bioassay tests to assess the duration of effectiveness of the insecticide
- Frequency and rates of retreatment
- Cost.

2.7.5 Combined use of vector control methods

More than one vector control method, with different levels of efficacy and requirements, may be used in a given area simultaneously or consecutively. Use of several methods necessitates the monitoring of indicators that measure:

- The effect of each method on its immediate or direct target.
- The relative contribution of each method.

Integrated vector management

Integrated vector management builds on selective vector control, which is defined as the targeted use of different vector control methods alone or in combination to prevent or reduce human-vector contact. In addition, integrated vector management should have the following attributes: cost-effectiveness, environmental soundness, inter-sectorality and sustainability. In most tropical countries, more than one vector-borne disease presents a public health problem. In local situations where several endophilic and endophagic vectors occur together and where biting activities or breeding sites are similar, control measures can be effective against several vector species at once, as has been shown for malaria and leishmaniasis. Programme management demands a sound understanding of the vectors, the ability to predict and react to the social and economic consequences of control actions and to changes in environmental risks, as well as an ability to accommodate to local differences in health activities.

2.7.6 Role of communities and other sectors in vector control

- **Community involvement**

Existing community structures, particularly in stable communities, must be used to implement vector control, with technical and financial guidance from the vector control programmes. This requires the provision to individuals of:

- Specific knowledge and skills (vector biology, type of interventions, preparation and/or performance of residual house-spraying, elements of environmental management).
- Skills in management and communication skills.

Local political support will ensure close interaction of the vector control staff with local leaders and community members from the planning stage to the management of control activities, taking into account the perceptions and cultural habits of the people.

- **Intersectoral collaboration** must aim at coordinating activities in order to ensure consistency of effort and eliminate work duplication. Certain vector control interventions (e.g. water management and intermittent irrigation) need interaction between the health services and other relevant sectors:
  - Resources and information sharing
  - Capacity-building
  - Development and observance of policies, legislation, and standards
  - Links between the public bodies involved in vector control and in development projects.

2.7.7 Reference

WHO. *Vector control: methods for use by individuals and communities.* Rozendaal JA, ed. Geneva: WHO, 1997
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3. DISEASES AND SYNDROMES

3.1 Diseases – sample format

Name of disease ICD-10 code

General introduction

Summary statement on the importance of the disease and the main measures for control

Causal agent(s) and main modes of transmission

- **Causal agent(s):**
- **Main modes of transmission:** with information on incubation, carrier state, case-fatality rate, etc.

Clinical description and case definition

- Clinical case definition or clinical description
  Laboratory criteria
  Case classification (humans)
  - ***Suspected***
  - ***Probable***
  - ***Confirmed***

Recommended interventions

- **Case management**
- **Prevention**
- **Epidemics**
  Conditions under which epidemics may occur
  Management of epidemics
- **Drug resistance monitoring**
  If applicable

Other aspects

- **Procurement of equipment and drugs**
  As appropriate, including specific requirements
- **Surveillance**
- **Special considerations/other interventions**
- **Indicators**
  As appropriate

Contacts and References

CONTACTS: Regional Offices
WHO Headquarters

REFERENCES:
WHO or other documents as appropriate

AIDS/HIV infection* B20-B24

** AIDS and HIV infection are handled as one entity from the point of view of prevention and control.*

General introduction

The Ninth General Programme of Work of WHO (9GPW, target 6.3) calls for a reduction in the incidence, prevalence and transmission of AIDS. Control measures are based on prevention and care strategies. Surveillance is necessary to assess national needs in education, supplies, and health care and to anticipate spread in the community.

HIV infection has spread to all parts of the world; 70% of the world total of cases and deaths occur in sub-Saharan Africa, where the impact of the disease at personal, family and societal levels (including education, work, economy and peace) is such as to affect decades of earlier development. In some countries AIDS has reduced life expectancy at birth by more than 10 years over the past few years.

Control implies both prevention (the mainstay of which is avoidance of unsafe sexual intercourse and, in some settings, the use of clean injecting material) and care (testing and counselling, treatment of opportunistic infections, specific antiretroviral treatment). The 2 elements – prevention and care – go hand in hand. They cannot be handled in isolation, but must take into account numerous societal, cultural and economic factors.

Causal agent and main modes of transmission

- **Causal agent:** A retrovirus (human immunodeficiency virus HIV) of which 2 types have been identified: HIV-1 and HIV-2. They are serologically distinct and their geographical distribution is different; their transmission characteristics are similar, with differences in efficiency of transmission. Subtype variations within both serotypes affect the possibility of vaccine development.
- **Main modes of transmission:** The infection is transmitted via body fluids, essentially blood and genital fluids (male and female). The main mechanisms are:
  - Unprotected sexual intercourse, hetero- or homosexual (risk of the order of 1% per episode of unprotected intercourse with a seropositive partner – in heterosexual intercourse, the risk is higher for women than for men)
  - Sharing of unsterile injecting/skin-piercing equipment (drug injection, tattooing, surgery) – variable risk of roughly the same order of magnitude as for unprotected sexual intercourse
  - Transfusion of infected blood (risk close to 100% per infected transfusion)
  - Vertical mother-to-child transmission during pregnancy or delivery (blood) and through breastfeeding (breast milk) – the combined risk of vertical transmission through blood and breast milk is estimated at 30% to 45% per pregnancy + breastfeeding until 6 months. The precise distribution of risks is still a matter of debate.

  NOTE: these risk values are in the absence of any intervention, and are given on a *purely indicative* basis.

  Most people infected with HIV develop detectable HIV antibodies within 1-3 months. Incubation is variable with a mean of about 10 years. The proportion of HIV-infected persons who will go on to develop AIDS is not precisely known, but some estimates range up to 70% during a period of 15 years after infection. The disease is ultimately fatal in the absence of treatment. Recourse to antiretroviral drugs and to effective prevention and treatment of opportunistic infections has improved survival and quality of life.

Clinical description and case definition

Different case definitions are used depending on the country, on population factors (children, adults, relative occurrence of opportunistic infections) and on the laboratory infrastructure and training available.

Case classification

This depends on the case definition. Please check with the national AIDS programme.

Recommended interventions

- **Case management includes**
  - **AIDS**
    - ♦ Treatment with antiretrovirals, which has proved effective in reducing the viral load and improving both health and survival.
    - ♦ Prevention, treatment or cure for opportunistic diseases in patients with HIV infection, for many of which effective treatment is available. Local health centres and small hospitals should obtain adequate facilities to diagnose and treat the commoner opportunistic infections.

    Initiatives undertaken by governments and international agencies in Africa (UNAIDS Drug Access Initiative) and in Latin America (Horizontal Technical Collaboration Group) endeavour to ensure a wide supply of appropriate treatment, although the high cost of drugs, together with infrastructure problems, still make it difficult to deliver drugs where they are needed.
  - **HIV**

    Individual surveillance of immune status based on clinical assessment and the monitoring of CD4 cells.
- **Prevention**

  This is based on:
  - Reducing sexual transmission through one or more of the following:
    - ♦ Postponing the start of sexual activity
    - ♦ Practising non-penetrative sex
    - ♦ Limiting the number of sexual partners
    - ♦ Consistently and correctly using condoms (male and female)
    - ♦ Preventing and treating common STIs, especially those that cause ulcerative lesions.

    These activities are to be accompanied by HIV/AIDS education, voluntary counselling and testing.
  - Avoiding transmission through infected material for injection/surgery/dentistry/other
  - Safety of injection equipment (sterilization techniques, "autodisable" syringes, etc.) for therapy, including dentistry, for immunizations or for recreational use (see *Injection safety*, page 31)
    - ♦ Setting up needle/syringe exchange programmes
    - ♦ Setting up drug treatment programmes if appropriate.
  - Avoiding transmission through transfusion:
    - ♦ Ensuring screening of blood for transfusions and for other blood products
    - ♦ Ensuring that blood tested positive is removed from the blood supply and not transfused
    - ♦ Minimizing recourse to transfusions
    - ♦ Encouraging auto-transfusion where possible.
  - Reducing vertical mother-to-child transmission:
    - ♦ Treatment of infected mothers and their baby according to national guidelines
    - ♦ Long-term multitherapy during pregnancy and childbirth according to national guidelines:
    - ♦ The most complex regimen includes antepartum and intrapartum zidovudine for the mother and postnatal doses for the infant; the simplest regimen requires a single dose of nevirapine at the onset of labour and a single dose for the newborn
    - ♦ Recourse to expressed breast milk from a seronegative nursing mother, or to artificial feeding.

NOTE 1: Not all these interventions are easy, since some deal with very fundamental items of human behaviour. Techniques for the replacement of maternal milk may present health risks (malnutrition, infection) for the child and also require support other than medical (avoidance of stigmatization, social support).

NOTE 2: For both HIV and AIDS, the benefits of care and prevention are interlocked: availability of care helps break down the denial and fear associated with HIV infection, in the same way that voluntary HIV counselling and testing can result in improved access to care. Antiviral drugs are expensive and their side-effects may be heavy. Communities and other stakeholders must become involved in developing standards for HIV-related care and support. In addition to drug treatment, this involves:

- Informing the community about available support and resources
- Identifying what the community can potentially contribute to care
- Sounding out the preferences of the community.

A comprehensive approach includes:

- Management of AIDS
- Management of opportunistic infections
- Improved nutrition
- Improvement of social conditions for the patient (including avoidance of stigmatization).

- **Epidemics**
  Transmission of HIV has in itself taken epidemic proportions. Localized outbreaks can occur in settings where non-sterile injection material is shared (hospitals, intravenous drug users, mass immunizations).
  HIV infections increase the risk of tuberculous disease in populations with high prevalence.
- **Drug resistance monitoring**
  Primary resistance to zidovudine (AZT) and to protease inhibitors has been reported.

Other aspects

- **Procurement of equipment and drugs**
  Condoms
  Drugs
- **Surveillance**
  For the purpose of surveillance, WHO and UNAIDS suggest a classification that describes the epidemic by its current state:
  - **Low-level epidemics:**
    - Infection largely confined to individuals within high-risk groups
    - Networks of diffusion rather loose
    - Virus only introduced recently
    - Numerical proxy: HIV prevalence not consistently >5% in any defined subpopulation.
    - Core Surveillance: Identify risk behaviours and groups at risk + selected groups
      - HIV serosurveillance in identified groups with risk behaviour
      - Sentinel serosurveillance in pregnant women in urban areas
      - Analysis of available STI data
      - Analysis of available data on blood donors.
  - **Concentrated epidemics:**
    - Infection spreading rapidly in a defined subpopulation
    - Not well-established in the general population
    - Networks of risk within the population
    - Numerical proxy: HIV prevalence consistently >5% in at least one defined subpopulation. HIV prevalence <1% among pregnant women in urban areas
    - Core Surveillance: Identify risk behaviours and groups at risk + selected groups
      - HIV serosurveillance in identified groups with risk behaviour
      - Annual sentinel serosurveillance in pregnant women in urban/high-exposure areas
      - Risk behaviour surveys among selected groups
      - HIV case-reporting
  - **Generalized epidemics:**
    - Infection well-established in the general population
    - Sexual networks within the population sufficient to maintain the epidemic
    - Numerical proxy: HIV prevalence consistently >1% for pregnant women
    - Core surveillance: Identify risk behaviours and groups at risk + selected groups
      - HIV serosurveillance in identified groups with high-risk behaviour (sex workers and clients)
      - Annual sentinel serosurveillance in pregnant women in urban/high-exposure areas
      - Surveillance of tuberculosis and other HIV-related illnesses
      - Risk behaviour surveys in general population, especially among young people
      - HIV case-reporting
      - Analysis of available STI data in the general population.

Contacts and References

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REFERENCES:

UNAIDS. *Report on the global AIDS epidemic.* June 2000. Geneva: UNAIDS,136 pp. UNAIDS/00.13E ISBN 92-9173-000-9.
WHO/UNAIDS. CD ROM: *Secon-generation surveillance for HIV. Compilation of basic materials*. Available from WHO and UNAIDS.
WHO. *The global AIDS Strategy* (WHO AIDS Series 11) WHO, Geneva, 1992
WHO: *HIV/AIDS and Sexually Transmitted Diseases, WHO Policy and Strategic Orientations.* WHO/ASD/96.2.

Anthrax A22

General introduction

Anthrax is a widespread zoonosis transmitted from domestic animals (cattle, sheep, goats, buffaloes, pigs and other) to humans by direct contact or through animal products. Human anthrax is a serious problem in several countries and has potential for explosive outbreaks (especially the gastrointestinal form); while pulmonary (inhalation) anthrax is mainly occupational, the threat of biological warfare attacks must not be forgotten. Anthrax has a serious economic impact on the trade of animal products.

In most countries anthrax is a notifiable disease. Effective control is based on prevention of anthrax in livestock; programmes based on prevention in humans alone are costly and likely to be ineffective except for industrial exposure. There is an effective vaccine for the latter case, and successful vaccines for livestock, particularly for herds with ongoing exposure to contaminated soil.

Causal agent and main modes of transmission

- **Causal agent:** Spore-forming *Bacillus anthracis*, a Gram-positive rod-shaped bacterium. Sporulation requires the presence of free oxygen (the organism remains in vegetative non-spore form within the anaerobic environment of the infected host).
- **Main modes of transmission:** it is largely through the uptake of spores that humans contract the infection, almost invariably from direct or indirect contact with animals. The routes of acquisition are:
  - A skin lesion (cutaneous anthrax, see *Clinical description* below)
  - Ingestion of contaminated food (gastrointestinal anthrax, see *Clinical description* below)
  - Inhalation of spore-laden dust (pulmonary anthrax, see *Clinical description* below)
  - The incubation period ranges from 1 to 7 days. Persons exposed to occupational hazards include those handling infected carcasses and those employed in the processing of bones, hides, wool and other animal products. Mechanical transmission by biting insects is a rare occurrence.

Clinical description and case definition

- **Clinical description (humans):** An illness with acute onset characterized by several clinical forms. These are:
  - *Localized (cutaneous) form:*
    - Skin lesion evolving over 1 to 6 days from a papular through a vesicular stage, to a depressed black eschar invariably accompanied by oedema that may be mild to extensive.
  - *Systemic forms:*
    - *Gastrointestinal:* abdominal distress characterized by nausea, vomiting, anorexia and followed by fever
    - *Pulmonary (inhalation):* brief prodrome resembling acute viral respiratory illness, followed by rapid onset of hypoxia, dyspnoea and high temperature, with X-ray evidence of mediastinal widening
    - *Meningeal:* acute onset of high fever possibly with convulsions, loss of consciousness, meningeal signs and symptoms; commonly noted in all systemic infections.

  Laboratory criteria: Laboratory confirmation by **one or more** of the following:
  - Isolation of *Bacillus anthracis* from a clinical specimen (e.g. blood, lesions, discharges)
  - Demonstration of *Bacillus anthracis* in a clinical specimen by microscopic examination of stained smears (vesicular fluid, blood, cerebrospinal fluid, pleural fluid, stools)
  - Positive serology (ELISA, Western Blot, toxin detection, chromatographic assay, fluorescent antibody test).

NOTE: It may not be possible to demonstrate *B. anthracis* in specimens if the patient has been treated with antimicrobials.

Case classification (humans)
- ***Suspected:*** A case that is compatible with the clinical description and has an epidemiological link to confirmed or suspected animal cases or contaminated animal products
- ***Probable:*** A suspected case with a positive reaction to allergic skin test (in non-vaccinated individuals)
- ***Confirmed:*** A suspected case that is laboratory-confirmed.

Recommended interventions

- **Case management**
  - *Mild uncomplicated cases (cutaneous without systemic involvement):*
    - Penicillin V, 500 mg every 6 hours for 5-7 days orally, or
    - Procaine penicillin, 1 million units intramuscularly every day for 3-7 days
  - *Severe cases (including all forms of systemic anthrax)*:*
    - Initially (until temperature returns to normal):
      - Penicillin G, 2 million units per day in slow (<300 mg/minute) intravenous injections of 0.5 million units every 6 hours, or
      - Intravenous (perfusion)
    - When temperature returns to normal:
      - Penicillin procaine, 1 million units intramuscularly every day for 3-7 days.

  * Antibiotherapy is less effective when the bacillus has produced high levels of toxin; gammaglobulin may be effective in such cases.

- **Prevention**
  Vaccination is required for animals when exported/imported (International Zoo-sanitary Code, Chapter 3.1.1). The vaccines must be stored in a refrigerator but not frozen.

  In humans, selective preventive vaccination may be considered in cases of occupational exposure. Vaccines are administered intramuscularly or by scarification; an annual booster dose is required.

- **Epidemics**
  In the case of animal outbreaks, the following precautions must be taken for exposed humans:
  - Check vaccination status and administer booster if needed
  - Use protective clothing (and face masks if there is a risk of aerosols)
  - Disinfect and dress any cuts and abrasions before putting on protective clothing
  - Avoid blood-spilling operations on infected/suspected animals/carcases.

  Outbreaks linked to occupation (e.g. working with goat hair) or consumption of infected meat have occurred among humans and may yield to removal of the offending material. Both for humans and for animals, report suspicious symptoms immediately.

Other aspects

- **Procurement of equipment and drugs**
  Human vaccines available from China, Russian Federation, United Kingdom and USA. Animal vaccines widely available.

- **Surveillance**
  The ratio of livestock cases to human cases is of the order of 10-20:1; it is ineffective to rely only on human case reports. Routine surveillance especially in high-risk groups (shepherds, slaughterhouse workers, veterinarians, wool/hide workers); unexplained sudden livestock deaths must be investigated.

  Immediate case-based reporting, mandatory for all cases, from the peripheral level (health care providers or laboratory) to intermediate and central levels of public health sector and to appropriate levels of the animal health sector.

  Routine monthly reporting of aggregated data on confirmed cases and investigation reports from the intermediate to central level in both the public health and the animal health sectors.

- **Special considerations/other interventions**
  Surveillance activities must be fully coordinated and shared between the public health and the animal health sectors, with administrative arrangements between the two sectors to facilitate immediate cross-notification and joint investigation of cases/outbreaks. Surveillance and control programmes are particularly important in high-risk areas, such as those with high pH/calcareous soils.

- **Indicators**
  Annual number of outbreaks of anthrax in animals and in humans, by geographical region.

Contacts and references

CONTACTS: WHO Regional Offices: see addresses on pages 40-42

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REFERENCES: WHO. *Guidelines for the Surveillance and Control of Anthrax in Humans and Animals.* 3rd edition. WHO/EMC/ZDI/98.6 Rev.3

Brucellosis (human) A23

General introduction

Brucellosis is the most widespread zoonosis transmitted from animals (cattle, sheep, goats, pigs, camels and buffaloes) through direct contact with blood, placenta, fetuses or uterine secretions, or through consumption of infected raw animal products (especially milk and milk products). Human brucellosis due to *Brucella melitensis* has serious public health consequences in areas where sheep and goat are raised. Brucellosis has an important worldwide impact on human health and the animal industry. In most countries brucellosis is a notifiable disease. Control measures are based on prevention.

Causal agent and main modes of transmission

- **Causal agents:** *Brucella abortus*, biovars 1-6, 9; *Brucella melitensis*, biovars 1-6; *Brucella suis*, biovars 1-5; *Brucella canis*.
- **Main modes of transmission:** Infected animals (mainly cattle, swine, sheep, goats, and less commonly dogs) and their products are the reservoirs and sources of infection (cattle farmers, slaughterhouse workers, consumers of raw milk and derivatives). Infection occurs by contact or by ingestion, with occasional cases of airborne infection in stables and pens. The incubation period is variable and long (1 week to 2 months and longer). The case fatality ratio in untreated patients is about 2%.

Clinical description and case definition [5]

- **Clinical description**
  An illness characterized by acute or insidious onset, with continued, intermittent or irregular fever of variable duration, profuse sweating particularly at night, fatigue, anorexia, weight loss, headache, arthralgia and generalized aching. Local infection of various organs may occur, with abscess formation.

  Laboratory criteria

  - Isolation of *Brucella* spp. from blood or other clinical specimen, **or**
  - Rose Bengal test – useful for screening, must be confirmed by one of the tests mentioned below
  - Brucella agglutination titre in one or more serum specimens obtained after onset of symptoms, to be interpreted as follows:
    - Standard tube agglutination test >160: brucellosis, **or**
    - Standard tube agglutination test <160: diagnosis to be confirmed by seroconversion or by one of the tests mentioned below:
  - ELISA IgG, 2-mercaptoethanol complement fixation test, Coombs IgG for detecting antilipopolysaccharide antibodies; and counterimmunoelectrophoresis with water-soluble proteins.

  Case classification

  - ***Suspected:*** A case that is compatible with the clinical description **and** epidemiologically linked to suspected/confirmed animal cases or contaminated animal products
  - ***Probable:*** A suspected case that has a positive Rose Bengal test
  - ***Confirmed:*** A suspected or probable case that is laboratory-confirmed.

[5] Updated for the present document by technical unit (see *Introduction*)

Recommended interventions

- **Case management**
  - Doxicycline 100 mg twice a day for 45 days + streptomycin 1 g daily for 15 days, **or**
  - Doxicycline 100 mg twice a day for 45 days + rifampicin 15 mg per kg body weight daily for 45 days

  Relapses occur in 5% of treated cases and must be treated like new cases
  Drainage/secretion precautions as appropriate.
- **Prevention**
  - Education to avoid consuming unpasteurized milk and milk derivatives
  - Barrier precautions for hunters and professionals at risk (butchers, cattle farmers, slaughterers)
  - Careful handling and disposal of afterbirths especially in cases of abortion
  - Ventilation of herd pens.

  Serological or other testing of animals. Immunization of herds may be envisaged. Elimination of infected herds.
- **Epidemics**
  Point-source epidemics: search for and recall incriminated produce (usually raw milk or cheese from an infected herd).
- **Drug resistance monitoring**
  Not applicable.

Other aspects

- **Procurement of equipment and drugs**
  Laboratory materials and equipment.
- **Surveillance**
  Routine surveillance particularly among high-risk groups (farmers, shepherds, workers in slaughterhouses, butchers, veterinarians, laboratory personnel).
  Mandatory early case-based reporting by health care providers or laboratory to upper levels of the public health sector as well as to the appropriate level of the animal health sector. In endemic countries where investigation of all reported cases may not be feasible, a representative proportion of reported cases should be investigated routinely.
- **Special considerations/other interventions**
  Control activities must be coordinated and shared between both public health and animal health sectors. Administrative arrangements between the 2 sectors must facilitate immediate cross-notification of cases, as well as joint investigations and control. Control programmes must be promoted in goat-raising areas.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42
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Buruli ulcer (*Mycobacterium ulcerans* infection) A31.1

General introduction

Buruli ulcer is a re-emerging disease endemic in at least 25 countries worldwide, mostly in the tropical regions. Awareness of the disease is low, which may lead to significant under-recognition and under-reporting. There is little knowledge on the extent of the disease at national and international levels. A good surveillance system is needed to provide better data and to allow monitoring of control efforts.

Causal agent and main modes of transmission

- **Causal agent:** The disease is caused by *Mycobacterium ulcerans*.
- **Main modes of transmission:** The mode of transmission is not known, hence no preventive strategies are possible at the moment. Recent evidence suggests that aquatic insects (*Naucoris* and *Dyplonychus* species) may be involved in the transmission of Buruli ulcer disease. Trauma to the skin appears to be the most likely means by which the organism enters the skin. There is no evidence to date to support transmission from person to person.

  There is little information on individual susceptibility to the infection. Males and females are equally affected and no racial or social group is exempt. Buruli ulcer often occurs close to rivers and stagnant bodies of water. In some situations, changes in the environment, such as irrigation and the building of dams, may have played a role in the resurgence of the disease. The incubation period is variable with an estimated average of 2-3 months.

Clinical description and case definition

- **Clinical description**
  Buruli ulcer is an infectious disease involving the skin, caused by *Mycobacterium ulcerans*, characterized by a painless nodule, papule, plaque or oedema, evolving into a painless ulcer with undermined edges, often leading to disabling sequelae.
- **Case definition and classification**
  There are two types of Buruli ulcer disease, active and inactive:
  - **Active:** Infections of different clinical forms.
    - *Papule*: raised skin lesions up to 1 cm in diameter
    - *Nodule*: painless, palpable firm lesion, up to 2 cm in diameter, situated in the subcutaneous tissue and usually attached to the skin
    - *Plaque*: usually painless, well-demarcated, elevated indurated lesion more than 2 cm in diameter
    - *Oedema*: diffuse, extensive, non-pitting, ill-defined margin, firm, may be painful with or without colour change over the affected skin
    - *Ulcer:* painless skin lesion characterized by a necrotic centre, undermined edges and oedematous skin. An early ulcerative lesion has a diameter of **less than 2 cm** and a late ulcerative lesion has a diameter of **more than 2 cm**.
  - **Inactive:** Healed lesions with characteristic depressed star-like scar with or without sequelae.

    A **sequel** of Buruli ulcer is defined as a complication resulting either directly from the disease (contracture deformities, loss of organs – breast, eye, genitalia) or as a result of treatment (amputation of limbs).
    Laboratory-confirmed case: a clinical case where laboratory investigations evidence one or more of the following:
    - Presence of acid-fast bacilli (Ziehl-Neelsen stain)
    - PCR positive
    - Characteristic histopathology.

Recommended interventions

- **Case management**
  Treatment by surgical excision of the lesion with or without split skin graft. Amputations of limbs may be necessary. Antibiotic treatment has been disappointing to date especially in extensive ulcerative cases.
- **Prevention**
  General cleanliness and prompt treatment of all injuries will be helpful. There is no vaccine for Buruli ulcer. BCG appears to offer limited protection.
  Increasing awareness within the affected population to encourage early reporting will reduce the current suffering associated with the disease.
- **Epidemics**
  Emerging disease with increasing burden on health facilities, although no epidemics have been described.
- **Drug resistance monitoring**
  Not applicable.

Other aspects

- **Procurement of equipment and drugs**
  Surgical facilities equipped to do skin grafting are essential to the management of cases.
  Blood transfusion services and facilities to screen blood for HIV and hepatitis B must be available. Laboratories must be equipped to undertake Ziehl-Neelsen staining for acid-fast bacilli and culture of *Mycobacterium ulcerans*. Histopathology and polymerase chain reaction (PCR) can be undertaken in external laboratories.
- **Surveillance**
  - Number of cases (new and recurrence) registered in a given time
  - Number of laboratory-confirmed cases
  - Age and sex distribution of the cases
  - Number of various clinical forms of cases
  - Number of patients presenting initially with disabilities
  - Number of patients with resulting sequelae after treatment
  - Number of deaths related to Buruli ulcer.
- **Special considerations/other interventions**
  - Previous residence or travel to a known endemic area must raise suspicion of Buruli ulcer
  - About 70% of the patients are children below 15 years of age
  - Most lesions are on the extremities: lower extremities are affected twice as often as upper extremities
  - In areas where the disease is unknown, first cases must be confirmed by laboratory diagnosis; in known endemic areas, sample cases may be confirmed for quality assurance.

Contacts and References

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REFERENCES: WHO, 2000. *Buruli ulcer (Mycobacterium ulcerans infection)*. WHO/CDS/CPE/GBUI.2000; www.who.int/gtb-buruli

Cholera A00

Notification to WHO universally required by *International Health Regulations*

General introduction

Cholera is prevalent in about 80 countries and causes an estimated 120 000 deaths each year. The world is currently experiencing the 7th pandemic. In Africa epidemics have become more frequent and case fatality rates are high. Refugees or displaced populations are at major risk of epidemics because of the conditions prevailing in camps (unsafe water, poor sanitation and hygiene).

Control of the disease requires standardized, appropriate patient management and preventive measures such as improvement of sanitation and living conditions (see *Sanitation*), together with surveillance and health education of the population at risk. Notification to WHO is required by the *International Health Regulations.*

Causal agent and main modes of transmission

- **Causal agent:** *Vibrio cholerae* O1, *Vibrio cholerae* O139
- **Main modes of transmission:** Ingestion of *V. cholerae* O1 or *Vibrio cholerae* O139 by:
  - Drinking contaminated water
  - Eating food (fruits and vegetables) contaminated through:
    - Water
    - Nightsoil
    - Contamination *during* preparation (rice, millet, food from street vendors)
  - Contaminated seafood
  - Indirect contamination (hands)

  The incubation period is very short (a few hours to 5 days).

Clinical description and case definition

- **Clinical description**
  In most cases, infection with *Vibrio cholerae* is asymptomatic or causes mild diarrhoea (asymptomatic carriers can transmit the infection). In 10-20% of cases there is severe diarrhoea and vomiting leading to dehydration. In the absence of appropriate treatment, the case fatality rate can range from 20% to 30%; proper management can reduce the case fatality rate to 1%.
- **Clinical case definition**
  - *In an area where the disease is not known to be present:*

    Severe dehydration or death from acute watery diarrhoea in a patient aged 5 years or more.
  - *In an area where cholera is endemic:*

    Acute watery diarrhoea, with or without vomiting in a patient aged 5 years or more.*
  - *In an area where there is a cholera epidemic:*

    Acute watery diarrhoea, with or without vomiting in any patient.

  * Cholera does appear in children under 5 years, but the inclusion of all cases of acute watery diarrhoea among the 2-4 year age group in the reporting of cholera would greatly reduce the specificity of reporting.

  Case classification
  - ***Suspected:*** A case that meets the clinical case definition
  - ***Probable:*** Not applicable
  - ***Confirmed:*** A suspected case that is laboratory-confirmed.

  Laboratory criteria

  Isolation of *Vibrio cholerae* O1 or O139 from stools in any patient with diarrhoea.

NOTE: Where cholera is rare or was previously unrecognized, initial cases must be confirmed by the laboratory (demonstration of toxigenic *V. cholerae* O1 or O139 in faeces or vomit).

Recommended interventions

- **Case management**
  Assess dehydration status: *none, some, severe* (refer to appendix on page 58)
  Treat dehydration
  Oral rehydration solution if *no* or *some* dehydration
  Oral rehydration + intravenous rehydration if *severe* dehydration
  Use antibiotics only for *severe* dehydration and after antimicrobial sensitivity testing, as locally recommended.
- **Prevention**
  - Provision of safe water
  - Hand-washing
  - Safe food (cook it, peel it or leave it)
  - Safe disposal of excreta
  - Safe latrines.

  ***Vaccines*:** The recently developed oral B subunit killed whole-cell (BS-WC) vaccine has shown convincing but transient protection against cholera under field conditions. Vaccination should be considered among the pre-emptive tools for the prevention of cholera in carefully evaluated emergency situations among high-risk populations, not as a method of containing an outbreak *after* occurrence. It should only be used as a public health measure in addition to other prevention and control measures (See WHO. *Potential use of oral cholera vaccines in emergency situations.* WHO, 1999. WHO/CDS/EDC/99.4).
- **Epidemics**
  Cholera control cannot be handled in isolation and requires coordination at national and regional levels, involving the community within preparedness control committees, and setting up communication lines to and from the laboratory and health authorities.

  The most effective actions involve health education and proper case management, provision of safe water (e.g. through boiling or chlorination) followed by improvements in sanitation. Laboratory confirmation is required for *initial* cases, but not once the diagnosis has been established in the region. Sample examination is also needed before the epidemic can be declared ended.

  In the presence of adequate infrastructures and together with other preventive measures, mass immunization with oral BS-WC vaccine is feasible and acceptable for the prevention of epidemics in large stable refugee populations. Recourse to mass immunization must be supported by a careful preliminary assessment of each emergency situation.

NOTE: There should be at least one reference laboratory in each country for identification of *Vibrio cholerae*. Once the presence of cholera is confirmed, it becomes unnecessary to confirm all subsequent cases (use the "suspected" case classification), but monitoring an epidemic must include laboratory confirmation of a small proportion of cases on a continuing basis.

- **Drug resistance monitoring**
  Drug resistance to some antibiotics (including TMP-SMX, tetracyclines and chloramphenicol) has been reported; refer to national and local information as regards antimicrobial sensitivity patterns and as regards regulations.

Other aspects

- **Procurement of equipment and drugs**
  For a population of 10 000 where 0.2% of the population are expected to fall ill in the first few days, the following stocks are required:
  - ***Rehydration supplies:*** 130 ORS packets, 24 bags Ringer's lactate + sets (1 litre); 3 scalp vein sets, 1 nasogastric tube (adults), 1 nasogastric tube (children).
  - ***Other supplies:*** 1 large water dispenser with tap; 4 litre bottles + 4 half-litre bottles for ORS, 8 tumblers, 4 teaspoons, 1 kg cotton wool, 1 reel of adhesive tape.
  - **Antibiotics**: (to be adapted according to local recommendations and antimicrobial sensitivity patterns): 96 capsules tetracycline 250 mg, 12 capsules doxycycline 100 mg, 60 tablets TMP20-SMX 100 mg.
  - **Material for stool samples:** containers, Cary Blair medium.

- **Surveillance**
  - *Routine surveillance* (together with surveillance of diarrhoeal diseases).
  - *Special surveillance:* risk areas (poor sanitation and water; poor hygiene/hand-washing; unsafe cooking/ conservation of food) or high-risk individuals (late diagnosis/treatment, malnutrition, concurrent diseases).
  - *Peripheral level:*
    - Immediate case-based reporting of suspected cases
    - Immediate investigation of all suspected cases and clusters.
    - Routine weekly/monthly reports on cases (aggregated data).
  - *Central level:*
    - Report initial suspected cases to WHO, with follow-up aggregated data.
- **Special considerations/other interventions**

  Preparation for a cholera outbreak involves the setting up of committees that include *both* health care workers *and* members of the community, particularly community leaders and people who command respect and support. The committees must coordinate with local health authorities and Ministry of Health personnel as well as nongovernmental organizations.

  Quarantine is not an effective control or containment measure and economic sanctions such as limitation of imports or exports cannot prevent the introduction of cholera. Mass chemoprophylaxis has also not been shown to be effective. Neither measure is useful or recommended.
- **Indicators**
  - Number of mothers with correct knowledge of home therapy for diarrhoea
  - Management of diarrhoea episodes
  - Incidence of diarrhoea
  - Deaths due to diarrhoea.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42

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REFERENCES:

WHO. *Guidelines for cholera control.* Geneva, 1993. ISBN 92 4254 49X

WHO. *Epidemic Diarrhoeal Disease Preparedness and Response: Participant's Manual.* Geneva, 1997. WHO/EMC/DIS/97.3.

WHO. *Epidemic Diarrhoeal Disease Preparedness and Response: Facilitator's Guide.* Geneva, 1997. WHO/EMC/DIS/97.4.

Website: www.who.int/emc/diseases/cholera/index.html

Appendix: Assessment of dehydration

- **Major signs of dehydration**
  - **General condition:** Depending on the degree of dehydration, a patient with diarrhoea, especially a child may be:
    - Lethargic or unconscious (general danger sign), or
    - Restless/irritable.

    Only children who cannot be consoled and calmed should be considered restless or irritable.
  - **Thirst, or child's reaction when offered to drink:**
    - *Unable to drink* if it cannot take fluid in the mouth and swallow it. For example, a child may not be able to drink because it is lethargic or unconscious
    - *Drinking poorly* if it is weak and cannot drink without help or swallow (only if fluid is put in the mouth)
    - *Drinking eagerly, thirsty* if it is clear that the patient wants to drink.
  - **Elasticity of skin**. When released, the skin pinch goes back:
    - *Very slowly* (longer than 2 seconds), or
    - *Slowly* (skin stays up for a brief instant), or
    - *Immediately*.

    In a child with marasmus (severe malnutrition), the skin may go back slowly even if the child is not dehydrated. In an overweight child, or a child with oedema, the skin may go back immediately even if the child is dehydrated.
- **Other signs include:**
  - Dryness of mouth and tongue
  - Sunken eyes. In a severely malnourished child who is visibly wasted (marasmus), the eyes may look sunken even if the child is not dehydrated. Even though the sign "sunken eyes " is less reliable in a visibly wasted child, it can still be used to classify dehydration.
- **Classification**

  Based on a combination of the above clinical signs, patients presenting with diarrhoea are classified into the following categories:
  1. Those who show 2 signs of dehydration, of which at least one of the following major signs: lethargic or unconscious, unable to drink or drinking poorly, very slow return of skin, and/or 1 of the following: very dry mouth or very sunken eyes, are said to have ***severe dehydration*** (fluid deficit greater than 10% of body weight) and require immediate IV perfusion associated with oral rehydration.
  2. Those who show 2 signs of dehydration, of which at least one of the following major signs: restless or irritable, drinking eagerly, slow skin return, and/or one of the following: dry mouth or sunken eyes, are said to have ***some dehydration*** (5% to 10% of body weight) and require active oral treatment with ORS solution. This classification includes both "mild " and "moderate" dehydration, the descriptive terms used in most textbooks.
  3. Patients with diarrhoea but no signs of dehydration are said to have ***no dehydration***; their fluid deficit is less than 5% of body weight. Although they lack distinct signs of dehydration, they must be given more fluid than usual to prevent dehydration from developing.

Variant Creutzfeldt-Jakob Disease (vCJD)

General introduction

The incidence of Creutzfeldt-Jakob Disease (CJD) and variant CJD (vCJD) is not currently monitored in many parts of the world. vCJD was recognized in the United Kingdom in 1996. An etiological link between vCJD and the agent of bovine spongiform encephalopathy (BSE) has been hypothesized. The size of the population exposed and susceptible to vCJD in the United Kingdom – and eventually in other parts of the world – is not known. This and other uncertainties relating to the potential length of the incubation period complicate any useful prediction of the future number of vCJD cases. Other populations may have also been exposed to the agent through importation of live cattle or cattle by-products from BSE-affected countries, or through the use of medicinal or cosmetic products derived from affected bovine tissues. Global surveillance of vCJD and other forms of CJD should lead to a better understanding of the disease, including potential causes of iatrogenic CJD as well as the distribution of various hereditary forms. It should also provide information towards protection against the risks of disease.

Causal agent and main modes of transmission

The nature of the ***causal agent*** is not yet fully elucidated.

- **Main modes of transmission:**
  - vCJD is supposed to be caused by the same agent as BSE, the exact route of exposure is uncertain, but is likely to be linked to contaminated foods of bovine origin
  - The incubation period is not known, but is measured in years, the average age at onset is younger than in sporadic CJD, but it is uncertain if this relates to exposure or to susceptibility
  - All those who have been identified to have vCJD have died, i.e., 100% case fatality rate
  - No screening test is currently available.

Disease forms and case definition

- **Sporadic CJD**
  - ***Possible CJD:***
    - Progressive dementia, **and**
    - EEG atypical or not known, **and**
    - Duration <2 years, **and**
    - **At least 2 out of the following clinical features:** myoclonus, visual or cerebellar disturbance, pyramidal, extrapyramidal dysfunction, akinetic mutism.
  - ***Probable CJD:***

    (in the absence of an alternative diagnosis from routine investigation)
    - Progressive dementia, **and**
    - At least 2 of the following 4 clinical features:
      - Myoclonus
      - Visual or cerebellar disturbance
      - Pyramidal / extrapyramidal dysfunction
      - Akinetic mutism, **and**
      - A typical EEG, whatever the clinical duration of the disease, **and/or**
      - A positive 14-3-3 assay for CSF and a clinical duration leading to death in <2years
  - ***Confirmed (definite) CJD:***
    - Neuropathological confirmation, **and/or**
    - Confirmation of protease-resistant prion protein (PrP) (immunocytochemistry or Western Blot)**, and/or**
    - Presence of scrapie-associated fibrils.
- **Iatrogenic CJD**
  - Progressive cerebellar syndrome in a recipient of human cadaver-derived pituitary hormone, **or**
  - Sporadic CJD with a recognized exposure risk.
- **Familial CJD**
  - Confirmed or probable CJD **plus** confirmed or probable CJD in a first degree relative, **and/or**
  - Neuropsychiatric disorder **plus** disease-specific PrP mutation.

NOTE: For purposes of surveillance, includes Gerstmann-Sträussler-Scheinker (GSS) syndrome and fatal familial insomnia (FFI).

- **Variant CJD (vCJD)**[6]
  Variant CJD cannot be diagnosed with certainty on clinical criteria alone. A definite diagnosis requires neuropathological confirmation. The following combinations of signs, symptoms and clinical investigations serve to define possible, probable and definite vCJD:

  I
  - Progressive psychiatric disorder
  - Clinical duration >6 months
  - Routine investigations do not suggest an alternative diagnosis
  - No history of potential iatrogenic exposure
  - No evidence of a familial form of TSE (transmissible spongiform encephalopathies).

  II
  - Early psychiatric symptoms (depression, anxiety, apathy, withdrawal, delusions)
  - Persistent painful sensory symptoms (frank pain and/or dysaesthesia)
  - Ataxia
  - Chorea / dystonia or myoclonus
  - Dementia.

  III
  - EEG unknown or does not show the typical appearance of sporadic CJD (generalized triphasic periodic complexes at approximately one per second)
  - Bilateral symmetrical pulvinar high signal on MRI brain scan (relative to other deep gray-matter nuclei).

  IV
  - Positive tonsil biopsy.

  NOTE: Tonsil biopsy not recommended routinely nor in cases with EEG appearances typical of sporadic CJD, but useful in suspect cases where the clinical features are compatible with vCJD and MRI does not show bilateral pulvinar high signal. The use of cerebral biopsy in living patients is to be discouraged unless its purpose is to arrive at an alternative diagnosis of a treatable disorder.

  Case classification
  - ***Possible***
    - A patient with the items under I above and at least 4 items under II, **and**
    - EEG does not show the typical appearance of sporadic CJD
  - ***Probable***
    - A patient with the items under I and at least 4 items under II, **and**
    - EEG does not show the typical appearance of sporadic CJD, **and**
    - Bilateral pulvinar high signal on MRI scan
  - ***Confirmed (definite)***
    - A patient with the items under I above, **and**
    - Neuropathological confirmation of vCJD (spongiform changes and extensive PrP deposition with florid plaques throughout the cerebrum and cerebellum)

  See under *Special considerations* for neuropathological criteria in CJD and other human transmissible spongiform encephalopathies.

