

SECOND EDITION



Managing epidemics

Key facts about major deadly diseases



World Health
Organization

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Managing epidemics: key facts about major deadly diseases, second edition

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Foreword

“Everybody knows that pestilences have a way of recurring in the world... There have been as many plagues as wars in history, yet always plagues and wars take people equally by surprise.”

Those words were written by the French writer Albert Camus in his classic novel *La Peste* – *The Plague* – in 1947. Seventy-six years later, they have a disturbing prescience.

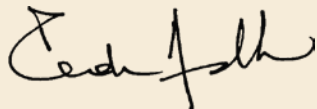
Outbreaks, epidemics and pandemics are a fact of nature, and a recurring feature of recorded history, from the Plague of Athens in 430 BCE, to the Black Death from 1346—1353, the 1918 influenza pandemic and now COVID-19.

But that does not mean we are helpless to prevent them, prepare for them or mitigate their impact. We are not prisoners of fate or nature. Viruses move fast, but data and knowledge can move even faster. With the right information, countries and communities can stay ahead of emerging risks and save lives. More than any humans in history, we have the ability to anticipate pandemics, to prepare for them, to unravel the genetics of pathogens, to detect them at their earliest stages, to prevent them spiralling into global disasters and to respond when they do.

This handbook is a valuable tool to help countries make progress in preparing for, detecting and responding to epidemics and pandemics. It offers expert guidance to help WHO country representatives and others to respond quickly in the earliest stages of an outbreak. The handbook describes in clear terms how to work together to prepare for and respond to epidemics, making the complexity of pandemics and epidemics more intelligible. People from different backgrounds can also find in this handbook common goals and clear united actions to take against infectious hazards.

COVID-19 will not be the last pandemic. We cannot predict when the next one will be, or which virus will cause it. But we can take the steps now, learning the lessons this pandemic has taught us, to ensure that when it arrives, we are all more ready than we were this time.

Future generations will judge us not by the crises we faced, but on how we reacted to them and the actions we took to prevent and prepare for the challenges of the future.



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Abbreviations

ACT Accelerator	Access to COVID-19 Tools Accelerator	DEET	N,N-diethyl-meta-toluamide	GMO	Genetically modified organisms
AFP	Acute flaccid paralysis	DENV	Dengue virus	GMMO	Genetically modified microorganisms
Ag-RDT	Antigen detection rapid diagnostic tests	EBOD	Ebola disease	GPEI	Global Polio Eradication Initiative
ARI	Acute respiratory infection	ECHO	European Community Humanitarian Office	GPLN	Global Polio Laboratory Network
AWD	Acute watery diarrhoea	EDTA	ethylenediaminetetraacetic acid	GTFCC	Global Task Force on Cholera Control
BI	Breteau Index	ELISA	Enzyme-linked immunosorbent assay	HACCP	Hazard analysis critical control point
bOPV	Bivalent oral polio vaccine	EIA	Enzyme immunoassays	HAI	Hemagglutination Inhibition Test
BSL	Biosafety level	EMO	Emergency Operations	HEPR	Health emergency preparedness, response and resilience
BVD	Bundibugyo virus disease (Ebola)	EOC-NET	Emergency Operations Centre Network	HIM	Health Emergency Information & Risk Assessment
CCHF	Crimean-Congo haemorrhagic fever	EPI	Expanded Programme on Immunization	HIV	Human immunodeficiency virus
CDC	United States Centres for Disease Control and Prevention	ERC	Emergency risk communication	HP	Highly pathogenic
CEPI	Coalition for Epidemic Preparedness Innovations	ERC	Ethics Review Committee	ICG	International Coordinating Group
CFE	Contingency Fund for Emergency	ERF	Emergency Response Framework	IER	Information Evidence and Research
CFR	Case fatality ratio	ETEC	Enterotoxigenic Escherichia coli	IFA	Immunofluorescence assays
CHIKV	Chikungunya virus	EVD	Ebola virus disease	IFRC	International Federation of the Red Cross and Red Crescent Societies
CNS	Central nervous system	EYE	Eliminate Yellow Fever Epidemics strategy	IHC	Immunohistochemistry
CPI	Country Health Emergency Preparedness & IHR	FAO	Food and Agriculture Organization of the United Nations	IHR	International Health Regulations
CSF	Cerebrospinal fluid	GISRS	Global Influenza Surveillance and Response System	ILI	Influenza-like illness
CTC	Cholera treatment centre	GLEAN	Global Leptospirosis Environment Action Network	IMD	Invasive meningococcal disease
cVDPVs	Circulating vaccine-derived polioviruses			IMS	Incident Management System
				IPC	Infection prevention and control
				IPV	Inactivated polio vaccine

IVM	Integrated vector management
JEE	Joint External Evaluation
LAMP	Loop-mediated isothermal amplification
LP	Low pathogenic
LMICS	Low- and middle- income countries
M&E	Monitoring and evaluation
MAT	Microscopic agglutination test
MERS	Middle East respiratory syndrome
MERS-CoV	MERS coronavirus
MOOCs	Massive open online courses
Mpox	Previously known as monkeypox
mRNA	Messenger RNA
MSF	Médecins sans Frontières
MVD	Marburg Virus Disease
NAAT	Nucleic Acid Amplification Tests
NAT	Nucleic acid tests
NICs	National Influenza Centres
NSAID	Nonsteroidal anti-inflammatory drug
NTD	Control of Neglected Tropical Diseases
OCV	Oral cholera vaccine
OIE	World Organization for Animal Health
OPV	Oral polio vaccine
ORP	Oral rehydration points

ORS	Oral rehydration solution
PCR	Polymerase chain reaction
PEPV	Post-exposure vaccination
PHEIC	Public health emergency of international concern
PHSM	Public health and social measures
PIP	Pandemic Influenza Preparedness Framework
PISA	Pandemic Influenza Severity Assessment
POL	Polio Eradication
PPE	Personal protective equipment
PPV	Primary preventive vaccination
PRNT	Plaque reduction neutralization test
R&D	Research and development
RCCE	Risk communication and community engagement
RDT	Rapid diagnostic tests
RIDT	Rapid influenza diagnostic tests
RNA	Ribonucleic acid
RT-PCR	Reverse transcription polymerase chain reaction
RVF	Rift Valley Fever
SAGE	Strategic Advisory Group of Experts on Immunization
SARI	Severe acute respiratory infections
SARS	Severe acute respiratory syndrome
SOCO	Single overriding communications objective
SOPs	Standard operating procedures
SPRP	Strategic Preparedness and Response Plan

SUDV	Sudan virus (Ebola)
SVD	Sudan virus disease (Ebola)
TAG-CO-VAC	Technical Advisory Group on COVID-19 Vaccine Composition
TAG-VE	Technical Advisory Group on SARS-CoV-2 Virus Evolution
TDR	Special Programme for Research and Training in Tropical Diseases
tOPV	Trivalent oral polio vaccine
UN	United Nations
UNCETDG	Committee of Experts on the Transport of Dangerous Goods
UNICEF	United Nations Children's Fund
VBD	Vector-borne diseases
VDPV	Vaccine-derived polioviruses
VOC	Variants of Concern
VOI	Variants of Interest
VRF	Viral haemorrhagic fever
WASH	Water, sanitation, hygiene
WCO	WHO Country office
WHA	World Health Assembly
WHO	World Health Organization
WHO MOOCs	WHO Massive Open Online Courses
WPV	Wild polioviruses
WRs	Country representatives
YF	Yellow fever
YFV	Yellow fever virus
ZIKV	Zika virus

About this handbook

Handbook purpose

Epidemics and pandemics of infectious diseases are occurring more often, and spreading faster and further than ever, in many different regions of the world. The background factors of this threat are biological, environmental and lifestyle changes, among others.

A potentially fatal combination of newly-discovered diseases, and the re-emergence of many long-established ones, demands urgent responses in all countries. Planning and preparation for epidemic prevention and control are essential.

The purpose of this Managing epidemics handbook is to provide expert guidance on those responses.