Recommended interventions

- **Case management**
  Supportive
- **Prevention**
  Avoiding exposures to BSE-causing agent
  Avoiding iatrogenic exposures
- **Epidemics**
  Not applicable
- **Drug resistance monitoring**
  Not applicable

[6] Updated for the present document by technical unit (see *Introduction)*

Other aspects

- **Procurement of equipment and drugs**
  Not applicable.
- **Surveillance**
  One centre should be identified at central level to carry out surveillance.
  All reporting should be case-based.
  All definite, probable and possible cases should be notified by the appropriate health care professionals (usually physicians, neurologists, psychiatrists, neuropathologists) to the centre responsible for surveillance.
  NOTE: Death registrations must be checked in order to identify cases not detected by routine surveillance.
- **Special considerations/other interventions**
  Neuropathological criteria for CJD and other human transmissible spongiform encephalopathies can be summarized as follows:
  - ***Creutzfeldt-Jakob disease:*** *sporadic, iatrogenic* (recognized risk) or *familial* (same disease in first-degree relative or disease-associated *PrP* gene mutation):
    - Spongiform encephalopathy in cerebral and/or cerebellar cortex and/or subcortical grey matter, **and/or**
    - Encephalopathy with prion protein (PrP) immunoreactivity (plaque and/or diffuse synaptic and/or patchy/perivacuolar types).
  - ***New variant CJD***
    - Spongiform encephalopathy with abundant PrP deposition, in particular multiple fibrillary PrP plaques surrounded by a halo of spongiform vacuoles ('florid' plaques, 'daisy-like' plaques) and other PrP plaques, and amorphous pericellular and perivascular PrP deposits especially prominent in the cerebellar molecular layer.
  - ***Gerstmann-Sträussler-Scheinker (GSS) disease:*** (in family with dominantly inherited progressive ataxia and/or dementia and one of a variety of PrP gene mutations):
    - Encephalo(myelo)pathy with multicentric PrP plaques.
    - Thalamic degeneration, variable spongiform change in cerebrum.
  - ***Kuru***
    - Spongiform encephalopathy in the Fore population of Papua New Guinea.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42

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REFERENCES

WHO. *WHO Infection Control Guidelines for Transmissible Spongiform Encephalopathies. Report of a WHO Consultation, Geneva, Switzerland, 23-26 March 1999].* WHO: Geneva, 2000. WHO/CDS/CSR/APH/2000.3 http://whqlibdoc.who.int/hq/2000/WHO_CDS_CSR_APH_00.3

Dengue

Dengue haemorrhagic fever (DHF) A.90

Dengue shock syndrome (DSS) A91

General introduction

Dengue fever (and related forms of dengue haemorrhagic fever – DHF – and dengue shock syndrome – DSS) occur in over 100 countries and territories and threaten over 2500 million people in tropical and subtropical regions. There is a high proportion of asymptomatic or quasi-asymptomatic infections and high epidemic potential. An estimated 500 000 patients, 90% of them below the age of 15, are hospitalized with DHF/DSS every year. WHO's efforts tend towards accelerating the development of a dengue vaccine.

Causal agent and main modes of transmission

- **Causal agents*:*** Dengue virus (4 serotypes: DEN-1, DEN-2, DEN-3, DEN-4)
- **Main modes of transmission:** Dengue viruses are transmitted to humans through the bites of infective female *Aedes aegypti* and a few other *Aedes* mosquito species. These generally acquire the virus while feeding on the blood of a viraemic person. Once infective – after 7 to 12 days – a mosquito can transmit the virus to susceptible individuals for the rest of its life; transovarial transmission to the next generation of mosquitoes has been demonstrated, albeit rarely. The virus circulates in the blood of infected humans for 2-7 days and the period from infective bite to the appearance of symptoms ranges from 3 to 14 days (usually about 1week).

Clinical description and case definition

- **Clinical description**
  - DENGUE FEVER

    An acute febrile illness of 2-7 days duration with 2 or more of the following manifestations: headache, retro-orbital pain, myalgia, arthralgia, rash, haemorrhagic manifestations, leucopaenia. Infants and persons under 15 may have a non-specific febrile illness with maculopapular rash. Older patients may have a mild febrile syndrome or the classical incapacitating disease.

    Laboratory criteria for confirmation of dengue infection

    One or more of the following:
    - Isolation of the dengue virus from serum, plasma, leukocytes, or autopsy samples
    - Demonstration of a 4-fold or greater change in reciprocal IgG or IgM antibody titres to one or more dengue virus antigens in paired serum samples
    - Demonstration of dengue virus antigen in autopsy tissue, serum or CSF samples (immunohistochemistry or immunofluorescence or ELISA)
    - Detection of viral genomic sequences in autopsy tissue, serum or CSF samples by polymerase chain reaction (PCR).
  - DENGUE HAEMORRHAGIC FEVER

    The WHO definition for dengue haemorrhagic fever is:
    - Fever or history of recent fever lasting 2-7 days
    - Thrombocytopaenia of 100 000 platelets or less per cc*

      * In practice, average of 3 platelets or less per oil-immersion field averaged on 10 fields
    - At least one of the following haemorrhagic manifestations: positive tourniquet test, petechiae/ecchymoses/purpura, haematemesis/melaena, other overt bleeding.
    - At least one of the following manifestations of plasma leakage due to increased vascular permeability: >20% rise in average haematocrit for age and sex, >20% drop in haematocrit following volume replacement, pleural effusions/ascites/hypoproteinaemia.
  - DENGUE SHOCK SYNDROME

    All of the above 4 criteria for DHF, plus
    - Evidence of circulatory failure (rapid weak pulse with narrow pulse pressure <20 mmHg), **or**
    - Cold clammy skin or restlessness, with hypotension for age.

    Critical shock and death occur within 12-24 hours. Patients may complain of acute abdominal pain.
    Most patients remain conscious until close to the terminal stage.

Case classification

- ***Suspected:*** A case compatible with the clinical description
- ***Probable:*** A case compatible with the clinical description with **one or more** of the following:
  - Serology
    - Reciprocal haemagglutination-inhibition antibody titre ≥1280
    - Comparable IgG enzyme immunoassay titre
    - Positive IgM antibody test in late acute or convalescent-phase serum specimen
  - Occurrence at same location and time as other confirmed cases of dengue fever.
- ***Confirmed:*** A case compatible with the clinical description, laboratory-confirmed.

Recommended interventions

- **Case management**
  - For dengue fever there are no specific case management techniques available, only symptomatic treatment. Acetylsalicylic acid (aspirin) is contraindicated because of its haemorrhagic potential.
  - For DHF, maintenance of the circulating fluid volume through intravenous perfusion is essential (watch out for signs of under- or overhydration). The following are warning signals for impending shock:
    - Sudden drop in body temperature
    - Profuse vomiting
    - Lethargy or restlessness
    - Acute abdominal pain.

    Blood transfusion may be considered in case of severe haemorrhage.
- **Prevention**

  The only method of prevention at present is through vector control:
  - Proper disposal of solid waste (including used tyres), improved water storage, application of insecticide to larval habitats (only temephos, methoprene or *Bacillus thuringiensis israelensis* (Bti) in water storage containers and animal drinking bowls), mosquito-eating fish, bednets, repellents (*see Vector control*)

  Progress is under way on a vaccine that protects against all 4 serotypes of dengue.
- **Epidemics**
  - Preparedness plan for triage and case management in health care centres and hospitals
  - Intensify source reduction measures, including community mobilization
  - Adulticide space spraying, where effective and appropriate.
- **Drug resistance monitoring**

  Not applicable.

Other aspects

- **Procurement of equipment and drugs**

  See *Vector control*
- **Surveillance**
  - **Areas where no dengue transmission has been detected but with *Aedes aegypti*, *Ae. albopictus* or other secondary mosquito vector species:** Surveillance of suspected cases with investigation of clusters of suspected cases for dengue.
  - **Areas where disease is endemic with seasonal variations in transmission, and areas where epidemic dengue occurs:** Routine weekly/monthly reporting of aggregated data of suspected, probable and confirmed dengue cases and DHF cases (to be considered separately) from peripheral to intermediate and central levels.
- **Special considerations/other interventions**

  Availability of basic laboratory tests for performing haematocrit and platelet counts.
  Rapid referral to more advanced facilities must be considered promptly.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42

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REFERENCES:

PAHO. *Dengue and dengue hemorrhagic fever in the Americas: guidelines for prevention and control.* PAHO scientific Publication N°548. Washington: PAHO, 1994. ISBN 92 75 11548 6.

WHO. *Dengue haemorrhagic fever: diagnosis, treatment, prevention and control.* Second edition. Geneva: WHO, 1997. ISBN 92 4 154500 3

WHO. *Strengthening implementation of the global strategy for dengue/dengue haemorrhagic fever prevention and control.* Geneva: WHO, 2000 (WHO7CDS7(DEN)/IC/2000.1)

WHO. *Preventing dengue and dengue haemorrhagic fever: a fact sheet for municipal and community leaders.* Geneva: WHO, 1994(CTD/FIL(DEN)/94.4) http://whqlibdoc.who.int/hq/1994/CTD_FIL(DEN)_/94.4.pdf

Diphtheria A36

General introduction

Diphtheria is a widespread severe pharyngeal infection with potential for epidemic spread. It involves primarily the nasopharyngeal mucosa, but can affect other mucosas and the skin (especially in Africa). Toxic effects of diphtheria include myocarditis, which can be fatal. Inapparent infections outnumber clinical cases. The control of diphtheria is based on 3 measures:

1. Ensuring high population immunity through immunization (primary prevention)
2. Rapid investigation and treatment of contacts (secondary prevention of spread)
3. Early diagnosis and proper case management (tertiary prevention of complications and deaths).

Causal agent and main modes of transmission

- **Causal agent:** *Corynebacterium diphtheriae*, toxicogenic strains
- **Main modes of transmission:** contact (usually direct, rarely indirect) with a patient or carrier. In rare cases, the disease may be transmitted through foodstuffs. The incubation period is usually 2 to 5 days but may be longer. In countries with high levels of immunization, the disease has become sporadic, but decreased immunization levels can lead to major epidemics, as in the former USSR in the mid-90s.

Clinical description and case definition

- ***Clinical description:*** upper respiratory tract illness with laryngitis or pharyngitis or tonsillitis **plus**
  - Adherent membranes of tonsils or nasopharynx

  Laboratory confirmation: Isolation of *Corynebacterium diphtheriae* from a clinical specimen.

  Classification
  - ***Suspected:*** Not applicable
  - ***Probable:*** A case that meets the clinical description
  - ***Confirmed:*** Probable case confirmed by laboratory or epidemiologically linked to a laboratory-confirmed case.
  - ***Carrier:*** Presence of *C. diphtheriae* in nasopharynx, no symptoms.

NOTE: Persons with positive *C. diphtheriae* identification but who do not meet the clinical description (e.g. asymptomatic carriers) must not be reported as probable or confirmed cases.

Recommended interventions

- **Case management**
  - *Patients*
    - Antitoxin: 20 000 to 100 000 units for 14 days intramuscularly **plus**
    - Antibiotics: Procaine penicillin 1.2 million units intramuscularly in 2 divided doses (children 25 000 to 50 000 units/kg/day in 2 divided doses) until patient can swallow, then orally (penicilllin V in 4 doses a day) for a total of 14 days
    - Isolation: strict (pharyngeal diphtheria) or contact (cutaneous diphtheria) for 14 days.
  - *Contacts*
    - Surveillance for 7 days, with throat culture
    - All must receive benzathine penicillin 1.2 million international units intramuscularly – if culture is positive, give antibiotics as for patients above.
  - *Carriers*
    - Benzathine penicillin 1.2 million international units intramuscularly (children 600 000 units) in a single dose.

- **Prevention**
  - *Immunization:* 3 doses of 0.5 ml DTP intramuscularly in outer part of thigh, according to national schedule (normally at age 6, 10, 14 weeks – if immunization is started later, there must still be an interval of 4 weeks between doses). Immunization to be completed preferably before the age of 6 months (26 weeks).

  DTP vaccine must be stored between 2°C and +8°C. The diphtheria and tetanus components of DTP are damaged by freezing – use shake test (see *Immunization*). The pertussis part is damaged by heat.

  DTP vaccine can be given to immunocompromised children and adults. It must *not* be given to children over 7 years of age or to any children who have shown a severe reaction to a previous dose of the vaccine (a combination of diphtheria and tetanus toxoids with reduced diphtheria content (Td) must be given instead). A booster dose at 10-year intervals is recommended for persons at higher risk of exposure (e.g. health workers).

  Adult contacts must avoid contact with children and must not be allowed to undertake food-handling until proven not to be carriers.
- **Epidemics**
  Identification and widespread immunization of close contacts and of other population groups involved, especially children
  If there is an epidemic among adults, identify and immunize the group(s) at highest risk.
- **Drug resistance monitoring**
  Not applicable.

Other aspects

- **Procurement of equipment and drugs**
  See *Immunization* (section 2.1).
- **Surveillance**
  - Routine monthly reporting of aggregated data of probable or confirmed cases from peripheral to intermediate and central levels; zero reporting required at all levels
  - All outbreaks must be investigated immediately and case-based data collected
  - In countries achieving low incidence (usually where immunization coverage is 85% to 90%) immediate reporting of case-based data for probable or confirmed cases from peripheral to intermediate and central levels
  - Aggregated data on probable or confirmed cases and on immunization coverage must be reported from national level to WHO Regional Offices according to regional specifications.
- **Special considerations/other interventions**
  Infants born to immune mothers are usually immune for 6 months.
  A clinical attack does not always induce lasting immunity.
- **Indicators**
  See *Immunization* (section 2.1).

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42

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REFERENCES:

WHO. *Immunization in practice*. *Module 1* - WHO/EPI/TRAM/98.01 (pages 3-4); *Module 2* - WHO/EPI/TRAM/98.02 (pages 6-9).
See also: *Immunization* in the present document.

Dracunculiasis B72

General introduction

Dracunculiasis, although rarely fatal, carries a heavy load of disability. An eradication programme is being implemented and has already eliminated the disease from Pakistan and India. Yemen has reported zero cases since 1997. Transmission was interrupted in Kenya in 1994, in Cameroon in 1997 (both countries report less than 10 imported cases for 2000), and in Senegal in 1997. Interruption of transmission has been achieved in all continents except Africa, where 13 countries reported indigenous cases in 2000 (see *Special Considerations*). There were over 96 000 cases in 1999 and a provisional total of about 75 000 in the year 2000, mainly in poor rural communities without a safe water supply.

Causal agent and main modes of transmission

- **Causal agent:** The Guinea worm *Dracunculus medinensis*, a nematode.
- **Mode of transmission:** The intermediate host is a water crustacean (*Cyclops*), encountered universally in stagnant water and ingested by drinking contaminated water. The larvae of *D. medinensis* are freed in the intestine and migrate in the tissues of the human host. The female gravid worm emerges through the skin after 1 year. To relieve the irritation caused by the emergence of the worm or for other reasons, the patient may step into the local water hole, where the larvae of *D. medinensis* will emerge in the water and complete the cycle.

Clinical description and case definition

- **Clinical description:** The emergence of the gravid female is accompanied by irritation and local infection, which often leads to lesions of the limbs with crippling. This may bring about severe losses in agricultural production since the symptoms often develop at the time of harvesting. Secondary bacterial infections are also of major concern.
- **Case definition:** [7] Anyone exhibiting or having a history of a skin lesion with the emergence of a Guinea worm within the previous year.

Recommended interventions

- **Case management**
  No drugs are currently available.

  Once a worm emerges, use a matchstick to roll it out gently. Never break the worm, and never pull it. Bandage the wound after applying an antibiotic ointment to prevent superinfection of the lesion, and 24 hours later remove the bandages and roll the part of the worm that has emerged. Repeat until the whole worm is removed. Although practised in certain endemic countries, surgical extraction is *NOT* recommended.
- **Prevention**
  - Keeping infected people away from sources of drinking-water.
    - Insecticide of choice for stagnant sources of water: Abate/temephos
    - Formulation and dosage: based on the estimated amount of water present
    - Time of application: usually twice a year, especially after a flood has receded
  - Filtration of water: use of nylon cloth filters for all drinking-water, including the use of filter straws
  - Health education: messages have been developed and adapted in all endemic countries.
- **Epidemics**
  Since 9 out of 10 people in many areas of Africa still have nothing else to drink but meagre quantities of impure water, exposure to dracunculiasis is always possible. The risk of an epidemic is present in previously endemic countries and those countries adjacent to endemic countries. In such cases, identify the geographical source of infection and undertake control as outlined above.
- **Drug resistance monitoring**
  Not applicable.

[7] Updated for the present document by technical unit (see *Introduction*)

Other aspects

- **Procurement of equipment and drugs**
  - Temephos, an insecticide for the intermediate host.
  - Suitable nylon or polyester monofilament filter.
- **Surveillance**
  - *Peripheral level (endemic and formerly endemic countries)*
    - Village-based surveillance aims to detect cases when the worm is pre-emergent or at latest 24 hours after the beginning of worm emergence, even in the most remote local villages
    - Community-oriented case-containment interventions are combined with surveillance to interrupt further transmission of the disease.
  - *Intermediate/Central level*
    - Reports (aggregated data) from all villages are sent to intermediate and central levels on a monthly basis, generally combined with supervision activities at all levels of the national dracunculiasis eradication programmes (when annual incidence is close to zero, cases must be reported on a weekly or daily basis).
  - *International level*
    - Reports are aggregated and sent from endemic countries to the international level on a monthly basis, and used as a policy basis and for managerial decisions by central programmes, as well as by external supporting agencies.
- **Special considerations/other interventions**
  Because of the need for health workers in newly identified endemic villages and the lack of trained workers in remote localities, training remains an important activity.
  Benin, Burkina Faso, Central African Republic, Côte d'Ivoire, Ethiopia, Ghana, Mali, Mauritania, Niger, Nigeria, Sudan, Togo and Uganda reported indigenous cases in 2000.
- **Indicators**
  - Short-term incidence of Guinea-worm cases
  - Projected long-term incidence of Guinea-worm cases
  - Geographical distribution of new cases of Guinea-worm.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42.

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REFERENCES:

CHIPPAUX J-Ph. *Le ver de Guinée en Afrique – méthodes de lutte pour l'éradication.* Paris : ORSTOM, 1994, 201 pp. ISBN 270991235.
WHO. *Dracunculiasis or Guinea worm.* WHO/CDS/CEE/DRA/99.2

Ebola and Marburg viral diseases A98.3, A98.4

(also applies to other haemorrhagic fevers)

General introduction

Ebola haemorrhagic fever is a rare but severe disease occurring primarily in areas of the African rain forest. The disease is characterized by person-to-person transmission through close contact with patients, dead bodies or infected body fluids. Marburg virus infections are extremely rare. They are similar to Ebola haemorrhagic fever and recommendations for both viral infections are the same.

Causal agent and main modes of transmission

- **Causal agents:** The Marburg and Ebola filoviruses are antigenically different, and there are at least 3 antigenically distinct geographical strains of Ebola (a fourth strain, called Reston, causes a haemorrhagic disease with clinical manifestations in nonhuman primates alone).
- **Main modes of transmission:** The natural reservoir of the virus is unknown. Significant outbreaks of the disease have until now mainly been related to nosocomial infections (see *Epidemics*). The incubation period ranges from 2 to 21 days, the most common range being estimated at 5-10 days.

Clinical description and case definition

- **Clinical description:** Initial symptoms include acute fever, diarrhoea that can be bloody (referred to as *diarrhée rouge* in francophone Africa) and vomiting. Headache, nausea and abdominal pain are common. Conjunctival injection, dysphagia and haemorrhagic symptoms (nosebleeds, bleeding gums, vomiting of blood, blood in stools, purpura) may further develop. Some patients may show a maculopapular rash on the trunk. Dehydration and significant wasting occur as the disease progresses. At a later stage, there is frequent involvement of the central nervous system, manifested by somnolence, delirium or coma. The case fatality rate ranges from 50% to 90% according to the virus.

  Laboratory criteria

  – ***Confirmatory:***
    - Positive Elisa antigen detection or IgM capture, **or**
    - Positive virus isolation (*only in a laboratory of biosafety level 4*), **or**
    - Positive skin biopsy (immunohistochemistry), **or**
    - Positive PCR with sequence confirmation.

  Case classification

  – ***Suspected:*** A case that is compatible with the clinical description.

  – ***Probable:*** *(in epidemic situation):*
    - Any person having had contact with a clinical case and presenting with acute fever, **or**
    - Any person presenting with acute fever and 3 of the following: headache, vomiting/nausea, loss of appetite, diarrhoea, intense fatigue, abdominal pain, general or articular pain, difficulty in swallowing, difficulty in breathing, hiccoughs, **or**
    - Any unexplained death.

  – ***Confirmed:*** Any suspected or probable case that is laboratory-confirmed.

  – ***Contact:*** *(in epidemic situation)*: An asymptomatic person having had physical contact within the past 21 days with a confirmed or probable case or his/her body fluids (e.g. care for patient, participation in burial ceremony, handling of potentially infected laboratory specimens).

  NOTE: In epidemic situations and after laboratory confirmation of a few initial cases, there is no need for individual laboratory confirmation and the use of "suspected or probable" case classifications is sufficient for surveillance and control purposes.

Recommended interventions

- **Case management**
  - *Supportive treatment.*

    The only way to prevent secondary infections is to minimize contact with the patient's lesions and body fluids using standard isolation precautions:
    - Isolation of patient
    - Restriction of access to patient wards
    - Use of protective clothing
    - Safe disposal of waste
    - Disinfection of reusable supplies and equipment
    - Safe burial practices.

    These can be implemented despite problems due to limited resources (see *References*).
- **Prevention**

  The following will help prevent explosive epidemics in areas potentially subject to Ebola-Marburg diseases:
  - Mobilization and education of the community
  - Advance preparations for the use of isolation precautions.
- **Epidemics**

  Epidemics of the disease in health care institutions with poor hygiene standards can be dramatically amplified through contact with patients or body fluids from infected patients (blood, vomitus, urine, stools, semen, saliva). The potential for explosive nosocomial infections constitutes the main threat to public health posed by the disease. Strict adherence to standard precautions with all patients has been shown to reduce the risk of transmission: during the 1995 Ebola haemorrhagic fever outbreak in Kikwit, no new cases were reported among health workers who used these precautions consistently.
- **Drug resistance monitoring:** Not applicable.

Other aspects

- **Procurement of equipment and drugs**

  A kit (protective material and clothing) is available from WHO for initial investigation activities. Material for protection and isolation (gloves, aprons, protective clothing, disinfectants) can often be made from locally available materials.
- **Surveillance**
  - ***In endemic areas and in the absence of an epidemic:*** Immediate reporting of suspected cases from the periphery to intermediate and central levels to ensure rapid investigation and laboratory confirmation.

  NOTE: Routine surveillance of Ebola haemorrhagic fever must be integrated with routine surveillance for other viral haemorrhagic fevers (e.g. Crimean-Congo fever, Lassa fever, Rift Valley fever, yellow fever).
  - ***In epidemic situations:***
    - Intensified surveillance and active finding of all suspected and probable cases for immediate isolation, and of all contact subjects for daily medical follow-up
    - The surveillance area must be monitored for a time corresponding to 42 days (corresponding to 2 maximum estimated incubation periods) after the date of death or hospital discharge of the last case
    - A "rumour registry" for systematic registration of rumours of cases reported by the population
    - A single source of official information is essential to ensure coherence and avoid confusion in the public.
- **Special considerations/other interventions:**

  Since extreme biohazard is associated with sampling, transportation and laboratory investigation, the strict application of biosafety procedures to specimens is essential. Shipping must be coordinated with the receiving laboratory.
- **Indicators:** Not applicable.

Contacts and References

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REFERENCES:

WHO/CDC. *Infection control for viral haemorrhagic fevers in the African care setting.* Geneva: World Health Organization, 1998. WHO/EMC/EST/98.2.

See also *Haemorhagic fevers* under *Syndromes* (page 179).

Japanese encephalitis A83.0

General introduction

Over a large part of East Asia, the Japanese encephalitis virus is the most common cause of encephalitis. The disease, which has extended southwards through Asia, is threatening Australia and the Pacific Islands. It has potential for outbreaks and can be associated with a high case fatality rate.

Causal agent and main modes of transmission

- **Causal agent:** Japanese encephalitis virus, of the family flavivirus.
- **Main modes of transmission:** Bloodsucking culicine mosquitoes (mainly *Culex tritaeniorhynchus*, *Cx. gelidus* and *Cx. fuscocephala*) transfer the virus to humans from infected animals, in most cases domestic pigs and wading birds. Human beings are not considered a reservoir for viral transmission. In most areas transmission starts in April or May and lasts until September or October. Where irrigation permits mosquito breeding throughout the year, transmission may occur even in the dry season. Incubation is 1 to 2 weeks.

Clinical description and case definition

- ***Clinical description:*** Japanese encephalitis is characterized by sudden onset of fever, chills and aches, including headaches and sometimes meningismus, particularly in adults. In children, gastrointestinal pain and dysfunction may dominate the initial stage of the disease and convulsions are common.

  Although the disease is often mild, some cases rapidly progress to severe encephalitis with mental disturbances, general or focal motor abnormalities and progressive coma. The encephalitis cannot be distinguished clinically from other central nervous system infections. Of the approximately 50 000 cases of Japanese encephalitis officially reported each year, about 10 000 end fatally; a high percentage of the survivors are left with neurological and psychiatric sequelae requiring extensive care.

  Laboratory criteria

  - ***Presumptive:*** Detection of an acute phase antiviral antibody response through one of the following:
    - Elevated and stable serum antibody titres to Japanese encephalitis virus through ELISA, haemagglutination/inhibition or virus neutralization assays, **or**
    - Japanese encephalitis virus-specific IgM in the serum.
  - ***Confirmatory:***
    - Detection of the Japanese encephalitis virus, antigen or genome in tissue, blood or other body fluid by immunochemistry or immunofluorescence or PCR, **or**
    - Presence of Japanese encephalitis virus-specific IgM in the CSF, **or**
    - A 4-fold or greater rise in Japanese encephalitis virus-specific antibody in paired sera (acute and convalescent phases) through IgM/IgG, ELISA, haemagglutination inhibition test or virus neutralization assay, in a patient with no history of recent yellow fever vaccination and where cross-reactions to other flaviviruses have been excluded.

  NOTE: Japanese encephalitis infections are common; the majority are asymptomatic. They may occur concurrently with other infections causing central nervous system symptoms; serological evidence of recent Japanese encephalitis viral infection may not be correct in indicating Japanese encephalitis to be the cause of the illness.

  Case classification

  - ***Suspected:*** A case that is compatible with the clinical description
  - ***Probable:*** A suspected case with presumptive laboratory results
  - ***Confirmed:*** A suspected case with confirmatory laboratory results.

Recommended interventions

- **Case management**
  There is no drug treatment for Japanese encephalitis other than supportive.
- **Prevention**
  For control, the following strategies based on the natural transmission cycle have been proposed:
  - Vector control
  - Water management (in cooperation with department/Ministry of irrigation and agriculture.

  Vaccination of humans (a freeze-dried, mouse brain-derived vaccine is advised).
  Vaccination of swine (virus-amplifying host associated with human epidemic disease).
- **Epidemics**
  Identification of infection among horses or birds provides epidemiological information; immunization of swine may have a significant effect, whilst immunization of horses is unlikely to. Outdoor spraying (fogging) may be used to abort urban epidemics.
- **Drug resistance monitoring**
  Not applicable.

Other aspects

- **Procurement of equipment and drugs**
  See *Vector control* (section 2.7); see *Immunization* (section 2.1) if vaccination is considered.
- **Surveillance**
  - Areas where no Japanese encephalitis transmission has been detected but the vector is present:
    Surveillance for acute central nervous system syndromes; investigation of clusters with fever.
  - Areas where disease is endemic with seasonal variation in transmission, or where epidemic Japanese encephalitis occurs:
    Routine weekly/monthly reporting of aggregated data on suspected, probable and confirmed cases from peripheral to intermediate and central level.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42.

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REFERENCES: See also *Immunization* and *Vector control* in the present document (sections 2.1 and 2.7).

Lymphatic filariasis B74

General introduction

Lymphatic filariasis is the second leading cause of permanent and long-term disability worldwide. It affects over 120 million persons in 80 countries, and over 40 million persons are seriously incapacitated by the disease; 20% of the world population is at risk of infection. Of those infected, roughly 1/3 are in India, 1/3 in Africa, and the rest in the Americas, Asia, and the Pacific. In 1997, resolution WHA50.29 called for the elimination of lymphatic filariasis as a global public health problem. The strategy adopted is based on:

a) the interruption of disease transmission

b) the treatment of the problems associated with disability control and prevention.

Causal agents and main modes of transmission

- **Causal agents:** the filariae *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori*
- **Modes of transmission:** transmitted by various species of mosquitoes, these parasitic filarial worms lodge in the human lymphatic system, producing millions of immature microfilariae that circulate in the blood. Microfilariae appear in the peripheral blood after 3 to 6 months for *Brugia malayi*, 6 to 12 months for *Wuchereria bancrofti*, often with nocturnal periodicity. When a mosquito thereafter bites the infected person, the microfilariae are picked up and the infection may be transmitted to others after about2 weeks.

Clinical description and case definition

- **Clinical description:**
  Filarial infection may be clinically asymptomatic (even in the presence of laboratory evidence of lymphatic and kidney damage); the disease may also present as one or more acute manifestations (fever, local swellings, tropical pulmonary eosinophilia syndrome, lymphangitis). Chronic complications include:
  - Lymphoedema or elephantiasis of the limbs
  - Damage to the genital organs (including hydrocoele in men)
  - Damage to the kidney (including chyluria) and lymphatic system.
- **Clinical case definition**
  Hydrocoele or lymphoedema in a resident of an endemic area for which other causes of these findings have been excluded.

  Laboratory criteria
  Positive parasite identification by:
  - Direct blood examination, or
  - Ultrasound, or
  - Positive antigen detection test.

  Case classification
  - ***Suspected:*** Not applicable.
  - ***Probable:*** A case that meets the clinical case definition.
  - ***Confirmed:*** A person with positive laboratory criteria even if he/she does not meet the clinical case definition.

Recommended interventions

- **Case management**
  - Hygiene measures for the affected body parts (and, when necessary, antibiotics and antifungal agents) can decrease the risk of adenolymphangitis:
    - Washing the affected parts twice daily with soap and water
    - Raising the affected limb at night
    - Exercising to promote lymph flow
    - Keeping nails short and clean
    - Wearing comfortable footwear
    - Using antiseptic or antibiotic creams to treat small wounds or abrasions, or in severe cases systemic antibiotics.
  - For the treatment of filarial carriers, the regimen recommended by the country is to be followed:
    - In areas where there is neither onchocerciasis nor loiasis: DEC 6 mg/kg single dose.
    - In areas where onchocerciasis has been excluded but not loiasis: individual clinical decision.

- **Prevention**
  The current strategy for filariasis control rests essentially on antiparasitic measures. To interrupt transmission, the entire at-risk population must be given a yearly, 1-dose regimen of the following:
  - *Areas with concurrent onchocerciasis:*
    - 400 mg of albendazole + ivermectin 150 micrograms per kg of body weight once a year for 4-6 years
  - *Areas with no concurrent onchocerciasis*
    - Diethylcarbamazine 6 milligrams per kg of body weight + albendazole 400 mg once a year, **or**
    - Diethylcarbamazine fortified salt for daily use for at least 6-12 months.

    NOTE: In areas with *concurrent loiasis* (sub-Saharan Africa rain forest), mass interventions cannot at present be envisaged systematically (unless onchocerciasis is a severe public health problem), because of the risk of severe adverse reactions in patients with high-density *Loa* infections (about 1 in 10 000 treatments).

  It is important to educate the population on the importance of compliance during mass chemotherapy.
  Special efforts for vector control are not required as regards lymphatic filariasis. They should be carried out under other existing vector control programmes such as anti-malaria vector control operations.
  See also *Mass chemotherapy* (section 2.8).
- **Epidemics**
  Because of relatively low infectivity and long incubation, outbreaks of filariasis are unlikely.
- **Drug resistance monitoring**
  Currently under investigation.

Other aspects

- **Procurement of equipment and drugs**
  US$0.05-$1.00 per person per year covers training, initial determination of prevalence, treatment, and post-treatment monitoring. See also *Mass chemotherapy and chemoprophylaxis.*
- **Surveillance**
  There are currently 3 options and the choice will depend on the local situation:
  1. Routine monthly reporting of aggregated data on probable and confirmed cases from periphery to intermediate level and to central level, **or**
  2. Sentinel population surveys (standardized and periodical), **or**
  3. Active case-finding through surveys of selected groups or through mass surveys.

  International: Annual reporting from central level to WHO (for a limited number of countries).

Special considerations/other interventions

- **Indicators**
  - Microfilaraemia rates
  - Antigenaemia rates
  - Incidence rates for adenolymphangitis attacks.

Contacts and References

CONTACTS:

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REFERENCES:

WHO. *Lymphatic filariasis.* WHO/CDS/CPE/SMT/2001.7

WHO. Training module on lymphatic filariasis for drug distributors (in countries where onchoerciasis is not co-endemic). WHO/CDS/CPE/CEE/2000.10 (Parts1 & 2)

*WHO. Training module on lymphatic filariasis for drug distributors (in countries where onchoerciasis is co-endemic).*WHO/CDS/CPE/CEE/2000.11 (Parts 1 & 2)

WHO. The programme to eliminate lymphatic filariasis – essential elements for medical personnel (in countries where onchoerciasis is not co-endemic). WHO/CDS/CPE/CEE/2000.12

WHO. The programme to eliminate lymphatic filariasis – essential elements for medical personnel (in countries where onchoerciasis is co-endemic). WHO/CDS/CPE/CEE/2000.13

WHO. *Preparing and implementing a national plan to eliminate filariasis (in countries where onchoerciasis is not co-endemic).* WHO/CDS/CPE/CEE/2000.15

WHO. *The programme to eliminate lymphatic filariasis* (in onchoerciasis co-endemic countries). WHO//CDS/CPE/CEE/2000.16

Webpage: www.filariasis.org

See also: *Mass chemotherapy/prophylaxis* in the present document (section 2.2).

Haemophilus influenzae b disease B96.3

General introduction

Haemophilus influenzae type b (Hib) is an important cause of infection in infants and children under 5; severe disease due to Hib is rare in adults. Among infants and children under 5, Hib is the leading cause of acute bacterial meningitis, accounting for 30% to 50% of all cases of bacterial meningitis in this age group. Severe bacterial pneumonia is the largest single remaining infectious disease killer of infants and children under 5 in the developing world, and Hib accounts for up to 1 in 5 of severe pneumonia cases in this group. WHO estimates that 400 000 children die each year of Hib disease in the absence of vaccination. Even with immediate proper treatment up to 25% of affected children may die. Permanent disabling sequelae such as deafness, learning disabilities, and difficulties in mobility may occur among those who survive infection. Safe and effective vaccines against Hib have been routinely used in many countries for over 10 years in the prevention of severe Hib disease, including meningitis and pneumonia. They reduce the risk of invasive Hib disease in children under 5 by more than 90%, and protect unimmunized populations by interrupting the chain of transmission. WHO recommends that Hib vaccine be included in routine infant immunization programmes in all countries where the disease is proven to be important and where resources permit.

Causal agent and main modes of transmission

- **Causal agents:** *Haemophilus influenzae* type b is one of 6 types (a, b, c, d, e, f) of encapsulated strains. Type b bacteria account for 95% of serious *H. influenzae* infections in children.
  H. influenzae strains live in the nose and throat of people and usually do not cause serious illness.
- **Main modes of transmission:**
  - Hib bacteria may spread throughout the body and become life-threatening (mostly in children under 5 years)
  - Hib bacteria pass from child to child in droplets of saliva when an infected child coughs or sneezes, and also when children share things they have put in their mouths.

  Transmission increases when many children spend prolonged periods of time together (day-care centres or crèches). Hib disease is most common in children under 5 years, and children between the ages of 4 and 12 months are at highest risk. At birth, maternal antibodies are adequate to protect most infants. Between 2 and 3 months of age, the level of these antibodies falls, and incidence of Hib infections increases. By 4 to 5 years of age, children develop their own immunity; Hib disease rarely occurs after that age.

Clinical description

- **Hib infections include:**
  - Bacterial meningitis – in developing countries, as many as 30% of cases result in death; 15% to 35% result in permanent neurological disabilities
  - Pneumonia – in developing countries, Hib is a major cause of pneumonia or acute lower respiratory infection among children; in Africa, up to 20% of pneumonia cases severe enough to be seen on chest X-ray are probably caused by Hib
  - Epiglottitis – without appropriate and immediate treatment, 50% of cases are fatal
  - Septicaemia ; septic arthritis; osteomyelitis; cellulitis; pericarditis.
- **Clinical description**

  Bacterial meningitis is characterized by fever of acute onset, headache and stiff neck. Meningismus is not a specific sign for Hib disease, and Hib disease cannot be diagnosed on clinical grounds.

  Laboratory criteria

  Isolation of *Haemophilus influenzae* type b or identification of Hib antigen from normally sterile fluids (CSF or blood).

  Case classification
  - ***Potential:*** (bacterial meningitis case): child with a clinical syndrome consistent with bacterial meningitis.
  - ***Confirmed:*** A case that is laboratory-confirmed.

  NOTE: Any person with Hib isolated from CSF or blood may be reported as a confirmed case, regardless of whether the clinical syndrome is meningitis.

Recommended interventions

- **Case management**
  Respiratory isolation.
  - Ampicillin 200-400 mg/kg/day parenterally for 7-10 days, **or**
  - Chloramphenicol 50 mg/kg/day for 7-10 days.
- **Prevention**
  - Respiratory isolation of patients
  - Prophylactic protection of:
    - Contacts (Rifampin orally 20 mg/kg once a day for 4 days, maximum dose 600 mg/day)
    - Household contacts where there are infants or unimmunized children under 3, other than the index case
    - Staff and children in day-care centres or crèches if more than 2 cases.

  Immunization schedule:
  - Three doses of 0.5 ml at monthly intervals, starting at 6 weeks or later (6, 10, 14 weeks), together with DTP, OPV, HepB (intramuscular administration in thigh or arm, not in the buttocks).

  Available vaccines protect against type b Haemophilus only. WHO recommends the use of conjugate Hib vaccine (to be combined with DTP or DTP-Hepatitis B vaccine according to national guidelines). The vaccine exists in single-dose and 10-dose vials, with specific diluents. No important side-effects (some redness, swelling and pain may occur). Storage temperature (2°- 8°C) same as DTP and HepB vaccines; Hib vaccine must never be frozen.

  NOTE: In routine programmes, all children must receive 3 doses of Hib vaccine in their first year, beginning after 6 weeks of age. For the first year after Hib immunization is introduced, managers must decide whether to immunize only children born after the date of introduction (gradual introduction strategy) or to include children born before that date as well (catch-up strategy).
- **Epidemics**
  Not applicable.
- **Drug resistance monitoring**
  In the USA, 30% of strains are resistant to ampicillin.

Other aspects

- **Procurement of equipment and drugs**
  Injection and reconstitution equipment.
- **Surveillance**
  - Routine monthly reporting of aggregated data of confirmed cases is recommended from the peripheral level to the intermediate and central levels
  - Zero reporting must be required at all levels
  - All potential cases must also be reported if laboratory performance indicators are to be monitored.

  NOTE: Laboratory confirmation is required for all cases, and the extent of surveillance will vary depending on the capabilities of individual countries. Surveillance does not need to be national in scope to fulfil goals. It is more important to have a well-functioning system in some areas than to have a nationwide system that functions poorly.
- **Special considerations/other interventions**
  Not applicable.
- **Indicators**
  Numbers of cases and deaths from Hib disease.

Contacts and References

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REFERENCES: See also *Immunization* in the present document (section 2.1)

Helminthiases (soil transmitted)

General introduction

More than 2000 million people worldwide (1 in 3) are affected by intestinal helminths, some of which can lead to severe diseases (hookworm anaemia). Worm infestations have proven to affect school and work performance and are therefore of economic importance. Yearly estimates of deaths from intestinal helminths worldwide are in the ranges of 10 000 for trichuriasis, 60 000 for ascariasis and 65 000 for hookworm infections.

Causal agent and main modes of transmission

- **Causal agents:** *Ascaris lumbricoides, Hookworm, Trichiuris trichiura*
- **Main modes of transmission:** Infection occurs through the ingestion of eggs (contaminated foods) or through active penetration of larvae in the soil (hookworm). Incubation is 4 to 8 weeks for *A. lumbricoides* and a few weeks to many months for hookworm disease; it is unspecified for *Trichiuris.*

Clinical description and case definition

- **Clinical description**
  - **Hookworm:**
    - Anaemia induced by intestinal blood loss.
  - **Other intestinal helminths:** symptoms include:
    - Intestinal manifestations (diarrhoea, abdominal pain)
    - Non-specific chronic symptoms
    - General malaise and weakness that may affect working and learning capacities
    - Long-term impact on physical growth.

  Symptoms are often mild and may go unrecognized in individuals.
- **Case definition and classification**
  - ***Ascariasis (suspected)***
    - Abdominal or respiratory symptoms, **and**
    - History of passing worms.
  - ***Ascariasis (confirmed):*** suspected case, **and**
    - Passage of *Ascaris lumbricoides* (anus, mouth, nose), **or**
    - Presence of *Ascaris lumbricoides* eggs in stools (microscope examination).
  - ***Hookworm infection (suspected):***
    - Severe anaemia for which there is no other obvious cause.
  - ***Hookworm infection (confirmed):*** suspected case and
    - Presence of hookworm ova in stools (microscope examination).
  - ***Trichuriasis (suspected):***
    - Bloody, mucoid stools.
  - ***Trichuriasis (confirmed):*** suspected case, **and**
    - Presence of *T. trichiura* eggs in stools.

Recommended interventions

- **Case management**
  For treatment, WHO recommends the following 4 drugs:
  - 400 mg albendazole, **or**
  - 2.5 mg/kg levamisole, **or**
  - 500 mg mebendazole, **or**
  - 10 mg/kg pyrantel (less commonly used because it is less easy to administer).

  NOTE 1: These drugs must not be given during the first trimester of pregnancy.

  NOTE 2: Where mass treatment with albendazole for filariasis is envisaged, chemotherapy of intestinal helminths will take place as part of the antifilarial chemoprophylaxis.