Although this publication is open to a wide readership, it is primarily intended to help World Health Organization (WHO) country representatives (WRs) to respond effectively and rapidly at the very start of an outbreak.

The handbook provides concise and basic up-to-date knowledge with which WRs can advise Ministries of Health in all countries. Specifically, it examines and explains in detail a total of 19 different infectious diseases and the necessary responses to each and every one of them.

These diseases have been selected because they represent potential international threats for which immediate responses are critical. Nearly all of them are subject to WHO's International Health Regulations (2005), hereafter IHR (2005), monitoring and are part of the Global Health Security Agenda.

The COVID-19 pandemic has re-enforced the importance of expert guided responses to contain and manage outbreaks of diseases both known and unknown. The handbook outlines this and other infectious disease threats, which pose an ongoing, unpredictable and inevitable risk to health and well-being.

The handbook focuses on practical and indispensable things to know about infectious diseases that are most important for national, political and operational decision-makers; it also links readers to more exhaustive WHO guidance. It has been developed in parallel with the creation of the WHO Massive Open Online Courses (MOOCs) on OpenWHO (<https://openwho.org>).

Handbook structure

The handbook is structured in three parts.

- **Part I: Epidemics of the 21st century** provides vital insights on the main features of the 21st century upsurge and the indispensable elements to manage them.
- **Part II: Be in the know—10 key facts about 19 deadly diseases** contains key information about 19 diseases (Ebola, Lassa fever, Crimean-Congo haemorrhagic fever (CCHF), yellow fever, Zika, chikungunya, dengue, malaria, animal influenza, seasonal influenza, pandemic influenza, Middle East Respiratory Syndrome (MERS), COVID-19, cholera, Mpox, plague, leptospirosis, meningococcal meningitis and poliomyelitis). This section provides tips on the interventions required to respond to epidemics of all these diseases.
- **Part III: Tool boxes** gives an overview and summarized guidance on some other important topics, including the role of WHO, the International Coordinating Group, tables for laboratory diagnosis collection, storage, packing and shipment of infectious substances, vector control, as well as vaccine development and types.

What's new in the second edition?

- ✓ **Part I of the handbook has been significantly updated** since the first edition published in 2018, with new information based on knowledge gained throughout the COVID-19 pandemic and Mpox global outbreak.
- ✓ **Response tips and checklists section** now aligns with the WHO Director-General's proposal on the global architecture for health emergencies set out in May 2022 at the 75th World Health Assembly and as per WHA Resolution 74.1 as well as the WHA Report 76/10.
- ✓ **New Focus sections** offer information on infodemic management, managing ethical issues and public health and social measures during epidemics and pandemics.
- ✓ **The content of disease-specific chapters has been updated**, including the addition of four new disease-specific chapters on dengue, malaria, COVID-19 and poliomyelitis.
- ✓ **Maps, tables and figures have been updated** based on latest statistics.
- ✓ **Tool boxes have been updated and a tool box has been added** that describes different types of vaccines.
- ✓ **A list of abbreviations has been added** to the start of the handbook for easy reference.

The handbook enables the three levels of WHO – its Headquarters, Regional Offices and Country Offices – to work efficiently together by building the foundations of a shared conceptual framework, which includes common terminology.

PART I

Epidemics of the 21st century

The re-emergence of infectious diseases



The threat continues

We are continuously learning about the unpredictable powers of nature. This is nowhere more true than in the continuous evolution of new infectious threats to human health that emerge – often without warning – from the natural environment.

The world continues to be sharply reminded time after time of the degree to which people in all countries, and on all continents, remain chronically vulnerable to infectious diseases, known and unknown.

In the 1970s, and for years afterwards, remarkable progress, including the development of new vaccines, antibiotics and other treatments and technologies, led mankind to proclaim victory over microbes. Many experts thought it was “the time to close the book on the problem of infectious diseases” (Jesse Steinfeld, MD, United States Surgeon General, 1969).

Here lay the roots of a dangerous complacency. The microbes didn’t go away. They just went out of sight. Instead, the focus turned to chronic, noncommunicable diseases, which came to receive much more attention. But nature was by no means in retreat. In fact, it seemed to return and took many health institutions and decision-makers by surprise.

Since 1970, more than 1,500 new pathogens were discovered, of which 70% proved to be of animal origin: a connection that deserves renewed scrutiny. Not all of them have had a public health impact but some of them have become famous. They included the Ebola virus in 1976 and more recently COVID-19.

Pause for a moment and reflect that HIV, a relatively new disease in human history, has infected about 70 million people in just 35 years, and killed an estimated 35 million people in the same period. Consider also, that over the last 45 years, Ebola has surfaced in many separate and deadly outbreaks, which often occur after long spells without reported cases. COVID-19, caused by a novel coronavirus, infected nearly 200 million people and killed over 4 million in the first 18 months since its emergence.

Even though the COVID-19 pandemic continues, we must ask the question: will this happen again?

The answer must be: Yes, it will. A new HIV, a new coronavirus, a new Ebola, a new plague, a new influenza pandemic are not mere probabilities. Whether transmitted by mosquitoes, other insects, contact with animals or person-to-person, the only major uncertainty is when they, or something equally lethal, will again arrive.

The obvious follow-up question is: so what are we doing about it? This purpose of this handbook is to provide as many answers as possible. In doing so it examines a range of challenges and real or potential solutions, ranging from the medical and technological to the social and political.



The 21st century: already a long list of infectious threats

To see the road ahead more clearly, we need to look over our shoulders – all the more so, because these early years of the 21st century have already been deeply scarred by so many major epidemics.

Take plague, one of the most ancient infectious threats. A thing of the past? By no means. A major outbreak in Madagascar in 2017 led to a total of at least 2,417 confirmed, probable and suspected cases, including 209 deaths. Most cases were of the more fatal pneumonic type, which is also transmissible from person to person, but there were also several hundred cases of bubonic plague. Nine countries and territories with trade and travel links to Madagascar were put on plague preparedness alert.

The lesson here is that, over time, diseases very rarely disappear. And there always seems to be room for new ones. Severe acute respiratory syndrome (SARS) was unheard of before 2003. But it affected more than 8,000 people, killing about one in ten of them, causing fear and panic across the world, and inflicting enormous economic damage, especially in Asian countries.

In 2009, a novel influenza virus, H1N1, started to spread, creating the first influenza pandemic of the 21st century. But – and this is a reason for cautious hope – it was not as severe as expected thanks to recent preparedness efforts. The importance of these efforts is a core issue in this handbook.

In 2012–2013, a new virus surfaced in the Middle East, causing an epidemic of what became Middle East respiratory syndrome (MERS) that spread fatally into many countries beyond that region.

The Ebola epidemic in West Africa (Guinea, Liberia and Sierra Leone) in 2014 was unlike the previous 24 localized outbreaks observed since 1976. Instead of being restricted geographically, this one seriously affected three African countries and spread to six other countries in three continents and sparked alarm worldwide.

In 2015, the Zika virus, transmitted by the *Aedes aegypti* mosquito, triggered a wave of microcephaly in Brazil. This disease causes dreadful damage in the brains of unborn babies. Almost 70 countries, one after another, then experienced their own Zika epidemic. There are probably many more to come, because most of the global intertropical zone has a high density of *Ae. aegypti* that transports the disease.

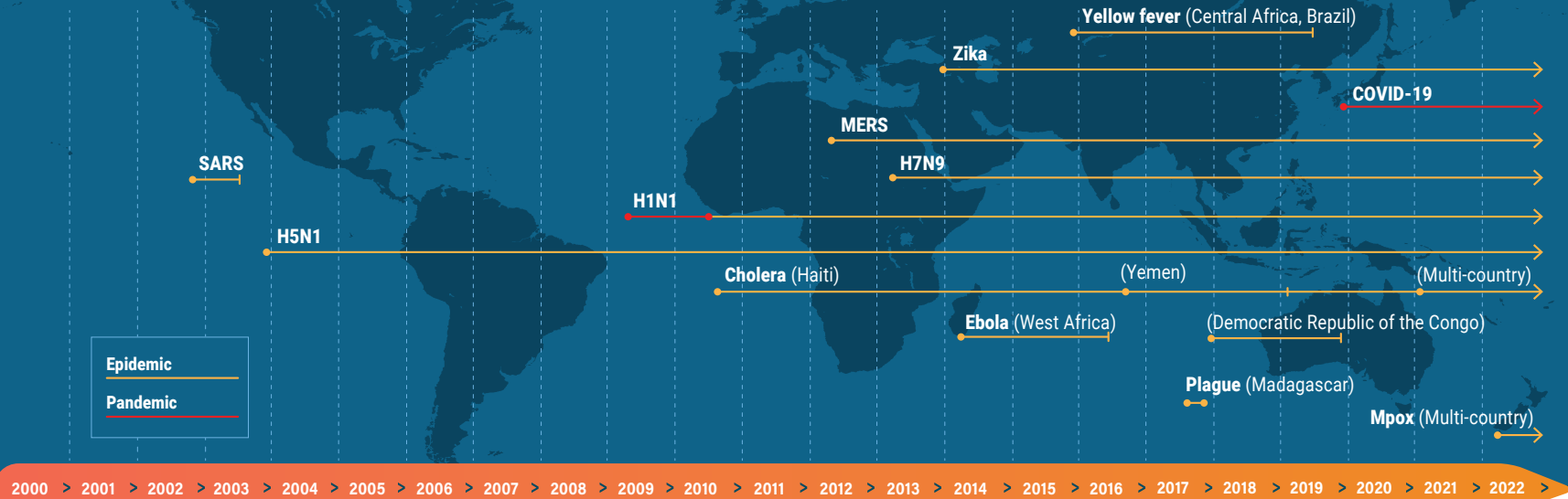
And of course, in 2019 a novel coronavirus of as-yet unknown origin emerged. First reported in Wuhan, China in late December 2019, COVID-19 spread at an unprecedented pace. Two months later, by March 2020, over 87 000 cases had been reported across 59 countries and its spread had been characterized as a pandemic.

We see a clear pattern taking shape. Old diseases – cholera, plague, yellow fever among them – often return, and new ones invariably arrive to join them (See Table on page 29).

Timeline

Major infectious threats in the 21st century & associated collaboration mechanisms

MAJOR EPIDEMIC AND PANDEMIC THREATS



INTERNATIONAL COLLABORATION EFFORTS TO FIGHT EPIDEMIC AND PANDEMIC THREATS

Gavi
Gavi, the Vaccine Alliance, is an international organization that was created in 2000 to improve access to new and underused vaccines for children living in the world's poorest countries.

GOARN
The Global Outbreak Alert and Response Network is a technical collaboration of existing institutions and networks who pool human and technical resources for the rapid identification, confirmation and response to outbreaks of international importance.

IHR (2005)
The International Health Regulations (2005) are an international law which helps countries work together to save lives and livelihoods caused by the international spread of diseases and other health risks. The IHR (2005) aim to prevent, protect against, control and respond to the international spread of disease while avoiding unnecessary interference with international traffic and trade.

IHR Review
PIP Framework
The Pandemic Influenza Preparedness (PIP) Framework brings together Member States, industry, other stakeholders and WHO to implement a global approach to pandemic influenza preparedness and response.

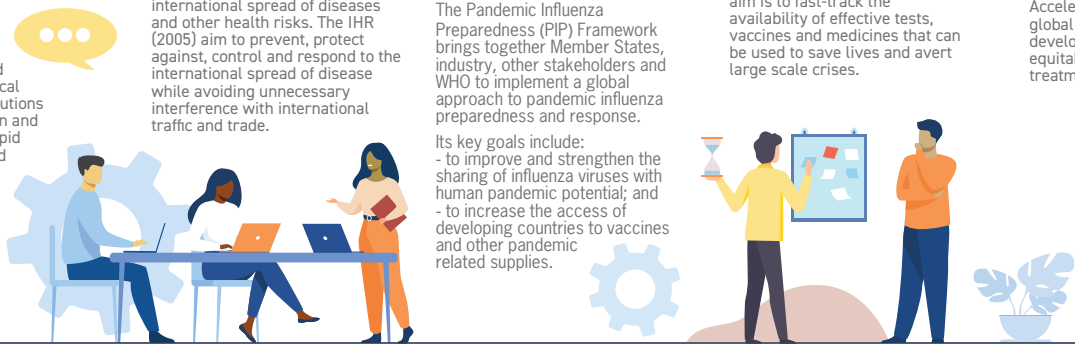
Its key goals include:
- to improve and strengthen the sharing of influenza viruses with human pandemic potential; and
- to increase the access of developing countries to vaccines and other pandemic related supplies.

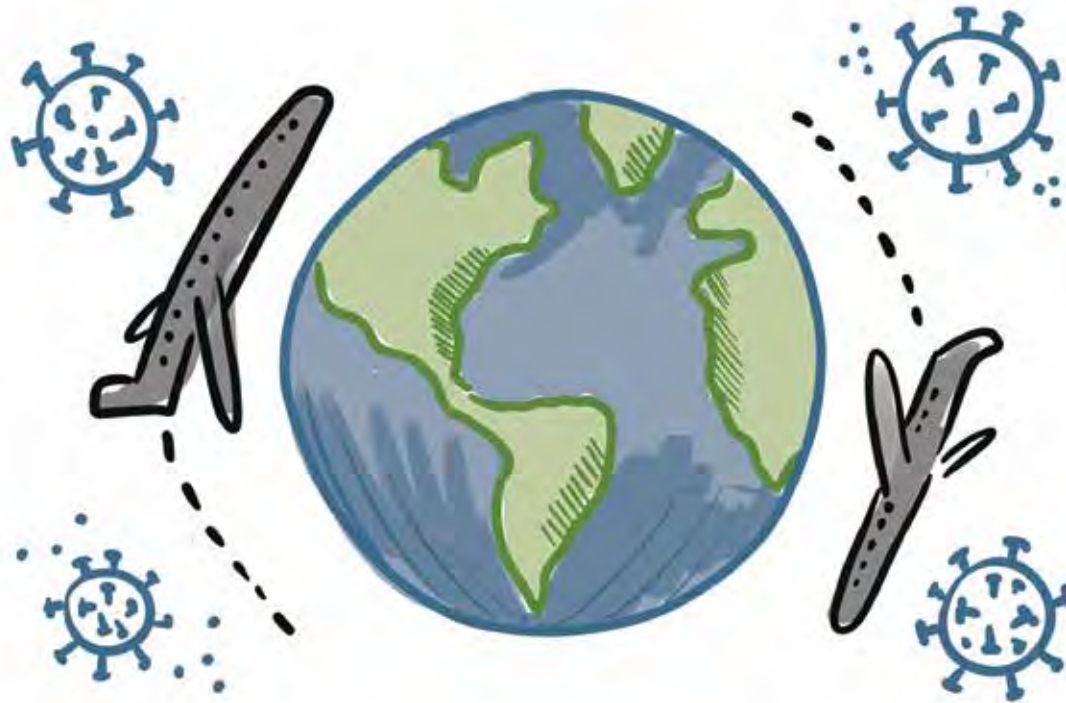
R&D Blueprint
R&D Blueprint is a global strategy and preparedness plan that allows the rapid activation of research and development activities during epidemics. Its aim is to fast-track the availability of effective tests, vaccines and medicines that can be used to save lives and avert large scale crises.

PIP Review
IHR Review
ACT Accelerator
Access to COVID-19 Tools (ACT) Accelerator, is a groundbreaking global collaboration to accelerate development, production, and equitable access to COVID-19 tests, treatments and vaccines.

INB
In December 2021, Member States established an intergovernmental negotiating body (INB), representing all regions of the world, to draft and negotiate a WHO convention, agreement, or other international instrument on pandemic prevention, preparedness and response.

Last updated: January 2023





Faster and further with a greater impact

This pattern has another, deeply troubling aspect. The epidemics in the 21st century are spreading faster and further than ever. Outbreaks that were previously localized can now become global very rapidly – just as fast, in fact, as an intercontinental aircraft can fly. Thus, an individual flying from one side of the world can introduce a new disease into the other, within hours, and before even showing symptoms. And in this way, far from its origins, the microbe finds a new home.