  NOTE 3: Iron supplementation is also recommended if required.
- **Prevention**
  - ***Overall:***
    - Personal hygiene, disposal of faeces, hand-washing, and clean food.
    - Improvements in sanitation standards (See *Sanitation*)
    - Community treatment for high-risk groups (children, pregnant women) as for individual treatment.
      - 400 mg albendazole (to be chewed before swallowing), **or**
      - 2.5 mg/kg levamisole, **or**
      - 500 mg mebendazole (to be chewed before swallowing), **or**
      - 10 mg/kg pyrantel (less commonly used).
  - ***Hookworm infection (suspected or confirmed) in addition:***
    - In highly endemic areas, wear shoes
    - Consider drug treatment and iron supplementation in pregnant women.
- **Epidemics**
  The soil-transmitted helminthiases are usually endemic, with little likelihood of rapid changes in incidence. Surveys may identify areas of particularly high endemicity where mass treatment will be warranted.
- **Drug resistance monitoring**
  This has only been identified in helminths infecting animals; there is no need at present for systematic monitoring among human infections. There is however a risk that drug resistance may develop. Strict adhesion to recommended dosages will help minimize this risk.

Other aspects

- **Procurement of equipment and drugs**
  In areas where soil-transmitted helminthiases are endemic, drugs are needed for individual treatment and for mass treatment or treatment of high-risk populations. The average cost in a school distribution campaign (including drugs, distribution, and monitoring activities) is approximately US$ 0.05 per child.
- **Surveillance**
  Not applicable.
- **Special considerations/other interventions**
  Control by drug administration can be classified according to intensity and prevalence of infection in the community as follows:
  - *High intensity* (10% or more of heavy infections* in the population), whatever the prevalence rate
    - Universal treatment once a year (twice a year for high-risk groups).
  - *Low intensity* (less than 10% of heavy infections* in the population)*/high prevalence* (50% or more infected)
    - Yearly community treatment targeted to high-risk groups (at least once a year).
  - *Low intensity* (less than 10% of heavy infections* in the population)*/low prevalence* (less than 50% infected)
    - Individual case management.

* WHO defines individual heavy infection as: 50 000 or more eggs per gram of faeces for *Ascaris;* 10 000 or more eggs per gram of faeces for *Trichiuris;* 4000 or more eggs per gram of faeces for hookworm.

The Bali conference (February 2000) has recognized the importance of helminthiasis control and asked WHO to

- Call on the governments of developed countries to contribute to relieveing poor people worldwideof this unnecessary burden of disease
- Ask governments of developing countries to include parasite control programmes as a matter of high priority on their national agendas.

The WHO objectives as regards the control of parastic infections are:

- Routine chemotherapy for at least 75% of schoolage children at risk, by 2010
- Routine chemotherapy in the framework of IMCI for children at risk (see pages 181 *sqq*)

Chemotheprapy for pregnant women in the framework of antenatal clinics.

- **Indicators**
  - % of heavy infections in the population
  - Coverage by interventions.

Contacts and References

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REFERENCES:

WHO. Montresor A., Crompton DWT, Bundy DAP, Hall A, Savioli L. *Guidelines for the evaluation of soil-transmitted helminthiasis and schistosomiasis at community level. A guide for managers of control programmes.* WHO, Geneva, 1998 (WHO/CDS/SIP/98.1).

WHO. Montresor A., Crompton DWT, Bundy DAP, Hall A, Savioli L. *Monitoring helminth control programmes. Guidelines for monitoring the impact of control programmes aimed at reducing the morbidity causes by soil-transmitted helminths and schistosomes, with particular reference to school-age children. A guide for managers of control programmes.* WHO, Geneva, 1998 (WHO/CDS/SIP/99.3).

See also: *Mass chemotherapy/prophylaxis* in the present document (section 2.2).

Viral hepatitis – faecal transmission

Viral hepatitis A B15
Viral hepatitis E B17.2

General introduction

Enterically transmitted hepatitis is a worldwide problem, with both sporadic cases and epidemic outbreaks. In developing countries, adults are usually immune and epidemics are uncommon, but improved sanitation leads to the presence of many susceptible adults in developing countries, where outbreaks – particularly institutional outbreaks – are increasing. Common-source epidemics may evolve explosively.

Causal agent and main modes of transmission

- **Causal agents:**
  Positive-strand RNA virus (picornavirus) of 27nm, Hepadnavirus (hepatitis A)
  Virus-like particle of 32nm (hepatitis E).
- **Main modes of transmission:** The virus is transmitted through faecal-oral contact; in practice, the reservoir is exclusively human. The agent of hepatitis A occurs in faeces, at peak levels in the week preceding the onset of symptoms and diminishing rapidly after symptoms appear; this information is not available for hepatitis E.

  Common source epidemics have been related to contaminated water and to the ingestion of molluscs or uncooked seafood from such waters, as well as to contamination via infected food handlers. The incubation period ranges from 15 to 50 days. Except in premature infants, most cases are probably noninfectious after the first week of jaundice.

  There is no evidence of a chronic form of the infection, although manifestations of the disease may persist for several months. Homologous immunity after infection probably lasts for life, at least for hepatitis A.

  The case fatality ratio for enterically transmitted hepatitis is usually low (<1:1000) but can be higher (up to 25:1000) for children under 5 and for those aged 50 and over. Among pregnant women infected with hepatitis E during late pregnancy, the disease may be fulminating and the case fatality rate may reach 20%.

Clinical description and case definition

- **Clinical description**
  Acute illness typically including acute jaundice, dark urine, anorexia, malaise, extreme fatigue and right upper quadrant tenderness. Biological signs include increased urine urobilinogen and >2.5 times the upper limit of serum alanine aminotransferase.
  NOTE 1: Most infections occur in early childhood; a variable proportion of adult infections is asymptomatic.

  Laboratory criteria
  - Hepatitis A: IgM anti-HAV positive
  - Hepatitis E: IgM anti-HAV and IgM anti-HBc (or Hbs Antigen) negative.

  NOTE 2: For patients negative for hepatitis A or B, further testing for a diagnosis of acute hepatitis C, D, or E is recommended (hepatitis E: IgM anti-HEV positive).

  Case classification
  - ***Suspected:*** A case that is compatible with the clinical description
  - ***Probable:*** Not applicable
  - ***Confirmed:***
    - A suspected case that is laboratory-confirmed, **or**
    - *For hepatitis A only*, a case compatible with the clinical description, in a person who has an epidemiological link with a laboratory-confirmed case of hepatitis A (household or sexual contact with an infected person during the 15-50 days before the onset of symptoms).

Recommended interventions

- **Case management**
  There is no specific treatment for acute viral hepatitis.
  Apply enteric precautions during the first 2 weeks of illness (in the case of an outbreak among neonates, this may be prolonged). Equipment contaminated with stools, urine or blood must be disposed of under sanitary conditions.
  Immunization of contacts:
  A good vaccine has been developed for hepatitis A, and is used for contacts in an outbreak. Immunoglobulin (0.02 ml/kg body weight IM) is reserved for special urgent cases. The efficacy of immunoglobulin has not been established for hepatitis E.
- **Prevention**
  - Investigation of contacts and source of infection – if hepatitis A occurs or is suspected in a food-handler
  - Improve hygienic and sanitary practices to eliminate faecal contamination of food and water; consider immunization of co-workers.
  - In countries where infection by the virus of hepatitis A tends to occur late in life (low and intermediate endemicity), vaccination can be recommended for uninfected persons at increased risk (chronic liver disease, men who have sex with men, injecting drug users, travellers to HAv-endemic countries, professionally exposed individuals).
  - In most developing countries, (asymptomatic) infections occur before the age of 5 in most children and routine immunization against hepatitis A is not considered useful in these countries.
- **Epidemics**
  Epidemics are uncommon, and occur mainly in low-prevalence countries in institutions such as day-care centres, institutions for the insane and/or institutions for the elderly. The most likely source is food-handling or, as in the cases of refugee camps, inadequate sanitation (both must be investigated and corrected).
- **Drug resistance monitoring**
  Not applicable.

Other aspects

- **Procurement of equipment and drugs**
  Immunoglobulin.
  See also *Sanitation*
- **Surveillance**
  - Routine monthly reporting of aggregated data of suspected cases, and if available, the number of confirmed cases of each type of hepatitis, from the peripheral level to intermediate and central levels
  - Zero reporting required at all levels.

  All outbreaks must be investigated immediately and confirmed serologically.
- **Special considerations/other interventions**
  Understanding the epidemiology and impact of viral hepatitis requires an understanding of the sequelae of hepatitis virus infection (asymptomatic chronic infection, chronic hepatitis, cirrhosis, primary liver cancer). This also requires data collection from sources not routinely used, including hospital surveillance data such as discharges, mortality (chronic hepatitis, cirrhosis, liver cancer) and cancer registers. Special seroprevalence surveys may be needed to measure prevalence of infection in the general population and in special groups (health care workers, blood donors, pregnant women, military recruits, patients with liver disease, people on dialysis, haemophiliacs), and ethnic subpopulations.

Contacts and References

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REFERENCES: See also: *Immunization* in the present document (section 2.1).

Viral hepatitis – parenteral and other transmission

Viral hepatitis B B16
Viral hepatitis D B17.0

General introduction

Hepatitis B accounts for an estimated 385 million carriers and more than 1 million deaths each year. Chronic infection and severe sequelae occur – an estimated 15% to 25% will die prematurely of either cirrhosis or hepatocellular carcinoma. The virus of hepatitis B may be the cause of up to 80% of all cases of hepatocellular carcinoma worldwide, and is second only to tobacco among known human carcinogens.

Control measures include ensuring transfusion safety and injection safety, and immunization. In 1992, the World Health Assembly targeted hepatitis B for reduced incidence/prevalence through the insertion of hepatitis B vaccine into national immunization programmes in all countries by 1997 (at the time of writing 128 countries have done this).

Hepatitis D shares many clinical and epidemiological characteristics with Hepatitis B; control measures are similar for the 2 agents.

Causal agent and main modes of transmission

- **Causal agents:**
  Hepadnavirus (hepatitis B), a 42-nm partially double-stranded DNA virus, with various geographical genotypes.
  The virus particles of hepatitis D are unable to infect a cell by themselves and require co-infection with HBV or superinfection of chronic HBV to undergo a complete replication cycle.
- **Main modes of transmission:** The virus is transmitted by percutaneous or permucosal exposure to blood or other infectious body fluids. It is found in highest concentrations in blood and serous exudates; lower concentrations are found in other body secretions, including saliva, semen and vaginal fluid. HBV is stable on environmental surfaces for at least 7 days, and indirect inoculation of HBV can also occur via inanimate objects. Faecal-oral or vector-borne transmission has not been demonstrated. The virus reservoir is man.

  Major modes of HBV transmission include sexual contact with an infected person, perinatal transmission from mother to infant (especially in hyperendemic areas), shared needles or syringes among injecting drug users, household contact (e.g. communally used razors and toothbrushes) and nosocomial exposure (transfusions, non-sterile parenteral equipment). Transmission of HBV in households occurs from child to child. The most important nosocomial exposures resulting in percutaneous hepatitis transmission include transfusion of blood or blood products that are not screened for hepatitis, unsafe injection practices (including excessive recourse to injections), and other inadequate infection control practices.

  In countries where HBV is highly endemic (HbsAg prevalence 8% or more), most infections occur during infancy and early childhood. In countries with an intermediate level of HBV endemicity (HBsAg prevalence 2%-7%), infections occur commonly in all age groups, although transmission during infancy and early childhood maintains a high rate of chronic infection. Where this level is low (HBsAg prevalence less than 2%), most infections occur in young adults, especially among those who belong to risk groups.

  The outcome of percutaneous hepatitis infection varies markedly depending on the age at which infection occurs. Among children under 5 years of age who become infected with HBV, fewer than 10% have signs or symptoms of acute disease, but chronic infection develops in 80%-90% of infants infected during the first year of life, and 30%-50% of children infected between 1 and 4 years of age. By comparison, 30%-50% of adults who become infected with HBV are symptomatic; only 2%-6% develop chronic infection.

Clinical description and case definition

- **Clinical description**

  HBV infection occurs in acute and chronic forms.

  – Acute illness typically includes acute jaundice, dark urine, anorexia, malaise, extreme fatigue, and right upper quadrant tenderness. Biological signs include increased urine urobilinogen and >2.5 times the upper limit of serum alanine aminotransferase. Onset of hepatitis D is usually abrupt.

  – The chronic form can be asymptomatic or can lead to cirrhosis and cancer of the liver. Asymptomatic acute HBV infection is common, particularly among children. In persons with chronic HBV or HCV infection, the risk of dying from cirrhosis or hepatocellular carcinoma, often after many years of asymptomatic chronic infection, is approximately 25% for those who become chronically infected during childhood and 15% for persons who become chronically infected at a later age.

  Laboratory criteria

  – Hepatitis B: positive hepatitis B surface antigen (HbsAg) **or** – preferably –IgM antibody to hepatitis B core antigen (anti-HBc)

  – Hepatitis D: HbsAg positive **or** IgM anti-HBc positive plus anti-HDV positive (as co-infection of hepatitis B)

  NOTE: HBsAg may be available, but a single positive test cannot distinguish acute from chronic infection. HBsAg positivity for more than 6 months indicates chronic infection.

  Case classification

  – ***Suspected:*** A case that is compatible with the clinical description.

  – ***Confirmed:*** A suspected case that is laboratory-confirmed.

Recommended interventions

- **Case management**

  – No specific treatment for acute viral hepatitis B or D. Alpha interferon and lamivudine are available for treatment of chronic hepatitis B in some countries.

  – Apply universal precautions to prevent exposure to blood and body fluids.

  – Equipment contaminated with blood or body fluids must be disinfected as soon as possible.

  Immunization of contacts:

  – Postexposure immunization beginning at birth is highly effective in preventing neonatal infections in infants of HBV-infected mothers. Optimum efficacy is achieved when vaccine is administered within 24 hours (preferably 12 hours) after birth. A total of 3 doses must be given (second and third doses at 1 and 6 months; the first dose may be accompanied by 0.5 ml of hepatitis B immunoglobulin if available). There is no evidence of efficacy if the vaccine is started more than 7 days after birth.

  – Where available and affordable, postexposure prophylaxis using hepatitis B vaccine and/or hepatitis B immune globulin is used after percutaneous or mucous membrane exposures to blood that contains HBsAg, and within 14 days of sexual contact with a person with acute HBV infection.

- **Prevention**

  – Routine universal infant vaccination is the essential element of strategies to prevent HBV infection. Monovalent and combination vaccines are available. Hepatitis B vaccine schedules are flexible, and the vaccine must be incorporated into national immunization schedules (see *General introduction*).

  – Where the level of HBV endemicity is high, routine infant vaccination will rapidly eliminate transmission because virtually all chronic infections are acquired among children under 5.

  – Where this level is intermediate or low, vaccinating infants alone will not substantially lower the disease incidence because most infections occur among adolescents and young adults. In these countries, special vaccination strategies for older children, adolescents and adults may be desirable.

  Other means to prevent HBV infection include:

  – Testing all donated blood for HBsAg by sensitive tests (enzyme immunoassay)

  – Avoiding and discouraging the use of paid donors

  – Preventing injection-associated transmission by reducing injection overuse and using safe injection practices, including appropriate use and disposal of needles and syringes

  – Appropriate disinfection and sterilization practices for equipment and environmental surfaces

  – Proper use of multi-dose medication vials.

- **Epidemics**
  Epidemics are uncommon, and occur mainly in low-prevalence countries in institutions such as haemodialysis centres and institutional care facilities. Aseptic techniques must be reinforced. If a plasma derivative is suspected, withdraw the product from use and trace all recipients of the same lot for cases linked to addiction, with possible post-exposure prophylaxis (serum derivatives).
- **Drug resistance monitoring**
  In cases of unsuccessful treatment with lamivudine, resistance to lamivudine must be investigated.

Other aspects

- **Procurement of equipment and drugs**
  Plasma-derived and recombinant hepatitis B vaccines are available, and are equivalent with respect to safety, immunogenicity, and efficacy. The vaccine purchased must meet all WHO biological requirements for hepatitis B vaccine and all requirements of the National Control Authority. Pooled procurements by several countries can result in significant reductions in vaccine price.
- **Surveillance**
  - Vaccine coverage, particularly the number of 3rd doses of hepatitis B vaccine administered to infants
  - Routine monthly reporting of aggregated data of suspected cases, and the number of confirmed cases of each type of hepatitis if available, from the peripheral level to intermediate and central levels (if country-wide surveillance is not possible, surveillance in sentinel areas or hospitals may provide useful information).
  - Zero reporting for patent cases of hepatitis required at all levels.

  All outbreaks must be investigated immediately and if possible confirmed serologically.

NOTE: In developed countries, surveillance for confirmed hepatitis B cases must use clinical and laboratory criteria.
Many countries do not have sufficient resources for the routine performance of the necessary tests; surveillance can then be limited to those sentinel sites where diagnostic testing is available. Whatever the type of surveillance, reports greatly underestimate the burden of acute hepatitis B, because children infected with HBV rarely develop symptoms. Other methods such as serological surveys to determine the prevalence of HBsAg and anti-HBc may be more suitable.

- **Special considerations/other interventions**
  Understanding the epidemiology and impact of viral hepatitis requires an understanding of the sequelae of hepatitis virus infection (asymptomatic chronic infection, chronic hepatitis, cirrhosis, primary liver cancer). This also requires data collection from sources not routinely used, including hospital surveillance data such as discharges, mortality (chronic hepatitis, cirrhosis, liver cancer) and cancer registers. Special sero-prevalence surveys may be needed to measure prevalence of infection in the general population and in special groups (health care workers, blood donors, pregnant women, military recruits, patients with liver disease, people on dialysis, haemophiliacs), as well as in ethnic subpopulations.

  Assessment for coverage of hepatitis B vaccine is similar to that for other vaccines. Hepatitis vaccine is given to infants (and in some industrial countries to adolescents) primarily to prevent the development of chronic liver disease and liver cancer. Serological testing to document sero-conversion in children is usually not necessary: studies show that vaccine is 85% to 100% effective in preventing chronic infection.

Contacts and References

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REFERENCES: See also: *Immunization* in the present document (section 2.1).

Viral hepatitis C B17.1

General introduction

A worldwide hepatitis, most common among injecting drug users and haemophiliac patients, also observed as a late development in patients who received multiple therapeutic injections under conditions of doubtful sterility (e.g. in the intramuscular treatment of schistosomiasis). Chronic infection is common in hepatitis C, and 5% to 20% of those infected may develop cirrhosis. There seems to be an association between HCV infection and hepatocellular carcinoma.

Causal agent and main modes of transmission

- **Causal agent:** Hepacavirus of approximately 50nm, single stranded, with various geographical genotypes.
- **Main modes of transmission:** the virus is transmitted by parenteral exposure to blood and plasma derivatives. It is found in highest concentrations in blood, and contaminated needles and syringes are the main vehicles of spread, either among parenteral drug users or through nosocomial transmission. The most important nosocomial exposures include transfusion of blood or blood products that are not screened for hepatitis C, injection overuse and unsafe injection practices, and other inadequate infection control practices. It may also be transmitted by sexual contact.

  The risk of transmission by household contact or sexual relations appears to be low, as is the case for mother-to-child transmission.

Clinical description and case definition

- **Clinical description:** HCV infection occurs in acute and chronic forms.
  - Acute illness typically including acute jaundice, dark urine, anorexia, malaise, extreme fatigue, and right upper quadrant tenderness; biological signs include increased urine urobilonogen and >2.5 times the upper limit of serum alanine aminotransferase
  - The chronic form, non specific, can lead to cirrhosis of the liver and to hepatocellular carcinoma.

  Laboratory criteria
  - Hepatitis C: anti-HCV positive – confirmation by PCR or Western Blot can be envisaged

  Case classification
  - ***Suspected:*** A case that is compatible with the clinical description
  - ***Confirmed:*** A suspected case that is laboratory-confirmed.

Recommended interventions

- **Case management**
  No specific treatment is available for acute viral hepatitis C. Alpha interferon in combination with ribavirin has an overall beneficial effect in about 25% of chronic hepatitis C cases.

  Apply universal precautions to prevent exposure to blood and body fluids. Equipment contaminated with blood or body fluids must be disinfected as soon as possible.
- **Prevention**
  Means to prevent HCV infection include:
  - Testing all donated blood for HCV by sensitive tests (enzyme immunoassay)
  - Avoiding and discouraging the use of paid donors
  - Preventing injection-associated transmission by reducing injection overuse and using safe injection practices, including appropriate use and disposal of needles and syringes.
  - Appropriate disinfection and sterilization practices for equipment and environmental surfaces
  - Proper use of multi-dose medication vials.
- **Epidemics**
  Epidemics are uncommon and occur mainly after (sometimes a long time after) mass injection programmes under unsafe conditions and in institutional care facilities. Aseptic techniques must be reinforced. If a plasma derivative is implicated, withdraw the product from use and trace all recipients of the same lot for additional cases and possible post-exposure prophylaxis with this product.
- **Drug resistance monitoring**
  Not applicable.

Other aspects

- **Procurement of equipment and drugs**
  See *Injection safety.*
- **Surveillance**
  - Routine monthly reporting of aggregated data of suspected cases, and if available, the number of confirmed cases of each type of hepatitis, from the peripheral level to intermediate and central levels
  - Zero reporting required at all levels

  All outbreaks must be investigated immediately and confirmed serologically.
- **Special considerations/other interventions**
  Understanding the epidemiology and impact of viral hepatitis requires an understanding of the sequelae of hepatitis B, C and D virus infection, such as asymptomatic chronic infection, chronic hepatitis, cirrhosis, and primary liver cancer. This also requires data collection from sources not routinely used, including hospital surveillance data such as hospital discharges, and mortality (chronic hepatitis, cirrhosis, liver cancer) and cancer registers. Special sero-prevalence surveys may be needed to measure prevalence of hepatitis B and C infection in the general population and in special groups (health care workers, blood donors, pregnant women, military recruits, patients with liver disease, people on dialysis, haemophiliacs, recipients of mass injection programmes, and ethnic subpopulations.

Contacts and References

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REFERENCES: See also: *Immunization* and *Injection Safety* in the present document (sections 2.1 and 2.5).

Influenza J10, J11

General introduction

Influenza (also known as 'flu) comes in seasonal epidemics that occur because of changes in the antigenic composition of the virus (antigenic drift). It can also cause worldwide epidemics (pandemics). It is responsible for severe morbidity and mortality (over 110 000 hospitalizations and 20 000 deaths a year in the USA alone). The virus can cause severe pneumonia or aggravate underlying medical conditions such as cardiovascular or chronic pulmonary disease, with staggering case fatality rates.

The early detection and characterization of new variants or subtypes of influenza virus allows for timely annual updates of a vaccine that can prevent deaths and alleviate illness in vulnerable groups of the population (children under 5 and persons aged 50 and over).

Causal agent and main modes of transmission

- **Causal agents:** The main agents are:
  - Influenza virus A, responsible for periodic pandemics and frequent epidemics
  - Influenza virus B, causing less frequent outbreaks.
- **Main modes of transmission:** Influenza is transmitted by respiratory secretions from person to person through sneezing or coughing. The disease is particularly transmissible within a week of clinical onset, and incubation is short (1 to 3 days).

Clinical description and case definition

- **Clinical description:** fever (often higher in children), cough, sore throat, runny or stuffy nose, headache, muscle aches, and often extreme fatigue. Most people recover completely within 1-2 weeks. However, compared with other viral respiratory infections, influenza causes more severe complications such as pneumonia, particularly in children, elderly people and other vulnerable groups.
- **Clinical case definition**
  A person with sudden onset of fever of >38°C and cough or sore throat in the absence of other diagnoses.
  Laboratory criteria
  - *Virus isolation:*
    - Swab or aspirate from the suspected individual, **or**
    - Direct detection of influenza viral antigen
  - *Serology:*
    - 4-fold rise in antibody titre between early and late serum.

  Case classification
  - ***Suspected:*** A case that meets the clinical case definition.
  - ***Confirmed:*** A case that meets the clinical case definition and is laboratory-confirmed (used mainly in epidemiological investigation rather than surveillance).

Recommended interventions

- **Case management**
  Isolation of the patient to prevent infection of others is optimal, but this may not always be practical. The antiviral drugs amantadine and rimantadine reduce the severity and duration of illness when taken within 2 days of the appearance of symptoms. The newer drugs zanamivir and oseltamivir are also used for treatment of uncomplicated cases. These drugs are not always available or licensed in developing countries.

  Antibiotics should not be resorted to unless bacterial complications develop.
- **Prevention**
  Vaccination is the single most effective preventive measure against influenza. It is especially recommended for elderly people and people with chronic underlying diseases (e.g. cardiopulmonary, diabetes) and must be given as a single shot. For children under 5, give 2 doses at 1 month interval.

  Immunization of persons on long-term salicylate therapy is particularly recommended to prevent the occurrence of Reye syndrome.

- **Epidemics** of influenza occur in many countries on all continents nearly every year; clinical attack rates range from 10% to 20% in the general community up to 50% and more in closed populations. Immunization of at-risk subjects before the start of the influenza season, planning for increased demands in health care and maintaining adequate supplies of antiviral drugs (if appropriate) help mitigate the impact of an epidemic. Reshuffling of gene segments (antigenic drift) with 2 different influenza A viruses may lead to worldwide epidemics (pandemics); there have been at least 3 influenza pandemics in the 20th century.
- **Drug resistance monitoring**
  Resistance has been shown against amantadine and rimantadine, while relevant resistance to zanamivir and oseltamivir has not yet been shown.

Other aspects

- **Procurement of equipment and drugs**
  Ensure adequate supply of vaccines each year especially for high-risk groups.
  Antiviral drugs should not replace vaccines as the primary preventive measure – they are recommended in some cases as an adjunct to vaccination.
- **Surveillance**
  Routine weekly reporting of case-based or aggregated data to central level (at least during the epidemic period). This may include:
  - Clinical cases (suspected)
  - Cases confirmed by laboratory
  - Virus isolates (type and subtype) through laboratory confirmation
  - Suspected/confirmed cases by sentinel practices (general practitioners/health institutions).

  Other sources of data include hospitals, clinics, emergency rooms, laboratories, vital statistics offices.
  International: Weekly aggregated data on confirmed cases from countries to WHO (FluNet) with information on extent of activity in the community.
- **Special considerations/other interventions**
  It is important to maintain and use:
  - Standard definitions
  - Standardized laboratory diagnostic reagents (available at WHO National Influenza Centres).

  The international influenza surveillance network (FluNet) serves as an early-alert information system for the global monitoring of influenza accessed through the internet, and ensures expanded geographic and national surveillance coverage. It allows for the early detection of influenza epidemics, the rapid isolation and characterization of influenza viruses, and the collection of morbidity and mortality data to estimate the impact and costs of outbreaks.
- **Indicators**
  - Number of cases
  - Number of deaths
  - Circulating virus types and subtypes
  - Number of individuals vaccinated, by age group, with emphasis on the elderly (50+).

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42.
WHO Headquarters, 20 Avenue Appia, CH-1211 Geneva 27, Switzerland - Communicable Diseases Surveillance and Response (CSR),
E-mail: stohrk@who.int and outbreak@who.int Tel: (41 22) 791 2529, Fax: (41 22) 791 4878/0746 attn CSR

REFERENCES:

WHO influenza surveillance/La surveillance de la grippe par l'OMS. *Weekly Epidemiological Record/Relevé épidémiologique hebdomadaire*, 1996, 71(47): 353-357.
WHO. *Influenza Pandemic Preparedness Plan – the role of WHO and Guidelines for National and Regional Planning.* WHO: Geneva. WHO/CDS/CSR/EDC/99.1
See also: *Immunization* in the present document (section 2.1).

Legionellosis

Legionnaires' disease A48.1

Non-pneumonic Legionnaires' disease (Pontiac fever) A48.2

General introduction

Legionnaires' disease is a disease with epidemic potential and a high case fatality rate. Outbreaks have been identified worldwide since the initial documented outbreak in the USA (1957).

Causal agent and main modes of transmission

- **Causal agents:** *Legionella*, most commonly *L. pneumophila* serogroup 1.
- **Main modes of transmission:** *Legionella* are common in rivers, lakes and moist soil, and often present in drinking-water supplies and other sources such as hot water systems, cooling towers, humidifiers, spas, etc. Infection occurs through inhalation of aerosols. The usual incubation period is 2-10 days for Legionnaires' disease and 24-48 hours for Pontiac fever. Person-to-person transmission has not been reported.

Clinical description and case definition

- **Clinical description**
  - LEGIONNAIRES' DISEASE is a multisystem disease the main clinical feature of which is pneumonia. It is characterized by initial anorexia, malaise, myalgia and headache, followed by high fever and chills, and by non-productive cough, abdominal pain/diarrhoea, confusion/delirium. It is not possible, clinically, to distinguish *Legionella* pneumonia from other pneumonias; suspicion should be raised through epidemiological information (e.g. immunosuppression, recent travel, hospitalization, gatherings). Age (>50), sex (M), smoking, alcohol consumption have been shown to be risk factors.

    Attack rates are often low (0.1% to 5% in the population at risk). The case fatality rate may be as high as 30% in hospitalized patients.
  - PONTIAC FEVER has the same initial manifestations as Legionnaires' disease but is not associated with pulmonary signs or symptoms or with death. It is thought to represent a reaction to inhaled antigen, rather than to bacteria. Attack rates can be high (up to 95%). Spontaneous recovery within 2-5 days is the rule.

Laboratory criteria

- ***Presumptive:*** One or more of the following:
  - Detection of specific *Legionella* antigen in respiratory secretions or urine
  - Direct fluorescent antibody staining of the organism in respiratory secretions or lung tissue.
- ***Confirmative:*** One or more of the following:
  - Isolation of *Legionella* from respiratory secretions, lung tissue, pleural fluid, or blood
  - A 4-fold or greater rise in specific serum antibody titre to *L. pneumophila* serogroup 1 by indirect immunofluorescence antibody test or microagglutination.

NOTE: Most European countries and others such as the United States now include the detection of *Legionella pneumophila* serogroup 1 antigen in urine as a confirmatory test rather than a purely presumptive test. This question – like that of the precise role of PCR in the diagnosis of legionellosis – is currently under consideration by the European Working Group for *Legionella* infections PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 SEQ - Tel: (44) 181 200 6868, Fax: (44) 181 200 7868, E-mail: respedsc@PHIS.co.uk

Case classification

- ***Suspected:*** Not applicable.
- ***Probable:*** A case compatible with the clinical description, with presumptive laboratory results.
- ***Confirmed:*** A case compatible with the clinical description, with confirmative laboratory results.

Recommended interventions

- **Case management**
  Specific treatment with erythromycin
  Isolation is not required.
- **Prevention**
  Regular cleaning and disinfection of water supply systems and of cooling towers. Tap water must not be used for respirator devices.
- **Epidemics**
  Identify common exposure and environmental sources of infection.
  Decontamination (hyperchlorination and/or superheating at 60-70°C of water supply).
- **Drug resistance monitoring**
  Not applicable.

Other aspects

- **Procurement of equipment and drugs**
  Erythromycin.
- **Surveillance**
  Immediate reporting of case-based data from periphery to intermediate and central levels. Identification of cases must prompt immediate investigation for risk factors and other cases (active case-finding).

  International: Since travel and stays in hotels are important risk factors, effective international surveillance is essential to identify and control the point source of infections.

  NOTE: Legionella infection is usually diagnosed after the patient's return to the country of residence and is therefore likely to be considered as a sporadic, single case. A surveillance scheme such as that of the European Working Group for Legionella Infections (v.supra) allows for the detection of clusters of cases (≥2 cases) with the same source of transmission collected in the same database. Environmental surveillance must be undertaken for known sources of outbreaks, to ensure that the organism is eradicated.
- **Special considerations/other interventions**
  Not applicable.
- **Indicators**
  Cluster(s) of cases.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42.

WHO Headquarters, 20 Avenue Appia, CH-1211 Geneva 27, Switzerland - Communicable Diseases Surveillance and Response (CSR)
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Leishmaniasis (cutaneous & mucocutaneous) B55.1, B55.2

General introduction

Cutaneous leishmaniasis is present on all continents (except Australia and Antarctica) in over 70 countries; Afghanistan, Brazil, Iran, Peru, Saudi Arabia and the Syrian Arab Republic report over 90% of all variants of cutaneous leishmaniasis cases (an estimated total of 1.5 million worldwide). The disease has several clinical forms: localized cutaneous leishmaniasis, diffuse cutaneous leishmaniasis, the most difficult to treat, and (in the western hemisphere mainly) mucosal leishmaniasis, which is the most severe form as it produces disfiguring lesions and mutilations of the face.

Causal agent and main modes of transmission

- **Causal agents:** The leishmaniases are caused by *Leishmania* species, protozoa transmitted by the bite of sandflies (genus *Phlebotomus* in the Old World and *Lutzomyia* in the New). Some 30 species of sandflies are proven vectors; the usual reservoir hosts are domestic and/or wild animals.
- **Main modes of transmission:** Female sandflies become infected by feeding from reservoir hosts. Most forms are zoonotic, humans being infected only secondarily, but in anthroponotic forms humans are believed to be the sole reservoir hosts. Incubation time varies (weeks to months).

Clinical description and case definition

- **Clinical description**
  Appearance of one or more skin lesions, typically on uncovered parts of the body. The face, neck, arms and legs are the most common sites. A nodule may appear at the site of inoculation and may enlarge to become an indolent ulcer. The sore may remain in this stage for a variable time before healing – it typically leaves a depressed scar. Other atypical forms may occur. In some individuals, certain strains can disseminate and cause mucosal lesions. These sequelae involve nasopharyngeal tissues and can be very disfiguring.

  Laboratory criteria
  Cutaneous, diffuse cutaneous and mucosal leishmaniasis
  - Positive parasitology (stained smear or culture from the lesion)
  - Mucosal leishmaniasis only: positive serology (immunofluorescent assay, ELISA).

- **WHO operational definitions:**
  A case of ***cutaneous leishmaniasis*** can be defined as a person showing clinical signs (skin or mucosal lesions) with parasitological confirmation of the diagnosis (positive smear or culture) and/or, *for mucosal leishmaniasis only*, serological diagnosis.

Recommended interventions

- **Case management**
  Humans are considered to be the sole reservoir in anthroponotic foci, and priority is thus given to early detection through clinical and parasitological diagnosis, followed by prompt treatment of the patients. Treatment is based on pentavalent antimonials as first-line drug, except when resistance exists. In the presence of resistance, second-line drugs must be used. In developing countries, standard amphotericin B, aminosidine plus pentavalent antimonials or pentamidine isethionate are the main alternatives.

  Although the disease is often self-limiting – except for the mucocutaneous forms – infections acquired in areas where mucocutaneous forms occur must be treated rapidly.

- **Prevention**
  - **Zoonotic cutaneous leishmaniasis:** Reservoirs are mainly rodents and control methods must be adapted to the biology of each species (anticoagulants, poison baits or deep ploughing to eliminate plants on which the rodent reservoir feeds). Vector control is not recommended since it produces a transient effect only. In the Americas, reservoir control is not applicable, as most of the reservoirs are sylvatic mammals, and vector control is restricted to environmental management measures.
  - **Anthroponotic cutaneous leishmaniasis:** Urban foci have been eliminated in Azerbaijan, Israel, Kazakhstan and Turkmenistan.

- **Epidemics**
  Epidemics are linked to human migrations from rural to poor suburban areas; in zoonotic foci, where mammals are the reservoir hosts, epidemics are related to environmental changes and movement of non-immune people to rural areas.
- **Drug resistance monitoring**
  Not applicable.

Other aspects

- **Procurement of equipment and drugs**
  See *Vector control* (section 2.7).
- **Surveillance**
  At peripheral level, individual patient records must be retained for investigation and case management.
  Routine monthly reporting of aggregated data of cases from periphery to intermediate and central level.
  Active case-finding through surveys of selected groups or mass surveys (standardized and periodical) is an alternative to estimate the prevalence of visceral leishmaniasis.

  International: Annual reporting from central level to WHO (limited number of countries).
- **Special considerations/other interventions**
  In most endemic countries, only a basic level of control exists. Funding, logistical and management problems cause difficulties in availability of drugs, quality of diagnosis and reliability of reporting system.
- **Indicators**
  The number of cases alone is of little help in determining priorities. New and simple tools have recently become available; their ease of use in the field has improved possibilities of control. They include:
  - Insecticide-treated bednets, a vector control approach that has proved useful in foci of cutaneous leishmaniasis
  - % of treatment failures, for the various drugs used.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42
WHO Headquarters, 20 Avenue Appia, Ch-1211 Geneva 27, Switzerland - Epidemic Disease Control (EDC)
E mail: desjeuxp@who.int Tel: (41) 22 791 38 70, Fax: (41) 22 791 48 78/91 38

REFERENCES: Desjeux P. Leishmaniasis: Public Health Aspects and Control. *Clinics in Dermatology*, 1996,14(5): 417-423.

Leishmaniasis (visceral) B55.0

General introduction

Bangladesh, Brazil, India and Sudan report more than 90% of all visceral leishmaniasis cases (a total of 0.5 million worldwide), with high case fatality ratios. Severe outbreaks have occurred in Nepal and in the northern states of India. Worldwide incidence is estimated at 500 000 each year and the population at risk at approximately 350 million.

Causal agent and main modes of transmission

- **Causal agents:** The leishmaniases are caused by 20-odd *Leishmania* species, protozoa transmitted by the bite of sandflies (genus *Phlebotomus* in the Old World and *Lutzomyia* in the New). Some 30 species of sandflies are proven vectors; the usual reservoir hosts include man and domestic and/or wild animals.
- **Main modes of transmission:** The female sandflies become infected by feeding from reservoir hosts. Most forms are zoonotic, humans being infected only secondarily, but in anthroponotic forms man is believed to be the only reservoir. Incubation time varies (2 to 6 months, ranging from 10 days to years).

Clinical description and case definition

- **Clinical description**
  An illness with prolonged irregular fever, splenomegaly and weight loss as its main symptoms
  Laboratory criteria
  - Positive parasitology (stained smears from bone marrow, spleen, liver, lymph node, blood or culture of the organism from a biopsy or aspirated material)
  - Positive serology (immunofluorescent assay, ELISA, Direct Agglutination Test).
- **WHO operational definition:**
  A case of **visceral leishmaniasis (VL)** is a person showing clinical signs (prolonged irregular fever, splenomegaly and weight loss) with serological (at peripheral geographical level) and/or (when feasible at central level) parasitological confirmation of the diagnosis. In endemic malarious areas, visceral leishmaniasis must be suspected when fever lasts for more than 2 weeks and no response has been achieved with anti-malarial drugs (assuming drug-resistant malaria has also been considered).

Recommended interventions

- **Case management**
  Humans are considered to be the sole reservoir in anthroponotic foci, and priority is thus given to early detection through clinical, parasitological and serological diagnosis, followed by prompt treatment of the patients. Treatment is based on pentavalent antimonials as first-line drug, except when resistance exists. In the presence of resistance, second-line drugs must be used.
  - In industrialized countries, liposomal amphotericin B allows very short treatment and hospitalization that compensate for the high price of the drug
  - In developing countries, standard amphotericin B, aminosidine plus pentavalent antimonials or pentamidine isethionate are the main alternatives.
- **Prevention**
  - ***Anthroponotic foci***

    Priority is given to the control of anthroponotic foci as these are at the origin of periodical and deadly epidemics of visceral leishmaniasis. Feasibility of control for anthroponotic foci relies on:
    - the limited dispersal of the vectors involved (*Plebotomus sergenti* and *P. argentipes* are restricted to the domestic and peridomestic areas)
    - the absence of an animal reservoir, and
    - transmission that occurs mainly man-to-man through the sandfly vector.

    Vector control, using residual insecticide house spraying or a more sustainable alternative method such as pyrethroid impregnated bednets, must be systematically associated to treatment. In China, anthroponotic visceral leishmaniasis has been eliminated from the north-eastern plains. As a side-effect of the attack phase of malaria eradication, visceral leishmaniasis almost disappeared in India in the 1960s.

- **Zoonotic foci**

  Activities concerning zoonotic foci are of lower priority except for *Leishmania*/HIV co-infections (see below: *Special considerations*) and for epidemics. Priority is given to detection/treatment of human cases. Dogs are the main domestic reservoirs; large-scale screening, followed if necessary by treatment or killing of dogs, is based on serological tests. Vector control through residual insecticide spraying of houses and of animal shelters is advisable only when the vector is restricted to the domestic and peridomestic areas.

- **Epidemics**
  There have been severe epidemics of visceral leishmaniasis among refugees and internally displaced persons in recent years, notably in Sudan. Action: see *Prevention* above. As for most epidemics, involvement of the community in preparedness committees is advisable.

- **Drug resistance monitoring**
  Drug resistance has been noted in recent years especially in Bangladesh, Brazil, Sudan and in India (Bihar State). Drug-resistant leishmaniasis may continue to spread as the number of patients co-infected with HIV increases (immunosuppression increases the number of parasites in the blood and facilitates a spiral of greater resistance, higher parasite levels and increased infective potential).

Other aspects

- **Procurement of equipment and drugs**
  See *Vector control* (section 2.7).

- **Surveillance**
  At peripheral level individual patient records must be retained for investigation and case management.
  Routine monthly reporting of aggregated data of cases from periphery to intermediate and central level.
  Active case-finding through surveys of selected groups or mass surveys (standardized and periodical) is an alternative to estimate the prevalence of visceral leishmaniasis.

  International: Annual reporting from central level to WHO (limited number of countries).

- **Special considerations/other interventions**
  In most endemic countries, only a basic level of control exists. Funding, logistical and management problems cause difficulties in availability of drugs, quality of diagnosis and reliability of reporting system.
  It is important to determine the most cost-effective surveillance and control strategies in order to reduce the case fatality ratio and the socioeconomic consequences of epidemics. Response to VL deadly epidemics deserves the highest priority.
  Although promising results have been obtained, there is no commercially available vaccine yet.

  Leishmania/HIV co-infections have already been reported from over 30 countries. The overlap of visceral leishmaniasis and AIDS is on the increase because the AIDS pandemic is spreading in rural areas and visceral leishmaniasis in suburban areas. In southern Europe, 25% to 70% of adult cases of visceral leishmaniasis are related to HIV infection and 1.5% to 9% of AIDS cases suffer from newly acquired or reactivated visceral leishmaniasis.

- **Indicators**
  The number of cases alone is of little help in determining priorities. New and simple control tools have recently become available; their ease of use in the field has improved possibilities of control. They include:
  - Reliable, easy to use and cheaper tests for serological diagnosis (dipsticks, direct agglutination test)
  - Insecticide-treated bednets, a vector control approach that has proved useful in foci of visceral leishmaniasis
  - % of treatment failures, for the various drugs used
  - Incidence of *Leishmania*/HIV co-infections
  - Proportion of population covered by the Visceral Leishmaniasis Control Initiative.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42

WHO Headquarters, 20 Avenue Appia, Ch-1211 Geneva 27, Switzerland - Epidemic Disease Control (EDC)
E mail: desjeuxp@who.int Tel: (41) 22 791 38 70, Fax: (41) 22 791 48 78/91 38

REFERENCES: WHO. *Manual on visceral leishmaniasis control*. WHO/LEISH/96.40, 1996.

Leprosy A30

General introduction

In 2000, several hundred thousand persons still live with leprosy. Control has improved with the introduction of multidrug therapy (MDT). WHA resolution 44.9 targeted the disease for elimination (less than 1 case/10 000 population) by the year 2000; although this target has been reached at the global level, at least 11 countries with a combined population of 1300 million have not yet reached it, for operational reasons. The approach to control and elimination includes the provision of multidrug therapy free of charge to all communities and areas, and appropriate and good diagnosis and treatment, with evaluation through epidemiological surveillance and programme monitoring.

Causal agent and main modes of transmission

- **Causal agent:** *Mycobacterium leprae*. This cannot be grown in bacteriological media or cell cultures.
- **Main modes of transmission:** Humans are the only significant reservoirs. The disease is in all likelihood transmitted from the nasal mucosa of a patient to the skin and respiratory tract of another person. Transmission requires close contact. Although the bacillus can survive up to 7 days in dried nasal secretions, indirect transmission is unlikely.

Clinical description and case definition

- **Clinical description**

  The clinical manifestations of the disease vary in a continuous spectrum between 2 polar forms:

  1. *Lepromatous (multibacillary) leprosy:* symmetrical and bilateral nodules, papules, macules and diffuse infiltrations, usually numerous and extensive; involvement of the nasal mucosa may lead to crusting, obstructed breathing and epistaxis; ocular involvement leads to iritis and keratitis.
  2. *Tuberculoid (paucibacillary) leprosy:* skin lesions single or few, sharply demarcated, anaesthesic or hypoaesthesic; bilateral asymmetrical involvement of peripheral nerves tends to be severe.
     Borderline leprosy has features of both polar forms and is more labile.
     Indeterminate leprosy is characterized by hypopigmented maculae with ill-defined borders; if untreated, it may progress to tuberculoid, borderline or lepromatous disease.

  The incubation period ranges from 9 months to 20 years. The disease is rarely seen in children under 3.

- **Case definition** (WHO operational definition)[8]
  - A case of leprosy is a person having one or more of the following, who has yet to complete a full course of treatment:
    - Hypopigmented or reddish skin lesion(s) with definite loss of sensation
    - Involvement of the peripheral nerves, as demonstrated by definite thickening with loss of sensation
    - Skin smear positive for acid-fast bacilli.
  - The operational case definition includes
    - Retrieved defaulters with signs of active disease
    - Relapsed cases who have previously completed a full course of treatment.

    It does not include cured persons with late reactions or residual disabilities.

  Laboratory criteria

  Alcohol-acid-fast bacilli in skin smears (made by the scrape-incision method).
  In the paucibacillary form the bacilli may be so few that they are not demonstrable. In view of the increasing prevalence of HIV and hepatitis B infection in many countries where leprosy remains endemic, the number of skin smear sites and the frequency of smear collection should be limited to the minimum necessary. In practice, laboratories are not essential for the diagnosis of leprosy.

  Case classification: on clinical grounds, leprosy cases can be classified as follows:
  - Multibacillary leprosy: more than 5 patches or lesions on the skin
  - Paucibacillary leprosy: 1 to 5 patches or lesions on the skin.

[8] Updated for the present document by technical unit (see *Introduction*)

Recommended interventions

- **Case management**
  Treatment by multidrug therapy (MDT) according to case classification
  - ***Adults with multibacillary leprosy:*** the standard regimen is a combination of the following for 12 months :
    - Rifampicin: 600 mg once a month
    - Dapsone: 100 mg once a day
    - Clofazimine: 50 mg once a day and 300 mg once a month.
  - ***Children*** must receive appropriately scaled-down doses (in child blister-packs).
  - ***Adults with paucibacillary leprosy:*** the standard regimen is a combination of the following for 6 months:
    - Rifampicin: 600 mg once a month
    - Dapsone: 100 mg once a day.
  - ***Children*** must receive appropriately scaled-down doses (in child blister-packs).

  Treatment is undertaken on an ambulatory basis. Patients must be advised to complete the full course of treatment and to seek care in the event of drug side-effects (allergic reaction) and immunological reactions (neuritis leading to damage of the peripheral nerve trunks).
- **Prevention**
  - Early detection and treatment of cases.
  - BCG vaccination can induce protection against the tuberculoid form of the disease; this is part of the control methods against tuberculosis in some countries and must not be undertaken specifically against leprosy.
  - Dapsone chemoprophylaxis is not recommended (limited effectiveness and danger of resistance).
  - Reducing contact with known leprosy patients is of dubious value and can lead to stigmatization.
- **Epidemics**
  Not applicable.
- **Drug resistance monitoring**
  Rifampicin-resistant strains of *M. leprae* have been reported when rifampicin is used alone; surveillance of resistance must be undertaken at selected regional reference centres.

Other aspects

- **Procurement of equipment and drugs**
  The national programme sets the amount of drugs required each year. Estimates are based on requirements for the previous year, adjusted in accordance with foreseen increases in the number of new cases through improved detection programmes.
- **Surveillance**
  Individual patient records at peripheral level for investigation and case management.
  Routine monthly reporting of aggregated data of all cases from periphery to intermediate level and from intermediate to central level.
  International: Quarterly and annual reporting of aggregated data from central level to WHO.
- **Special considerations/other interventions**
  Multiple drug therapy is available free of charge through WHO. MDT drugs must be given in blister packs, free of charge, to all patients.
- **Indicators**
  - Number of cases detected each year
  - Number of registered cases
  - Number of patients on MDT
  - Number cured by MDT.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42
WHO Headquarters, 20 Avenue Appia, CH-1211 Geneva 27, Switzerland - Eradication and Elimination of Diseases (CEE/CDS)
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REFERENCES:

WHO. *Expert Committee on Leprosy. Seventh Report.* Geneva: WHO, Technical Reports Series N°874, 1998.
WHO. *Guide to eliminate leprosy as a public Health Problem.* WHO/LEP/00.14

Leptospirosis A27

General introduction

A highly endemic worldwide zoonosis in countries with a humid subtropical or tropical climate. Leptospirosis often peaks seasonally, sometimes in outbreaks, and is often linked to occupation. Feral and domestic animal species may serve as sources of infection with one of the pathogenic *Leptospira* serovars, through contact with the urine or tissues of infected animals or a urine-contaminated environment, mainly surface waters, soil and plants. The course in humans ranges from mild to lethal. Leptospirosis, a disease with manifestations ranging from mild (flu-like) to severe and potentially fatal, is underreported in many countries because of difficult clinical diagnosis and lack of diagnostic laboratory services.

Causal agents and main modes of transmission

- **Causal agents:** Pathogenic leptospires belong to the genus *Leptospira* (long corkscrew-shaped bacteria, too thin to be visible under the ordinary microscope); dark-field microscopy is required. The more than 200 pathogenic serovars clustered into 25 serogroups cannot be differentiated on the basis of morphology.
- **Main modes of transmission:** Wild and domestic animals constitute the reservoir of infection, transmitted through contact of mucous membranes or broken skin with water, moist soil or vegetation contaminated with the urine of infected animals (swimming or immersion); occasional infection occurs through ingestion/inhalation of food/droplet aerosols of fluids contaminated by urine. The incubation usually lasts about 10 days (from 2 to 30 days).

Clinical description and case definition

- **Clinical description:**
  The usual presentation is:
  - Acute febrile illness with headache, myalgia and prostration associated with any of the following symptoms:
    - Conjunctival suffusion
    - Meningeal irritation
    - Anuria or oliguria and/or proteinuria
    - Jaundice
    - Haemorrhages (from the intestines; lung bleeding is notorious in some areas)
    - Cardiac arrhythmia or failure
    - Skin rash

  and
  - A history of exposure to infected animals or an environment contaminated with animal urine.

  NOTE: Other common symptoms include nausea, vomiting, abdominal pain, diarrhoea, arthralgia. The clinical diagnosis is difficult where diseases with symptoms similar to those of leptospirosis occur frequently.

  Laboratory criteria
  - Isolation from blood or other clinical materials through culture of pathogenic leptospires. A positive PCR may also be considered.
  - Positive serology, preferably Microscopic Agglutination Test, using a range of *Leptospira* strains for antigens that must be representative of local strains.

  Case classification
  - ***Suspected:*** A case that is compatible with the clinical description.
  - ***Probable:*** Not applicable.
  - ***Confirmed:*** A suspect case that is confirmed in a competent laboratory.

Recommended interventions

- **Case management**
  Early treatment with antibiotics. Severe cases are usually treated with high doses of intravenous benzylpenicillin (30 mg/kg up to 1.2 g IV 6-hourly for 5-7 days), amoxicillin, ampicillin or erythromycin. Less severe cases are treated orally with antibiotics such as doxycycline (2 mg/kg up to 100 mg orally 12-hourly for 5-7 days), tetracycline, ampicillin or amoxicillin.
  Third-generation cephalosporins, such as ceftriaxone and cefotaxime, and quinolone antibiotics may also be effective.
  Jarisch-Herxheimer reactions may occur after the start of antimicrobial therapy.

  Isolation must cover disinfection of soiled articles and should preferably cover body fluid precautions, although interhuman transmission is rare.
- **Prevention**
  The large number of serovars and of infection sources and the wide difference in transmission conditions make of leptospirosis an unlikely candidate for national eradication. Preventive measures, which must be based on a knowledge of those groups at higher risk of infection and of local epidemiological factors, include:
  - Identifying and controlling the source of infection
  - Interrupting the transmission route, thereby preventing infection or disease in the human host:
    - Wearing protective clothes
    - Disinfecting contaminated surfaces such as stable and abattoir floors
    - Marking areas with increased risk exposure (warning signs).
  - Preventing infection or disease in human hosts:
    - Selective vaccination
    - Prophylaxis
    - Information.

  Control of leptospirosis in terms of eradication is not possible in feral animals but control measures can be highly effective in small, defined populations (dogs, certified cattle herds). Selective local rodent control (baiting and management) may be important.
- **Epidemics**
  Conditions leading to an increase of contaminated surface water or soil, such as rain, floods and disasters increase the risk of leptospirosis and may lead to epidemics. During periods of drought both humans and animal reservoirs may be attracted to spare water places hence increasing the risk of infection. In a suspected outbreak, attempts to diagnose leptospirosis must be encouraged to enable prompt treatment. For outbreaks in remote or areas with poor access, local use of screening tests to detect antibody is helpful. When an outbreak of leptospirosis is suspected or identified, and if it has been possible to identify the serovar concerned, the source must be identified and appropriate environmental measures must be implemented, with public information to people at risk (including clinicians and health care workers and health authorities).
- **Drug resistance monitoring**
  No reports of resistance for common antibiotics (*see above Case management*) and no guidelines for monitoring. Testing of antibiotic resistance in individual clinical cases is not useful since it requires considerable time.

Other aspects

- **Procurement of equipment and drugs**
  Several levels of laboratory service can be considered:
  - Simple screening methods for anti-Leptospira antibodies are available for use at the periphery. Basic equipment: containers for serum, (Pasteur) pipettes, centrifuge, freezer.
  - Limited provincial or national level (more complex serological methods and cultures; checking activities at peripheral level). Additional equipment: dark-field microscope; also (optional) ELISA reader, pH meter, incubator, micropipettes.
  - Elaborate provincial or national level for complex diagnostic methods, a quality control system with a check of activities at second level, provisional typing of isolates. Additional equipment: sterile syringes, millipore filters, autoclave (traditional pressure cooker), deep freezer, automatic dispensers, accurate scales.
  - International/regional reference laboratory for culture collections, typing, outbreak investigations, reference strains, reagents, and antisera, and quality checks on performance in other laboratories.
- **Surveillance:** Immediate case-based reporting of suspected or confirmed cases from peripheral level (hospital/general practitioner/laboratory) to intermediate level. All cases must be investigated.

  Routine reporting of aggregated data of confirmed cases from intermediate to central level (levels 3 and 4 above). Hospital-based surveillance may give information on severe cases of leptospirosis. Serosurveillance or enhanced serosurveillance through the use of questionnaires may inform on whether leptospiral infections occur or not in certain areas or populations,

detecting changing trends in infecting serovars, sources, and (risk) occupations and hospitalization rates associated with leptospirosis.

The International Leptospirosis Society* collects worldwide data: Royal Tropical Institute (KIT), Department of Biomedical Research, NH Swellengrebel Laboratory. Meibergdreef 39, 1105 AZ Amsterdam, The Netherlands
Tel: 31 20 566 5441 Fax: 31 20 697 1841 E-mail: r.hartskeerl@kit.nl
ILS home page: http://www.med.monash.edu.au/microbiology/staff/adler/ilspage.htm

- **Special considerations/other interventions**
  Leptospirosis is often confused with other diseases or not considered at all. In all cases of fever with unknown origin, leptospirosis must be included in the differential diagnosis. Exposure to infection sources may not always be obvious to the clinician or patient.

  It is advisable to include veterinary experts and departments in the control management team.

- **Indicators:**
  - Increased numbers of (suspected) cases of leptospirosis
  - Multiple cases with a putative common history of exposure
  - Presence of (new) serovars in animals and/or increase of the percentage carriers
  - Climatological or seasonal conditions (monsoons, El Niño, harvest time)
  - Disasters (hurricanes, floods, earthquake).

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42.

WHO Headquarters, 20 Avenue Appia, CH-1211 Geneva 27, Switzerland, - Communicable Diseases Surveillance and Response (CSR)
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REFERENCES:

Faine S, Adler B, Bolin C, Perolat P. *Leptospira and leptospirosis*. Melbourne: MediSci, 1999

WHO. *WHO-ILS guidelines on leptospirosis*. Terpstra WJ, ed. (in preparation).

Malaria B50-54

General introduction

Malaria, the most highly prevalent tropical disease, has high morbidity and mortality rates and a high economic and social impact. The disease is currently endemic in 106 countries and territories. The ROLL BACK MALARIA (RBM) project was founded as a global partnership in 1998 by WHO, UNDP, UNICEF and the World Bank with the goal of halving the world's malaria burden by 2010 – this is estimated at almost 300 million episodes of acute illness and over 1 million deaths a year. The strength of the RBM partnership lies in the strength of its constituent elements (governments, civil society and non-governmental organizations, research institutions, professional associations, UN and development agencies, development banks, the private sector and the media). RBM builds on recent successful efforts in malaria-affected countries and regions to improve and support capacity to scale up action against malaria and on the *Global Strategy for Malaria Control* (9GPW) with 4 key technical interventions:

1. Rapid diagnosis and prompt effective treatment with appropriate medications, including home treatment.
2. Use of multiple preventive methods and vector control measures as appropriate.
3. Prevention of the ill effects of malaria during pregnancy.
4. Early detection, containment and prevention of epidemics.

Malaria control ultimately aims to prevent mortality and reduce social and economic loss by reducing morbidity. It is carried out in some communities as part of primary health care activities; in other areas, given the importance of malaria as a public health problem, malaria control may serve to stimulate the development of effective local health systems. In many countries, preventive interventions are implemented by centrally managed programmes in cooperation with local health services. Since most cases are treated at home or by private practitioners, the integration of home and private treatment in surveillance and control is a challenge for malaria control.

Effective planning of malaria control activities requires:

- A core group of malaria experts within the Ministry of Health to develop evidence-based strategies, assist health districts in technical matters, planning, implementation and evaluation, and to consolidate partnership with other ministries and development agencies around interventions impacting on mortality
- Functioning general health services, trained staff and health workers at community level
- Intersectoral cooperation at local, national and international levels.

Causal agents and transmission

- **Causal agents:** Human malaria is caused by 4 species of protozoan parasites of the genus *Plasmodium* (*P. falciparum*, *P. vivax*, *P. malariae*, *P. ovale)*. *P falciparum*, the most prevalent species, is responsible for the majority of malaria deaths.
- **Main modes of transmission:** From the blood of an infected person, parasites enter the female blood-sucking anopheline mosquito, develop in the gut and lodge in the salivary glands. When the infective mosquito takes a new blood meal, parasites are transmitted and carried by the blood to the liver where they multiply. After 9 to 16 days the parasites return to the blood and invade the red cells, where they multiply again, progressively breaking down the red cells. This induces bouts of fever and severe anaemia. The incubation period after an infective bite is 1 to 4 weeks for *P. malariae*, 1 to 2 weeks for others – prophylaxis may lengthen this pre-patent period. Of the almost 400 species of anopheline mosquitoes, some 40 may transmit the parasite. Each has its preferred breeding grounds, feeding patterns and resting place. Sensitivity to insecticides is also variable. Knowledge of the ecology and biting habits of the local insect vector and of the behaviour of people in endemic areas is important in order to choose the most effective methods of prevention.
- **Population at risk:** In endemic regions, where transmission can be very high (over 300 infective bites per person per year), people are continuously infected and gradually develop immunity to the disease. Until they have acquired such immunity, morbidity in children and pregnant women during first pregnancies is severe and mortality is high. In less endemic regions where malaria transmission is low, immunity develops more slowly and irregularly, putting all age groups at risk of developing severe disease. In such areas, epidemics may lead to high mortality in adults and children when not controlled in time.

Clinical description and case definition

- **Clinical manifestations of uncomplicated malaria**
  Signs and symptoms may vary:
  - Many patients experience fever with chills.
  - Common but non-specific symptoms include otherwise unexplained headache, back pain, sweating, myalgia, nausea, vomiting.
  - Splenomegaly and anaemia are common signs.

  Untreated or partially treated *P. falciparum* infection can quickly (sometimes within24 hours) lead to severe manifestations such as coma, generalized convulsions, renal failure, hypoglycaemia, hyperpyrexia, haemoglobinuria, shock, spontaneous bleeding, pulmonary oedema , disturbances of fluid, and electrolyte, balance and eventually death. In reasonably well equipped referral hospitals, case fatality rate from severe malaria is estimated to be around 10%.

- **Case definition**
  The clinical case definitions for malaria vary according to local epidemiological patterns, diagnostic capabilities and local perceptions of the disease. Each national malaria control programme must adapt and introduce indicators to improve applicability to local epidemiology and control targets.
  Laboratory criteria
  Demonstration of malaria parasites in blood films (mainly asexual forms) using light microscopy or an rapid diagnostic tests ("dipsticks") for detection of parasite antigen in the blood.
  Case classification (Twentieth Expert Committee on Malaria, 1998)

  – *In areas without access to laboratory-based diagnosis:*
    - ***Probable uncomplicated malaria:*** A person with symptoms and/or signs of malaria who receives anti-malarial treatment.
    - ***Probable severe malaria:*** A patient who requires hospitalization for symptoms and signs of severe malaria and receives anti-malarial treatment.
    - ***Probable malaria death:*** Death of a patient diagnosed with probable severe malaria.

  – *In areas with access to laboratory-based diagnosis:*
    - ***Asymptomatic malaria:*** A person with no recent history of symptoms and/or signs of malaria who shows laboratory confirmation of parasitaemia.
    - ***Confirmed uncomplicated malaria****:* A patient with symptoms and/or signs of malaria who received anti-malarial treatment, with laboratory confirmation of diagnosis:
    - ***Confirmed severe malaria****:* A patient who requires hospitalization for symptoms and/or signs of severe malaria and receives anti-malarial treatment, with laboratory confirmation of diagnosis.
    - ***Confirmed malaria death****:* Death of a patient diagnosed with probable severe malaria, with laboratory confirmation of diagnosis.
    - ***Malaria treatment failure:*** A patient with uncomplicated malaria without any clear symptoms suggesting another concomitant disease who has taken a correct dosage of anti-malarial treatment, and who presents with clinical deterioration or recurrence of symptoms within 14 days of the start of treatment, in combination with parasitaemia (asexual forms).

NOTE: "Probable" and "confirmed" denote mutually exclusive categories, as do "uncomplicated" and "severe". Some Health Services record malaria cases as "suspected malaria" until the microscopic diagnosis becomes available, after which the case becomes one of "confirmed malaria". These services must avoid double counting, and must record confirmed cases as a subset of suspected cases.

Recommended interventions

- **Case management**
  Management of uncomplicated malaria

In the few remaining areas where there is no known chloroquine resistance (mainly the Americas north of the Panama canal), oral chloroquine remains the standard recommended treatment for P. vivax and for P falciparum infections. Primaquine can be used as an antirelapse treatment in *P. vivax* and *P. ovale* infections.

In some Asian and South American countries, multi-drug resistance of *Plasmodium falciparum* is common. This has led to new therapeutic approaches, such as artemisinin-based combination therapies, which are being promoted in such areas as effective first line treatment together with appropriate support such as microscopy and rapid diagnostic tests (RDT). In several East African countries, single-dose sulfadoxine/pyrimethamine is being adopted as first-line treatment, on account of its low cost and ease of use. However, growing resistance to this drug in some countries in Africa leads to concern that its usefulness will be time-limited. Effective but more expensive artemisinin-based combination therapies are being introduced by RBM partners as part of national antimalarial drug policies. An informal technical consultation convened by WHO in 2001, concluded that combination therapy be incorporated into National Policies in preference to monotherapy and recommended that effective

combination options be considered for field testing.

Management of severe malaria

Parenteral quinine remains effective, but intramuscular artemether or intravenous artesunate is increasingly recommended because of its greater ease of use and safety. Artesunate suppositories are now being tested as pre-referral treatment, especially among children.

In pregnant women, artesunate and artemether are the drugs of choice for severe malaria during the 2nd and 3rd trimesters because, unlike quinine, they do not induce hypoglycemia. Data on the safety of these drugs during the 1st trimester are still limited, and they should therefore not be used during that period if quinine is available,.

- **Prevention**

— **Personal protection and vector control measures:** *Insecticide-treated bednets and other materials (ITMs)* have proven highly efficacious in reducing morbidity and mortality in areas of high, moderate and low malaria transmission in Africa. They have the potential for reducing transmission when used on a large scale.

♦ *Preventive Intermittent Treatment* at least twice during pregnancy (2nd and 3rd trimesters) is advisable for primi- and secundi-gravidae living in areas where transmission is high. HIV-positive pregnant women may need to receive such treatment on a monthly basis, and during all pregnancies. The drug of choice for this purpose is sulfadoxine-pyrimethamine (SP). In areas where SP is no longer effective, a safe alternative still needs to be identified.

♦ *Regular chemoprophylaxis*, where necessary in combination with stand-by treatment following strong clinical suspicion or an appropriate laboratory diagnosis, is recommended for travellers from non-endemic areas and as a short-term measure for soldiers, police and labour forces serving in highly endemic areas[9]. It must be complemented by personal protection against mosquito bites.

♦ *Indoor residual spraying* is the most effective intervention for prevention in some epidemiological situations such as controlling epidemics, maintaining transmission at the lowest possible level, maintaining eradication or truncating short seasonal transmission periods. They must be guided by local epidemiological and entomological knowledge.

♦ Other vector control measures such as *larviciding* may be of benefit in specific and well documented situations such as in cities, periurban areas and development projects impacting on environment where breeding sites are well known and mapped out.

Environmental management deserves to be used more often by the local community for collective protection from vectors and other communicable diseases, and incorporated into the comprehensive planning of development projects. Large-scale environmental management requires specialized teams.

- **Epidemics**

Malaria epidemics occur in areas where essential factors for transmission are marginal or seasonally absent. This is the case in highlands, semi-arid zones and periurban settings where population is generally non-immune. In such situations, human interventions may lead to environmental modifications that create suitable breeding sites and allow transmission to start on an epidemic mode. Meteorological factors such as unexpected or prolonged rainfall or above normal temperatures may lead to a sudden transmission increase of epidemic magnitude. Premature termination of efficient control measures also permits the reestablishment of malaria endemicity in a non immune population. The association of deteriorating social and economic conditions such as drought and famine renders populations highly vulnerable to the disease, especially as a result of population movements that bring non-immunes into areas with high levels of transmission. Areas of epidemic risk and risk factors must be identified on the basis of the epidemiological history and ecological and social characteristics. Relevant meteorological indicators include rainfall, humidity and temperature. Information on population movements and environmental change is also essential. Control of a malaria epidemic involves:

(i) Identifying zones and populations at risk.

(ii) Developing early warning and detection/verification systems to prevent or control epidemics in a timely manner.

(iii) Selecting cost-effective measures in advance; this includes the selection and stock of effective antimalarial drugs and insecticides, or re-impregnation of ITMs if pre-epidemic coverage and use of nets were already high.

(iv) As part of the response:

— Managing uncomplicated and severe malaria cases through existing health care facilities, mobile clinics and (if relevant) mass drug administration of effective and safe drugs (preferably one-dose) to all the population at risk or to all those with fever

— Preventing the spread of the epidemic (in time and space) through the timely use of vector control measures such as indoor spraying with residual insecticides.

(v) Developing preparedness plans of action and budget with other ministries and partners. The unit responsible for malaria within the Ministry of Health must provide technical input to the authorities coordinating disaster response.

9 See current edition of *International travel and Health* (WHO) for country-specific details and annual updates

- **Drug resistance monitoring and antimalarial drugs policy development**
  Resistance of *P. falciparum* to antimalarial drugs, especially chloroquine, is of major concern throughout the world. There is also growing evidence of *P. vivax* resistance to chloroquine in some endemic countries. A monitoring system for drug efficacy and resistance must incorporate the following:
  - Systematic use of agreed upon *in vivo* WHO protocols to document/monitor *P. falciparum*/*P. vivax* resistance to common antimalarials in use,
  - Collection and analysis of data at country, sub regional and regional level to be used as evidence to develop country and sub regional antimalarial drug policy
  - Notification by health services of suspected or confirmed treatment failures (using clinical criteria in the absence of laboratory facilities). Quality of drugs used must be monitored.

Other aspects

- **Procurement of equipment and drugs**
  National malaria therapy guidelines must detail known adverse effects of drugs and define conditions, such as pregnancy, in which specific drugs are contraindicated for prophylactic and/or therapeutic use. This is particularly vital with the coming use of combination therapies.
- **Surveillance (RBM monitoring and evaluation framework)**
  The monitoring and evaluation framework identifies five "critical areas" that relate directly to the RBM objectives:
  (i) impact on malaria burden (mortality, morbidity and economic losses)
  (ii) improvements in malaria prevention and disease management, including the prevention and control of epidemics
  (iii) related health sector development
  (iv) intersectoral linkages (to be created or reinforced)
  (v) support and partnerships.
  All regions and RBM countries should use this framework to develop their own monitoring and evaluation system. Within this system, indicators for each critical area could vary between sub-regions, regions and countries according to local malaria epidemiology and actual RBM strategy. The principal monitoring and evaluation system of RBM at regional, sub-regional and country levels should be based on a small number of core indicators for each of the critical areas in the monitoring and evaluation framework. These should be intervention- and result-oriented and provide information for action at the relevant operational levels.
- **Proposed core indicators for RBM monitoring and evaluation**

At least two indicators, one process and one outcome, should be selected for each critical area.

I. Impact

- Crude death rate among target groups
- Malaria death rate (probable and confirmed cases) among target groups
- % of probable and confirmed malaria deaths among patients with severe malaria admitted to a health facility
- Number of cases of severe malaria (probable and confirmed) among target groups
- Number of cases of uncomplicated malaria (probable and confirmed) among target groups
- Annual Parasite Incidence (API) among target groups (by region/according to the epidemiological situation).

II. Malaria prevention and disease management

Prevention

- % of countries having introduced pyrethroids for public health use and insecticide-treated materials in the list of essential drugs and materials
- % of service providers (health personnel, CHW…) trained in techniques of treatment of nets and/or indoor spraying according to national policy
- % of households having at least one treated bednet
- % of pregnant women who have taken chemoprophylaxis or intermittent drug treatment, according to national drug policy
- % of antenatal clinic staff trained in preventive intermittent antimalarial treatment for pregnant women.

Prevention and control of epidemics

- % of countries with epidemic prone areas/situation having a national preparedness plan of action for early detection and control of epidemics
- % of malaria epidemics detected within two weeks of onset and properly controlled.

Early diagnosis and prompt treatment

- % of health personnel involved in patient care trained in malaria case management and IMCI
- % of health facilities able to confirm malaria diagnosis according to the national policy (microscopy, rapid test etc.)
- % of patients hospitalised with a diagnosis of severe malaria and receiving correct antimalarial and supportive treatment according to the national guidelines
- % of patients with uncomplicated malaria getting correct treatment at health facility and community levels according to national guidelines within 24 hours of the onset of symptoms.

III. Health Sector Development

Health Policy

- % of districts with plans of action reflecting national health policy
- % of districts using health information for planning
- % of countries having a policy of universal coverage for all with a basic package including relevant malaria control activities.

Service Delivery

- % of health facilities reporting no disruption of stock of antimalarial drugs, as specified in the national drug policy, for more than one week during the previous 3 months.

Community Action

- % of countries having national guidelines for malaria prevention and treatment including training of all the informal health providers and recommendations for home treatment of febrile illness/suspected malaria, recognition of the most frequent signs of danger for children, prevention of malaria during pregnancy and use of insecticide treated materials
- % of villages/communities with at least one Community Health Worker trained in management of fever and recognition of severe febrile illness
- % of mothers/caretakers able to recognize signs and symptoms of danger of a febrile disease in a child under 5 years.

IV. Intersectoral linkages

- % of countries with established multisectoral and inter-agencies partnership
- % of countries having established official linkages, including the elaboration of research agenda of public health interest, between research institutions and Ministry of Health.

V. Support/Partnership

- % of countries with agreed national RBM budget met by donor funding
- % of countries with functional sentinel sites for surveillance efficacy of 1st and 2nd line antimalarial drugs
- Number of anmtimalarial drugs that have progressed to the level of Phase III trials.

Contacts and References

CONTACTS: Regional Offices: see addresses on pages 40-42

AFRO (Regional Office for Africa): Fax 26 34 70 56 19, Tel 26 34 70 74 39

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EMRO (Regional Office for the Eastern Mediterranean): Fax 20 34 83 89 16, Tel 20 34 82 02 23

EURO (Regional Office for Europe) Fax 45 39 17 18 18, Tel 45 39 17 17 17

SEARO (Regional Office for South-East Asia): Fax 911 13 31 86 07, Tel 911 13 31 78 04

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REFERENCES

WHO. *Vector control for malaria and other mosquito-borne diseases.* Geneva: WHO, 1995. Technical Report Series n°857. ISBN 92 4 120857 0.

WHO. *WHO Expert Committee on Malaria. Twentieth Report.* Geneva: WHO, 1993. Technical report Series N° 892. ISBN 92 4 120892 9.

WHO. *The use of antimalarial drugs. Report of an informal consultation, 13-17 November, 2000*. WHO/CDS/RBM/2001.33

WHO. *Antimalarial Drug combination therapy. Report of a WHO technical consultation, 4-5 April 2001.* WHO/CDS/RBM/2001.35

WHO. The African Summit on Roll Back Malaria, Abuja, April 25, 2000. WHO/CDS/RBM/2000.17

WHO. *Management of severe malaria, a practical handbook.* 2000. ISBN 92 4 154523 2

WHO. *Framework for monitoring progress and evaluation outcomes and impact. 2000.* WHO/CDS/RBM/2000.25

WHO. *Malaria diagnosis: New perspectives, report of a joint WHO/USAID informal consultation.* Geneva: WHO, 2000. WHO/CDS/RBM/2000.14

WHO. *Malaria Early Warning Systems, a framework for field research in Africa.* Geneva: WHO, 2001. WHO/CDS/RBM/2001.32

WHO. *Drug resistance in malaria. A background document for the WHO global strategy*., 2001. Geneva: WHO, WHO/CDS/DRS/2001.4

WHO. *Insecticide Treated Materials. Report of the Third meeting of the technical support network.* 2001. Geneva: WHO, WHO/CDS/RBM, 2001.36

WHO. *Malaria control among refugees and displaced population*,, 1998. Geneva: WHO, CTD/MAL/96.6

WHO. Framework for developing, implementing and updating antimalarial treatment policy in Africa. A guide for country malaria control programmes. WHO Regional Office for Africa *(in press)*.

WHO. *International Travel and Health, vaccination requirements and health advice* . Geneva: WHO, 2001. ISBN 92 4 258026 0

Measles B05

General introduction

Measles is a major childhood killer in developing countries, accounting for about 875 000 deaths a year, over 50% of the estimated 1.6 million child deaths due to vaccine-preventable diseases. It remains the leading cause of vaccine-preventable death worldwide and may ultimately be responsible for more child deaths than any other single microbe, because of complications such as pneumonia, diarrhoea and malnutrition.

Measles is currently targeted for a 50% mortality reduction by 2005. Accelerating measles control or achieving measles elimination is based on 5 strategies:

1. Routine immunization (measles vaccination is extremely cost-effective)
2. Supplementary immunization
3. Enhanced surveillance
4. Vitamin A supplementation
5. Adequate case management

There are 2 phases of measles control:

1. Mortality reduction phase

Districts are in the mortality reduction stage if:

- Measles is *endemic,* incidence is high, with high mortality, **and**
- Measles immunization coverage is low – less than 80% coverage, **and**
- Wild poliovirus is endemic.

NOTE: Districts and countries in this phase must focus on achieving the measles mortality and morbidity goals mentioned earlier and in meeting basic surveillance, monitoring and immunization requirements to accelerate achievement of these goals.

2. Outbreak prevention and elimination* phase

* During the elimination phase, endemic transmission cannot occur over a wide territory and the introduction of an imported case does not lead to sustained transmission; intervention meaures are nevertheless still required.

Districts are in the outbreak prevention/ elimination stage if:

- Measles mortality is less than 1%
- Vaccine coverage is above 80%
- Circulation of wild poliovirus has been interrupted as certified by adequate level of AFP surveillance indicators.

NOTE: Districts and countries in this phase must focus on forecasting/preventing intermittent outbreaks that may occur even with high coverage, and on stopping low-level transmission. Measles elimination goals can be met only if they are set at national level and considered as part of a multi-country or regional effort. WHO recommends that measles elimination be attempted only in regions that are poliomyelitis-free.

Causal agent and main modes of transmission

- **Causal agent:** Measles virus of the genus Morbillivirus, family Paramyxoviridae.
- **Main modes of transmission:** Transmitted via airborne droplets, direct contact with nasal or throat secretions, or by articles freshly soiled with nose and throat secretions. Measles is one of the most highly communicable diseases in man, with a basic reproductive rate of 17-20 (i.e. the introduction of 1 case of measles in a completely susceptible community generates 17-20 new cases). The incubation period (to onset of fever or rash) is normally 7 to 18 days. The case fatality rate in developing countries is normally 3% to 5% but may reach up to 30% in some situations.

Clinical Case definition and Case Classification [10]

- **Clinical case definition**

  Any person with
  - Fever, **and**
  - Maculopapular (non-vesicular) rash, **and**
  - Cough, coryza (i.e. runny nose) or conjunctivitis (i.e. red eyes).

  Or
  - Any person in whom a clinician suspects measles infection.

  Laboratory criteria

  Presence of measles-specific IgM antibodies.

[10] Updated for the present document by technical unit (see *Introduction*)

Case classification

- ***Clinically confirmed:*** A case that meets the clinical case definition
- ***Laboratory-confirmed:*** *(only for outbreak confirmation and during the outbreak prevention/elimination phase)*. A case that meets the clinical case definition and is laboratory-confirmed **or** a case meeting clinical definition and epidemiologically linked by direct contact to a laboratory-confirmed case in which rash onset occurred 7-18 days earlier.

Recommended interventions

- **Case management**
  - ***Uncomplicated measles***

    Under normal circumstances, supportive therapy, with access to further care if complications develop.
  - ***Complicated measles***
    - Follow the recommendations for case management of uncomplicated measles **and**
    - Refer to health facility for adequate management of complications:
      - Clean eye lesions and treat with 1% tetracycline eye ointment 3 times a day for 7 days
      - Vitamin A supplementation (to minimize the risk of potentially blinding eye lesions)
      - Clean ear discharge and treat with antibiotics
      - Treat malnutrition and diarrhoea with sufficient fluids and a high-quality diet
      - Treat pneumonia with antibiotics.

  Vitamin A and treatment of complications of measles (e.g. fluids for diarrhoea and antibiotics for pneumonia) are effective in reducing severity and the risk of death.

Recommended Vitamin A schedule

Age	*Immediately on diagnosis*	*Following day*
Infants <6 months	50 000 IU	50 000 IU
Infants 6-11 months	100 000 IU	100 000 IU
Children 12+ months	200 000 IU	200 000 IU

- **Prevention**
  A single dose of live attenuated measles vaccine after 9 months of age will induce active immunity in >85% of susceptible individuals. A second dose may increase immunity levels to as high as 99%.
  Measles vaccine is effective and safe and it can be combined with other live vaccines. The main reason for the persistence of the disease burden is underutilization of the vaccine.
- **Epidemics**
  The thresholds to determine whether or not an outbreak or epidemic occurs will be based on local epidemiological conditions and immunization objectives. For instance, the Region of the Americas chose to define an outbreak as 3 or more cases in a defined geographical area within a 1-month period.
  In all measles outbreaks, strengthening routine immunization is a priority, together with raising awareness of vaccination and ensuring effective case management (including Vitamin A supplements). Ad hoc immunization activities may not have a substantial impact on the course of a measles outbreak; even when they are successful, the cost per prevented case can be very high. If it is decided to implement supplementary vaccination campaigns, these must focus on as yet unaffected areas where the outbreak is likely to spread, starting at once without waiting for completion of the outbreak investigation.
- **Drug resistance monitoring**
  Not applicable.

Other aspects

- **Procurement of equipment and drugs**
  See *Immunization (section 2.1)*
- **Surveillance**[11]
  - ***Control phase:*** When measles is endemic, routine monthly reporting of aggregated data of clinical measles cases by age group and immunization status from peripheral to intermediate and central level. Only outbreaks (not each case) must be investigated.
  - ***Outbreak prevention/Elimination phase***: Case-based surveillance – every case reported and investigated immediately from peripheral to intermediate level, and included in the weekly reporting system. Laboratory specimens must be

[11] Updated for the present document by technical unit (see *Introduction*)

collected from every sporadic case. Suspected measles outbreaks must be confirmed by conducting serology on the first 5-10 cases only. Urine samples for virus isolation must be collected from sporadic and outbreak cases (approximately 10 cases from each chain of transmission) to allow genetic characterization of circulating virus in order to assess viral circulation and importation patterns. Zero reporting required at all levels during all phases.

- **Special considerations/other interventions**
  - **Frequency of complications**

    At least 3 out of 4 cases in developing countries may have at least one complication and some have multiple systems involvement. The main causes contributing to high case fatality rate are pneumonia, diarrhoea and croup. Measles can also lead to life-long disabilities, including blindness, brain damage and deafness. Of measles deaths, 98% occur in developing countries, where vitamin A deficiency is common. Low vitamin A status is associated with a higher rate of complications and a higher death rate, as vitamin A deficiency and measles have similar effects on epithelia and the immune system. Half the cases of childhood corneal blindness in developing countries are attributable to vitamin A deficiency, and half to measles infection.
  - **Immunization safety**

    Accelerated measles control and elimination activities require strict attention to injection safety.
  - **Refugees and special populations**

    Outbreaks in closed communities or institutions such as refugee camps, hospitals and military barracks may necessitate immediate supplementary immunization activities whatever the circumstances. In refugee camps, vaccination of all children below 5 years of age is indicated as soon as they arrive in the camp. Delay in implementing this may result in increased morbidity and mortality.
  - **Vitamin A supplementation**

    In countries with a vitamin A deficiency problem, the provision of high-dose vitamin A supplements every 4-6 months:
    - Protects against blindness
    - Reduces the risk of all-cause mortality by 23%.

    In such countries, vitamin A supplements must be provided at the time of routine measles vaccination (9 months). Supplementary campaigns of immunization against measles must also be used as an opportunity for the provision of vitamin A supplementation to all children whose age puts them at risk of measles, whether immunized or not.
    Supplementary dosage:
    - Infants 6-11 months 100 000 IU
    - Children 12 months and over 200 000 IU

- **Indicators**
  - ***Control phase***
    - Incidence rate by month, year, and geographic area
    - Measles vaccine coverage by year and geographic area (including municipalities)
    - DTP1-measles or BCG-measles dropout rate
    - Completeness/timeliness of monthly reporting
    - Proportional morbidity (compared to other diseases of public health importance)
    - Proportion of known outbreaks that were investigated
    - Age-specific incidence rate
    - Cases by age group and immunization status: age groups suggested 0-5 months, 6-11 months, 12-23 months, 2-4 years, 5-9 years, 10-14 years, 15-19 years, 20-24 years, 25-29 years, 30 years and over.
  - ***Outbreak prevention/measles elimination phase:*** same as control phase plus the following
    - Performance indicators *Target*
      - % of weekly reports received =80%
      - % of cases* notified =48 hours of rash onset =80%
      - % of cases* investigated =48 hours of notification =80%
      - % of cases* with adequate specimen** and lab results =80%
      - % of confirmed cases with source of infection identified =80%

* All cases that meet the clinical case definition**

** Adequate specimen is a blood specimen collected within 28 days of rash onset

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42.

WHO Headquarters: 20 Avenue Appia, CH-1211 Geneva 27, Switzerland - Vaccines & Other Biologicals/Expanded Programme on Immunization (VAB/EPI)
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REFERENCES

WHO. *Measles: mortality reduction and regional elimination – strategic plans 2001-2005.* WHO: Geneva, 2001 WHO/V&B/01.13
http://whqlibdoc.who.int/hq/2001/WHO_V&B_01.13.pdf

See also: *Immunization* and *Mass chemotherapy/prophylaxis* (vitamin A) in the present document (sections 2.1 and 2.2)

Meningococcal disease A39

General introduction

Meningococcal disease occurs sporadically and in epidemics of meningococcal meningitis; the majority of cases occur in children under 5 years. Sub-Saharan Africa is the most severely affected area, particularly in the "meningitis belt" from Senegal to Ethiopia, but epidemic meningococcal disease can affect any country.