For example, the influenza pandemic of 2009 reached all continents in less than nine weeks. In recent outbreaks, yellow fever made it all the way from Angola to China, but, fortunately, there were only imported cases with no sustainable circulation in the mosquito population.

In 2015, it took just one traveller returning home to the Republic of Korea after spending time in the Middle East to bring MERS back. The consequences: 186 cases, 36 deaths and outbreak-related losses of approximately US\$ 8 billion, all in the space of two months.

COVID-19 follows a similar and amplified trajectory. Within a few months of its emergence, nearly all nations and territories had reported cases. In many, the virus became widespread in communities despite public health and social measures (PHSM). The result – a complex emergency with profound impacts on lives and livelihoods globally and trillions of economic losses.

Thus, 21st century epidemics can spread more widely and more quickly, potentially affecting ever-greater numbers of people. They also can have a ruinous impact on the economy of the affected country and spill over into the global economy, disrupting travel, trade and livelihoods.

Ready and able to detect the next outbreak

As the world grapples with the impact of COVID-19, we must not be complacent. The next threat is on the horizon. Given the effects of globalization, intense mobility of human populations, and relentless urbanization, it is likely that the next emerging virus will also spread fast and far. It is impossible to predict the nature of this virus or its source, or where it will start spreading.

But we can say, with a high degree of certainty, that when it comes there will be a) an initial delay in recognizing it; b) a serious impact on travel and trade and; c) a public reaction that includes anxiety, or even panic and confusion, that could be amplified by an infodemic.

The concept of global health security, a central issue in this handbook, represents a new determination by, or on behalf of, human society to protect itself from the health impact and social disruption caused by outbreaks. It encompasses a spectrum of ways and means that offer worldwide protection against the threats of infectious diseases, backed by revised and more powerful IHR (2005).

But to make the world safer, global health security depends crucially on much greater awareness, cooperation and collaboration between individual countries, agencies, organizations and communities. The continuing scientific uncertainty around disease emergence requires even more collaboration and global awareness than has previously existed, not least to improve early detection.

Recent outbreaks, however, show how difficult this can be, even with good public health surveillance systems. Early recognition of emergence typically starts with clinicians who can detect unusual clusters of severe cases, take samples to allow laboratory diagnostics and alert surveillance units.

Often, poorer communities around the world, especially those in remote areas, lack easy access to care. This has major implications when an infectious threat occurs. The Ebola outbreak in West Africa remained undiagnosed for more than two months. This time lag allowed the virus to spread unseen and to reach capital cities where the outbreaks grew into large epidemics. In such circumstances, it is essential to raise clinicians' awareness and provide them with the relevant knowledge and diagnostic tools to enable them to perform effectively as detectors and first-line responders and protect them with personal protective equipment (PPE).

As we have signalled earlier, another indispensable element of increasing health security is preparedness. This should be flexible enough to adapt to any novel agent but should be directed primarily at known pathogens because some of them are likely to behave differently than previously. The recent plague outbreak in Madagascar, described earlier, is a good example of known diseases with new patterns.

In addition, the fear generated by the emergence of a previously unknown infection may be greatly out of proportion to its real public health impact. Fear often generates inadequate decisions or inappropriate behaviours, including stigma of certain at-risk populations. The impact on travel and trade and on economies can be disproportionate, as was seen in the Republic of Korea during the MERS epidemic. To a certain extent, global health security also encompasses economic and human security. Thus, risk communication is critical to minimize the social, political and subsequently economic impact of an epidemic, and this is also a major focus of this publication.





One Health and emerging and re-emerging pathogens

Epidemics are sparked either by the re-emergence of pathogens that have been familiar for a long time, but now threaten new, immunologically vulnerable populations, or are newly emerging ones. They come in a daunting array of species of bacteria, viruses, fungi and parasites. Some are borne in contaminated water or food, others are carried in the air we breathe and by human touch.

As noted earlier, 70% of emerging human pathogens come from animals. This is a burgeoning threat, because animals are intensively farmed, transported for trade and kept in close contact with other species and humans in marketplaces.

Early detection often relies on close collaboration between human health, animal health and wildlife sectors (the One Health approach); otherwise, early signals of emergence in animals or the environment are often missed. This collaborative approach, another pivotal element of global health security, can also contain outbreaks at an early stage by reducing animal-to-human transmission.

Because these diseases are rare and outbreaks are generally contained quickly, these epidemics have not been a priority among the research community or manufacturers in the development of medical countermeasures. Nevertheless, more research is needed to precisely identify the modes of transmission and medical countermeasures.

Today's harsh reality is, that there is as yet no vaccine or treatment for most emerging diseases. This is not as hopeless as it might seem at first. WHO has developed a Research & Development (R&D) Blueprint for action to prevent epidemics: it is a global strategy and preparedness plan that allows the rapid activation of R&D activities during epidemics. Its aim is to fast-track the availability of effective tests, vaccines and medicines that can be used to save lives and avert large scale crisis. We have seen evidence of these mechanisms in the rapid development of vaccines to counter COVID-19, with multiple vaccines entering Phase III clinical trials in less than a year since the identification of the virus. However, outbreak responses have to rely primarily on PHSM to reduce human transmission, and on controlling the source of infection (for instance by culling of infected animals/elimination of the reservoir). Thus, to prevent the spread of emerging diseases, it is vitally important to ensure early detection of a new pathogen and the start of human-to-human transmission.

Enhanced international information and virus sharing among laboratories is being actively encouraged and pursued. This is necessary to enable research and development of countermeasures. The results of this sharing are potentially life-saving interventions (vaccines, diagnostics and therapeutics). But they also need to be underpinned by specific mechanisms to ensure they become widely available and accessible on an equitable basis.

Overall, there is a need for greater collaborative efforts towards preparedness and early response against infectious hazards. The Pandemic Influenza Preparedness (PIP) Framework brings together Member States, industry, other stakeholders and WHO to implement a global approach to pandemic influenza preparedness and response. Efforts in the first ten years of the PIP Framework include strengthening global laboratory surveillance networks through the Global Influenza Surveillance and Response System (GISRS), the creation of data sharing and reporting platforms such as FluNet, the certification of 11 new National Influenza Centres (NICs), over 5 million enrollees in the OpenWHO training platform, amongst other achievements.

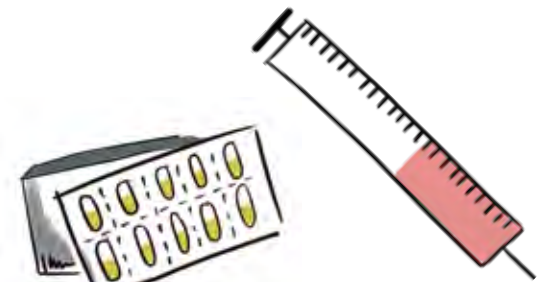
In April 2020, in response to the COVID-19 pandemic, WHO and partners including governments, scientists, businesses, civil society, philanthropists and global health organizations launched the Access to COVID-19 Tools (ACT) Accelerator. Involved organizations included the Bill & Melinda Gates Foundation, the Coalition for Epidemic Preparedness Innovations (CEPI), FIND (the global alliance for diagnostics), Gavi The Vaccine Alliance, The Global Fund, Unitaid, Wellcome, the World Bank and WHO. This initiative aimed to support a rapid and coordinated global effort to accelerate development, production and equitable access to COVID-19 tests, treatments and vaccines. COVAX is the vaccines pillar of the ACT-Accelerator. Co-led by Gavi The Vaccine Alliance, CEPI and WHO, it aims to accelerate the development and manufacture of COVID-19 vaccines, and to guarantee fair and equitable access for every country in the world.

Known epidemics: still a severe threat

Fortunately, control programmes are already widely applied for some known epidemic diseases, such as cholera, HIV infection, influenza, meningitis, malaria, tuberculosis and yellow fever.