Immunization of the entire population at risk with bivalent A, C vaccines must be considered in order to halt epidemics due to A and C serogroup meningocci. In some countries, vaccine is used for close contacts of patients with meningococcal disease due to A, C, Y or W135 serogroups in order to prevent secondary cases. Immunization is also indicated for people travelling to areas of high endemicity or epidemic risk.

Causal agent and main modes of transmission

- **Causal agent:** *Neisseria meningitidis*, a Gram-negative microorganism.
- **Main modes of transmission:** Transmission is by aerosol or direct contact with the respiratory secretions of infected persons (including symptomless carriers). The incubation period is 2 to 10 days. Most infections are subclinical and many infected people become symptomless carriers. Climatic conditions in the dry season and overcrowding favour epidemics, as do upper respiratory tract infections. Waning immunity among the population against a particular strain may also facilitate the occurrence of an epidemic.

Clinical description and case definition

- **Clinical description:** Meningococcal meningitis usually starts suddenly with intense fever and headache, nausea, vomiting, photophobia, neck stiffness, with/without purpuric rash and neurological signs (lethargy, delirium, coma and/or convulsions). Infants may present illness with neither sudden onset nor stiff neck.
  Even with early and adequate therapy the case fatality rate is between 5% and 10%. It may exceed 50% in the absence of treatment. Up to 15% of those who survive may suffer neurological sequelae (deafness, mental retardation). A less common but often fatal form of meningococcal disease is meningococcal septicaemia, characterized by rapid circulatory collapse and a haemorrhagic rash.
- **Clinical case definition**
  An illness with sudden onset of fever (>38.5°C rectal or >38.0°C axillary) **and one or more** of the following:
  - Neck stiffness
  - Altered consciousness
  - Other meningeal sign **or** petechial or purpural rash.

  In patients under 1 year, suspect meningitis when fever accompanied by bulging fontanelle.

  Laboratory criteria
  - Positive CSF antigen detection, **or**
  - Positive culture.

  Case classification
  - ***Suspected:*** A case that meets the clinical case definition.
  - ***Probable:*** A suspected case as defined above **and:**
    - Turbid CSF (with or without positive Gram-stain), **or**
    - Ongoing epidemic and epidemiological link to a confirmed case.
  - ***Confirmed:*** A suspected **or** probable case with laboratory confirmation.

Recommended interventions

- **Case management**

  Meningococcal disease is a medical emergency requiring admission to a hospital or health centre; isolation is not necessary. Antimicrobial therapy must be instituted as soon as possible after lumbar puncture.

  Oily chloramphenicol intramuscularly (100 mg/kg up to 3 grams in a single dose) is the drug of choice in epidemics, particularly in areas with limited health facilities. A further dose can be given after 48 hours if no improvement. Where scales are not available, doses may be set according to age as follows:

1-8 wks	2-11 mths	1-2 yrs	3-5 yrs	6-9 yrs	10-14 yrs	15+ yrs
0.25 g	0.5 g	1.0 g	1.5 g	2.0.	2.5 g	3.0 g
(1 ml)	(2ml)	(4 ml)	(6ml)	(8ml)	(10ml)	(12 ml)

  Other antibiotics – more costly and/or requiring administration for a longer time (penicillin G, ampicillin, ceftriaxone) – are also effective. Supportive treatment must include maintenance of hydration.

- **Prevention**

  In endemic situations and small clusters or closed populations (extended household, boarding schools), chemoprophylaxis may be considered for close contacts (rifampicin, ciprofloxacin, ceftriaxone or other as advised by the health authorities – but not penicillin or chloramphenicol). Vaccination may be used for close contacts (A, C, Y, or W135 serogroups) to prevent secondary spread around a sporadic case.

- **Epidemics**

  Epidemics of cerebrospinal meningitis usually spread rapidly to a peak within weeks but may last several months in the absence of vaccination. Polysaccharide vaccines are available against serogroups A, C, Y, W135. A mass immunization campaign that reaches at least 80% of the entire population with serogroup A and C vaccine can halt an epidemic due to meningococci of these serogroups. Other than mass immunization, there is no effective means of interrupting transmission during an epidemic.

  Deciding when an epidemic is occurring or likely to occur (setting thresholds linked to action)

  – *Alert threshold (population 30 000 or more):*
    - 5 cases per 100 000 inhabitants per week, in 1 week.
  – *Alert threshold (population less than 30 000):*
    - 2 cases in 1 week **or**
    - Increase in the number of cases compared to previous non-epidemic years.
  – *Uses of alert threshold:*
    1. Sound early warning and launch investigation at the start of an epidemic
    2. Check epidemic preparedness
    3. Start a vaccination campaign if there is an epidemic in a neighbouring area
    4. Prioritize areas for vaccination campaigns.

  If a meningitis epidemic has been confirmed in a neighbouring area, crossing the alert threshold is sufficient to implement full-scale epidemic control measures.

  – *Epidemic threshold (population 30 000 or more)*
    - 15 cases/100 000 inhabitants per week, in 1 week
    - 10 cases/100 000 inhabitants per week, in 1 week when the epidemic risk is high, e.g. when:
      - Alert threshold is reached early in the dry season, **or**
      - No meningitis epidemic in district for at least 3 years and vaccination coverage against meningococcal meningitis in target population less than 80%.
      - Other factors, such as high population density, may increase the risk of an epidemic.
  – *Epidemic threshold (population less than 30 000)*
    - 5 cases in 1 week, **or**
    - Weekly doubling of the number of cases over a 3-week period.

  Other situations must be studied on a case-by-case basis, taking into account epidemic risk.

  – *Uses of epidemic threshold:*
    1. Confirm the emergence of an epidemic
    2. Step up control measures (mass vaccination and case management).

Actions

- At the start of the dry season:
  - Reactivate meningitis surveillance, including zero reporting
  - Place stocks of vaccines, treatment drugs and injection equipment for rapid mobilization.
- *When the alert threshold is reached:*
  - Inform regional and national health authorities
  - Initiate a field investigation
  - Confirm the agent and the serogroup
  - Strengthen the surveillance system
  - Reactivate the epidemic management committee
  - Check that vaccines, medications and injection equipment are in place
  - Remind health personnel of the treatment protocol
  - In case of an epidemic in a neighbouring area: mass vaccination.
- *When the epidemic threshold is reached, in addition:*
  - Inform the population
  - Conduct mass vaccination
  - Distribute drugs, injection equipment and treatment guidelines to all local health facilities
  - Treat cases according to guidelines adapted for use during epidemics.
- *Special situations* (e.g. refugees, displaced persons) call for immediate response, including mass vaccination, when 2 cases of meningococcal disease are confirmed in 1 week, even if there is no epidemic nearby.

- **Drug resistance monitoring**
  Recent reports of decreased sensitivity (France, Vietnam) may warrant this type of surveillance in future.

Other aspects

- **Procurement of equipment and drugs**
  In areas where epidemics may occur regularly:
  - Diagnostic material for *N. meningitidis*
  - Oily chloramphenicol
  - Injection equipment
  - Lumbar puncture equipment
  - Vaccine (1 dose per vaccinee + 4% to 10%, if a mass vaccination is scheduled).

  Oily chloramphenicol suspension is available from:
  I.D.A. International Dispensary Association
  P.O. Box 37098, NL-1030 AB Amsterdam, The Netherlands
  Tel: +31 2040 33 051, Fax: +31-20 40 31 854, Email: info@ida.nl
  and from:
  Laboratoires LAFRAN 1, route de Stains, F-94387 Bonneuil/Marne CEDEX, France
  Tel: +33 143 39 99 90, Fax: +33 143 39 78 00, Email: lafran@libertysurf.fr

- **Surveillance**
  At peripheral level, individual patient records must be maintained (particularly for contact tracing).
  Immediate reporting of all suspected or probable cases from peripheral level to intermediate level.
  All cases must be investigated. Follow-up data on the organism identified and on patient outcome to be sought by the intermediate level. Routine weekly/monthly reporting of aggregated or case-based data from intermediate to central level.
  Microbiological data on serogroup and genotype data from parallel surveillance using reference laboratories may be useful for epidemiological analysis.
  NOTE 1: In countries with limited surveillance infrastructure, 2 approaches to clinical surveillance can be combined:
  1. A limited amount of data reported from all health sites (e.g. new cases and deaths by week)
  2. More extensive data reported from selected referral health centres.

  NOTE 2: Surveillance of vaccine coverage may be undertaken in areas of mass vaccination or where vaccination for meningococcal disease is part of routine vaccination.

- **Indicators**
  - Weekly incidence rate
  - Number of reported cases
  - Trends in the number of cases over time and compared to previous year
  - Vaccination coverage (in case of mass immunization campaigns).

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pp. 40-42
WHO Headquarters: 20 Avenue Appia, CH-1211 Geneva 27, Switzerland - Communicable Diseases Surveillance and Response (CSR)
E-mail: Hardimanm@who.int and outbreak@who.intTel: (41 22) 791 2572, Fax: (41 22) 791 4878/0746 attn CSR

REFERENCES:

WHO: *Control of meningococcal disease – WHO practical guidelines*. 2nd edition, 1998 WHO/EMC/BAC/98.3
Detecting meningococcal meningitis epidemics in highly-endemic African countries/Détecter une épidémie de méningite à méningocoque dans les pays d'Afrique à forte endémicité. *Weekly Epidemiological Record/Relevé épidémiologique hebdomadaire*, 2000, 75(38): 306-309.
See also: *Mass chemoprophylaxis/chemotherapy* and *Immunization* in the present document (sections 2.1 and 2.2).

Viral meningitis A87

General introduction

Viral meningitis occurs worldwide, sporadically and also as an epidemic disease. Case fatality rates are generally low; infection may have potential long-term sequelae in those affected (mostly children), but the disease is rarely severe and recovery is usually complete.

Causal agents and main modes of transmission

- **Causal agents:** multiple viral etiologies (mumps, enteroviruses, coxsackie viruses, echoviruses, arboviruses, measles, herpes simplex, adenoviruses, etc.).
- **Main modes of transmission:** vary according to the infectious agent, mainly faecal-oral or by aerosol. Incubation variable according to the infectious agent.

Clinical description and case definition

- **Clinical description:** Sudden onset of febrile illness with signs and symptoms of meningeal involvement. A rash, transient paresis and encephalitic manifestations may be present; active illness usually lasts at most 10 days. Neuromuscular residual signs may occur for about 1 year and usually clear up completely.
- **Clinical case definition**
  A case with fever =38.5°C **and one or more** of the following:
  - Neck stiffness
  - Severe unexplained headache
  - Neck pain and **2 or more** of the following
    - Photophobia
    - Nausea
    - Vomiting
    - Abdominal pain
    - Pharyngitis with exudates.

  For **children <2 years of age** a case is defined as
  - A case with fever =38.5°C **and one or more** of the following
    - Irritability
    - Bulging fontanelle.

  Laboratory criteria
  Confirmation of the specific virus on cell culture (including polymerase chain reaction (PCR) if possible).

  Case classification
  - ***Suspected:*** A case that meets the clinical case definition.
  - ***Probable:*** A suspected case with **one or more** of the following:
    - Normal CSF glucose and normal or mild increase (>50 mg/dl) in CSF protein
    - Moderate increase CSF cells (<500/mm^3) and lymphocyte predominance (>50%)
    - CSF positive for viral genomic sequences using PCR
    - Epidemiological link to a confirmed case.
  - ***Confirmed:*** A suspected or probable case with laboratory confirmation.

Recommended interventions

- **Case management**
  Symptomatic. Enteric precautions are indicated for 7 days until after onset of illness or until a nonenteroviral etiology has been established.
- **Prevention**
  Not applicable apart from those prevention measures specific to the etiology if known.
- **Epidemics**
  For enteroviral outbreaks:
  - Identify source if possible
  - Apply enteric precautions: sanitation, hand-washing.
- **Drug resistance monitoring**
  Not applicable.

Other aspects

- **Surveillance**
  At the peripheral level, individual patient records must be maintained.
  Immediate reporting of all suspected or probable cases from peripheral to intermediate and central levels.
  All cases must be investigated. Follow-up data on identified organism and patient outcome to be sought by the intermediate and central level.
  Routine weekly reporting of aggregated or case-based data from intermediate to central level.
  A parallel surveillance using reference laboratories for viral diseases may provide more detailed virological data on specific causal agents on a national basis; these are very useful for epidemiological analysis.
- **Special considerations/other interventions**
  Not applicable.
- **Indicators**
  Not applicable.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42.

WHO Headquarters: 20 Avenue Appia, CH-1211 Geneva 27, Switzerland - Communicable Diseases Surveillance and Response (CSR)
E-mail: lavanchyd@who.int and outbreak@who.int Tel: (41 22) 791 4878, Fax: (41 22) 791 4878/0746 attn CSR

Onchocerciasis (River blindness) B73

General introduction

Onchocerciasis is endemic in 37 countries of Africa, the Arabian peninsula and the Americas. Control of the disease is the result of a 25-year old programme that uses larviciding for vector control in order to interrupt transmission and, since 1988, has been combined with mass treatment by ivermectin – a safe, effective microfilaricidal drug. The global strategy for controlling onchocerciasis is based on the yearly administration of ivermectin to affected populations (twice yearly in the Americas).

The first step in control is to map the endemicity of onchocerciasis in known or potentially endemic areas. The second is to implement cost-effective and sustainable ivermectin delivery, focusing on methods involving community-based treatment.

Once onchocerciasis is under control (as is currently the case in 11 West African countries), the risk of recrudescence must be kept to a minimum. In the Onchocerciasis Control Programme in West Africa (OCP), participating countries will ensure that, during the phasing-out period (1998-2002), detection and control of onchocerciasis recrudescence become a routine function of national disease surveillance and control services. In the Americas, in addition to the main goal of eliminating morbidity from *Onchocerca volvulus* by the year 2007, the elimination of parasitic transmission is considered a realistic goal.

Causal agent and main modes of transmission

- **Causal agent:** *Onchocerca volvulus*, a nematode filaria.
- **Main modes of transmission:** The adult form of *Onchocerca volvulus* can live in the human body for up to 14 years and is often found encased in fibrous subcutaneous nodules. Each adult female produces millions of microfilariae that migrate under the skin and through the eyes, giving rise to a variety of dermal and ocular symptoms. The vector for onchocerciasis is the blackfly (genus *Simulium* – in Africa and the Arabian peninsula mainly *S. damnosum* complex and *S. neavei* group; in America mainly *S. ochraceum, S. metallicum* and *S. exiguum* complexes), the larvae of which live in fast-running waters – this has led to the name "river blindness". Blackflies live for up to 4 weeks and African species can cover hundreds of kilometres in flight. The female blackfly may ingest microfilariae by taking a blood meal from an infected person. A few microfilariae may transform into infective larvae within the blackfly after several days; they are then injected into the person from whom the next blood meal is taken and subsequently develop into adult parasites. The life-cycle of the parasite is completed in about 1 year. Symptoms begin 1 to 3 years after infection, usually at the time when adult females begin to produce microfilariae.

Clinical description and case definition

- **Clinical description:** Persons suffering from onchocerciasis may experience rashes, papular skin lesions, subcutaneous nodules, intense itching and depigmentation of the skin; lymphadenitis, which results in "hanging groin" and elephantiasis of the genitalia; and general debilitation. Eye lesions lead to serious visual impairment including blindness.
- **Clinical case definition**
  In an endemic area, a person with fibrous nodules in subcutaneous tissues. These must be distinguished from lymph nodes or ganglia.

  Laboratory criteria

  Presence of one or more of the following:
  - Microfilariae in skin snips taken from the iliac crest (Africa) or scapula (Americas)
  - Adult worms in excised nodules
  - Typical ocular manifestations, such as slit-lamp observations of microfilariae in the cornea, the anterior chamber, or the vitreous body
  - Serology (especially for non-indigenous persons).

  Case classification
  - ***Suspected:*** A case that meets the clinical case definition
  - ***Probable:*** Not applicable.
  - ***Confirmed:*** A suspected case that is laboratory-confirmed.

Recommended interventions

- **Case management**
  Administration of ivermectin once a year (twice a year in the Americas) over a period of at least 15 to 20 years* will reduce infection to insignificant levels and prevent the appearance of clinical manifestations. The recommended dosage is equivalent to 150 microgrammes per kilog of body weight (in practice, dosage is according to height, using 1 to 4 tablets of 3 mg). Ivermectin is a filaricide and effective against adult worms.
  Established clinical manifestations are treated by ivermectin.
  * Based on computer simulations, currently recommended by OCP for asymptomatic individuals in an endemic area

- **Prevention**
  OCP's principal method for controlling onchocerciasis has been to interrupt the cycle of transmission by eliminating the blackfly. Simulium larvae are destroyed by application of specifically researched insecticides through aerial spraying to breeding sites in fast-flowing rivers. Once the cycle of disease has been interrupted for about 14 years the reservoir of adult worms dies out in the human population, thus eliminating the source of the disease.
  Annual treatment prevents clinical disease. In the Americas, the strategy of twice-yearly mass treatment aims at stopping transmission as well as eliminating the clinical manifestations of the disease.

- **Epidemics**
  Recrudescence of transmission may occur and can be managed by the administration of ivermectin if mass treatment programmes can maintain good treatment coverage.

- **Drug resistance monitoring**
  The risk of resistance to ivermectin is remote but a cautious approach must nevertheless be adopted – techniques to monitor resistance are being developed.

Other aspects

- **Procurement of equipment and drugs**
  Ivermectin is available free from the manufacturer for onchocerciasis programmes, contact WHO.

- **Surveillance**
  - **In zones where onchocerciasis is endemic:**

    Active case-finding (skin snips, ophthalmological examination, diethylcarbamazine patch test) through surveys. Distribution of the disease can be targeted to those villages identified through rapid epidemiological assessment and through rapid epidemiological mapping of onchocerciasis (REMO), techniques that use noninvasive assessment of nodule rates and environmental characteristics to identify areas at risk for high endemicity of onchocerciasis.
  - **In the onchocerciasis-freed zones of West Africa:**
    - *Surveillance in sentinel villages:* To detect recrudescence of infection, a minimum of 260 sentinel villages in onchocerciasis-freed zones of West Africa have been kept under periodic surveillance (once every 3 years). They are located near former productive larval breeding sites and had high prevalence rates prior to beginning of control activities. In areas where recrudescence is identified (incidence >1%), the administration of ivermectin is instituted for a period of 15 to 20 years.
    - *Routine surveillance*: All suspected cases must be investigated locally, with routine reporting of aggregated data from peripheral to intermediate and central levels. This is in continuous development at country level through training of health staff.
    - *Migration investigation*: If a case is detected in the course of epidemiological surveillance, a migration investigation is systematically carried out to identify origin of infection and take appropriate action.

- **Special considerations/other interventions**
  The approach recommended and promoted by APOC is community-directed treatment with ivermectin (CDTI) with distribution house-to-house or at central meeting points in the village, using distributors selected by the community who have attended training and capacity-building sessions organized by local health staff. Communities are informed about adverse effects, most of which – such as oedema, itching and headaches – are benign and transient; more seroius effects must be reported and referred to local health authorities for management.
  In small areas inaccessible by helicopter, ground application of larvicides may be considered.

- **Indicators**
  - Trends in the number of cases in sentinel areas
  - Evidence of resettlement in formerly abandoned settlements (population displacement)
  - Reduced ocular disease and skin disease in (hyper)endemic areas (where infection prevalence rates are >60% and where nodule rates are >40%)
  - Reduced life expectancy, poverty, malnutrition, unemployment in (hyper)endemic areas.

Contacts and References

CONTACTS: WHO Regional Offices

AFRO (Regional Office for Africa), Parirenyatwa Hospital, POB BE 773, Harare, Zimbabwe Tel: 001 321 733 9244, Fax: 001 321 733 9020

AMRO/PAHO (/Regional Office for the Americas/Pan American Health Organization)

Communicable Diseases Program, Division of Diseases Prevention and Control, 525 Twenty-third St. NW, Washington DC 20037, USA

Email: ehrenbej@paho.org Tel: 001 202 974 3894, Fax: 001 202 974 3632

EMRO (Regional Office for the Eastern Mediterranean), WHO Post Office Abdul Razzak Al Sanhouri Street, Naser City, Cairo 11371, Egypt

Tel: 202 670 2535, Fax: 202 670 2492 or 202 670 2494

WHO Headquarters: 20 Avenue Appia, CH-1211 Geneva 27, Switzerland

Onchocerciasis Control Programme/African Programme of Onchocerciasis Control

Control Liaison Office (ACP/APOC) E-mail: daribia@who.int and Surveillancekit@who.intTel: (41 22) 791 3883/2111, Fax: (4122) 791 4190

REFERENCES:

APOC. *Community-directed treatment with ivermectin (CDTI). A practical guide for trainers of community-directed distributors.* APOC/WHO, Ouagadougou, 1998

Samba EM. *The Onchocerciasis Control Programme in West Africa – an example of effective public health management.* WHO: Geneva, 1994. ISBN 9242561688

WHO. *Onchocerciasis and its control – report of a WHO Expert Committee on Onchocerciasis Control.* WHO Technical Report Series N° 852. WHO: Geneva, 1995. ISBN 924120852X

WHO. TDR/OCP/APOC. 1996. *Community-directed treatment with ivermectin*. Report on a multi-country study. TDR/AFR/RP/96.1

See also: *Mass chemoprophylaxis/chemotherapy* in the present document (section 2.2).

Pertussis (whooping cough) A37.0

General introduction

Pertussis is a major cause of childhood morbidity and mortality. Each year sees an estimated 20-40 million new cases, 90% of which occur in developing countries, and an estimated 200 000 to 300 000 fatalities. Case fatality rates in developing countries can reach 15%. Although pertussis may occur at any age, most cases of serious disease and most fatalities are observed in early infancy.

High routine coverage with effective vaccine is the mainstay of prevention. Surveillance data on the disease can monitor the impact of vaccination on disease incidence and help identify outbreaks and high-risk areas.

Causal agent and main modes of transmission

- **Causal agent:** *Bordetella pertussis*, a Gram-negative bacillus.
- **Main modes of transmission:** Pertussis is transmitted by discharges from respiratory mucous membranes of infected persons via the airborne route. Humans are the only hosts. The disease is most communicable in the early stages from the onset of the catarrhal stage up to paroxysmal cough, with a secondary attack rate of up to 90% among non-immune household contacts. Untreated patients may be contagious for up to 3 weeks after the onset of paroxysmal cough in the absence of treatment or up to 5 days after onset of treatment, although communicability diminishes rapidly after the catarrhal stage. The incubation period usually lasts 7 to 10 days and rarely more than 14 days.

Clinical description and case definition

- **Clinical description:** Initial catarrhal stage with irritating cough that gradually becomes paroxysmal. In younger infants, periods of apnoea may follow the coughing spasms. Pneumonia is a relatively common complication (reported 21.7% of cases in developed countries); otitis, haemorrhages (subconjunctival petechiae and epistaxis), convulsions, encephalopathies and death occur more rarely. The disease lasts 4 to 8 weeks. Complications are more frequent and severe in younger infants. In developed countries the case fatality ratio among infants less than 1 month has been reported to be around 1%.
- **Clinical case definition**
  A case diagnosed as pertussis by a physician, **or**
  A person with a cough lasting at least 2 weeks **with at least one** of the following symptoms:
  - Paroxysms (i.e. fits) of coughing
  - Inspiratory "whooping"
  - Post-tussive vomiting (i.e. vomiting immediately after coughing).

  Laboratory criteria
  - Isolation of *Bordetella pertussis*, or
  - Detection of genomic sequences by polymerase chain reaction (PCR)
  - Positive paired serology.

  Case classification
  - ***Clinical case:*** A case that meets the clinical case definition
  - ***Confirmed:*** A clinical case that is laboratory-confirmed.

Recommended interventions

- **Case management**
  Treatment for 7 to 10 days with erythromycin or erythromycin estolate or – in case of allergies to erythromycin – with trimethoprim sulfamethoxazole (contraindicated during pregnancy); symptomatic treatment and supportive case management.
- **Prevention**
  The administration of vaccines is the most rational approach to pertussis control; for more than forty years the use of whole-cell vaccine against pertussis (wP) has been effective in preventing pertussis.
  The more efficacious vaccines, whether wP or acellular (aP) protect more than 80% of recipients. Although the use of aP vaccines is less commonly associated with adverse reactions (usually mild to moderate), price considerations affect their use and wP vaccines are the vaccines of choice for most countries. The vaccine should be given in 3 doses at 4-week intervals starting at the age of about 6 weeks. The precise regimen may vary from country to country and may include booster doses.

- **Epidemics**
  The highly contagious nature of the disease leads to large numbers of secondary cases among non-immune contacts. Prophylactic antibiotic treatment (erythromycin) in the early incubation period may prevent disease, but difficulties of early diagnosis, costs involved and concerns related to the occurrence of drug resistance all limit prophylactic treatment to selected individual cases. Priority must be given to:
  - Protecting children less than 1 year old and pregnant females in the last 3 weeks of pregnancy because of the risk of transmission to the newborn.
  - Stopping infection among household members, particularly if there are children aged less than 1 year and pregnant women in the last 3 weeks of pregnancy.

  The strategy relies on chemoprophylaxis of contacts within a maximum delay of 14 days following the first contact with the index case. Index cases must avoid contact with day-care centres, schools and other places regrouping susceptible individuals for up to 5 days after the beginning of treatment or up to 3 weeks after onset of paroxysmal cough, or till the end of cough, whichever comes first.
  All contact cases must have their immunization status verified and brought up to date.
- **Drug resistance monitoring**
  As for other agents sensitive to antibiotic therapy.

Other aspects

- **Procurement of equipment and drugs**
  See *Vaccination*
- **Surveillance**
  - Routine monthly reporting of aggregated data of suspected and confirmed cases from peripheral level to intermediate and central level. Zero reporting required at all levels.
  - All outbreaks must be investigated immediately and laboratory-confirmed. During an outbreak, information on age groups and immunization status of cases must be collected.
  - In countries with low pertussis incidence (where DTP3 coverage is usually >80%), case-based surveillance, active surveillance, sentinel surveillance and/or occasional surveys and/or laboratory confirmation for suspected cases can be considered. Suspect cases must be immediately notified to public health.

  International: Aggregated data of clinical (suspected) and confirmed cases in routine surveillance reports of countries to WHO Regional Offices according to regional specifications.
- **Special considerations/other interventions**
  Current vaccines not recommended for persons above 7 years of age (decreased benefit/risk ratio). Acellular vaccines (aP) could make immunization of older individuals possible.
- **Indicators**
  Coverage with DTP3 (target: at least 80% in all districts).

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42.

WHO Headquarters: 20 Avenue Appia, CH-1211 Geneva 27, Switzerland - Vaccines & Other Biologicals (VAB)/Vaccine Assessment and Monitoring (VAM)
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REFERENCES:

Edelman K, Nikkari S, Ruuskanen O, et al. Detection of *Bordetella pertussis* by polymerase chain reaction and culture in the nasopharynx of erythromycin-treated infants with pertussis. *Pediatric Infectious Diseases Journal*,1996, 15 8(1):54-57.

Ivanoff B, Robertson SE. Pertussis: a worldwide problem. *Developments in Biological Standardization*, 1997, 89(1): 3-13.

La coqueluche. Protocole d'intervention – Mise à jour 1999. Québec. Ministère de la Santé et des Services sociaux, Direction générale Santé publique, 1999, Québec, Canada, ISBN 2-550-34801-X.

WHO. Pertussis vaccines. WHO position paper/Les vaccins anticoquelucheux. Note d'information de l'OMS. *Weekly Epidemiological Record/Relevé épidémiologique hebdomadaire*, 1999, 71(18):137-143.

WHO. *Immunization in practice*. Module 1 WHO/EPI/TRAM/98.01 (pages 3-4). Module 2 WHO/EPI/TRAM/98.02 (pages 6-9).

See also: *Immunization* in the present document (section 2.1).

Plague (human) A20

Notification to WHO universally required by *International Health Regulations*

General introduction

The disease is endemic in many countries and often has epidemic potential. Plague is transmitted to humans through flea bites or direct exposure to respiratory droplets or infected animal tissues. Surveillance of human and animal disease is important to predict and detect epidemics and to monitor control measures.

Causal agent and main modes of transmission

- **Causal agent:** *Yersinia pestis*
- **Main modes of transmission:** Plague is transmitted among rodents and from rodents to other animals via wild rodent fleas, cannibalism, or (possibly) contaminated soil. Indirect transmission through the bite of a flea is the most common route.

  Human infection most frequently occurs when an epizootic develops among rats in centres of human population, following contact with infected wild rodents. Commensal rat fleas, including plague-infected fleas, leave the bodies of rats killed by plague to seek another blood meal and may bite human beings. People can be infected directly from a plague-infected rodent or other animal while handling, skinning or cutting up meat. The plague agent also penetrates the human body through skin lesions or mucous membranes of the mouth, nose or eyes.

  Humans who contract the disease may subsequently become infective to other people. Bubonic plague is only occasionally transmitted between humans, either through the bites of human fleas (*Pulex irritans*) infected after biting patients in the septicaemic stage, or through direct contact between a healthy person and an infected person. When primary bubonic plague develops into secondary pneumonic plague, airborne transmission of the infective agent may take place via the respiratory route, leading to primary pneumonic plague among close contacts. Infection through direct contact with objects contaminated with sputum from pneumonic plague patients can lead to the development of bubonic plague. The case fatality ratio is 25% to 50% in untreated bubonic plague; untreated pulmonary plague is nearly always fatal.

Clinical description and case definition

- **Clinical description**
  - ***Bubonic plague:*** A local cutaneous proliferation, not usually clinically evident, follows inoculation. In some cases, a vesicle, pustule or ulcer develops at the inoculation site. The infection spreads via the lymphatics to regional lymph nodes, causing inflammation and swelling in one or more nodes (buboes). After 2 to 6 days, patients typically experience a sudden onset of illness characterized by headache, chills, fever, malaise and pain in the affected regional lymph nodes, which may not be clinically enlarged at this stage. Symptoms may progress rapidly, the regional lymphadenitis becoming excruciatingly tender and painful. Small to moderately enlarged buboes may be masked by extensive perinodal inflammation and oedema.
  - ***Septicaemic plague:*** Primary septicaemic plague is a progressive, overwhelming bloodstream infection with *Yersinia pestis* in the apparent absence of a primary lymphadenopathy. Without a bubo to prompt a suspicion of plague, the correct diagnosis may easily be overlooked. Septicaemic plague occurs in all age groups, but the elderly appear to be at greatest risk. The host response may result in a wide spectrum of pathological events including disseminated intravascular coagulopathy, multiple organ failure and adult respiratory distress. Disseminated intravascular coagulation can lead to arteriolar thrombosis, haemorrhages in the skin, serosal surfaces and organ parenchymata, and can sometimes result in tissue necrosis.
  - ***Pneumonic plague****:* Primary pneumonic plague is the most fulminating and fatal form of plague. The incubation period is usually 1 to 13 days. Onset typically manifests by a sudden onset of chills, fever, headache, body pains, weakness and chest discomfort. Cough, sputum production, increasing chest pain, difficulty in breathing, hypoxia and haemoptysis become prominent as the disease rapidly progresses. Death usually ensues if specific antibiotic therapy is not begun within 18-24 hours of disease onset. Pulmonary complications may include localized areas of necrosis and cavitation, pleurisy with effusion, and adult respiratory distress syndrome.

- **Case definition**

  Disease characterized by rapid onset of fever, chills, headache, severe malaise, prostration, **with**

  – *Bubonic form:* extreme painful swelling of lymph nodes (buboes)

  – *Pneumonic form:* cough with blood-stained sputum, chest pain, difficult breathing.

  NOTE: Both forms can progress to a *septicaemic form* with toxaemia; sepsis without evident buboes rarely occurs.

  Laboratory criteria

  – Isolation of *Yersinia pestis* in cultures from buboes, blood, CSF or sputum, **or**

  – Passive haemagglutination (PHA) test, demonstrating an at least 4-fold change in antibody titre specific for F1 antigen of *Y. pestis* (haemagglutination inhibition test in paired sera).

  Case classification

  – ***Suspected:*** A case compatible with the clinical description. May or may not be supported by laboratory finding of Gram-negative bipolar coccobaccili in clinical material (bubo aspirate, sputum, tissue, blood).

  – ***Probable:*** A suspected case **with**

    ♦ Positive direct fluorescent antibody (FA) test for *Yersinia pestis* in clinical specimen, **or**

    ♦ Passive haemagglutination test, with antibody titre of at least 1:10, specific for the F1 antigen of *Y. pestis* as determined by the haemagglutination inhibition test (HI), **or**

    ♦ Epidemiological link with a confirmed case.

  – ***Confirmed:*** A suspected or probable case that is laboratory-confirmed.

Recommended interventions

- **Case management**

  When human plague is suspected on clinical and epidemiological grounds, diagnostic specimens (sputum, blood, bubonic fluid) must be obtained immediately. The patient must be started on specific antimicrobial therapy without waiting for a definitive answer from the laboratory.

  Suspect plague patients with evidence of pneumonia must be isolated and managed under respiratory droplet precautions. Streptomycin 2 g/day (or 30 mg/kg/day up to a total of 2 g/day), given intramuscularly for 10 days or until 3 days after temperature has become normal is the most effective antibiotic for plague. Other antibiotics (gentamycin, chloramphenicol, doxycycline, oxytetracycline) may be used according to local guidelines.

  Tetracyclines are effective in the primary treatment of patients with uncomplicated plague:

  Oral loading dose of 15 mg/kg not to exceed 1g in all, followed by 25-50 mg/kg/day (up to a total of 2 g/day) for 10 days.

- **Prevention**

  Persons in close contact with pneumonic plague patients, or likely to have been exposed to fleas infected with *Yersinia pestis*, to have had direct contact with body fluids or tissues infected with *Y. pestis*, or exposed to known infectious materials, must receive antibiotic preventive therapy if the exposure was in the previous 6 days. The preferred antimicrobials for prevention are tetracycline, doxycycline, or trimethoprim-sulfamethoxazol (TMP-SMX). Administration of an antibiotic prior to exposure may be indicated when persons must be present for short periods in plague areas under circumstances in which exposure to plague sources (fleas, pneumonic cases) is difficult or impossible to prevent. Hygiene and sanitation will assist in the prevention of rodent and flea-borne diseases.

  Plague vaccines do not protect against primary pneumonic plague. Their use is indicated only for persons at high risk of contact with *Y. pestis* (field workers, laboratory technicians, etc.); vaccination is of little use during outbreaks since it requires a month or more to provide a protective immune response.

- **Epidemics**

  The first step in controlling an outbreak of plague is to interrupt transmission by controlling the flea vectors on rodents in expanding circles from the focus of infection.

  Rodent control in affected areas (rodenticides, environmental management, ensuring rodent-proof food storage) must follow ***after*** intensive flea control programmes have been carried out. When appropriate, clothing must be dusted with insecticide powder, and insect repellents must be used daily.

  Contacts: see above under *Prevention*.

- **Drug resistance monitoring**

  Multiresistant strains of *Yersinia pestis* have recently been isolated in Madagascar. Monitoring of antibiotic resistance is therefore recommended in areas endemic for plague.

Other aspects

- **Procurement of equipment and drugs**
  - Insecticides and insecticide dusting equipment
  - Rodenticides and rat control equipment
  - Streptomycin and IM injection equipment.
- **Surveillance**
  - *In all situations:* Immediate case-based reporting of suspected cases from peripheral level to intermediate and central level. Laboratory-based reporting of all confirmed cases required in all situations.
  - *During an outbreak:* Intensified active case-finding and contact-tracing in order that treatment can start for cases and contacts; environmental measures; community education. A daily report of the number of cases and contacts as well as their treatment status and vital status must be produced. A weekly report must summarize the outbreak situation, the control measures taken, and those planned to interrupt the outbreak.

  International: Mandatory reporting of all suspected and confirmed cases to WHO within 24 hours.
- **Special considerations/other interventions**

  Epizootic surveillance:
  - Periodical surveys of rodent populations and of their fleas, and monitoring of plague activity in these populations; this alerts public health authorities to increased human plague risks, thus allowing prevention and control measures to be implemented before human cases occur
  - Ports in the vicinity of endemic zones must be put under surveillance and undergo periodic deratting to prevent the growth of rodent populations
  - Serological surveillance of wild carnivores and of roaming dog and cat populations is advisable in all areas bordering on endemic areas.
- **Indicators**
  - Increased rat mortality (“ratfalls”)
  - Number of human cases.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42.

WHO Headquarters: 20 Avenue Appia, CH-1211 Geneva 27, Switzerland - Communicable Diseases Surveillance and Response (CSR)
E-mail: **dayaldragerr@who.int** and **outbreak@who.int** Tel: (41 22) 791 2132, Fax: (41 22) 791 4878/0746 attn ISR

REFERENCES: *Plague Manual: Epidemiology, Distribution, Surveillance, and Control*. Geneva: WHO, 1999: WHO/CDS/CSR/EDC/99.2

Poliomyelitis A80

General introduction

Poliomyelitis has been targeted for ***eradication***, i.e. interruption of transmission for the infectious agent (9GPW 6.1). Surveillance of acute flaccid paralysis (AFP) in the latter stages of control is critical for eradication to take place. No indigenous cases of poliomyelitis have been reported in the Western hemisphere since 1991 – the Region of the Americas is certified as poliomyelitis-free and the Western Pacific Region has officially been certified poliomyelitis-free in 2000; importation remains a threat in both Regions. The European region has not reported indigenous wild poliovirius transmission since 1998. The disease is still a serious problem in the Indian subcontinent, as well as in West and Central Africa and the Horn of Africa. In the rest of the world, it is on the verge of eradication. Until global eradication is achieved, all poliomyelitis-free areas, including industrialized countries, remain at risk as regards the importation of wild poliovirus.

The main poliomyelitis eradication strategies are:

- Achieving and maintaining high routine immunization with 4 doses of oral poliovirus vaccine (OPV)
- National immunization days (NIDs) targeting all children aged <5 years.
- Surveillance for all cases of acute flaccid paralysis (AFP) in children aged <15 years, including those considered to arise from Guillain-Barré syndrome, and virological testing of stool specimens from all AFP cases
- House-to-house mopping-up campaigns targeting the final foci of wild poliovirus transmission in one or more countries (administering OPV to 1 million children or more).

Causal agents and main modes of transmission

- **Causal agents:** Poliovirus (*Enterovirus*) types 1, 2 or 3.
- **Main modes of transmission:** Transmission is from person to person, mainly faecal-oral. Both wild virus and oral vaccine virus can be transmitted from carriers and patients during the incubation period (7 to 14 days). Occasional pharyngeal spread also occurs.

Clinical description and case definition

- **Clinical description:** All 3 types of wild poliovirus may cause paralysis, although most infections remain asymptomatic. Intramuscular injections during the incubation period may precipitate paralysis. Initial symptoms include fever, fatigue, headaches, vomiting, constipation (or less commonly diarrhoea), stiffness in the neck, and pain in the limbs. A small percentage of cases (1 or less per 100 infected susceptible persons) develop flaccid paralysis, usually affecting the lower limbs. Bulbar paralysis may also occasionally occur, leading to respiratory muscle involvement and death unless artificial respiration is resorted to.
- **Case definition:** In view of the ongoing eradication effort, intensified surveillance targets:
  - All children under 15 with acute flaccid paralysis (AFP), including those considered to have Guillain-Barré syndrome*, **or**
  - Persons at any age diagnosed as suspect poliomyelitis cases.

  * For practical reasons, Guillain-Barré syndrome will be considered as poliomyelitis until proved otherwise.

  Case classification
  - ***Suspected:*** A case that meets the clinical case definition
  - ***Confirmed:*** AFP from whom wild poliovirus is isolated (see diagram at the end of this item)
  - ***Polio-compatible:*** AFP clinically compatible with poliomyelitis, but without adequate virological investigation (see diagram at the end of this item).

Recommended interventions

- **Case management**

  Supportive treatment only:
  - Respiratory support (iron lung, positive pressure ventilator)
  - Moist heat and physical therapy to stimulate the muscles
  - Anti-spasmodic drugs.

  Isolation if hospitalized, disinfection of discharges, faeces and soiled articles, and immediate reporting of further cases.
- **Prevention**

  Immunization:
  - ***Oral poliovirus vaccine (OPV)***

OPV is a live vaccine including live attenuated strains of all three virus types, given by mouth. It is easily administered by health workers or volunteers, induces a good humoral (antibody) and mucosal (intestine) immune response and is 4 times cheaper than inactivated poliovirus vaccine (IPV). OPV is the only vaccine of choice for poliomyelitis eradication because it achieves much better mucosal immunity than IPV and can therefore disseminate in the community whilst limiting the dissemination of wild poliovirus.

WHO-recommended immunization schedule for both routine and supplementary immunization:

- Basic immunization at birth, 6, 10 and 14 weeks
- Supplemental OPV immunization for poliomyelitis eradication, using National Immunization Days (NIDs), sub-NIDs, and mop-up campaigns, during which two OPV doses are given at an interval of 1 month to all children under 5 years, preferably during the season of low transmission for enteroviruses (cooler season).

– ***Inactivated poliovirus vaccine (IPV).***

IPV, which can only be given by intramuscular injection and requires trained health workers, elicits an excellent antibody response, but only minimal intestinal mucosal response; it is much more expensive than OPV (see below: *Special considerations*).

- **Epidemics**

Where wild poliovirus transmission has not yet been interrupted, the intensity of transmission and risk of epidemics are highest during the warm summer months. Measures include:

– Nationwide supplementary immunization campaigns using OPV in all endemic countries

– 'Mopping-up' campaigns with OPV, targeting the remaining virus reservoirs and outbreaks.

For the control of outbreaks, OPV is used even in countries where IPV is used for the routine programme (see *Special considerations*).

- **Drug resistance monitoring**

Not applicable.

Other aspects

- **Procurement of equipment and drugs**

See *Immunization*
IPV: syringe, trained health care workers.
OPV: vaccine only, can use untrained workers.

- **Surveillance**

Active surveillance is essential during the current eradication phase. It includes weekly visits by public health staff in order to find cases and sensitize clinicians in selected hospitals and health facilities likely to see cases (“sentinel facilities”). Weekly line-listed data on cases of AFP are expected from all countries.

Aggregated data of AFP cases must be included in routine monthly surveillance reports.
Zero reporting is required at all levels for polio and AFP.

As regards AFP cases (suspect poliomyelitis cases)

– All cases must be reported immediately

– All cases must be investigated within 48 hours (case-based data), and

– Stool specimens must be collected within 14 days of paralysis onset.

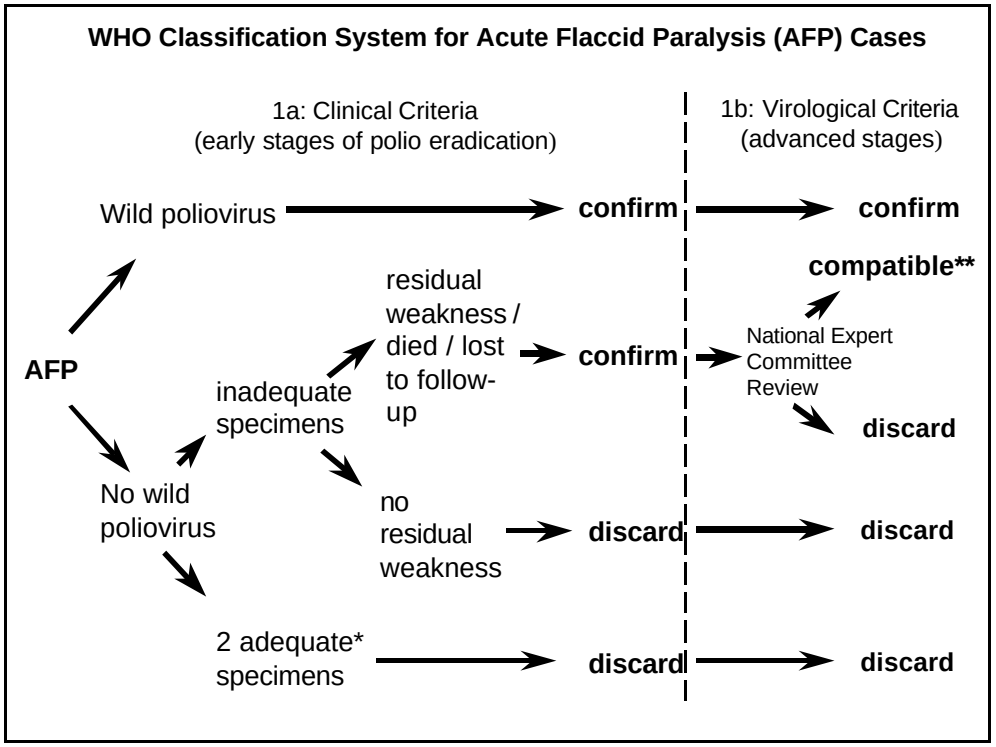
More than 99% of all infected susceptible persons remain asymptomatic. Isolation of wild poliovirus indicates the presence of wild poliovirus in a large area, which must be specially targeted during the next scheduled national immunization days (NIDs) or during mopping-up immunization campaigns.

- **Special considerations/other interventions**

– ***OPV or IPV?***

- When a person immunized with *IPV* is infected with wild poliovirus, the virus can still multiply inside the intestines and be shed in stools, with a risk of continued circulation of wild virus.
- When a person immunized with *OPV* is infected with wild poliovirus, the virus cannot multiply. OPV is thus the vaccine of choice wherever a poliomyelitis outbreak must be contained. However, 1 in every 3 million doses of OPV can cause paralysis either in the vaccinated child, or in a close contact. For this reason countries where the incidence of poliomyelitis is extremely low – such as Canada, France, the Netherlands, all Nordic countries and the USA – resort to IPV. In some countries, a single dose of trivalent OPV is given to all children under 5 in the neighbourhood of a confirmed case.

- **Indicators**
  - Rate of AFP not due to poliomyelitis per 100 000 persons less than 15 (non-poliomyelitis AFP rate – the rate should be at least 1/100 000 at national and provincial levels, indicating that the surveillance system is sufficiently sensitive to identify wild poliovirus wherever this may still circulate
  - Proportion of AFP cases from whom 2 adequate specimens were collected within 14 days of onset of paralysis – 2 adequate specimens must have been collected in at least 80% of all AFP cases
  - Number of confirmed poliomyelitis cases
  - Routine immunization coverage with 3 doses of OPV (OPV3 coverage).



***** "Adequate specimens" means 2 specimens collected 24-48 hours apart and within 14 days of onset of paralysis. The specimen arriving at the laboratory must be of adequate volume (approximately 8-10 grams), have appropriate documentation (laboratory request form) and be in "good condition" (evidence that the reverse cold chain was maintained (presence of ice or temperature indicator), no leakage, no desiccation).
****** "Compatible cases" indicate surveillance failures and must be monitored for clustering in space and time.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42
WHO Headquarters: 20 Avenue Appia, CH-1211 Geneva 27, Switzerland - Vaccines & Other Biologicals (VAB)/Expanded Programme on Immunization (EPI)
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REFERENCES:

WHO. *Field guide for supplementary activities aimed at achieving polio eradication* – 1996 revision. Geneva: WHO, 1996: WHO/EPI/GEN/95.01Rev1.
Electronic: www.polioeradication.ch

See also: *Immunization* in the present document (section 2.1).

Rabies A82

General introduction

Rabies, present on all continents and endemic in most African and Asian countries, is a fatal zoonotic viral disease, transmitted to humans through contact (mainly bites and scratches) with infected animals, both domestic and wild. An estimate of at least 40 000 human deaths occur each year worldwide, most of them in the developing world (mainly in Asia), and an estimated 10 million people receive post-exposure treatment after being exposed to animals suspected of rabies.

There is no specific treatment for rabies, which is a fatal disease. WHO promotes:

- Human rabies prevention through:
  - Well-targeted post exposure treatment using modern vaccine types and , when appropriate, antirabies immunoglobulin
  - Increased availability of modern rabies vaccine.
- Dog rabies elimination through mass vaccination of dogs and dog population management.

Causal agent and main modes of transmission

- **Causal agent:** The rabies virus, a rhabdovirus of the genus *Lyssavirus*.
- **Main modes of transmission:** Hosts are usually *Canidae*, including dogs (responsible for more than 99% of all human deaths from rabies), foxes, coyotes, wolves, and jackals; also cats, skunks, raccoons, mongooses, bats, and other biting animals. A bite or a scratch introduces virus-laden saliva from a rabid animal. The incubation period usually ranges from 2 to 10 days but may be longer (up to 7 years).

Clinical description and case definition

- **Clinical description**
  - Paresis or paralysis, delirium, convulsions
  - Without medical attention, death in about 6 days, usually due to respiratory paralysis.
- **Clinical case definition**

  An acute neurological syndrome (encephalitis) dominated by forms of hyperactivity (furious rabies) or paralytic syndromes (dumb rabies) progressing towards coma and death, usually by respiratory failure, within 7 to 10 days after the first symptom if no intensive care is instituted.

  Laboratory criteria

  One or more of the following:
  - Detection of rabies viral antigens by direct fluorescent antibody (FA) in clinical specimens, preferably brain tissue (collected post mortem)
  - Detection by FA on skin or corneal smear (collected ante mortem)
  - FA positive after inoculation of brain tissue, saliva or CSF in cell culture, or after intracerebral inoculation in mice or in suckling mice
  - Detectable rabies-neutralizing antibody titre in the CSF of an unvaccinated person
  - Identification of viral antigens by PCR on fixed tissue collected post mortem or in a clinical specimen (brain tissue or skin, cornea or saliva)
  - Isolation of rabies virus from clinical specimens and confirmation of rabies viral antigens.

  Case classification

  HUMAN RABIES**:**
  - ***Suspected:*** A case that is compatible with the clinical case definition.
  - ***Probable:*** A suspected case plus history of contact with a suspected rabid animal.
  - ***Confirmed:*** A suspected case that is laboratory-confirmed.

  HUMAN EXPOSURE TO RABIES:
  - ***Possibly exposed:*** A person who had close contact (usually a bite or scratch) with a rabies-susceptible animal in (or originating from) a rabies-infected area.
  - ***Exposed:*** A person who had a close contact (usually a bite or scratch) with a laboratory-confirmed rabid animal.

Recommended interventions

- **Management of cases and potential cases (bitten patients)**
  Immediate and thorough cleaning of the wound with soap, followed by ethanol or aqueous iodine
  Post exposure prophylaxis: administration of rabies immunoglobulin in case of severe exposure (WHO category 3)
  Vaccine treatment as soon as possible, followed by additional vaccine injection according to the regimen chosen – vaccines with a potency at least 2.5 IU per dose according to one of the following schedules.
  - *Intramuscular schedules:* volume of 1 dose after reconstitution – 0.5 ml for purified vero cell vaccine (PVRV), 1 ml for purified primary chick embryo cell vaccine (PCECV) and currently also for purified duck embryo vaccine (PDEV):
    - 1 dose on days 0, 3, 7, 14 and 28. All intramuscular injections to be given into deltoid region or into anterolateral area of the thigh muscle in small children. Never inject the vaccine in the gluteal region.
    - 2-1-1 regimen: 2 doses on day 0 (one in the deltoid region of the right arm and the other in the deltoid region of the left arm). 1 dose in the deltoid region on day 7 and 1 on day 21. This regimen is particularly recommended when no immunoglobulin is required i.e. when contact consists in nibbling of uncovered skin, minor scratches or abrasions without bleeding, or licks on broken skin.
  - *Intradermal schedules:* the following intradermal regimens have been shown to be immunogenic:
    - *2-site intradermal method* (2-2-2-0-1-1) for use with PVRV, PCECV and HCDV (see commercial denominations on next page) at 0.1 ml per intradermal injection site – days 0, 3 and 7: 1 intradermal dose at each of 2 sites, intradermally on upper arm, over each deltoid. Days 28 and 90: 1 intradermal dose at 1 site, on upper arm.
    - *8-site intradermal method* (8-0-4-0-1-1) for use with human diploid cell vaccine (HDCV) and PCECV, where the intramuscular dose is 1 ml after reconstitution. REGIMEN: Day 0: 0.1 ml reconstituted vaccine at each of 8 sites using the contents of a whole vial. Inject intradermally over deltoid, lateral thigh, suprascapular region and lower quadrant of the abdomen. Day 7: 0.1 ml of vaccine at each of 4 sites over deltoids and thighs. Days 28 and 90: 0.1 ml of vaccine at 1 site, over deltoid. This regimen is particularly recommended for severe exposure when no immunoglobulin is available.
- **Prevention**
  - Immunize all dogs and cats owned by an individual or by the community and destroy ownerless dogs
  - Immunize any person with proven exposure to rabies patients
  - Humans at high risk (e.g. laboratory personnel, professions at high risk) must receive pre-exposure immunization: 3 injections of an intramuscular dose on days 0, 7, 28.

  Pre-exposure vaccine regimen: 1 dose of a cell culture or purified duck embryo vaccine on days 0, 7 28. A few days variation is acceptable. The dose is 1 standard intramuscular dose (1 ml or 0.5 ml according to vaccine type). The vaccine may be given intradermally (0.1 ml on days 0, 7, 28) except if antimalarial chemoprophylaxis (e.g. chloroquine) is being used concurrently, when intramuscular injections are preferable, since the antibody response may be impaired if the intradermal method is used.
- ***Epidemics*** (animals only; the disease is sporadic in humans):
  Undertake a dog immunization campaign: 75% of the dog population must be vaccinated within 1 month.
  Immunize domestic animals and (through bait) wild animals as appropriate.
  Enact and enforce legislative measures regarding stray dogs.
  Selective and humane capture and elimination of dogs may be conducted in outbreak situations.
- **Drug resistance monitoring**
  Not applicable.

Other aspects

- **Procurement of equipment and drugs**
  - A 1-ml syringe and a needle for each intramuscular injection (intradermal syringes for intradermal vaccination)
  - Vaccine amounts: between 2 and 5 vials, depending on the method used.

  Only the following vaccines meet WHO safety, potency and efficacy requirements when used for post-exposure intradermal treatment of rabies:
  - Human diploid cell vaccine (HDCV): Rabivac ™
  - Purified vero cell vaccine (PVRV): Verorab, Imovax, Rabies vero, TRC Verorab ™
  - Purified chicken embryo cell vaccine (PCECV): Rabipur ™
- **Surveillance**
  - SURVEILLANCE OF CASES OF HUMAN RABIES: Immediate reporting of suspected and confirmed cases and reporting of post-exposure treatment (by the diagnosing physician and the laboratory) from peripheral to intermediate and central levels; rapid exchange of information with the services in charge of animal rabies surveillance/ control. Epidemiological investigation of outbreaks and all rabies foci, identifying sources of infection and humans or animals exposed or possibly exposed.
  - SURVEILLANCE OF HUMAN EXPOSURE TO RABIES: At peripheral level, especially in rabies-infected areas, reports of patients with a history of animal contact (usually a bite/scratch) must be investigated at once. Offending animals, especially wild, must be submitted for laboratory tests whenever possible. Domestic animals concerned must be put under observation for 10 days.

    In an endemic zone and if the species concerned is susceptible to rabies, the case must be treated as an emergency and should not wait for the results of laboratory tests or those of animal observation where the nature of the contact has involved licks on broken skin, nibbling on abrasions, bites or scratches, or contamination of mucous membranes with saliva (WHO category 2 or 3 exposure criteria). The same applies when the suspected animal is unknown. Case-based and aggregated data on human cases and post-exposure treatment must be sent regularly from peripheral to intermediate and central levels.
  - SURVEILLANCE IN ANIMAL POPULATIONS: Where the disease is endemic or could be reintroduced, undertake laboratory-based surveillance of animal rabies and similar conditions among wild and domestic species that are most likely to be reservoirs of disease. Encourage immediate submission of brain specimens from any suspected animal for laboratory diagnosis when human exposure occurs. Domestic animals at the origin of human exposure and that cannot be killed must be kept under observation for 10 days. Rapid exchange of information between services in charge of human and animal rabies surveillance and control is essential.
- **Special considerations/other interventions**

  It is theoretically possible for person-to-person rabies transmission to occur since secretions may contain the virus, although this has not been described. As a precaution, medical and nursing staff must wear mask, gloves, and goggles. In hospitals and other institutions caring for a number of rabid patients, pre-exposure vaccination of medical and nursing personnel must be considered. Organs of patients with rabies or any neurological disease should not be used for transplantation.
- **Indicators**
  - Number of human cases
  - Number of episodes of animal bites requiring antirabies intervention.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42

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REFERENCES:

WHO. WHO Expert Committee on Rabies. Eighth report. Technical Report Series N 852. Geneva: WHO, 1992. ISBN 92 4120 8244

WHO. *Laboratory Techniques in Rabies.* 4th edition. Meslin F-X, Kaplan MM, Koprowski H., eds. Geneva: WHO, 1996. ISBN 92 41544791

Rubella B06

Congenital rubella syndrome P35.0

General introduction

Rubella is a common cause of childhood rash and fever; its public health importance relates to the teratogenic effects of primary rubella infection in pregnant women. Congenital rubella syndrome (CRS) is an under-recognized public health problem in many developing countries. The estimated mean incidence of the syndrome per 100 000 live births is lowest in the Eastern Mediterranean region (77.4, range 0 to 212) and highest in the Americas (175, range 0 to 598). WHO estimates the annual number of cases in developing countries at over 100 000. By 1999, 105 of the 214 countries and territories reporting to WHO had introduced rubella vaccine in their national immunization programmes.

Causal agent and main modes of transmission

- **Causal agent:** Rubella virus, of the genus *Rubivirus* of the family *Togaviridae*
- **Main modes of transmission:** The rubella virus is spread by droplets in the air from the nose and pharynx of infected people, or by direct contact with nasal or pharyngeal secretions. Infants with CRS also shed large quantities of the virus in urine. Infants born to immune mothers are usually protected for 6 to 9 months. Active immunity is acquired by natural infection or by vaccination.
  In unvaccinated populations, rubella is primarily a disease of childhood although it occurs among adolescents and adults more often than does measles or chicken pox. Where children are vaccinated against rubella, adolescent and adult infections are more important.

Case definition and case classification

- **Recommended case definition**

  Rubella

  – ***Suspected rubella case***

  Any person in whom a health worker suspects rubella infection in the presence of :
  - Fever, **and**
  - Maculopapular rash (non-vesicular), **and**
  - One of the following: cervical, suboccipital, or post-auricular adenopathy; or arthralgia/arthritis.

  At the measles/rubella elimination phase, suspected measles and suspected rubella are combined in a single febrile rash illness surveillance category for suspected cases.

  – ***Laboratory-confirmed rubella case***

  Because of difficulties in the clinical diagnosis of rubella, laboratory confirmation is required. A laboratory-confirmed rubella case is a suspected case with a positive blood test for rubella-specific IgM.

  – ***Epidemiologically confirmed rubella case***

  Epidemiologically-confirmed rubella case is a patient with a febrile rash illness who has not had a blood test and has an epidemiological linkage to a laboratory-confirmed case of rubella.

  Congenital Rubella Syndrome (CRS)

  – ***Suspected CRS case***
  - Any child under 1 year in whom a health worker suspects CRS – when the child presents with heart disease and/or suspicion of deafness, and/or one or more of the following eye signs: white pupil (cataract); diminished vision; pendular movement of the eyes (nystagmus); squint; small eye ball (microphthalmos); enlarged eye ball (congenital glaucoma)
  - Any child where there is a maternal history of suspected or confirmed rubella during pregnancy, even if the child shows no signs of CRS.

  Health workers must refer all suspected CRS cases to a qualified physician.

  – ***Clinically confirmed CRS case***

  A case in which a qualified physician detects at least 2 of the following:
  - Cataract(s)/ congenital glaucoma/ congenital heart disease/ loss of hearing/ pigmentary retinopathy, **or**

  A case in which a qualified physician detects at least one of the following:
  - Purpura/ splenomegaly/ microcephaly/ mental retardation/ meningoencephalitis/ radiolucent bone disease/ jaundice with onset less than 24 hours after birth.

  – ***Laboratory-confirmed CRS case:*** An infant with a positive blood test for rubella IgM who has clinically-confirmed CRS.

  – ***Congenital rubella infection (CRI):*** An infant with a positive blood test for rubella IgM who does not have clinically-confirmed CRS is classified as having congenital rubella infection (CRI).

Recommended interventions

- **Case management**
  Rubella
  - ***Uncomplicated rubella***

    No specific therapy is necessary or indicated in uncomplicated rubella.
  - ***Complicated rubella***

    Arthritis can be severe in adults. When weight-bearing joints are affected, rest is encouraged. Symptoms readily respond to aspirin therapy. Corticosteroids are not indicated.
    In rubella encephalitis, care is supportive, with adequate maintenance of fluids and electrolytes. Thrombocytopaenia is usually self-limited. In patients who do not recover rapidly and in those with severe bleeding, treatment with intravenous immunoglobulin must be considered.
  - ***Congenital rubella syndrome (CRS)***

    Most babies with CRS are contagious at time of birth and must therefore be placed in isolation.
    Clinical manifestations of CRS are varied, and symptoms are manifested during the first few months of life. In asymptomatic infants no particular management problems occur. Long-term problems (deafness, cardiac or neurological problems, immunological defects, multiple handicaps) require specialized treatment.
- **Prevention**
  The following rubella vaccines are available:
  - Monovalent rubella vaccine
  - Measles and rubella vaccine (MR)
  - Measles, mumps and rubella vaccine (MMR).

  Prior to the introduction of rubella vaccination in the national programme, it is necessary to assess:
  - The level of susceptibility to rubella in women of child-bearing age (antenatal serosurveys)
  - The importance of CRS
  - The adequacy of current immunization services (proxy: measles vaccine coverage) and the capacity of the health system to ensure high coverage and ensure immunization safety without detracting from other public health interventions
  - Government commitment to maintain high rubella vaccine coverage.

  Planners may use one of the following strategies:
  1. Prevention of CRS: women of child-bearing age and adolescent girls are the primary target group.
  2. *Elimination of rubella and CRS*: infants are the primary target group.
- **Outbreaks**
  Rubella outbreaks leading to CRS have been documented in Panama in the mid-80s and in Greece, Oman and Sri Lanka in the 90s. Once rubella has been identified as the cause of an outbreak of a febrile rash illness, particular attention must be paid to the detection of rubella in women of childbearing age. Rubella outbreaks may continue for two or more years and a small outbreak often heralds a larger one.

Other aspects

- **Surveillance**
  - **Rubella**

    Countries where rubella vaccine has been incorporated in the national immunization programme: surveillance must focus on CRS.
    Countries where rubella vaccine has been incorporated in the national immunization programme but a rubella elimination target has not been set: the surveillance system must monitor rubella vaccine coverage in all age groups in addition to CRS; consider establishing antenatal serosurveillance at selected sentinel sites to monitor rubella susceptibility in pregnant women.
    Countries with a rubella elimination target: case-based surveillance for all febrile rash illnesses, with laboratory assessment of each case for measles and, if negative, for rubella.
  - **Congenital rubella syndrome (CRS)**

    Active surveillance for CRS cases with special emphasis on follow-up of women exposed in the first 16 weeks of pregnancy can be conducted during a rubella outbreak and for 9 months after the last case is reported.

    Comprehensive system to detect suspected CRS cases in infants who present a range of different health services. Suspected cases must be investigated, with full clinical and laboratory investigation. CRS incidence must be reported as the annual number of CRS cases per 1000 live births.

- **Immunization safety**
  Accelerated rubella/CRS control and elimination activities require strict attention to injection safety.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42.
WHO Headquarters: 20 Avenue Appia, CH-1211 Geneva 27, Switzerland - Vaccines and Biologicals/Expanded Programme on Immunization (VAB/EPI)
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REFERENCES:

Cutts FT, Vynnycky E. Modelling the incidence of congenital rubella syndrome in developing countries. *International Journal of Epidemiology*, 1999;28(6): 1176-1184

See also: *Immunization* in the present document (section 2.1).

Schistosomiasis B65

General introduction

Schistosomiasis has the second highest prevalence for tropical diseases (following malaria) and is a leading cause of severe morbidity in large parts of Africa, Asia and the Americas. 600 million persons are at risk worldwide, of whom 200 million are infected and 20 million are severely ill. About 85% of cases and almost all those severely affected are to be found in Africa. Urinary schistosomiasis is endemic in 53 countries in the Middle East and most of Africa. Intestinal schistosomiasis currently occurs in at least 55 countries in Africa and Asia.

Because schistosomiasis is a chronic insidious disease, it is poorly recognized in the early stages. It is linked to water and agricultural development schemes and becomes a threat to development as disease occurs in adulthood. The primary goal for WHO is to control the disease (morbidity control). Once this has been achieved, the reduction and (in some countries) the elimination of the risk of schistosomiasis through strong surveillance and control programmes can be contemplated.

Causal agents and main modes of transmission

- **Causal agents:** The agents of schistosomiasis are fluke worms:
  - *Schistosoma haematobium*, agent of urinary schistosomiasis worldwide
  - *Schistosoma mansoni*, agent of intestinal schistosomiasis worldwide
  - *Schistosoma intercalatum*, agent of intestinal schistosomiasis encountered in West Africa
  - *Schistosoma japonicum*, agent of intestinal schistosomiasis endemic in China, Indonesia, Philippines
  - *Schistosoma mekongi*, agent of intestinal schistosomiasis encountered in Cambodia and Laos.
- **Main modes of transmission:** The eggs of schistosomes leave the human body in urine or faeces according to species, hatch in water and liberate larvae (miracidia) that penetrate into freshwater snail hosts (genus *Biomphalaria* for *S. mansoni*, *Bulinus* for *S. haematobium* and *S. intercalatum*, *Oncomelania* for *S. japonicum,* and *Neotricula* for *S. mekongi*). After several weeks, cercariae emerge from the snails and penetrate the human skin (during wading, swimming, washing). Within the body, cercariae develop to maturity and subsequently migrate to the lungs, the liver, and the veins of the abdominal cavity or the bladder plexus. Eggs escape through the bowel or urinary bladder. Human discharge of eggs may last in excess of 10 years; infected snails release cercariae throughout their lifetime (3 weeks to 3 months).

Clinical description and case definition

- **Clinical description**
  In an area endemic for *Schistosoma haematobium,* the pathognomonic sign of urinary schistosomiasis is haematuria. Intestinal schistosomiasis has a non-specific clinical picture of abdominal pain, diarrhoea, blood in stool, with possible hepato(spleno)megaly.
- **Case definition and classification**
  - **URINARY SCHISTOSOMIASIS: endemic areas (moderate or high prevalence)**
    - ***Suspected:*** Not applicable
    - ***Probable:*** Not applicable
    - ***Confirmed:*** A person with visible haematuria, **or** with positive reagent strip for haematuria, **or** with eggs of *S. haematobium* in urine (microscope).
  - **URINARY SCHISTOSOMIASIS: non-endemic areas and areas of low prevalence**
    - ***Suspected:*** A person with visible haematuria, **or** with positive reagent strip for haematuria, and possibly infective water-contact
    - ***Probable:*** Not applicable
    - ***Confirmed:*** A person with eggs of *S. haematobium* in urine (microscope).
  - **INTESTINAL SCHISTOSOMIASIS: endemic areas (moderate or high prevalence)**
    - ***Suspected:*** A person with non-specific abdominal symptoms, blood in stool, hepato(spleno)megaly
    - ***Probable:*** Not applicable
    - ***Confirmed:*** A person with eggs of *S. mansoni*, *S. japonicum, S. mekongi* or *S. intercalatum* in stools (microscope).

NOTE: The probability that non-specific symptoms are due to schistosomiasis increases with the endemic level. It is ethically admissible to treat suspected cases presumptively with praziquantel (therapeutic trial); this is more cost-effective than microscopically confirming cases in endemic areas.

- **INTESTINAL SCHISTOSOMIASIS: non-endemic areas and areas of low prevalence**
  - ***Suspected:*** A person with non-specific abdominal symptoms, blood in stool, hepato(spleno)megaly and possibly infective water-contact
  - ***Probable:*** Not applicable
  - ***Confirmed:*** A person with eggs of *S. mansoni*, *S. japonicum, S. mekongi* or (possibly) *S. intercalatum* in stools (microscope); a person with a positive reaction to immunoblot test.

Recommended interventions

- **Case management**
  - Praziquantel is the drug of choice against all schistosome parasites. A single oral dose of 40 mg/kg is generally sufficient to give cure rates of between 80% and 90% and dramatic reductions in the average number of eggs excreted.
  - Oxamniquine has been the drug of choice for the Brazilian national control programme over the last 20 years, but has been replaced by praziquantel, mainly because of the lower cost of the latter drug.
- **Prevention**
  - Creation of alternative, safe water sources to reduce infective water contact
  - Proper disposal of faeces and urine to prevent viable eggs from reaching bodies of water containing snail hosts
  - Health education to promote early care-seeking behaviour, use of safe water (if available) and proper disposal of excreta
  - Reduction of snail habitat and snail contact (in irrigation and agriculture practices) – environmental management
  - Treatment of snail-breeding sites with molluscicides (if costs permit).
- **Epidemics**
  - Examine for schistosomiasis and treat all infected patients
  - Improve water supply and minimize contact
  - Molluscicide in areas with high snail densities.
- **Drug resistance monitoring**

  Resistance to oxamniquine has been documented in the field since 1973. Low cure rates with praziquantel (despite normal intensity reduction rates), as reported from Senegal in the early 1990s, are likely when the number of parasites is particularly high. In Egypt, where praziquantel has been in massive use for years, 2% of patients still excrete eggs after 3 praziquantel treatments. In mice, some isolates require 2-6 times the normal dose to achieve a 50% reduction in worm load.

Other aspects

- **Procurement of equipment and drugs**

  Praziquantel treatment for 1 person requires on average 3 tablets of 600 mg in 1 dose. The cost of 1 tablet of 600 mg is now less than US$ 0.10), bringing the total drug cost of 1 treatment to about 35 US cents.
- **Surveillance**

  Data from general health statistics often underestimate the prevalence but may nevertheless indicate a relatively high prevalence in a particular area. Surveillance of schistosomiasis has to take into account the distribution of the disease in geographical foci – adjacent areas may have very different patterns and rates. Surveillance must be incorporated in the primary health care system.
  - **For low-prevalence zones, and where eradication is targeted:**

    Routine monthly reporting of aggregated suspected or confirmed cases from peripheral level to intermediate and central level.
  - **For endemic zones:**

    Particularly in zones endemic for intestinal schistosomiasis, where surveillance through the primary health care system has less epidemiological value, ad hoc surveys to evaluate the prevalence and intensity of infection in the community may be required. Children of school age have been identified as good indicators of the endemic level in the general population and as an appropriate group for investigation.
    Yearly reporting of aggregated data from peripheral level to intermediate and central levels.

  International: Yearly reporting from the central level to WHO.

- **Special considerations/other interventions**

  In 1984 the Expert Committee on the Control of Schistosomiasis endorsed a strategy for morbidity control, of which the cornerstone was regular chemotherapy. The availability of praziquantel through large-scale community-based distribution has proven successful in Asia and Latin America and has boosted schistosomiasis control. In sub-Saharan Africa, however, this type of (mainly donor-funded) programme has been shown to be unsustainable.

  WHO has recently defined a strategy to implement morbidity control, based on the delivery of regular chemotherapy to high-risk groups (early symptomatic patients, school-age children and special occupation groups) through the health and educational systems already in place. The core of this package is the coverage of school-age children; in terms of morbidity control, benefits will extend with time to the whole community. In order to further increase the cost-effectiveness of control interventions, integration with the control of other parasitic diseases has to be sought for. The most "natural" association in this respect is with the control of soil-transmitted helminths (similar morbidity, wide geographical overlap, similar control objectives and high-risk groups, same methods and channels to implement control). This strategy has been endorsed in the Bali Declaration of February 2001 (see *Soil-transmitted helminths*).

  NOTE: Because of decreased demand, the production of oxamniquine may come to an end. This would be a dangerous situation, because it would leave praziquantel as the only available antischistosomal drug, with serious consequences in the event that the parasite develops resistance to praziquantel.

- **Indicators**
  - Numbers/rates of reported suspected/probable/confirmed cases
  - Prevalence and intensity of infection in school-age children or communities.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42

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WHO Headquarters: 20 Avenue Appia, CH-1211 Geneva 27, Switzerland - Strategy Development & Monitoring for Parasitic Diseases & Vector Control (PVC)
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REFERENCES:

WHO. *Report of the WHO Informal Consultation on Schistosomiasis Control.* Geneva, World Health Organization, 1998. Document WHO/CDS/CPC/SIP/99.2

WHO. Montresor A, Crompton DWT, Hall A. et al. *Guidelines for the evaluation of soil-transmitted helminthiasis and schistosomiasis at community level.* Geneva: WHO, 1998. WHO/CTD/SIP/98.1

WHO. Schistosomiasis and soil-transmitted helminths/Schistosomiase et helminthiases d'origine tellurique. *Weekly Epidemiological record/Relevé épidémiologique hebdomadaire*, 2001, **76**(10): 74-76 http://www.who.int/wer/pdf/2001/wer7610.pdf

See also: *Mass chemo/prophylaxis*/chemotherapy in the present document (section 2.2).

Shigellosis A03

General introduction

The estimate of the number of deaths due to shigellosis is of the order of 1 million per year worldwide, mostly in children less than 10 years of age. Outbreaks commonly occur in places of overcrowding and where personal hygiene is poor. High rates of morbidity and mortality occur among displaced populations in developing countries. Reporting of cases is traditionally very poor.

Causal agents and main modes of transmission

- **Causal agents:** *Shigella dysenteriae* (12 serotypes), *S. flexneri* (13 serotypes), *S. boydii* (18 serotypes) and *S. sonnei* (1 serotype).
  Shigella dysenteriae type 1 (Sd1) differs from other *Shigella* serogroups in 3 important ways:
  - Sd1 causes large and prolonged epidemics
  - Antimicrobial resistance occurs more frequently
  - Infection with Sd1 is more severe, of longer duration and more often fatal.
- **Main modes of transmission:** *Shigella* most often contaminate via the oral route, after which they invade the colonic mucosa where they cause cell death and kill adjacent epithelial cells. As few as 10-100 ingested organisms can cause infection.

Clinical description and case definition

- **Clinical description:** Persons infected with *Shigella* may experience bloody stools with abdominal cramps, and rectal pain.
- **Case definition:** diarrhoea with visible blood in the stools.

  Laboratory criteria: Isolation of *Shigella* from the stools

  Case classification
  - ***Suspected:*** A case corresponding to the clinical definition
  - ***Probable:*** Not applicable
  - ***Confirmed:*** A case corresponding to the clinical definition with laboratory confirmation.

Recommended interventions

- **Case management**
  All patients to receive supporting treatment (ORS and frequent small meals).
  The sensitivity of local strains must guide the choice of antibiotics.The following table provides an indication of treatments

Agent	Resistance		Dose (for 5 days)	
	S. dysenteriae type 1	Other *Shigella*	Adults	Children
Ampicillin	Frequent	Variable	1 gramme 4 times a day	25 mg/kg 4 times a day
TMP-SMX	Frequent	Variable	TMP 160 mg SMX 800 mg 2 times a day	TMP 5 mg/kg + SMX 25mg/kh 2 times a day
Nalidixic acid	Increasing	Uncommon	1 gramme 4 times a day	15 mg/kg 4 times a day
Pivmecillinam	Uncommon	Rare	400 mg 4 times a day	20 mg/kg 4 times a day
Ciprofloxacin	Rare	Rare	500 mg 2 times a day	15 mg/kg 2 times a day
Norfloxacin	Rare	Rare	400 mg 2 times a day	10 mg/kg 2 times a day
Enoxacin	Rare	Rare	200 mg 2 times a day	5 mg/kg 2 times a day

a Dose varies according to the weight of the child, but must never be greater than the "adult" dose

b New quinolones have not yet been approved for use in children below 12 years of age. There is growing evidence, however, that they will prove both safe and effective. They are already used by some workers to treat children with serious illness caused by strains of Sd1 resistant to all other available agents

- **Prevention**
  Prevention comprises basic sanitary and hygiene measures: hand-washing facilities, purified water supplies, improved water delivery and sewage control, latrines, boiling water and supervision of food-handlers.
  Because of the emergence of multidrug resistant *Shigella* strains, a safe and effective vaccine is highly desirable. This is under development but has not yet been effectively developed for general use.

- **Epidemics**
  Large and prolonged epidemics occur only with Sd1. They require coordination at the national level, planning within the community, and communication lines to and from the laboratory and health authorities at regional and central levels. The most effective action is provision of safe water (e.g. through boiling or chlorination) followed by improvements in sanitation as well as proper case management.
  Laboratory confirmation is required at the beginning of an epidemic but it is not necessary for all cases or contacts. Since multidrug resistance is widespread, regular antibiotic sensitivity monitoring is paramount in order to guide antibiotic treatment.
- **Drug resistance monitoring**
  Multidrug-resistant strains occur, particularly for *Shigella dysenteriae* type 1. The choice of antibiotic must be made according to the sensitivity pattern of the local strain (See *References*).

Other aspects

- **Procurement of equipment and drugs**
  For a population of 10 000 where 0.2% of the population are expected to fall clinically ill in the first few days, the following stocks are required:
  - *Rehydration supplies:* 20 ORS packets, 4 bags Ringer's lactate + sets (1 litre); 1 scalp vein set.
  - *Other supplies:* 1 large water dispenser with tap; 1 litre bottle, 1 half-litre bottle, 2 tumblers, 1 teaspoon, 1 kg cotton wool, 1 reel of adhesive tape.
  - *Antibiotics* (to be adapted according to local sensitivity patterns): 400 tablets nalixidic acid 1 g; 60 tablets TMP20-SMX 100 mg.
  - *Material for stool samples:* containers, slides, culture media.
- **Surveillance**
  - *Routine surveillance* (together with surveillance of diarrhoeal diseases).
  - *Special surveillance:* risk areas (poor sanitation and water; poor hygiene/hand-washing; unsafe cooking/ conservation of food) or high-risk individuals (late diagnosis/treatment, malnutrition, concurrent diseases).
  - *Peripheral level*:
    - Immediate case-based reporting of suspected cases
    - Immediate investigation of all suspected cases and clusters
    - Routine weekly/monthly reports on cases (aggregated data).
- **Special considerations/other interventions**
  Not applicable.
- **Indicators**
  - Number of outbreaks.
  - Mothers with correct knowledge of home therapy for diarrhoea
  - Management of diarrhoea episodes
  - Incidence of diarrhoea
  - Deaths due to diarrhoea.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42.

WHO Headquarters: 20 Avenue Appia, CH-1211 Geneva 27, Switzerland -Communicable Diseases Surveillance and Response (CSR/EDC)
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REFERENCES:

WHO. Guidelines for the control of epidemics due to Shigella dysenteriae type 1. Geneva WHO, 1995. WHO/CDR/95.4

WHO. *The management and prevention of diarrhoea; practical guidelines,* 3rd ed. Geneva, WHO, 1993 (ISBN 92-4-154454-6).

Ivanoff BM, Neira MP. Vaccination contre les maladies diarrhéiques et la fièvre typhoïde: état actuel et perspectives. *Annales de médecine interne*, 1998, 149(6): 340-350.

Tetanus neonatorum A33

General introduction

In developing countries, the disease still causes an estimated 500 000 infant deaths and 50 000 maternal deaths each year. The case fatality rate can reach 80%.

The disease is targeted for **elimination** – less than 1 case per 1000 live births in every district of every country (9GPW). The 3 primary strategies towards this goal are:

1. High tetanus toxoid coverage – at least 90% for all women of childbearing age
2. Provision of clean delivery services
3. Identification of high-risk areas and immunization of women of childbearing age in these areas.

Causal agent and main modes of transmission

- **Causal agent:** *Clostridium tetani*, an anaerobic microorganism that develops best when oxygen concentration is low.
- **Main modes of transmission:** The disease occurs through infection of the umbilical cord or umbilical stump (infants) or of the genital tract (mothers) with tetanus spores during delivery. The main sources of infection are:
  - Spore-carrying instruments (use of unsterile tools)
  - Dirty hands
  - Spore-carrying material covering the umbilicus (e.g. dung poultices).

  The spores convert to tetanus bacilli in the presence of necrotic tissue with reduced oxygen potential. The bacteria itself is not an invasive organism, and infection with *Clostridium tetani* remains localized. However, the toxin produced by the bacteria migrates to its site of action in the central nervous system, where it blocks the release of inhibitory neurotransmitter substances into neural synapses.

Clinical description and case definition

- **Clinical description:** In the newborn, the disease is characterized by inability to suck and convulsions. The average incubation period is about 6 days (range 3-28 days). The case fatality rate is high (100% in untreated cases, up to 80% even if treated). In the postpartum mother, presenting syndromes are those of adult tetanus (painful contractions, abdominal rigidity, opisthotonos and occasional *risus sardonicus*).
- **Case definition and classification (infants)**
  - ***Suspected case:*** Any neonatal death between 3 and 28 days of age in which the cause of death is unknown; or any neonate reported as having suffered from neonatal tetanus between 3 and 28 days of age and not investigated.
  - ***Confirmed case:*** Any neonate with a normal ability to suck and cry during the first 2 days of life, who between 3 and 28 days of age cannot suck normally, **or** any neonate who becomes stiff or has convulsions (i.e. jerking of the muscles) or both.

  Hospital-reported cases of neonatal tetanus are considered confirmed cases.
  The diagnosis is purely clinical and does not depend upon laboratory or bacteriological confirmation.

Recommended interventions

- **Case management**
  Supportive treatment combined with high sedation.
- **Prevention**
  The most effective strategy is the immunization of pregnant women at risk:
  - Women in whom the latest immunization against tetanus occurred more than 10 years ago
  - All cases where the conditions of asepsis during delivery may be in doubt.

  In some countries, women receive tetanus toxoid protection (usually 0.5 ml injected into the muscle of the upper arm) as soon as they have reached child-bearing age:
  - 1st dose (TT1) at 1st contact with woman of childbearing age or as soon as possible during pregnancy
  - 2nd dose (TT2) 4 weeks at least after the first, preferably at least 2 weeks before delivery
  - 3rd dose (TT3) at least 6 months after TT2
  - 4th dose (TT4) at least one year after TT3
  - 5th dose (TT5) at least one year after TT4.

- **Epidemics**
  Not applicable.
- **Drug resistance monitoring**
  Not applicable.

Other aspects

- **Procurement of equipment and drugs**
  See *Immunization*.
- **Surveillance**
  The number of confirmed neonatal tetanus cases must be reported as a separate item from other (non-neonatal) tetanus in routine monthly surveillance reports. Zero reporting required at all levels.
  Active surveillance in major health facilities on a regular basis (at least once a year).
  In "low risk" geographical areas (incidence <1/1000 live births with effective surveillance), all suspect cases must be investigated to confirm the case and identify the cause.
  Community surveillance in "silent" areas (i.e. where routine reporting is not functional but where, from other indicators, neonatal tetanus could be a problem).
- **Special considerations/other interventions**
  There may be mild pain, redness, warmth or swelling for 1-3 days at the injection site after a tetanus toxoid injection, especially after later doses.
  If the patient suffers from malaria or AIDS at the same time as tetanus toxoid is being given, the immune response may be hampered.
- **Indicators**
  - Number of cases of neonatal tetanus per 1000 live births
  - % of newborns protected at birth*.

  * Record during DTP1 visits whether the infant was protected at birth (PAB) because of the mother's tetanus toxoid status and/or delivery status (clean/unclean). % PAB is the ratio of infants protected to total live births. The mother of an unprotected child must receive a dose of tetanus toxoid at the same visit and be followed up with subsequent doses for protection.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42.

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REFERENCES:

WHO. *Immunization in practice.* Module 1 WHO/EPI/TRAM/98.01 (pages 12-3), Module 2 WHO/EPI/TRAM/98.02 (pages 15-16).
WHO. *Field guide for neonatal tetanus elimination*. WHO/V&B/99.14.
See also: *Immunization* in the present document (section 2.1).