However, even if medical countermeasures are available, these diseases remain a threat for many of the world's populations, either because of their rapidly evolving nature (for example influenza) or because equitable access to effective medical countermeasures is difficult. There are many reasons for limited access to vaccines: production capacity does not meet the demand (for example yellow fever and pandemic influenza); explosive outbreaks exhaust the available vaccines (for example meningitis); the absence of markets prevents access to the intervention in case of emergencies (for example the oral cholera vaccine); or global inequities in purchasing power and manufacturing capacity, coupled with patent protection and limited technology transfer. In addition, in many affected countries, the weakness of the existing health care system prevents effective access to medical interventions (such as diagnostics and treatment).

Therefore, although it is reassuring that sound knowledge and a range of potential control interventions are available, expert guidance must be constantly updated to incorporate scientific and technological progress. Equally important, access to life-saving interventions must be improved in all settings worldwide.



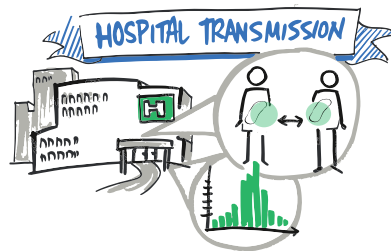
Strengthening health systems: essential in epidemics

Strong health systems are needed to mitigate the impact of epidemics, protect the health workforce and ensure continuity of health services during and after. Epidemics and pandemics put health systems under great pressure and stress. The sudden influx of large numbers of sick individuals to health facilities stretches the systems' capacity and resources, even more so, and more noticeably where resources are already scarce.

When an epidemic emerges and spreads, it inevitably draws most of health responders' attention and monopolizes most of the health system's human and financial resources, as well as medical products and technologies. Indeed, COVID-19 has seen ongoing shortages and inequitable distribution of these products and technologies. For example, shortages of PPE necessary to safely provide care during the COVID-19 pandemic.

People, efforts and medical supplies all shift to respond to the emergency. This often leads to the neglect of basic and regular essential health services. People with health problems unrelated to the epidemic find it harder to access health care services. Some may die as a result of disruptions that overwhelm health systems. Mortality rates of other diseases for which people could not get treatment may rise. For example, during COVID-19 as health systems were stretched beyond their capacities, we saw interruptions to essential health services and inequitable access to alternative forms of service delivery, such as telemedicine.

Furthermore, health care settings, and especially emergency rooms, can become hubs of infectious disease transmission during epidemics. Many people can get infected there if prevention and control measures are not properly implemented. This is particularly true for unknown and emerging pathogens (for instance MERS). A delay in the recognition of the disease will lead to delay in applying the right protection measures. Infected patients will be able to transmit the disease because health care workers, family members and other patients will not know how to protect themselves. Because health care settings and emergency rooms are usually crowded, the lack of appropriate infection prevention and control (IPC), for example through triage, isolation and other precautions, can have significant impacts. For example, during the COVID-19 pandemic there were reports of people delaying care seeking at hospitals or other health facilities for fear of being exposed to the virus.

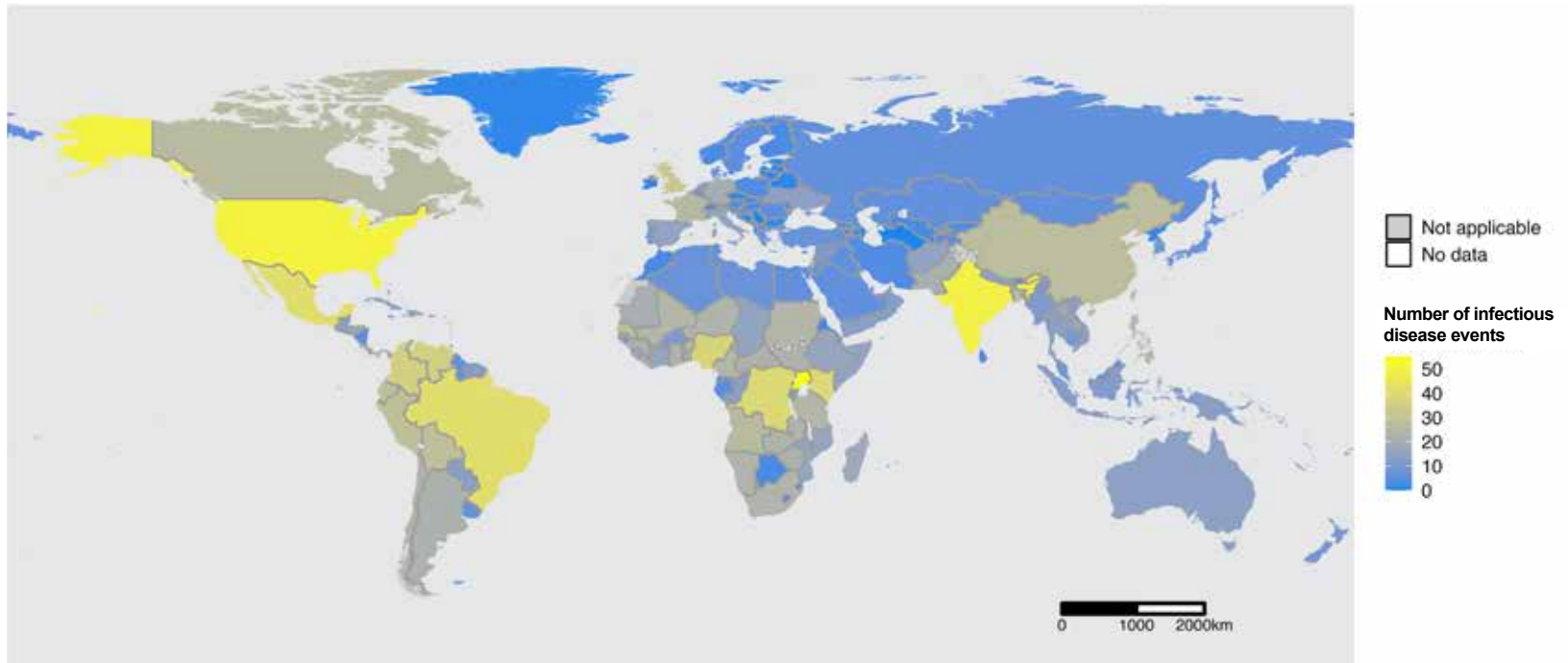


Health systems resilience after epidemics may be challenging for unprepared health systems. Indeed, if the health system is ill-prepared to cope with infectious disease epidemics, health workers at the frontline of the response may themselves become infected and die. Tragic as such cases are, they have wider consequences. In countries that have health worker shortages, the loss of several health workers further weakens the health system. It takes years to train new medical staff and rebuild the health workforce. In the meantime, other constraints burden the health system, which still must provide regular services.

Long-term substantial investments should therefore be made to strengthen health systems so that they are able to provide safe, effective and high-quality health services before, during and after epidemics. Critical elements include an appropriate health financing system and a fit-for-purpose workforce that is trained, safe and provided with PPE. In addition, access to essential medical products and technologies and a business continuity plan are critical to ensure that health systems are strong enough to withstand the increased needs and to mitigate the impacts of very disruptive epidemics.

Reported epidemics

Acute infectious disease events reported to WHO (2011–2021)



Source: World Health Organization
Map production: WHO Health Emergencies Programme
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Acute public health events* for selected infectious diseases (2011–2021)

												TOTAL
Avian/Animal influenza	5	2	1	3		5	5	3	2	5	16	47
Chikungunya	1	3	4	24		5	3	3	2		1	46
Cholera	24	24	11	1	19	16	14	23	19	4	12	167
Crimean-Congo haemorrhagic fever	1		3		4	2	8	4	8	3	3	36
Dengue	8	10	7	6	7	5	12	13	16	4	10	98
Ebola virus disease	1	3		3				2	2		1	12
Lassa fever	2	1	2	1	2	2	7	3	6	1	4	31
Malaria	2	2			3	3	11	4	8	3	7	43
Marburg virus disease				1			2				1	4
Measles	19		7	11	13	7	15	25	15	3	5	120
Meningococcal disease/Meningitis	11	11	3	4	4	8	10	7	2	2	2	64
MERS		3	5	9	2	1	1	5	4	1	2	33
Nipah virus	1		1					1	2	1	1	7
Poliomyelitis	10	1	4	3	2	2	3	13	16	6	16	76
Rift Valley fever	2				2	3	3	3	3	1	2	19
Yellow fever	2	3	3		1	5	1	5	2	6	3	31
Zika				2	15	63	5	3	1		2	91
	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	

* A public health event is an outbreak of a disease reported to WHO. One event may consist of one or several case reports or clusters. Time and space linked reports are merged and counted as one event.