Trachoma A71

General introduction

Trachoma is the major infective and preventable cause of blindness. An estimated 146 million people are affected by the disease and 6 million are blind because of it. It is seen in poor, underserved rural areas in 46 developing countries of Africa and Asia. Elimination programmes are already being implemented in 16 priority countries using the WHO *SAFE* strategy, which relies on:

- ***S***urgery for trichiasis
- ***A***ntibiotic treatment for active cases
- ***F***acial cleanliness (education on personal hygiene)
- ***E***nvironmental improvement (water availability, provision of latrines and garbage removal systems).

Causal agent and main modes of transmission

- **Causal agent:** *Chlamydia trachomatis*, serovars A, B, Ba, C.
- **Main modes of transmission:** Trachoma spreads through contact with contaminated ocular or nasal discharges, either directly (finger) or indirectly (tissues, flies – *Musca sorbens*). It occurs in areas where poor hygiene and poor access to water are common. Populations at risk include children below 10 years (active infectious disease) and women older than 15 years (blinding disease).

Clinical description and case definition

After an incubation period of 5 to 12 days it begins as a mild conjunctivitis and then explodes as a keratoconjunctivitis, characterized by large amounts of ocular and nasal discharge. The active stage of the disease is characterized by swollen eyelids, abundant discharges, follicles and hyperaemia of the inner part of the upper eyelids. The chronic stage is characterized by cicatrization with the development of conjunctival scars and a variable degree of deformation of the upper tarsal plate; consequent inversion of the eyelashes (trichiasis) can bring on corneal lesions. The final degree of visual acuity (from normal vision to blindness) depends on the extent of corneal involvement.

Re-infections cause complications leading to trichiasis, conjunctival scarring, corneal lesions and ultimately blindness.

- **Case definition (in endemic areas)**
  - Presence of more than 5 lymphoid follicles in the tarsal conjunctival lining of the upper eyelid
    - Greater than 0.5 mm in diameter
    - With diffuse conjunctival inflammation.
  - Presence of one of the following signs helps qualify for diagnosis of trachoma:
    - Epithelial keratitis, mostly marked in the upper third of the cornea
    - Pannus
    - Scars of characteristic configurations in the upper tarsal conjunctiva
    - Limbal follicles or their sequelae (Herbert's pits).

Laboratory diagnosis

- Detection of intracellular chlamydial elementary bodies in epithelial cells of conjunctival scrapings (Giemsa-stained smears)
- Immunofluorescence
- Chlamydial antigen detection by enzymatic immunoassay
- DNA detection
- Isolation of the agent in special cell culture
- PCR test.

Recommended interventions

- **Case management**
  - *Topical* treatment with 1% tetracycline eye ointment
    - Twice a day for 6 consecutive weeks, **or**
    - Twice a day for 5 days a month for 6 consecutive months.
  - *Systemic* treatment with a single oral dose of azithromycin (children 20 mg/kg, adult 1 g) has proved to be effective for individual treatment.

  For trichiasis, urgent eyelid surgery is required to prevent progression to irreversible blindness.
- **Prevention**
  Appropriate personal and environmental hygiene prevents infection from trachoma. Facial cleanliness is important since the disease spreads from ocular and nasal discharges. Flies help to spread trachoma when they rest on the periocular areas and fly control measures (including building and maintaining fly-proof latrines) are effective in controlling the infection. Health education on cleanliness and fly control is essential.
- **Epidemics**
  Epidemics of trachoma may occur in endemic countries in concurrence with bacterial conjunctival infections occurring as seasonal epidemics (beginning or end of rain season). These conjunctival infections may facilitate and aggravate the onset and course of trachoma. See *Prevention* above.
- **Drug resistance monitoring**
  No recorded resistance to the topical preparation of tetracycline, the main drug used in trachoma control.

Other aspects

- **Procurement of equipment and drugs**
  - Surgical tools to perform trichiasis surgery (Trichiasis Surgery Kit).
  - Tetracycline eye ointment 1%.
  - Kit described in WHO Manuals for trachoma control (see References).
- **Surveillance**
  Based on the national health system capacity.
  - *District level:* reported cases or trichiasis and screening for active trachoma cases.
  - *Central/National level:* aggregated data from hospital records and survey/screening activities by the national coordinator for the prevention of blindness.
  - *International level:* report of aggregated available data sent to WHO yearly.
- **Special considerations/other interventions**
  The ***SAFE*** trachoma prevention strategy allows prevention of blindness in advanced cases and prevents/reduces the transmission of infection.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42

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REFERENCES:

Francis V, Turner V. *Achieving community support for trachoma control. A guide for district health work.* Geneva: WHO, 1993. WHO/PBL/93.36.

Mariotti SP, Prüss A. *The SAFE strategy – preventing trachoma. A guide for environmental sanitation and improved hygiene/La stratégie CHANCE – prévenir le trachome. Guide d'assainissement et d'hygiène.* Geneva: WHO, 2000. WHO/PBD/GET/00.7 Rev.1.

WHO. *Primary health care level management of trachoma control.* Geneva: WHO, 1993. WHO/PBL/93.33.

WHO. *Future approaches to trachoma control*. Geneva: WHO, 1996. WHO/PBL/96.56

Treponematoses, non venereal

General introduction

Non venereal treponematoses currently occur under 3 main forms.

1. Endemic syphilis (*bejel*) in eastern Mediterranean and Asian countries and in arid areas of tropical Africa
2. Yaws or *framboesia*, primarily in rural tropical areas of Africa, Central and South America, South-East Asia, the Caribbean and equatorial islands of the Pacific.
3. Pinta, a dyschromic treponematosis observed among isolated rural populations of South America.

In all 3 forms, lesions can become secondarily infected and painful to the point of disability, especially if located on the palms and soles. Late destructive lesions occur after 5 years or more.

Control activities initiated in the late 1960s have led to a considerable diminution of the venereal treponematoses, particularly yaws, but interruption of these activities has been followed by a resurgence (460 000 new cases of endemic treponematoses reported to WHO in 1997).

Causal agents and main modes of transmission

- **Causal agents:** *Treponema pallidum* (bejel), *T. pertenue* (yaws), *T. carateum* (pinta).
- **Main modes of transmission:** The site of entry is usually:
  - For yaws, a pre-existing abrasion, laceration, or insect bite; transmission by direct, non-sexual contact with the exudate or serum from infectious lesions (papules, papillomata or macules); late lesions (deep ulcers, gangosa, bone, and hyperkeratotic palmar and plantar lesions) are not infectious
  - For endemic syphilis: contact with early infectious lesions of skin and mucosae, directly or indirectly (common eating utensils)
  - Pinta, which is not highly contagious, is presumably transmitted by direct and prolonged contact with early dyschromic lesions – trauma often provides a portal of entry.

  The incubation period is 2 weeks to 3 months. The case fatality rate is usually low.

Clinical description and case definition

- **Clinical description**
  - Bejel - Mucous patches in mouth, with moist papules on skin folds and drier lesions on trunk and extremities. Plantar and palmar hyperkeratosis with painful fissuring. Late inflammatory lesions of skin, long bones or nasopharynx.
  - Yaws - Painless initial lesion (papilloma) on the face or extremities, which proliferates slowly or may ulcerate. Secondary papillomata appear before or shortly after the initial lesion heals – if located on the palm or sole, they are very painful. Secondary manifestations include periostitis of the shin (sabre shins) or fingers (polydactylitis). Late lesions occur in 20% of patients, with destruction of skin and bone. The disease, rarely fatal, can be very disabling.
  - Pinta - A scaling painless papule with satellite lymphadenopathy on the back of hands or feet, or legs. Secondary maculopapulous erythematous rash evolving into tertiary areas of dyspigmentation (blue/violet/brown discoloration), rich in treponemata. Scars occur as a final stage and do not contain treponemata. The disease is not fatal and does not lead to disability.

  Laboratory confirmation
  - Darkfield or direct fluorescent antibody examination showing *Treponema*
  - Treponemal serological tests
  - Nontreponemal serological texts (initial and early stages only).

Recommended interventions

- **Case management**
  600 000 units of benzathine benzylpenicilin for all cases and contacts aged under 10 years, and 1 200 000 units for those aged over 10 years, in a single intramuscular injection.
- **Prevention**
  Treatment of asymptomatic contacts is justified and mass treatment is recommended if the prevalence rate for active disease surpasses 5%.
- **Epidemics**
  Mass treatment of the total population with benzathine benzylpenicillin.
- **Drug resistance monitoring**
  True penicillin resistance has not been observed, although failure of penicillin treatment has occurred in some Western Pacific Islands, mainly for operational reasons.

Other aspects

- **Procurement of equipment and drugs**
  Benzathine benzylpenicilin:
  - 1 200 000 units multiplied by number of subjects aged 10 years and above in the population, plus 10%
  - 600 000 units multiplied by number of subjects aged under 10 in the population, plus 10%

  Injection equipment and material.
- **Surveillance**
  Periodic resurveys are essential and must begin 6 months after the implementation of mass treatment. The timing of subsequent resurveys will depend upon the prevalence (in high-prevalence areas they must be more frequent than in low prevalence areas), but will usually be at intervals of 2 years.
- **Special considerations/other interventions**
  Fatal anaphylaxis from hypersensitivity to penicillin must be taken into account.
- **Indicators**
  - Number of cases.
  - Seroprevalence.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42.

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REFERENCES:

See also *Mass chemo/prophylaxis/chemotherapy* in the present document (section 2.2).

Trypanosomiasis, African B56-0, B56-1

General introduction

About 40 000 new cases of African trypanosomiasis are reported each year from 36 countries in tropical Africa (latitudes 15°N to 20°S); the estimated number of cases is between 350 000 and 450 000 and over 60 million people are at risk of infection. Only 4 to 5 million of those at risk are currently under surveillance. Trypanosomiasis attacks the labour force and hampers production and work capacity. The disease is fatal in the absence of treatment. The reservoir is mainly human for *Trypanosoma brucei gambiense*, and mainly animal (cattle, wild ruminants) for *T. b. rhodesiense*. Outbreaks occur when human-fly contact is intensified or through movements of hosts or of infected flies. In epidemic situations, the prevalence can be higher than 70%. An intercountry approach is essential. The leading principles of trypanosomiasis control are:

- Reduction of the human reservoir through early diagnosis and treatment of infected individuals
- Reduction of man-fly contact through adapted vector control.

Causal agents and main modes of transmission

- **Causal agents:**
  - *Trypanosoma brucei gambiense* (tropical forest, central and West Africa)
  - *Trypanosoma brucei rhodesiense* (savanna, mainly eastern and southern Africa).
- **Main modes of transmission:** Infection occurs after an infected *Glossina* species bites the victim and transmits the trypanosome. The parasite then multiplies in the blood and lymph glands and after a variable delay crosses the blood-brain barrier, provoking major, often irreversible, neurological disorders that lead to death. The incubation period is short for *Trypanosoma brucei rhodesiense* (3 days to a few weeks); it can take years for *T. b gambiense.*

Clinical description and case definition

- **Clinical description:**
  In the early stages, a painful chancre*, which originates as a papule and evolves into a nodule, may be found at the primary site of a tsetse fly bite. There may be fever, intense headache, insomnia, painless lymphadenopathy, anaemia, local oedema and rash. In the later stage, there is cachexia, sleep disturbance, and signs of central nervous system impairment. The disease may run a protracted course of several years in the case of *Trypanosoma brucei gambiense*. In the case of *T. b. rhodesiense*, the disease has a rapid and acute evolution. Both diseases are always fatal without treatment.
  * Chancre is rare in *T. b. gambiense* infection.

  Laboratory criteria
  - ***Presumptive:*** serological: card agglutination trypanosomiasis test (CATT) for *Trypanosoma brucei gambiense* only or immunofluorescent assay for *T. b rhodesiense* mainly and possibly for *T. b. gambiense*
  - ***Confirmative***: parasitological: detection (microscopy) of trypanosomes in blood, lymph node aspirates or CSF.

  Case classification
  - ***Suspected *:*** A case that is compatible with the clinical description, and/or
    - with a positive serology
    - without a positive parasitology.
  - ***Confirmed:*** A case with positive parasitology, with or without clinical symptoms.**

    * In the early stage or early in the late stage of the disease there are often no clinical signs or symptoms associated with the disease. Suspicion is then based on local risk of contracting the disease and the local historical disease background.

    ** Confirmed positive healthy carriers are a major public health risk. As a reservoir of parasites, they disseminate the disease and must be treated as soon as possible.

Recommended interventions

- **Case management**
  - ***Trypanosoma brucei gambiense***
    - 1st stage of disease (without CSF impairment): Ambulatory pentamidine IM for 7-10 days dose of 4 mg base/kg/day.
    - 2nd stage (CSF impairment): Hospitalization with a series of 3 or 4 melarsoprol IV injections of 3.6 mg/kg/day, with a rest period of 7 days between injections.
  - ***T. b. rhodesiense***
    - 1st stage: Ambulatory suramin – 1 intramuscular injection of 1 gram per week for 6 weeks.
    - 2nd stage: Hospitalization. Melarsoprol treatment, same as for the second stage of a *T. gambiense* infection. Check patients at 3, 6, 12, 24 months for relapses.

NOTE: Melarsoprol is effective for treatment of trypanosomiasis of either type with CSF anomalies, but it may have severe toxic side-effects (see *Special Considerations*). In case of melarsoprol treatment failure, use:

- *T. gambiense* infection: eflornithine 400 mg/kg body weight in 4 perfusions a day (every 6 hours) for 7 or 14 days
- *T. b. rhodesiense* infection: there is no effective second-line drug at the time of writing.

- **Prevention**
  - Tsetse fly control programmes: traps and screens (may be impregnated with insecticides) – see *Vector control* (section 2.7)
  - Containment of the human reservoirs through population screening and chemotherapy
  - Public education on how to protect oneself against the bites of the tsetse fly
  - Prohibition of blood donation from those who live (or have stayed) in endemic areas.
- **Epidemics**
  - Mass surveys to identify affected areas
  - Early identification of infection in the community, followed by treatment
  - Urgent implementation of tsetse fly control measures.
- **Drug resistance monitoring**
  Melarsoprol treatment failure for *Trypanosoma brucei gambiense* is as high as 35% in Ugandan foci. A melarsoprol resistance surveillance network has been established by WHO.

Other aspects

- **Procurement of equipment and drugs**
  - *Eflornithine, suramin:* through WHO and MSF
  - *Pentamidine:* through WHO
  - *Melarsoprol:* from manufacturer
- **Surveillance**
  The surveillance system will use a village-based definition using 4 classes:
  - Village of unknown epidemiological status
  - Suspected village
  - Endemic village
  - Disease-free village.

  In the context of control programmes, surveillance provides valuable village-based data, with the precise geographic location of each village using the global positioning system (GPS). Data are analysed using the geographical information systems (GIS).
  Information collected at village level is aggregated at the intermediate/central level and reported to WHO.
  In areas not covered by control activities, results of serological surveys will give indications of the endemicity status.
- **Special considerations/other interventions**
  Reactive encephalopathy from melarsoprol in up to 10% of patients (fatal outcome in about half the cases).

Contacts and References

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Trypanosomiasis, American B57

(Chagas disease)

General introduction

Targeted by WHO for **elimination** by the year 2000 (Resolution WHA51.14), American trypanosomiasis currently affects 25 countries with 16-18 million people infected and about 40 million at risk of infection. The disease is prevalent in South America and in Central America. The disease is potentially fatal and the chronic cardiac lesions are irreversible; one third of those infected develop incapacitating cardiac damage. Infection can also be acquired through blood transfusion and from mother to child.

The infection can be effectively eliminated through interruption of vector transmission and systematic screening of blood donors. Interruption of transmission has been successful in some countries of the Southern Cone of South America (Brazil, Chile, Uruguay); surveillance is necessary to monitor prevention and control measures.

Causal agent and main modes of transmission

- **Causal agent:** *Trypanosoma cruzi (Schizotrypanum cruzi)*, a protozoan seen in humans both as a flagellate and as an intracellular parasite without a flagellum.
- **Main modes of transmission:**
  Vectors (blood-sucking "kissing bug" species of *Reduviidae: Triatoma*, *Rhodnius*, *Panstrongylus*) are infected when biting a parasitaemic animal or person and carry the parasite in their gut and ultimately in their faeces. Infection of mammalian hosts occurs when fresh bug faeces (deposited on human skin during feeding) contaminate the conjunctivae, mucous membranes or skin abrasions (including the bite wound).

  Transmission may also occur through transfusion of infected blood (and during organ transplantation from chagasic donors or through accidental laboratory infections).

  Disease reservoirs include man and many species of domestic and wild animals. The incubation period after an insect bite is 5-14 days, after transfusion 30 to 40 days. Organisms may persist throughout life in the blood of the vertebrate hosts whether or not symptoms are present. The vector becomes infective 10 to 30 days after biting an infective host and remains so for life (up to 2 years).

Clinical description and case definition

- **Clinical description**
  The main clinical signs of the acute disease are mainly fever, malaise, hepatosplenomegaly and lymphadenopathy in the acute phase. Many patients present without clinical signs. An inflammatory response at the site of infection (chagoma) may last up to 8 weeks.
  The disease leads in the long run to chronic cardiac lesions and/or enlargement of the digestive viscera and to peripheral neuropathies in up to 30% of those infected.

  Laboratory criteria
  - Positive parasitology (direct, xenodiagnosis, blood culture), **and/or**
  - Positive serology for *Trypanosoma cruzi* antibodies (IgM and/or conversion from negative to positive in recent infections), indirect haemagglutination test (IHA), indirect immunofluorescent antibody test (IFAT), direct agglutination test (DA), Western Blot, chemoluminescence and ELISA.

  Case classification
  - ***Suspected:*** Not applicable.
  - ***Probable*** (*endemic areas*): A case with unexplained fever, hepatosplenomegaly and a *chagoma* (inflammation at site of infection).
  - ***Confirmed:*** A clinically compatible case that is laboratory-confirmed.
  - ***Congenital:*** A newborn with:
    - Positive parasitology (direct, xenodiagnosis, culture), **or**
    - Positive serology 6 to 8 months after delivery

    when there is no other potential means of transmission.
  - ***Indeterminate:*** Positive serology for *T. cruzi* antibodies alone, no other clinical findings related to the disease (e.g. in blood donors).
  - ***Chronic:*** Positive serology or parasitology with chronic cardiac lesions and/or enlargement of the digestive viscera and/or peripheral neuropathies.

Recommended interventions

- **Case management**
  Management of confirmed cases to be undertaken only under the supervision of health personnel (anti-parasite treatment only).
  No isolation necessary, but blood must be handled with the same biosafety measures as any other infected material either in ambulatory care or for hospitalized patients.
  - ACUTE PHASE/RECENT CHRONIC PHASE (probable or confirmed case)

    Nifurtimox in 3 daily doses for 30 to 60 days
    - (up to 40 kg) 10-12 mg/kg body weight
    - (over 40 kg) 8 mg/kg body weight

    OR
    Benznidazole in 3 daily doses for 30 to 60 days
    - (up to 40 kg) 7.5 mg/kg body weight
    - (over 40 kg) 8 mg/kg body weight
  - RECENT CHRONIC PHASE (probable or confirmed case)

    Benznidazole in 3 daily doses for 30 to 60 days
    - (up to 40 kg) 7.5 mg/kg body weight
    - (over 40 kg) 8 mg/kg body weight
  - CONGENITAL*

    Nifurtimox in 3 daily doses for 60 days, 10-15 mg/kg per day, **or**
    Benznidazole in 3 daily doses for 60 days, 10 mg/kg per day
    NOTE: check white blood cells and platelets after 72 hours before continuing treatment
  - CHRONIC CASE

    Benznidazole, 5 mg/kg in 3 daily doses for 60 to 90 days, **or**
    Nifurtimox 8-10 mg/kg in 3 daily doses for 60 to 90 days.
- **Prevention**
  Vector control has until now depended on vertical programmes to carry out activities: To insert the control programme into PHC requires a network of laboratory services with different facilities at different levels for diagnosis.
  - Construct or repair walls and roofs in order to eliminate shelters for reservoir and vector species
  - Use residual-action insecticides (household spraying, fumigant canisters, insecticide paintings)
  - Environmental management of the peri-domestic area.

  Prevention of transmission by blood transfusion requires screening of blood donors.
  Secondary prevention of congenital Chagas disease requires serological diagnosis of the infection in pregnant women, confirmation of the infection in newborns, followed by treatment.
- **Epidemics**
  Rare events related to ingestion of crude palm tree fruit extracts containing infected vectors and/ or uncooked small mammals containing *Trypanosoma cruzi* have been reported**.** Such events are to be dealt with using the standard acute phase procedures described above.
- **Drug resistance monitoring**
  Strains of *Trypanosoma cruzi* resistant to nifurtimox and or benznidazole have been described. They seem to be much more common in Brazil than in Argentina, Chile and Uruguay.
  Insecticide resistance
  Natural occurrence of resistance to carbamates among *Rhodnius* vectors has been reported, but resistance to other insecticides (such as pyrethroids), has up to now only been a laboratory finding without effect on operational programmes. Appropriate selection of insecticide products is important for the result of spraying with residual insecticides. An intercountry network of laboratories (RELCOT) monitors insecticide resistance of the vectors.

Other aspects

- **Procurement of equipment and drugs**
  See also *Vector control*
- **Surveillance**
  In endemic areas, sentinel surveillance may be the only feasible method at present.
  Serological surveys (standardized and periodical) among age groups 0-4 for surveillance and control. Where possible, routine surveillance should be part of primary health services. At peripheral level, individual patient records must be maintained. Routine monthly reporting of aggregated data from peripheral level to intermediate level. Routine biannual reporting of aggregated data to central level.

  All blood donations must be screened locally.
- **Special considerations/other interventions**
  Because of variation in specificity of the tests, cut-off points must be defined locally using a standard serum panel provided by the reference laboratories of the intercontinental network for standardized serology (currently in Brazil and Argentina).
  A national laboratory network must be set up in those countries where Chagas disease is endemic.
- **Indicators**
  - Parasitological
    - *Trypanosoma cruzi* infection rate
    - Number of cases identified from transfusion donors
    - Number of cases with positive serology**,** by age / sex / month / means of diagnosis.
  - Entomological
    - Infestation rate (% with presence of vectors) for:
      - Housing unit (House + peridomicile)
      - House
      - Peridomicile
      - Locality
    - Number of houses and localities subject to annual vector control
  - Clinical
    - Incidence of acute Chagas disease
    - Serological prevalence by age group
    - Serological prevalence among blood donors

Contacts and References

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REFERENCES:

Salvatella R, Rosa R. La interrupción en Uruguay de la transmisión vectorial de *Trypanosoma cruzi*, agente de la enfermedad de Chagas, por control de *Triatoma infestans. Revista de Patologia tropical* 2000, 29(2): 213-231.
WHO. Organización Panamericana de la Salud/Organización Mundial de la Salud. *Tratamiento etiologico de la enfermedad de Chagas. Conclusiones de una consulta tecnica.* OPS/HCP/HCT/140/99.
WHO. *Report of the Expert Committee on the Control of Chagas Disease.*Technical Report Series (in preparation)

Tuberculosis A15-A19

General introduction

Every year 8 million people become sick and about 2 million die from tuberculosis. WHO recommends a control strategy (called DOTS), but by 1999 only 20% of estimated new infectious cases of tuberculosis received it and tuberculosis remains the single most important killer among infectious diseases. Insufficient recourse to DOTS (especially in countries with severe tuberculosis burdens), the association with HIV infection, and development of drug resistance because of inadequate treatment are major concerns. The objective of tuberculosis control is to reduce morbidity, mortality and transmission until tuberculosis is no longer a threat to public health. The WHA has endorsed the following operational targets for tuberculosis control by the year 2005:

1. Successful treatment of 85% of detected new smear-positive cases
2. Detection of 70% of estimated (incident) smear-positive cases.

Causal agent and main modes of transmission

- **Causal agent:** *Mycobacterium tuberculosis* complex (rarely *M. bovis* or *M. africanum*).
- **Main modes of transmission:** Tuberculosis is transmitted through the air (milk from infected cattle can also transmit *M. bovis*). Infectious droplets produced by the cough of tuberculosis patients dry out in the air and infectious nuclei reach the lung alveoli where bacilli multiply and disseminate via the blood or the lymphatic system. Untreated patients with pulmonary tuberculosis and smear-positive sputum on direct microscopy are the main sources of transmission, each such patient infecting on average 20-30 persons in 2 years. Appropriately treated patients become non-infectious in 2-4 weeks.

  Primary infection, which may occur 2 to 10 weeks after exposure, can cure spontaneously or progress to disease. Bacilli may remain latent for many years or a lifetime and may produce late disease when the immune status of the patient deteriorates (through age or associated factors). The lifetime risk of developing active tuberculosis among infected individuals is around 10% (mostly in the first 2 years after infection). Among individuals infected with both the tubercle bacillus and with HIV, the cumulative lifetime risk approaches 50%. Infection with HIV increases the risk of tuberculosis disease in patients infected with *M. tuberculosis*, because HIV infection breaks down the immunological barriers in the individual. Areas of high prevalence for HIV infection therefore show increases of tuberculosis incidence (up to 5-fold in some countries). Among persons with untreated tuberculosis disease the case fatality rate is about 50%; treatment can reduce this to 3%-5%, provided there is no HIV co-infection.

  Extra-pulmonary tuberculosis is non-infectious. Childhood tuberculosis cases (pulmonary infiltrates, miliary tuberculosis, meningeal and other extrapulmonary tuberculosis) are usually not infectious.

Clinical description and case definition

- **Clinical description**
  - *According to site:*
    - Pulmonary (involving lung parenchyma) — ICD10: A15.0-A15.3, A16.0-A16.2
    - Extra-pulmonary — ICD10: A15.4-A15.9, A16.3-A19.9
  - *According to bacteriology:*
    - Sputum smear-positive (PTB+) — ICD10: A15.0
    - Sputum smear-negative/unknown
    - Includes culture-positive tuberculosis with negative sputum smear: — ICD10: A15.1
  - *According to previous treatment:*
    - New case (no treatment or less than 1 month of treatment)
    - Relapse: patient previously treated for tuberculosis who has been declared cured or “treatment completed” and is diagnosed with a bacteriologically positive tuberculosis (smear or culture)
    - Other cases needing treatment
      - *Failure:* patient who, while on treatment, is sputum smear-positive at 5 months or later during the course of treatment.
      - *Returning after default:* patient who returns to treatment with positive bacteriology, following interruption of treatment for 2 months or more
      - *Chronic case:* patient who is sputum-positive at the end of a re-treatment regimen.
- **Case definition**
  A patient in whom tuberculosis has been bacteriologically confirmed or has been diagnosed by a clinician.

Recommended interventions

- **Case management – the DOTS strategy**
  DOTS is the most cost-effective strategy available for controlling the tuberculosis epidemic today. It has 5 components:
  1. Government commitment to sustained tuberculosis control activities
  2. Case detection by sputum smear microscopy among symptomatic patients (e.g. adults with cough) who spontaneously report to health services
  3. Standardized short-course treatment regimen of 6 to 8 months for at least all confirmed sputum smear positive cases, with directly observed treatment (DOT) for at least the initial 2 months (the drugs to be used are those recommended by national guidelines)
  4. A regular, uninterrupted supply of all essential anti-tuberculosis drugs
  5. A standardized recording and reporting system that allows assessment of treatment results for each patient and of the overall tuberculosis control programme.

- **Prevention**
  Cure of infectious patients is the best prevention as it stops transmission of the infectious agent.
  BCG vaccination as early in life as possible provides a degree of effective protection for children (up to 80%), particularly against severe forms such as tuberculous meningitis.

  Chemoprophylaxis of infected individuals with isoniazid for 6 months reduces the risk of disease by 80-90%, mainly in child contacts of smear-positive tuberculosis patients and in HIV-infected individuals. An alternative to isoniazid is to give rifampicin/pirazynamide for 2 months.

  Environmental protection: air renewal (outside ventilation); sunlight and UV light kill the infectious agent.

- **Epidemics**
  The spread of HIV infection has resulted in extensive epidemics of tuberculosis, increasing the expected incidence and mortality up to 5-fold. Micro-epidemics can occur in schools, nursing homes, shelters for the homeless, and hospitals with HIV patients. Migration from high-prevalence areas or countries increases the incidence in low-prevalence areas. Cases must be rapidly diagnosed and treated, and contacts must be identified and provided with preventive treatment. HIV has also facilitated the epidemic spread of drug-resistant strains.

- **Drug resistance monitoring**
  Monitoring of anti-tuberculosis drug resistance through surveys or ongoing surveillance follows standard laboratory and epidemiological guidelines. Laboratory quality control helps assess proficiency testing, and an internationally recognized external laboratory must undertake the validation of collected data. Where ongoing surveillance is not feasible, surveys are recommended every 3-5 years in order to assess trends. The level of drug resistance is a good indicator of programme performance. In new cases it suggests the level of circulating strains in the community, and in previously treated cases it reflects how the programme has performed in the past.

Other aspects

- **Procurement of equipment and drugs**
  This must be undertaken according to national programme procedures. Estimates can be based on the requirements for the previous year, adjusted in accordance with foreseen increases in the number of new cases through improved detection programmes – a buffer stock must also be foreseen.

- **Surveillance**
  Monitoring trends of notified cases (total tuberculosis and smear-positive pulmonary tuberculosis) from country reports, mortality (vital statistics) and drug resistance (periodic surveys or routine surveillance based on standard WHO/IUATLD protocol). Monitoring of treatment outcomes in patient cohorts. Age and sex distribution of smear-positive cases.

- **Special considerations/other interventions**
  - Health education to the community on:
    - Recognition of symptoms (prolonged cough) leading to consultation in a health facility
    - Curability and availability of free drugs in the public health system
    - Need to complete regular therapy until cure.
  - Control of contacts of infectious cases (especially children).
  - Coordination with HIV/AIDS for the diagnosis and treatment of tuberculosis among persons infected with HIV.
  - Information to patients including offers of voluntary testing for prognosis and counselling.
  - Quality of tuberculosis control:

    High quality of tuberculosis control depends on:
    - Quality of standard procedures for diagnosis including quality control of sputum smear microscopy
    - Quality of treatment through procurement of known quality drugs in sufficient quantities and ensuring their regular intake
    - Quality of care through staff training, patient education and on-site visits to health care facilities where tuberculosis is treated.
  - Programme monitoring by cohort analysis through (usually quarterly) reports of treatment outcomes.
- **Indicators**
  - Annual tuberculosis case notification
  - Percent of registered smear-positive cases successfully treated (cured and completed treatment)
  - Notification rates (total and new smear-positive)
  - Percent of newly registered patients.

Contacts and References

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REFERENCES:

Crofton J, Horne N, Miller F. *Clinical tuberculosis.* London: Teaching Aids at Low Cost (TALC)/International Union against Tuberculosis and Lung Diseases, Macmillan. 2d ed., 1999. 222 pp. ISBN 0333724305.

Rieder, H. *Epidemiological basis of tuberculosis control.* IUAT: Paris, 1999. ISBN 29 5042 3884.

WHO, 1997. *Treatment of Tuberculosis – Guidelines for National Programmes.* WHO/TB/97.220.

WHO, 1998. *Tuberculosis Handbook.* WHO/TB/98.253.

WHO, 1999. *What is DOTS? – a guide to understanding the WHO-recommended TB control strategy known as DOTS.* WHO/CDS/CPC/TB/99.270 http://www.who.int/gtb/publications/index.htm

Typhoid fever A01.0
Paratyphoid fevers A01.1-A01.4

General introduction

Systemic bacterial diseases of worldwide occurrence, with an estimated 600 000 deaths and 17 million cases each year. Relapses occur in 3%-4% of cases. Complications include intestinal perforation and haemorrhage, but mild or inapparent forms are common, especially in endemic areas, mainly where sanitation is poor.

Causal agent and main modes of transmission

- **Causal agents:**
  - **Typhoid fever:** *Salmonella typhi* (new nomenclature: *Salmonella enterica* serovar Typhi)
  - **Paratyphoid fever:** *Salmonella paratyphi* A, B and rarely C (new nomenclature: *Salmonella enterica* serovar Paratyphi A, B and C)

  The ratio of disease from *S. enterica* serovar Typhi to that caused by *S. enterica* serovar Paratyphi A, B and C is about 10:1.
- **Main modes of transmission:** Ingestion of food and water contaminated by faeces and urine of patients and carriers. Faecal carriers occur in about 2% of infected adults. Chronic carriers are most common among persons infected at an older age, especially women and often in patients with biliary tract abnormalities. Patients with concurrent *Schistosoma haematobium* are at higher risk of becoming urinary carriers of *Salmonella enterica*.

  Infection occurs through ingestion of the organisms in food (shellfish, fruit, vegetables) contaminated at the source or during handling (hands or instruments soiled by faeces/urine of infected person). Flies may infect the food in which the organism then multiplies to attain an infective dose.

Clinical description and case definition

- **Clinical description**

  Typhoid fever (due to *Salmonella enterica* serovar Typhi) may vary from a mild illness with low-grade fever and malaise to a severe picture of sustained fever, diarrhoea or constipation, malaise, anorexia, severe headache. Intestinal ulceration can produce intestinal haemorrhage or perforations. The incubation period ranges from 3 days to 1 month (usual range 1 to 2 weeks) according to the size of the infecting dose. The case fatality rate may reach 10% (less than 1% with prompt treatment).

  Paratyphoid fever due to *S. enterica* serovar Paratyphi A, B or C is clinically similar but milder. The incubation period ranges from 1 to 10 days and the case fatality rate is much lower than for typhoid fever.

  HIV infection and sickle cell anaemia are host factors that affect the severity of the disease and complications.

  Laboratory criteria

  Isolation of the relevant serovars of *Salmonella enterica* from the stool or blood of a patient.

  Case classification
  - ***Suspected:*** A patient with fever of at least 38°C for 3 or more days
  - ***Confirmed:*** A suspected case with laboratory confirmed positive blood culture.
  - ***Carriers:*** *S. enterica* serovar Typhi organisms persisting in stools or urine for >1 year after onset of the disease.

Recommended interventions

- **Case management**

  Supportive care such as oral or intravenous rehydration, antipyretics and appropriate nutrition for severe cases. Antibiotherapy (chloramphenicol, ampicilline, ciprofloxacine or trimethoprim-sulfamethoxazol TMP-SMX) must be offered to all patients. Patients with concurrent schistosomiasis must be treated with praziquantel.
- **Prevention**
  - Early isolation and typing of the causal agent in order to identify the source of the outbreak and facilitate control
  - Safe food-handling
  - Personal hygiene including hand-washing
  - Access to safe water
  - Fly control.
- **Immunization:** (WHO position as of February 2001)

  Immunization may be considered in endemic areas for travellers, populations in refugee camps, microbiologists and school-age children or where multidrug-resistance is common (see *References*).

- **Epidemics**
  These often occur as point-source epidemics, from healthy carriers to food (including use of contaminated utensils). Outbreaks may occur through person-to-person contamination (faecal-oral transmission via contaminated hands or instruments). Direct faecal contamination of untreated water supplies may cause extensive outbreaks.
  Investigations must pinpoint the source and mode of infection to identify corrective measures for application (chlorination/ boiling of water, selective elimination of suspect food).
- **Drug resistance monitoring**
  Resistant strains of *Salmonella* have been identified in several areas of the world – all isolates must be checked for drug resistance (chloramphenicol, ampicillin, ciprofloxacine, trimethoprim-sufamethoxazol).

Other aspects

- **Procurement of equipment and drugs**
  Sufficient stocks of drugs and of laboratory isolation and testing material.
- **Surveillance**
  - Practitioners must be aware of the importance of requesting examination of stool specimens or rectal swabs for public health purposes, especially in cases where food- or water-borne transmission is suspected.
  - All suspected outbreaks of typhoid/paratyphoid must be reported and investigated.
  - After the outbreak investigation, a minimum data set must be collected at intermediate and central levels, including key variables on the nature and extent of the outbreak (time, place, person, possible source).
- **Special considerations/other interventions**
  Surveillance and control activities must be linked with food safety and control authorities.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42.

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REFERENCES:

Ivanoff BM, Levine MM. Typhoid fever: continuing challenge from a resilient bacterial foe. *Bulletin de l'Institut Pasteur*, 1997, 95(3): 129-142.
WHO. Typhoid vaccines. WHO position paper/Vaccins contre la typhoïde : position de l'OMS. *Weekly Epidemiological Record/Relevé épidémiologique hebdomadaire*, 2000, 32(75): 257-264.
www.who.int/vaccines/intermediate/typhoid.htm
See also: *Immunization* in the present document (section 2.1).

Scrub typhus (Tsutsugamushi disease) A75.3

General introduction

Scrub typhus (mite-borne typhus, Tsutsugamushi disease) is an acute infectious disease that is emerging and re-emerging in South-East Asia and the south-western Pacific region. It can have a case fatality rate of up to 30% if untreated. Epidemics occur when susceptible individuals are brought into endemic areas (e.g. during military operations). In some countries (e.g. Japan) it is a notifiable disease. Multidrug resistance has been documented in Thailand.

Surveillance is essential to a better understanding of the epidemiology of the disease and to the detection and control of outbreaks. Training in diagnostic techniques is often required.

Causal agent and main modes of transmission

- **Causal agent:** *Orientia tsutsugamushi*, a Rickettsia (formerly *Rickettsia tsutsugamushi*)
- **Main modes of transmission:** Infection in humans occurs through the bite of infected larval mites. The incubation period is 6 to 21 days.

Clinical description and case definition

- **Clinical description**
  A disease with a primary "punched out" skin ulcer (eschar*) where the bite(s) occurred, followed by acute onset of fever after several days, along with headache, profuse sweating, conjunctival injection and lymphadenopathy. Within a week, a dull maculo-papular rash** appears on the trunk, extends to the extremities and disappears in a few days. Cough is also common. Defervescence within 48 hours following tetracycline therapy strongly suggests a rickettsial etiology.

  * Eschar may be absent in some geographic areas and in highly endemic areas where reinfection is frequent.

  ** Rash may be overlooked in patients with dark or sunburned skin.

  Laboratory criteria
  - Isolation of *Orientia tsutsugamushi* by inoculation of patient's blood in white mice (preferably treated with cyclophosphamide at 0.2 mg/g intraperitoneally or intramuscularly on days 1,2 and 4 after inoculation).
  - Serology: Detection of specific IgM
    - at 1:100 or higher by enzyme immunoassay, **or**
    - at 1:32 dilution or higher by immunoperoxidase, **or**
    - at 1:10 dilution or higher by indirect immunofluorescence.

  Case classification
  - ***Suspected:*** A case that is compatible with the clinical description.
  - ***Confirmed:*** A suspected case with laboratory confirmation.

  NOTE: Serological tests are complicated by the antigenic differences between various strains of the causal agent.

Recommended interventions

- **Case management**
  Tetracyclines, loading dose followed by divided doses daily until the patient is afebrile, or chloramphenicol.
  If treatment is started within 3 days of onset, a second course must be given after 6 days.
- **Prevention**
  - Prevent contact with mite vectors (repellents, impregnated clothes and blankets)
  - Local insecticide treatment against mites
  - For exposed small groups, prophylaxis with small doses of doxycycline once a week for 7 weeks prior to exposure.
- **Epidemics**
  - Mite control
    - Removal of patches of vegetation likely to harbour mites
    - Spraying of vegetation islands likely to harbour mites around human habitations and sites.
  - Daily observation of at-risk populations; immediate treatment on appearance of signs/symptoms.
- **Drug resistance monitoring**

  Thailand has reported multi-resistance of *Orientia* to drugs and follow-up must be considered in this regard.

Other aspects

- **Procurement of equipment and drugs**
  Insecticide and repellents.
- **Surveillance**
  Immediate case-based reporting of all suspected cases from the peripheral level to the intermediate and central level. All suspected cases and outbreaks must be confirmed.
  A parallel laboratory surveillance system reports all confirmed cases to the central level.

Contacts and References

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Yellow fever A95.9

Notification to WHO universally required by *International Health Regulations*

General introduction

Yellow fever is a mosquito-borne viral haemorrhagic fever that strikes over 200 000 people and causes over 30 000 deaths each year in tropical regions of Africa and South America; it is maintained by sylvatic transmission of virus involving forest-dwelling mosquitoes and monkeys. Transmission to humans may occur in forest transition zones; the disease may subsequently enter an urban cycle through *Aedes aegypti*. Yellow fever is undergoing a major resurgence especially in Africa, and many cities are now threatened with epidemics. A safe and effective vaccine has been available for 60 years, but the number of people infected over the last two decades has increased and yellow fever is now a serious public health issue again. During epidemics, case fatality rates may exceed 50% for unimmunized adults and 70% for children.

Strategies for yellow fever control include control of *Ae. aegypti* in urban centres, infant immunization, vaccination campaigns, outbreak prevention, epidemic detection and control.

Causal agent and main modes of transmission

- **Causal agent:** arthropod-borne *Flavivirus*. The prevailing view is that there are only 2 genotypes of yellow fever in Africa and at most 2 genotypes in South America.
- **Main modes of transmission**
  The virus is carried from one animal to another (horizontal transmission) by biting vector species of *Aedes* or *Haemagogus* mosquitoes. Humans and monkeys are the main species to be infected. The mosquito can also pass the virus via infected eggs to its offspring (vertical transmission). The eggs produced are resistant to drying and lie dormant through dry conditions, hatching when the rainy season begins. The mosquito is thus the true reservoir of the virus, ensuring transmission from one year to the next. The incubation period is very short (3 to 6 days).

  Yellow fever persists as a zoonosis in tropical areas of Africa and America. In the equatorial forest, transmission is mainly enzoonotic and human infection is sporadic. In humid or semi-humid savanna areas, cyclic epizootics occur in monkey populations and epidemics with interhuman transmission – most epidemics of yellow fever occur in these zones. In the dry savanna, sylvatic vector populations are too low or active for too short a period to sustain an epizootic. If the virus is introduced into urban areas or in regions where the human population lives in close association with *Aedes aegypti*, explosive outbreaks of urban yellow fever may occur. Since 1985, major outbreaks have been recorded in Angola, Benin, Burkina Faso, Cameroon, Gabon, Ghana, Guinea, Kenya, Liberia, Mali, Mauritania, Nigeria, Senegal and Sierra Leone. Serological evidence of transmission has occurred in Brazil.

  The vectors in Africa can be classified as:
  - Domestic – mainly *Aedes aegypti*
  - Semi-domestic *Ae. furcifer*, *Ae. africanus*, *Ae. luteocephalus*
  - Wild (all other species).

  The vectors in America can be classified as:
  - Domestic – mainly *Ae. aegypti*
  - Wild (all other species).

Clinical description and case definition

- **Clinical description**
  Characterized by acute onset of fever followed by jaundice within 2 weeks of onset of first symptoms. Haemorrhagic manifestations and signs of renal failure may occur.

  There are 2 disease phases for yellow fever. While some infections have no symptoms whatsoever, the first "acute" phase is normally characterized by fever, muscle pain (with prominent backache), headache, shivers, loss of appetite, nausea and/or vomiting. Often, the high fever is paradoxically associated with a slow pulse. Most patients improve after 3 to 4 days and their symptoms disappear, but 15% enter a "toxic phase" within 24 hours. Fever reappears, the patient rapidly develops jaundice and complains of abdominal pain with vomiting. Bleeding can occur from mouth, nose, eyes and/or stomach. Once this happens, blood appears in the vomit and faeces. Kidney function deteriorates; this can range from abnormal protein levels in the urine (albuminuria) to complete kidney failure with no urine production (anuria). Half the patients in the "toxic phase" die within 10-14 days. The remainder recover without significant organ damage.

  Laboratory criteria
  - Isolation of yellow fever virus, **or**
  - Presence of yellow fever specific IgM or a 4-fold or greater rise in serum IgG levels in paired sera (acute and convalescent), **or**

- Positive post-mortem liver histopathology, **or**
- Detection of yellow fever antigen in tissues by immunohistochemistry, **or**
- Detection of yellow fever virus genomic sequences in blood or organs by PCR.

Case classification

- ***Suspected:*** A case that is compatible with the clinical description.
- ***Probable:*** Not applicable.
- ***Confirmed:*** A suspected case that is laboratory-confirmed (national reference laboratory) or epidemiologically linked to a confirmed case or outbreak.

Recommended interventions

- **Case management**
  No specific treatment for yellow fever. Dehydration and fever can be corrected with oral rehydration salts and paracetamol. Superimposed bacterial infections must be treated with an appropriate antibiotic. Intensive supportive care may improve the outcome but is rarely available in poorer, developing countries.
- **Prevention**
  Vaccination is the single most important measure for preventing yellow fever:
  - In endemic areas, vaccination must be given routinely through the incorporation of yellow fever vaccine in routine child immunization programmes.* Current yellow fever vaccines have a shelf-life of up to 2 years at a temperature of –20°C or +4°C.**

  * Current EPI/WHO policy does not recommend mixing different vaccines in the same syringe before injection.

  ** Yellow fever vaccine is not recommended for symptomatic HIV-infected persons or other immuno-suppressed individuals; for theoretical reasons it is not recommended for pregnant women

  Routine mosquito control measures
  - Eliminating potential mosquito breeding sites.
- **Epidemics**
  Under epidemic conditions, the following must be implemented:
  - Mass vaccination, and
  - Emergency mosquito control measures:
    - Eliminating potential mosquito breeding sites
    - Spraying to kill adult mosquitoes (emergency measure only).
- **Drug resistance monitoring**
  Not applicable.

Other aspects

- **Procurement of equipment and drugs**
  See *Immunization* and *Vector control.*
- **Surveillance**
  In populations where vaccination coverage is low, surveillance is critical for prompt recognition of outbreaks and rapid implementation of immunization campaigns.

  Routine weekly/monthly reporting of aggregated data on suspected and confirmed cases from peripheral to intermediate and central level. Zero reporting required at all levels.

  Immediate reporting of suspected cases from peripheral to intermediate and central levels.

  All suspected cases and outbreaks must be investigated immediately and laboratory-confirmed. Case-based surveillance must be implemented in countries identified by WHO as being at high risk for yellow fever. Specimens must be collected to confirm an epidemic as rapidly as possible. Priority is on collecting specimens from new or neighbouring areas (other than the area where the epidemic is already confirmed).

  International: Mandatory reporting of all suspected and confirmed cases within 24 hours to WHO.
- **Special considerations/other interventions**
  Ready access to laboratory testing is essential for confirming cases of yellow fever, as many other diseases have similar symptoms. WHO has recently recommended that every country at risk should have at least 1 national laboratory where basic yellow fever blood tests can be performed.
  Vaccination is highly recommended for travellers to high-risk areas.
- **Indicators**
  - Number of outbreaks
  - Number of cases.

Contacts and References

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REFERENCES:

Vainio, J, Cutts, F. *Yellow fever.* Geneva: World Health Organization, 1998. WHO/EPI/GEN/98.11

See also: *Immunization* and *Vector control* in the present document (sections 2.1 and 2.7).

3.2 Syndromes: Overview of some syndromic approaches

Illness – the reason for attendance at a health unit – is often represented by a complex of signs and symptoms that constitute a syndrome. A single syndrome may be caused by different etiological agents; the ultimate role of the health care provider is to identify the etiological agent and to provide appropriate care. It may however be necessary to provide appropriate care even if the etiological agent has not (or not yet) been identified. The *syndromic case management approach* uses an algorithmic format to define what constitutes a given syndrome and decide on the action to be taken, such as:

- Simple home care or specific treatment at home
- Simple care or specific treatment at primary care level
- Urgent referral for treatment/hospitalization
- Referral for further assessment or (in chronic patients) re-evaluation of treatment.

Strategies for the control of ill-health (including communicable diseases) include:

- Reduction of impact on the community:
  - Reduction of mortality
  - Reduction of human suffering (morbidity/disability)
  - Reduction or elimination of transmission (in the case of communicable diseases).
- Improved and/or more effective use of health facilities.

The syndromic approach, which is used mainly but not exclusively at the peripheral level of health care, is applied for instance in the following cases as part of WHO disease control programmes:

- Sexually transmitted infections
- Haemorrhagic fevers
- Integrated Management of Chilhood Illness (IMCI)*
  - Cough or deficient breathing
  - Diarrhoea
  - Fever
  - Ear problems.

* Measles and malaria, which are diseases and not syndromes, are also components of IMCI.

Sexually transmitted infection syndromes (STI)

Epidemiology

WHO estimates that around 340 million new cases of curable sexually transmitted infections (STIs) occurred throughout the world in 1995 in adults aged 15-49 years. In developing countries, STIs and their complications rank in the top 5 disease categories for which adults seek health care. In women of childbearing age, STIs – even excluding HIV – are second only to maternal factors as causes of disease, death and healthy life lost. The scale of the STI problem is too big to be dealt with in specialized STI centres alone: the management of STIs must expand and become part of primary health and other health centres.

The integration of HIV/AIDS programmes with STI prevention and care programmes is economically advantageous and is strongly recommended. Almost all measures for preventing sexual transmission of HIV and STIs are the same, as are the target audiences. Clinical services offering STI care are important not only for diagnosis and treatment but also for information and education. The presence of an untreated STI (ulcerative or non-ulcerative) can also enhance both acquisition and transmission of HIV by a factor of up to 10. STI treatment is thus an important HIV prevention strategy in a general population.

NOTE: STIs often exist without symptoms (up to 70% of women with gonococcal and/or chlamydial infections may be symptom-free). Both symptomatic and asymptomatic infections can lead to the development of serious complications. For women and newborn babies, these include:

- Cervical cancer
- Pelvic inflammatory disease
- Chronic pelvic pain
- Fetal wastage
- Ectopic pregnancy
- Infertility, particularly in women
- Pneumonia in infants *(Chlamydia*)
- Blindness (neonatal gonococcal ophthalmia).

Congenital syphilis is an important and significant cause of infant morbidity and mortality. In adults, the cardiac, neurological and other consequences of syphilis can be fatal.

Some types of genital warts lead to genito-anal cancers.

Main STI pathogens

More than 20 pathogens are transmissible through sexual intercourse – oral, anal or vaginal.

- The main bacteria are:
  - *Neisseria gonorrhoeae* (causing gonorrhoea)
  - *Chlamydia trachomatis* (chlamydial infections)
  - *Treponema pallidum* (syphilis)
  - *Haemophilus ducreyi* (chancroid)
  - *Calymmatobacterium granulomatis* (granuloma inguinale, donovanosis).
- The main viruses are:
  - Human immunodeficiency virus (HIV)
  - Herpes simplex virus (herpes)
  - Human papillomavirus (genital warts)
  - Hepatitis B virus
  - Cytomegalovirus.
- The main parasites are:
  - *Trichomonas vaginalis* (vaginal trichomoniasis)
  - *Candida albicans* – vulvovaginitis in women; inflammation of glans penis and of the foreskin in men.

Case definitions, complications and consequences of STIs

- **Clinical case definition**
  - URETHRAL DISCHARGE SYNDROME: Urethral discharge in men, with or without dysuria.
  - GENITAL ULCER SYNDROME: Genital ulcer on penis or scrotum in men and on labia, vagina or cervix in women, with or without inguinal adenopathy.
  - VAGINAL DISCHARGE SYNDROME: Abnormal vaginal discharge (amount, colour and odour), with or without lower abdominal pain, or specific symptoms or specific risk factors (without examination).

  Laboratory criteria for confirmation
  - URETHRAL DISCHARGE SYNDROME: Laboratory confirmation of organism if possible (Gram-stain for intracellular diplococci), but this is not essential for the case definition, which is syndrome-based.
  - GENITAL ULCER SYNDROME / VAGINAL DISCHARGE SYNDROME: Laboratory confirmation of organism if possible, but this is not essential for the case definition, which is syndrome-based.

  Case classification
  Not applicable.

Syndromic case management of STIs

The traditional method of diagnosing STIs is through laboratory tests. However, these are often unavailable or too expensive. WHO has recommended syndromic management of STIs in patients presenting with symptoms of STI since 1990. The main features of syndromic management are :

- Classification of the main causal pathogens by the clinical syndromes produced (*see above*)
- Use of flowcharts derived from this classification to manage a particular syndrome
- Treatment for all important causes of the syndrome
- Notification and treatment of sex partners
- No expensive laboratory procedures required.

The syndromic approach offers accessible and immediate treatment that is effective and efficient; syndromic case management of STIs using flowcharts is more cost-effective than diagnosis based on clinical examination or laboratory tests. However, the following factors may hinder effective prevention and care of STIs:

- *Many cases are asymptomatic***,** especially in women – asymptomatic individuals will not know that they have an STI and hence will not seek care and will continue to be infected and infective.
- *Even with symptoms, some people may be reluctant to seek STI care,* out of ignorance, embarrassment or guilt; patients may also be deterred by unfriendly attitudes of staff, lack of privacy or confidentiality, or an intimidating setting of the service.
- *Ignorance of STIs, their causes, symptoms, cures and possible consequences may constitute obstacles to resolving problems of STIs and HIV/AIDS*. Ignorance of STIs and AIDS can exist in all types of people and all age groups, but is usually more widespread among adolescents and young people – the very people who have poor access to STI care services –, are likely to be more sexually active, and are unlikely to be in stable sexual relationships.
- *STI services may be absent or unsuitable.* They may not exist in a particular locality, or may be difficult to access, especially for women and young people, or may lack privacy or confidentiality. Clients may be deterred from attending by the stigma attached to STI clinics. In the case of men who have sex with men, the health-care provider may not look for or recognize a rectal STI.
- *The prescribed treatment may be substandard.* Treatment for many STIs is effective when the correct drugs are given, but government health departments sometimes opt for cheaper substandard treatments. This perpetuates infection and may encourage the rapid emergence of resistant organisms.
- *It may be difficult to notify spouse(s) or sex partner(s).* Such notification is important for interrupting the transmission of STIs and preventing possible reinfection, but patients may be reluctant to inform their sex partners out of fear, embarrassment, or unawareness of the importance of doing so. In resource-poor settings, it is usually impractical for notification to be done by the health sector.

Prevention and care of STIs

- *Primary prevention*, concerned with the entire community and aiming at curbing the acquisition of infection, can be promoted through health education, and involves items such as promoting safer sex behaviour, encouraging the use of condoms and abstinence from sex.
- *Secondary prevention* involves treating infected people. The bacterial infections and trichomoniasis are curable; viral infections are not curable, but some can be controlled. Except as regards HIV and viral STIs, treatment interrupts the chain of transmission by rendering the patient non-infectious; it is thus highly cost-effective in its own right, especially when the benefits of reduced HIV transmission are taken into account.
- *Integration* into primary health care facilities, maternal and child health centres, family planning clinics and private clinics makes STI services accessible to more people than are currently served and especially to sexually active adolescent females. It also has the advantage that people seeking care can avoid the potential stigma of going to a dedicated STI clinic. STI care must be expanded to embrace the "public health package", the components of which are discussed in more detail below.
  - ***Comprehensive case management of STIs,*** including early detection of symptomatic and asymptomatic infections through:
    - *Identification of the syndrome*. The syndromic case management approach, using flowcharts, is well suited to settings where laboratory facilities are limited or unavailable. A diagnosis can be made within a short time without expensive and complex laboratory tests.
    - *The provision of appropriate antibiotic treatment:* whatever means are used for diagnosis, availability and use of effective antibiotics are an essential requirement. In the public and in the private sector, drugs must be available at the first point of contact for a patient with an STI. The use of ineffective or partially effective drugs results in an escalation of costs, as patients repeatedly seek treatment for the same condition or its complications, and also leads to the appearance of resistant strains.
    - *Educating the patient:* all patients must be made thoroughly aware of the need to follow a full course of medication, and made to understand that during treatment they are still infectious to others; for this reason at least they must be advised to abstain from sex during the course of treatment.
    - *Counselling* must be available – for example in chronic cases of genital herpes or warts – whether for individuals or for couples in a sexual relationship.
    - *Providing information on partner notification and treatment:* contacting sex partners of patients with STIs, persuading them to present themselves to STI services and treating them promptly and effectively are essential to STI control programmes. These activities must take into account social and cultural factors in order to avoid ethical and practical problems such as rejection and violence, particularly against women. Health and social workers and the media must educate people about the reasons for partner notification and alert them to the possibility that in future they may be notified by their sex partner of an infection and that treatment is important. The treatment of partners of STI patients is particularly important in gonorrhoea and chlamydial infections, which are asymptomatic in most women.
    - *Controlling congenital syphilis and neonatal conjunctivitis:* congenital syphilis occurs in about a third of newborns among women with untreated syphilis; prenatal screening and treatment of pregnant women for syphilis is cost-effective even in areas of very low prevalence. Women should be motivated to attend antenatal clinics early in pregnancy, where they will be routinely tested and, if necessary, treated for syphilis promptly and appropriately. Because of the prevalence of gonorrhoea and chlamydial infections in developing countries and the risks for newborn children (gonococcal or chlamydial ophthalmia), routine prophylactic treatment for such ophthalmia at birth is recommended.
    - *Monitoring drug sensitivity:* health authorities must regularly monitor and detect the emergence of resistance to STI drugs. This will allow for adaptation of treatment protocols.
  - ***Promotion of safe sex behaviour:*** governmental bodies and NGOs must develop and disseminate messages promoting safer sex and educating people about risk reduction. Schools and community-based programmes must provide appropriate sex education to adolescents before sexual activity starts. Such education has been shown to delay the onset or frequency of sexual intercourse rather than increase promiscuity.
  - ***Condom programming*** (from condom promotion to planning and management of supplies and distribution): governmental bodies and NGOs must provide barrier contraceptives against unwanted pregnancy and against infection, and must also educate people about condoms and encourage their use. Health authorities must ensure adequate supplies of good-quality condoms at health facilities and at various other distribution points in the community. Social marketing of condoms outside the health sector is another way of increasing access and use.
  - ***Promotion of health-care-seeking behaviour:*** health authorities must encourage people who have STI symptoms or suspect they may have contracted an STI to seek health care early. Patients seeking STI care must be received in a friendly setting where they can be interviewed and treated in privacy.

- ***Integration of STI control:*** to reduce the obstacles faced by people seeking care, health authorities must combine STI care activities and other health-care facilities (primary health care and reproductive health-care facilities, private clinics and others). Efforts must be made to improve any hostile or judgemental attitudes of health-care workers towards patients with STIs.
- ***Specific services for populations with high-risk behaviours:*** Young people, and men who have sex with other men, are among those in need of friendly and confidential services.

Contacts and References

CONTACTS: WHO Regional Offices: see addresses on pages 40-42

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REFERENCES:

UNAIDS. *Sexually transmitted diseases: policies and principles for prevention and care.* Geneva: UNAIDS, 1997. UNAIDS/97.6.

WHO. *Management of sexually transmitted diseases.* Geneva: WHO/GPA, 1997. WHO/GPA/TEM/94.1 Rev1

WHO/WPRO. *Syndromic case management of sexually transmitted diseases: a guide for decision-makers, health care workers, and communicators.* WPRO : Manila, 1997.

Website: www.unaids.org ; http://www.unaids.org/publications/documents/impact/std/stdcontroltue.pdf

Haemorrhagic fevers

Epidemiology

Acute haemorrhagic fever syndromes can be attributed to dengue (dengue haemorrhagic fever), Ebola-Marburg viral diseases, Lassa fever, yellow fever, Rift Valley fever, hantavirus infections, Crimean-Congo haemorrhagic fever and other viral, bacterial or rickettsial diseases with a potential to produce epidemics. All cases of acute haemorrhagic fever syndrome, whether single or in clusters, should therefore be notified early, without waiting for the causal agent to be identified, according to a syndromic approach. Surveillance of acute haemorrhagic fever syndrome is aimed at early detection and control of cases in order to avoid epidemics and the possible international spread of the disease.

Recommended clinical description

- **Clinical case description (revised *International Health Regulations*)**
  Acute onset of fever of less than 3 weeks duration in a severely ill patient **and**
  Any 2 of the following:
  - Haemorrhagic or purpuric rash
  - Epistaxis
  - Haematemesis
  - Haemoptysis
  - Blood in stools
  - Other haemorrhagic symptom, **and**
  - No known predisposing host factors for haemorrhagic manifestations.

NOTE: During epidemics, most infected patients do not show haemorrhagic symptoms and a specific case definition, according to the suspected or proven disease, has to be used. See disease-specific case definitions in this manual for Ebola, Lassa, dengue, and yellow fever, or specific WHO Outbreak Control Guidelines (available for Ebola haemorrhagic fever, dengue haemorrhagic fever, yellow fever).

Case management

Supportive treatment

The only way to prevent secondary infections is to minimize contact with the patient's lesions and body fluids using standard isolation precautions:

- Isolation of patient
- Restriction of access to patient wards
- Use of protective clothing
- Safe disposal of waste
- Disinfection of reusable supplies and equipment
- Safe burial practices.

These can be implemented despite problems due to limited resources (see *References*).

Other aspects

- **Procurement of equipment and drugs**
  A kit of protective material and clothing is available from WHO for initial investigation activities. Most of the material for protection and isolation (gloves, aprons, protective clothing, disinfectants) can be obtained or adapted from locally available materials.
- **Surveillance**
  - ***In endemic areas and in the absence of an epidemic:***
    - Immediate reporting of suspected cases from the periphery to intermediate and central levels to ensure rapid investigation and laboratory confirmation.
  - ***In epidemic situations:***
    - Intensified surveillance and active finding of all suspected and probable cases for immediate isolation, and of all contact subjects for daily medical follow-up
    - The surveillance area must be monitored for a time corresponding to 42 days (corresponding to twice the maximum estimated incubation periods) after the date of death or hospital discharge of the last case.

- A "rumour registry" for systematic registration of rumours of cases reported by the population
- A single source of official information is essential to ensure coherence and avoid confusion in the public.

- **Special considerations/other interventions**
  Since extreme biohazard may be associated with sampling, transportation and laboratory investigation, the strict application of biosafety procedures to specimens is essential. Shipping must be coordinated with the receiving laboratory.
  Acute haemorrhagic fever syndrome is one of the syndromes subject to notification to WHO in the revised *International Health Regulations* (pending implementation);
- **Indicators**
  Not applicable.

Contacts and References

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REFERENCES:

WHO/CDC. *Infection control for viral haemorrhagic fevers in the African care setting.* Geneva: World Health Organization, 1998. WHO/EMC/EST/98.2

Integrated Management of Childhood Illness (IMCI)

In 1998, more than 50 countries had childhood mortality rates in excess of 100 per 1000 live births. Every year more than 10 million children in these countries die before their fifth birthday; 7 in 10 of these deaths are due to acute respiratory infections (mostly pneumonia), diarrhoea, measles, malaria or malnutrition – and often due to a combination of these conditions. Many sick children are not properly assessed or treated by health care providers, who often lack diagnostic tools, laboratory tests, or X-rays and must rely on history, signs and symptoms to determine a course of management that makes the best use of available resources. Specific interventions (such as childhood vaccinations, oral rehydration for diarrhoea, antibiotics for pneumonia, prompt treatment of malaria, improvements in breastfeeding practices) have shown great success, but an integrated approach to the management of sickness in children can achieve better outcomes.

The strategy known as Integrated Management of Childhood Illness (IMCI) stems from the needs of curative care; it also deals with nutrition, immunization and other elements of disease prevention and health promotion. The IMCI guidelines deal with children less than 5 years old – the age group that bears the highest burden of deaths from common diseases – and cover most, but not all, of the major reasons a sick child is brought to a clinic. IMCI clinical guidelines do not cover management of trauma or other emergencies due to accidents or injuries. A child with chronic problems or less common illnesses may require special care. IMCI management procedures use a limited number of essential drugs and encourage active participation of carers in the treatment of children. They must be adapted to the conditions in each country.

The IMCI clinical guidelines are based on the following principles:

- A ***limited number of carefully selected clinical signs*** can be used, based on evidence of their sensitivity and specificity, and taking into account conditions and realities of first-level health facilities.
- A combination of individual signs leads to a ***classification*** rather than to a diagnosis. The classification indicates the severity of the condition and calls for specific action(s) based on whether the child:
  - must be urgently referred to another level of care
  - requires specific treatment (such as antibiotics or antimalarial treatment), or
  - may be safely managed at home.
- As part of their assessment, all sick children must be examined for "***general danger signs***" indicating a need for immediate referral or admission to hospital.
  - for infants aged 1 week up to 2 months: diarrhoea, bacterial infection
  - for children aged 2 months up to 5 years: diarrhoea, cough or difficult breathing, fever, ear problems.
  - Children must also be routinely assessed for items such as ***nutritional/immunization status*** and ***feeding problems***.

Outpatient management of infants aged 1 week to 2 months[12]

Among sick young infants (1 week* to 2 months), some clinical signs differ from those in older children. A young infant's illness can rapidly progress to death; it is thus essential to pay attention to *possible bacterial infection* (in addition, problems attributable to noncommunicable disorders such as feeding problems or low weight and immunization status must be taken into account).

All sick young infants must be assessed first for signs of possible bacterial infection. The most informative and easiest to check signs of possible bacterial infection in sick young infants are:

- ***Convulsions*** as for older children (see below).
- ***Fast breathing:*** 60 per minute or more is the cut-off rate to identify fast breathing in this age group. The count must be repeated, because the breathing rate of a young infant is often irregular.
- ***Chest indrawing:*** Mild chest indrawing is normal in a young infant because of softness of the chest wall. Severe chest indrawing is very marked and easy to see. It is a sign of pneumonia or other serious bacterial infection in a young infant.
- ***Temperature*** (whether ***fever*** or ***hypothermia***) may equally indicate bacterial infection. Fever is uncommon in the first 2 months of life. It may indicate a serious bacterial infection, and may be the *only* sign of a serious bacterial infection. Young infants can also respond to infection by dropping their body temperature to below 35.5°C axillary (36°C rectal).
- ***Nasal flaring*** (when an infant breathes in) and ***grunting*** (when an infant breathes out) are an indication of troubled breathing and possible pneumonia, although they are not specific signs.
- ***Lethargy***, ***unconsciousness*** or ***less than normal movement*** indicate a serious condition.
- ***A bulging fontanelle*** (when an infant is not crying), ***convulsions*** (as part of the current episode), ***skin pustules***, ***umbilical redness*** or ***pus draining from the ear*** are other signs indicating possible bacterial infection.

[12] * These guidelines are not applicable to new-borns less than 1 week old, who are often sick from conditions related to labour and delivery or have conditions that require special management asphyxia, sepsis from premature ruptured membranes or other intrauterine infection, birth trauma, immature lungs, jaundice).

A sick young infant with possible ***serious bacterial infection*** must be referred urgently to the hospital after giving intramuscular benzylpenicillin (or ampicillin) plus gentamicin, treatment to prevent hypoglycemia, and advice to the mother on keeping the young infant warm. Other types such as a ***mild*** or ***localized bacterial infection*** may be treated at home with oral antibiotics and seen in follow-up within 2 days.

Outpatient management of children aged 2 months up to 5 years

The assessment procedure includes:

1. History taking and talking with the carer about the child 's problem, to avoid overlooking signs or symptoms – the understanding and motivation of the carer are key to the success of home treatment.
2. Routine checks for **general danger signs** in all children:
   - ***Convulsions or a history of convulsions during the current illness.*** This may simply be the result of fever or may be associated with meningitis, cerebral malaria or other life-threatening conditions.
   - ***Unconsciousness or lethargy.*** An unconscious or lethargic child is likely to be seriously ill. These signs may be associated with many conditions (e.g. cerebral malaria, meningitis.
   - ***Inability to drink or breastfeed,*** either because the child is too weak or because it cannot swallow for another reason (e.g. thrush).
   - ***Severe vomiting.*** This may be a sign of serious illness; it is also important because the child will not be able to take oral medication or fluids for rehydration.

If a child has ***one or more of the above danger signs***, it must be considered ***seriously ill*** and will almost always need referral to start treatment for severe illnesses without delay, after a quick assessment for the most important causes of serious illness and death – acute respiratory infection (ARI), diarrhoea, fever (especially associated with malaria and measles). At all times, a rapid assessment of nutritional status is essential.

3. After checking for **general danger signs**, the health care provider must check for **main symptoms**. The IMCI clinical guidelines suggest the following 4 symptoms:

   - **cough or difficult breathing (can be life-threatening)**
   - **diarrhoea (can be life-threatening)**
   - **fever (can be life-threatening)**
   - **ear problems (a main cause of childhood disability in low-and middle-income countries).**

Cough or **difficult breathing:**

The following 3 key clinical signs are used to assess a sick child:

1. The ***respiratory rate*** distinguishes children who have pneumonia from those who do not. Fast breathing has the best combination of sensitivity and specificity to detect pneumonia in children under 5. The point at which fast breathing is considered to be fast depends on the child 's age:

Child's age	*Cut-off point for fast breathing*
2 months to 12 months	50 breaths/minute or more
12 months to 5 years	40 breaths/minute or more

2. ***Lower chest wall indrawing***, defined as the inward movement of the bony structure of the chest wall with each inspiration, is a useful indicator of severe pneumonia. Agitation, a blocked nose or breastfeeding can all cause temporary chest indrawing, and this sign must only be taken into account if it is *consistently present in a calm child*.
3. ***Stridor*** is a harsh noise made when the child inhales (breathes ***in***). Children who have stridor when calm have a substantial risk of obstruction and must be referred.

A combination of the above clinical signs leads to the classification of children presenting with cough or difficult breathing into 3 categories:

1. ***Those who require referral*** for possible severe pneumonia (any general danger sign) or very severe disease (chest indrawing or stridor in a calm child). Such children most likely will have life-threatening invasive bacterial infections or diseases. This warrants the use of injectable antibiotics.
2. ***Those who require antibiotics as outpatients*** because they are highly likely to have bacterial pneumonia (all children with a fast respiratory rate for age – fast breathing, as defined above, detects about 80% of children with pneumonia in need of antibiotic treatment).
3. ***Those who simply have a cough or cold and do not require antibiotics***. Such children may require a safe remedy to relieve cough, and normally will improve in 1 or 2 weeks. However, a child with chronic cough (more than 30 days) needs to be further assessed/referred to exclude problems such as tuberculosis, asthma, whooping cough.

Diarrhoea

This must be routinely checked in ***every child*** brought to the clinic. A child presenting with diarrhoea must first be assessed for general danger signs and the person who cares for the child must be asked if the child has cough or difficulty in breathing. A child with diarrhoea may have 3 potentially lethal conditions:

1. Acute watery diarrhoea (including cholera)
2. Dysentery (bloody diarrhoea)
3. Persistent diarrhoea (diarrhoea lasting more than14 days).

All children with diarrhoea must be assessed for:

- Signs of dehydration
- Duration of diarrhoea.
- Presence of blood in the stool (dysentery)

Signs of dehydration in children

All children with diarrhoea must be checked for ***dehydration***.

- **Major signs of dehydration**
  - ***Child's general condition:*** Depending on the degree of dehydration, a child with diarrhoea may be
    - Lethargic or unconscious (general danger sign), **or**
    - Restless/irritable.

NOTE: Only children who cannot be consoled and calmed should be considered restless or irritable.

  - ***Thirst*** or ***child's reaction when offered to drink***. A child is said to be:
    - *Unable to drink* if it cannot take fluid in the mouth and swallow it. For example, a child may not be able to drink because it is lethargic or unconscious
    - *Drinking poorly* if it is weak and cannot drink without help or swallow (only if fluid is put in the mouth).
    - *Drinking eagerly, thirsty* if it is clear that the child wants to drink.
  - ***Elasticity of skin***. When released, the skin pinch goes back:
    - *Very slowly* (longer than 2 seconds), **or**
    - *Slowly* (skin stays up for a brief instant), **or**
    - *Immediately*.

    NOTE: In a child with marasmus (severe malnutrition), the skin may go back slowly even if the child is not dehydrated. In an overweight child, or a child with oedema, the skin may go back immediately even if the child is dehydrated.

- **Other signs** include:
  - Dryness of mouth and tongue
  - Sunken eyes. The eyes of a dehydrated child may look sunken. In a severely malnourished child who is visibly wasted (marasmus), the eyes may look sunken even if the child is not dehydrated. Even though the sign "sunken eyes " is less reliable in a visibly wasted child, it can still be used to classify the child 's dehydration.

Based on a combination of the above clinical signs, children presenting with diarrhoea are classified into the following categories:

1. Those who show 2 signs of dehydration, with at least one of the following major signs: lethargic or unconscious, unable to drink or drinking poorly, very slow return of skin, and/or one of the following: very dry mouth or very sunken eyes, are said to have ***severe dehydration*** (fluid deficit corresponding to 10% or more of body weight) and require immediate IV perfusion associated with oral rehydration.
2. Those who show 2 signs of dehydration, with at least one of the following major signs: restless or irritable, drinking eagerly, slow skin return, and/or 1 of the following: dry mouth or sunken eyes, are said to have ***some dehydration*** (5% to 10% of body weight) and require active oral treatment with ORS solution. This classification includes both "mild " and "moderate" dehydration, the descriptive terms used in most paediatric textbooks.
3. Patients with diarrhoea but no signs of dehydration are said to have ***no dehydration***; their fluid deficit is less than 5% of body weight. Although these children lack distinct signs of dehydration, they must be given more fluid than usual to prevent dehydration from developing.
   Most diarrhoeal episodes are caused by agents for which antimicrobials are not effective: antibiotics should not be used routinely for treatment of diarrhoea. Anti-diarrhoeal drugs may have dangerous side-effects; they have no place in the treatment of diarrhoea in children.

After assessment for dehydration, the person caring for a child with diarrhoea must be asked how long the child has had diarrhoea and if there is blood in the stool. This will allow identification of children with persistent diarrhoea and dysentery.

Duration of diarrhoea

Persistent diarrhoea is defined as an episode of diarrhoea, with or without blood, beginning acutely and lasting at least 14 days. It accounts for up to 15% of all diarrhoea episodes and for 30% to 50% of deaths from diarrhoea. It is usually associated with weight loss and with serious non-intestinal infections. Many children who develop persistent diarrhoea are malnourished, greatly increasing the risk of death. Persistent diarrhoea almost never occurs in exclusively breastfed infants.

Children with severe persistent diarrhoea and any degree of dehydration must not be managed at the outpatient health facility but referred to a hospital. As a rule, treatment of dehydration must be initiated first, unless there is another severe classification.

Children with persistent diarrhoea and no signs of dehydration can safely be managed as outpatients, at least initially.

Proper feeding is the most important aspect of treatment for children with persistent diarrhoea. Routine treatment of persistent diarrhoea with antimicrobials is not effective. Some children, however, have infections that require specific antimicrobial therapy. The persistent diarrhoea of such children will not improve until these infections are diagnosed and treated.

Blood in the stool

If the mother or person caring for the child reports blood in the child's stool, the child is classified as having dysentery. It is not necessary to examine the stool microscopically or perform laboratory tests to diagnose dysentery. Bloody diarrhoea in children under 5 is usually a sign of invasive enteric infection and carries a substantial risk of serious morbidity and death. About 10% of all diarrhoea episodes in children under 5 years are dysenteric and account for up to 15% of all diarrhoeal deaths. Dysentery is especially severe in infants and children who are undernourished, who develop clinically evident dehydration during their illness, or who are not breastfed. All children with dysentery (bloody diarrhoea) must be treated promptly. The sensitivity of local strains must guide the choice of antibiotics.The following table provides an indication of treatments.

Agent	Resistance		Dose (for 5 days)	
	S. dysenteriae type 1	Other *Shigella*	Adults	Children
Ampicillin	Frequent	Variable	1 gramme 4 times a day	25 mg/kg 4 times a day
TMP-SMX	Frequent	Variable	TMP 160 mg SMX 800 mg 2 times a day	TMP 5 mg/kg + SMX 25mg/kh 2 times a day
Nalidixic acid	Increasing	Uncommon	1 gramme 4 times a day	15 mg/kg 4 times a day
Pivmecillinam	Uncommon	Rare	400 mg 4 times a day	20 mg/kg 4 times a day
Ciprofloxacin	Rare	Rare	500 mg 2 times a day	15 mg/kg 2 times a day
Norfloxacin	Rare	Rare	400 mg 2 times a day	10 mg/kg 2 times a day
Enoxacin	Rare	Rare	200 mg 2 times a day	5 mg/kg 2 times a day

a Dose varies according to the weight of the child, but must never be greater than the "adult" dose

b New quinolones have not yet been approved for use in children below 12 years of age. There is growing evidence, however, that they will prove both safe and effective. They are already used by some workers to treat children with serious illness caused by strains of Sd1 resistant to all other available agents

All patients to receive supporting treatment (ORS and frequent small meals).

Fever

All sick children must be checked for ***fever*** (body temperature above 37.5°C axillary or 38°C rectal). Fever is often the main reason for bringing children to the health centre; it may be caused by minor infections, but also be the most obvious sign of a life-threatening illness, particularly malaria (especially *Plasmodium falciparum*), or other severe infections, including meningitis, typhoid fever, measles. When diagnostic capacity is limited, it is important first to identify those children who need urgent referral with appropriate pre-referral treatment (antimalarial or antibacterial).

A child presenting with fever must first be assessed for ***danger signs*** as above (cough or difficult breathing, diarrhoea and other obvious causes of fever such as ear infection or sore throat).The following must also be assessed:

- ***Stiff neck:*** a sign of meningitis, cerebral malaria or other severe febrile disease. If the child is conscious and alert, check stiffness by asking the child to bend the neck to look down, or gently bending the child's head forward – it must move freely.
- ***Risk of malaria and other endemic infections***: where routine microscopy is not available or results may be delayed, the risk of malaria transmission must be defined. The same applies where other endemic infections with public health importance for children under 5 are present (e.g. dengue haemorrhagic fever, relapsing fever). In such situations, the national health authorities normally adapt the IMCI clinical guidelines to local conditions.
- ***Duration of fever:*** most fevers due to viral illnesses cease within a few days. A fever that has been present every day for more than 5 days can mean that the child has a more severe disease such as typhoid fever.
- ***Measles:*** children with fever must be assessed for signs of current or previous measles within the last 3 months.
- ***Runny nose:*** in areas where malaria risk is low, a child with fever and a runny nose probably has a common cold and does not need an antimalarial.
- All children with fever and any general ***danger sign*** or ***stiff neck*** are classified as having **very severe febrile disease** and must be urgently referred to hospital after pre-referral treatment with antibiotics. Where *Plasmodium falciparum* malaria is present, children must also receive a pre-referral dose of an antimalarial (see malaria). Further classifications will depend on the level of malaria risk in the area.
- In a **high malaria risk area** or season, children with fever and no general danger sign or stiff neck must be classified as having malaria, for which treatment must be given
- In a **low malaria risk area** or season, children with fever (or history of fever) and no general danger sign or stiff neck are classified as having malaria and given an antimalarial provided they have :
  - No runny nose (a sign of ARI)
  - No measles
  - No other obvious cause of fever (pneumonia, sore throat, etc.).

Children *with* clinical signs of other possible infections need follow-up. If their fever lasts more than 5 days, they must be referred for further assessment of prolonged pyrexia.

- In a **no malaria risk area** or season, children with no general danger sign and no stiff neck must be assessed to distinguish possible bacterial infections, which require antibiotic treatment, from non-complicated viral infections.

All children with fever lasting more than 5 days must be referred for further assessment. Children with high fever, defined as an axillary temperature greater than 39.5°C (or rectal greater than 39°C), must be given a single dose of paracetamol to combat hyperthermia.

Ear problems

A child with an ear problem may have an ear infection. When otoscopy is not available, look for the following clinical signs:

- ***Tender swelling behind the ear.*** The most serious complication of an ear infection is a deep infection in the mastoid bone, usually with tender swelling behind one ear. In infants, this swelling may also occur above the ear. When both tenderness and swelling are present, the sign is considered positive. It must not be mistaken for swollen lymph nodes.
- ***Pain.*** In the early stages of acute otitis, a child may have ear pain, which usually causes it to become irritable and rub the ear frequently.
- ***Discharge or pus.*** When a mother reports ear discharge, check for pus drainage from the ears and find out how long the discharge has been present.

Based on the clinical signs above, the child 's condition can be classified as follows:

1. Mastoiditis, which must be referred to the hospital for treatment, after receiving a dose of antibiotic and a single dose of paracetamol for pain.
2. Acute ear infection (pain or ear discharge for less than 14 days), which must be treated for 5 days with the same first-line antibiotic as for pneumonia.
3. Chronic ear infection (over 14 days). Dry the ear by wicking. Antibiotics are not normally recommended because they are expensive and their efficacy is not proven.

Contacts and References

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REFERENCES: WHO. *Handbook IMCI IntEgrated Management of Childhood Illness.* Geneva: WHO, 2000. WHO/FCH/CAH/OO.12

http://www.who.int/child-adolescent-health

3.3 Foodborne salmonelloses

General introduction

Salmonellosis is one of the most frequently reported foodborne diseases worldwide. Each year, an estimated 5000 persons die and 325 000 are hospitalized among the 76 million cases annually reported to the US Centers for Disease Control and Prevention (CDC) in the U.S. alone. Of all cases, 96% are estimated to be caused by food. Incidence of salmonellosis per 100 000 for the year 1997 was 14 in the USA and 38 in Australia. In the European Union, estimates range from 16 cases per 100 000 (Netherlands) to 120 cases in parts of Germany.

Causal agents and main modes of transmission

- **Causal agents:** Over 2000 salmonella serovars are known to cause illness in humans
  - **Main modes of transmission:** A wide range of foods has been implicated in foodborne illness due to *Salmonella*; poultry is a principal source. Raw meats, poultry, eggs, milk and dairy products, fish, fresh produce (e.g. raw sprout), and unpasteurized juices are associated with foodborne salmonelloses. *Salmonella* serovars are found in the intestinal tract and faeces of animals; while *Salmonella enteritidis* is also found in the inside of raw shell eggs. In the case of raw sprout, the seeds may be contaminated by animal faeces. In the case of unpasteurized juice, fruits such as oranges and apples may have been contaminated by animal faeces during growing and harvesting.

Clinical description and case definition

- **Clinical case definition**
  The clinical case definition varies with the specific disease.
  Laboratory criteria for confirmation
  Isolation of pathogen.
  Case classification
  - ***Suspected:*** A case that meets the clinical case definition of a specific foodborne disease.
  - ***Probable:*** Not applicable.
  - ***Confirmed:*** A suspected case in whom laboratory investigation confirms the presence of one or more foodborne pathogens in a clinical specimen.

Recommended interventions

- **Case management**
  Rehydration and electrolyte replacement.
  Antibiotherapy may lead to carrier state or even aggravate the infection. Its use must be restricted to patients with extra-intestinal complications, infants under 2 months, the elderly, or persons with sickle-cell disease or HIV infection.
- **Prevention**
  See *Food safety* (page 28)
  The development of food safety systems for the reduction of health risk that apply along the entire food chain, from the primary producer to the consumer, is highly recommended. For selecting risk management strategies, outputs from microbiological risk assessment are desirable although the technique of microbiological risk assessment has only recently been developed. The first international risk assessment on *Salmonella* spp. in eggs and broilers by the Joint WHO/FAO activity will be published in 2002.
  Establish a Salmonella control programme in cooperation with animal health authorities.
- **Epidemics**
  Identify the source and implement control measures.
- **Drug resistance monitoring**
  Antibiotic resistance is common and must be monitored in cooperation with animal health authorities.

Other aspects

- **Procurement of equipment and drugs**
  Rehydration equipment and supplies
- **Surveillance**
  Parallel systems of surveillance may be used, depending on specific surveillance objectives:
  - Routine immediate reporting of case-based data on suspected cases from the peripheral level to the intermediate level (notifications). Routine weekly reporting of aggregated data on suspected and confirmed cases from the peripheral to intermediate and central levels.
  - Routine weekly case-based or aggregated reporting from laboratories on confirmed cases to intermediate and central levels.
  - Sentinel surveillance (through reporting physicians or laboratories).*
  - Community studies.
  - All outbreaks must be investigated and notified to the intermediate and central level.

  * Sentinel surveillance or community studies can provide detailed epidemiological and microbiological information, and may give a better picture of the true incidence and impact of disease in a defined population, but are likely to miss outbreaks and thus do not necessarily represent a valid approach to outbreak detection.
- **Special considerations/other interventions**
  Human surveillance must be linked with the food safety and control authorities.
  Some diseases (e.g. salmonellosis) have a specific surveillance system that requires reference laboratories for detailed serotyping.

Contacts and References

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