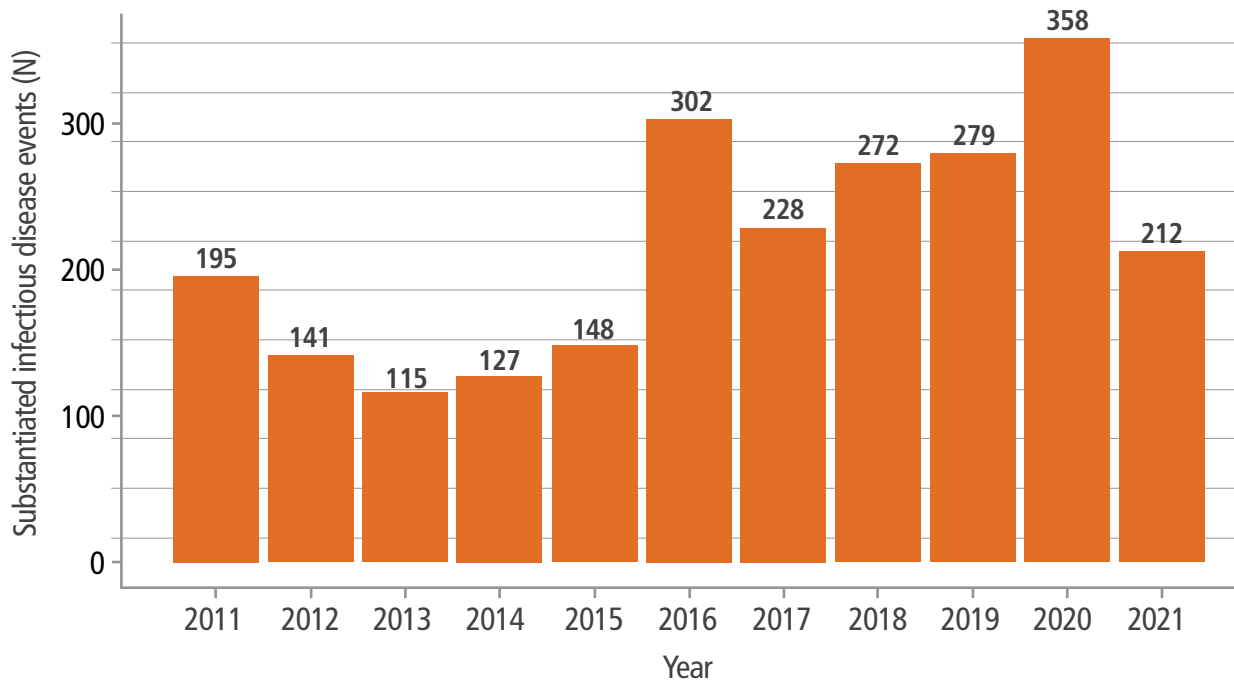
Heatmap for selected infectious diseases:

- Top 10 most commonly reported infectious diseases selected in the 11-year time period.
- Priority diseases in WHO R&D blueprint

Note:

Events of acute watery diarrhoea have **not** been included as cholera

Number of acute public health events* of infectious disease typology by year (2011–2021)



Source: data reported to WHO

* A public health event is an outbreak of a disease reported to WHO. One event may consist of one or several case reports or clusters. Time and space linked reports are merged and counted as one event.



Challenges and risk factors for 21st century epidemics



The face of epidemics and pandemics has changed in the recent past and continues to do so. Many new factors contribute to an increase in the transmissibility and severity of infectious diseases.

New lifestyles spread diseases further

New and more intense factors amplify the transmission of diseases, either because they increase contacts between people, or between animals and people. In an era of rapid global change, many of these factors are almost inevitable. Among them are the fast and intense mobility of people, with increased transport and international travel, and greater inter-connectivity between megacities, which are major transport hubs for aircraft, trains, road vehicles and ships.

These human activities highlight the profound changes in land use, agricultural practices and food production over the past century. New lifestyles and ways of extracting and using natural resources continue to accelerate global climate and ecological change. As our planet changes, so too does our risk of infectious diseases. Deforestation, urban sprawl and human encroachment into previously untouched habitats intensify our interactions with wildlife and the pathogens they harbour. Changing and intensified food production, from live poultry and animal markets to deforestation for expanded large-scale agriculture, also leads to increased contact between people and wildlife. Some of the animals that humans are increasingly in contact with (bats for example) are likely sources of new pathogens. At the same time, ever increasing climate-mediated disasters create humanitarian emergencies where infectious diseases can take hold and quickly spread.



Globalization also means increased trade among countries in addition to greater movement of people within and between them. For decades, more and more people have been migrating from the countryside into cities in search of better jobs and improved living standards. Unprecedented levels of urbanization and swelling populations of city dwellers inescapably pose greater risks of infectious disease transmission.

These risks similarly apply to densely populated areas on the periphery of cities, where rural areas overlap with urban sprawl. Here, close and repeated contacts between people and livestock,

domestic animals and wildlife raise the likelihood of new epidemics. To make matters worse, these peri-urban areas tend to be disadvantaged and local people have less access to health care facilities. The double jeopardy here is that their infections may go undetected and untreated, while the options for detection, prevention and control are reduced. The Ebola outbreak in 2014 dramatically demonstrated this.

Regrettably, the early years of the 21st century have seen many humanitarian emergencies, the massive displacement of populations fleeing from civil unrest, political instability, conflicts, wars and natural disasters. Millions of people have been uprooted from their homes and become either refugees, asylum-seekers or economic migrants, and find themselves living in often overcrowded conditions that also increase infection risks. Conflicts and wars not only cause civilian casualties and displacement, they destroy health care facilities exactly when and where they are most needed. Limited access to health care, constrained health systems and inadequate IPC practices in these settings also contribute to increased risk of virulence and mortality from epidemic diseases.

Revisiting traditional control measures

We have also seen that many traditional containment measures are challenging to put in place and sustain. Measures such as quarantine can be at odds with people's expectations of more freedom, including freedom of movement. Digital technologies for contact tracing became common in response to COVID-19. These, however, come with privacy, security and ethical concerns. Containment measures should be re-examined in partnership with the communities they impact.

The use of antibiotics to treat infections and control outbreaks has been a turning point in the 20th century. Yet, antimicrobial resistance is now on the rise. This is a major concern because a resistant infection may kill, can spread to others and requires finding new ways to treat and limit the spread of the disease. Antimicrobial resistance occurs naturally, but is facilitated by the inappropriate use of medicines, for example using antibiotics for viral infections such as cold or flu. Among major infectious diseases, the treatment of tuberculosis is the most affected, and there are now strains of the microorganism that are multi-drug resistant. In the animal sector, using antibiotics to promote animal growth also contributes to the threat of antimicrobial resistance.

Equity and solidarity

Epidemics are complex events. Complex in their origins, their spread, their effects and their consequences. Effects that can be at one and the same time medical, social, political and economic. The global impact of a single pathogen may vary significantly between settings and there is no one-size-fits-all intervention strategy.

Equity and solidarity issues are often part of the picture. Access to medical countermeasures remains difficult, especially for low-income countries and countries facing humanitarian emergencies. This difficulty is worsened when vaccine or treatment production is limited. Market mechanisms do not ensure a fair distribution of resources based on public health demands. Global mechanisms, matched with global solidarity, are needed to ensure fair and equitable access to life-saving interventions during crises. A number of organizations are dedicated to this goal (among them are CEPI, New Vaccines for a Safer World, the ICG, Gavi The Vaccine Alliance, the Pandemic Influenza Preparedness Framework, the ACT-Accelerator) but more efforts are required.



A new information ecosystem

A new word has entered the public health vocabulary: infodemic. An infodemic is an overabundance of information, accurate or not, in the digital and physical space, accompanying an acute health event such as an outbreak or epidemic. Such information is spread instantly and internationally through the growing popular use of mobile phones, social media, the Internet and other communication technologies. An infodemic causes confusion and can lead to risk-taking behaviours that can harm health. False or misleading information is dangerous. It can also lead to mistrust in health authorities, cause widespread public reluctance to adopt well-founded infection control measures, delay essential interventions, and in doing so undermine the public health response. To understand this new threat, we need infodemiology, the multidisciplinary science of managing infodemics. Infodemiology relies on systematic use of risk- and evidence-based analysis and approaches to manage the infodemic and reduce its impact on health behaviours during health emergencies.

To counter an infodemic, we need two conceptual shifts: 1) social listening and infodemic insights and 2) empowering communities.

Thus, we are recognizing that preventing and controlling the complex epidemics of the 21st century requires not only new technologies, but new skills and new attitudes across the public health community. Infodemic management is examined at greater length in *Focus 2: Managing an Infodemic* (page 51).

¹ https://link.springer.com/chapter/10.1007/978-3-031-27789-4_1

Key insights into infectious disease epidemics



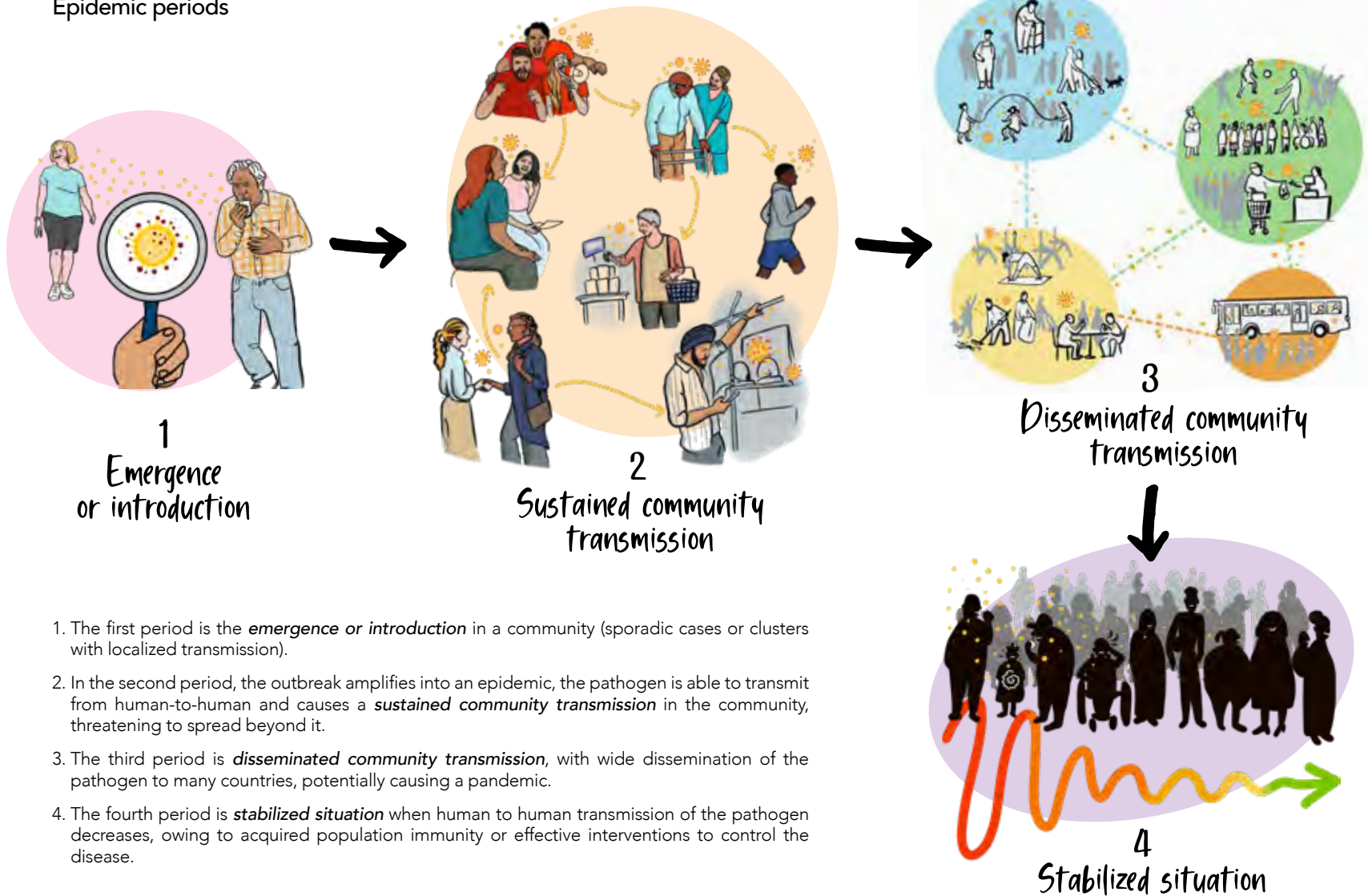
A whole-of-society approach is needed to tackle 21st century epidemics so that the diverse drivers of disease are taken into consideration: genetics and biological factors, ecology and the physical environment, human behaviour and demographics, social, political and economic factors and so on.

This increasing convergence of many factors that drive and amplify outbreaks requires multi-disciplinary, multi-sectoral and multi-faceted approaches.

Moreover, because epidemics are social problems as much as medical ones, we need to move beyond the traditional biomedical approaches to them. Social sciences should be an integral part of surge capacities by adding social scientists to the team of first responders. Such a change allows us to address issues of fear and trust within the social context. Engaging communities and empowering them in advance as part of preparedness ensures that there is a better understanding of the human ecology. Linking community and biomedical perspectives enhances effective partnerships, as does building upon pre-existing relationships to respond to epidemics.

Because new infectious disease threats usually start locally, understanding their dynamics is important to deny them the opportunity to spread further among people and overwhelm health systems. The dynamics of epidemic and pandemic diseases typically occur in four periods, although not all epidemic diseases necessarily go through each period.

Epidemic periods



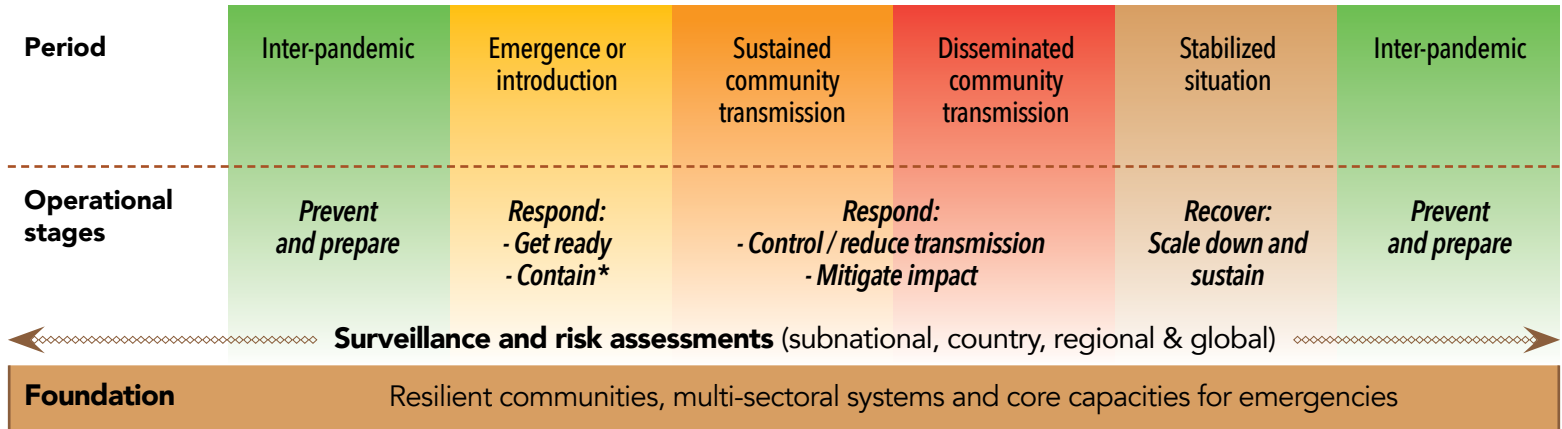
1. The first period is the *emergence or introduction* in a community (sporadic cases or clusters with localized transmission).
2. In the second period, the outbreak amplifies into an epidemic, the pathogen is able to transmit from human-to-human and causes a *sustained community transmission* in the community, threatening to spread beyond it.
3. The third period is *disseminated community transmission*, with wide dissemination of the pathogen to many countries, potentially causing a pandemic.
4. The fourth period is *stabilized situation* when human to human transmission of the pathogen decreases, owing to acquired population immunity or effective interventions to control the disease.



The dynamics of epidemics, as described above, define the response and the sequence of interventions that then become necessary. Here, there are four crucial operational stages:

1. **Prevent and prepare:** the anticipation of new and re-emerging diseases to facilitate faster detection and response.
2. **Respond – get ready and contain:** the containment of the disease at the early stages of transmission.
3. **Respond – control / reduce transmission and mitigate the impact:** the control and mitigation of the epidemic/pandemic during its amplification.
4. **Recover – scaledown and sustain:** the scaling down and elimination of the risk of outbreak or eradication of the infectious disease.

Epidemic periods and response interventions



* Containment aims to stop transmission by reducing the effective reproduction number (R) to below one. This requires highly stringent application of measures, is resource intensive and time sensitive. Containment measures may halt, delay or reduce the spread and overall impact of the pandemic and may be considered as part of a country's national preparedness plan. Operational decisions need to be based on risk assessments that account for pathogen, exposure and contextual factors including health and socio-economic capacities and vulnerabilities.

Prevent and prepare: In this first stage of response, emergence cannot be predicted, but it can certainly be anticipated. The anticipation of risks enables a focus on the most likely threats. Anticipation encompasses forecasting the most likely diseases to emerge, and the quick identification of the drivers that will worsen the impact or facilitate the spread. Preparedness plans, based on lessons learned from past experiences, should contain a variety of scenarios to allow for a reactive response to the unexpected.

Respond – get ready and contain: Emerging and re-emerging diseases include new ones about which there is little scientific knowledge. These often require investigation into their sources at the same time as the use of coordinated, rapid-containment measures. New diseases require new interventions. And because they appear irregularly or rarely, constant vigilance is needed along with proactive risk assessment and the development of new management tools.

Early detection allows for rapid implementation of containment measures, which are key to reducing the risk of amplification and potential international spread. Early detection begins in the health care setting, so health workers must be trained to recognize potential epidemic disease and quickly report an unusual event, such as an unusual cluster of cases or deaths. Health workers must also know how to protect themselves by employing IPC measures and understand how to prevent outbreak amplification in health care facilities. The risk of community transmission and mortality can also be reduced by isolating severely-ill patients in health care settings to prevent household transmission and protect care givers at home.

Once a new disease is recognized by the health system, early laboratory confirmation is essential. When this cannot be done at country level, the affected countries must be confident they can count on the support of a network of regional or global laboratories. It is critically important for global health security that there is a system for safely taking samples and shipping specimens to relevant laboratories in full compliance with biosafety and biosecurity regulations.

Effective and rapid containment of emerging diseases is just as vital as early detection to avoid a large-scale epidemic. Rapid containment should start as soon as the first case is detected regardless of the etiology, which is most likely to be unknown. It requires skilled professionals to safely implement the necessary countermeasures. Pre-training of these professionals is essential to guarantee the safety and efficiency of the operations.

Unfortunately, containment at the source is often impossible.



Respond – control and mitigate: Once the infectious disease threat reaches an epidemic or pandemic level, the goal of the response is to mitigate its impact and reduce its incidence, morbidity and mortality, as well as minimize its disruptions to economic, political and social systems. At this stage, it is important to prevent further spread, both geographically or into groups and communities not yet infected. This stage requires a lot of preparedness and has often been neglected.

Recover – scale down and sustain: There are several options when phasing out of the acute period of the disease towards elimination and eradication.

Firstly, phasing out requires control and mitigation leading to the development of a programmatic approach to manage the disease as for other endemic diseases (for example H1N1 influenza pandemic).

Secondly, control of a disease may lead to its elimination as a public health problem, which means that it is sufficiently controlled to prevent an epidemic from occurring in a defined geographical area (for example yellow fever). Elimination means that the disease is no longer considered as a major public health issue. However, intervention measures (surveillance and control) should continue to prevent its re-emergence.

Eradication of a disease (for example smallpox) is much more difficult and rarely achieved. Eradication involves the permanent elimination of its incidence worldwide. There is no longer a need for intervention measures.

Three criteria need to be met to eradicate a disease:

- There must be an available intervention to interrupt its transmission.
- There must be available efficient diagnostic tools to detect cases that could lead to transmission.
- Humans must be the only reservoir.



Response tips & checklists

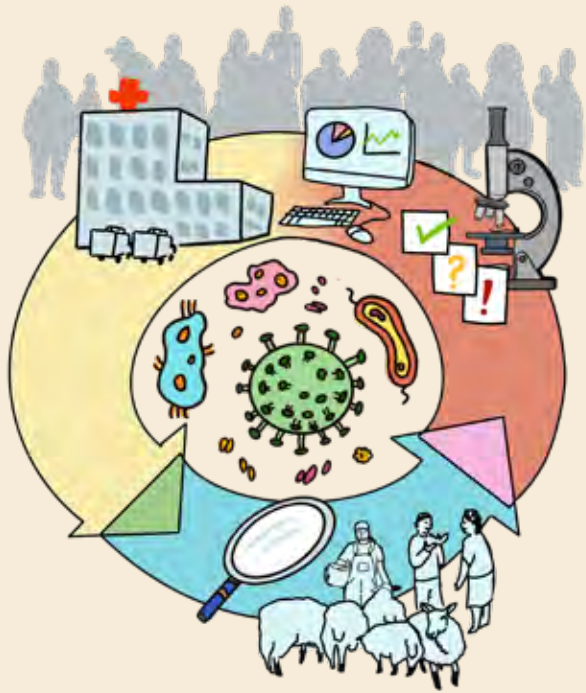


A comprehensive outbreak response is always complex, comprising many components that should be coordinated harmoniously to strengthen health emergency preparedness, response and resilience, also known as HEPR.

The following response tips are used to organize ideas and to make sure no important point is overlooked. In this handbook, specific tips are listed for each disease, which will help keep focus on essential elements of each response. They are organized into five main components:

- Collaborative surveillance
- Community protection
- Clinical care
- Access to countermeasures
- Emergency coordination

The checklists will help you assess what is important and necessary for the response. The outbreak response varies depending on the disease. For some diseases treatment is essential; for other diseases, vaccination is vital.



Collaborative surveillance

Surveillance provides information about factors including emergence, transmission, susceptibility, morbidity and mortality of an infectious hazard. Decision-makers and programme implementers need accurate and timely information about these factors to best initiate and adjust response measures. To tackle the health threats of the 21st century, a collaborative surveillance approach is key. Such an approach spans systems and data sources. Collaborative surveillance includes:

- 1) National surveillance capacities, including disease, threat and vulnerability surveillance.
- 2) The laboratory infrastructure and capacity necessary for pathogen and genomic surveillance.
- 3) Collaborative approaches for risk assessment, event detection and response monitoring.

In every event, information is necessary to monitor it, measure the impact of interventions and to guide decision-making throughout the crisis. There are two particular types of information: surveillance of the disease, and information on the interventions (process and output indicators), which show the coverage and impact of the interventions being performed. Surveillance provides information on the number of cases and deaths by period and place (people, time and place). Information on the interventions enables knowing which ones are performed and what is their coverage and impact.

Collaborative surveillance means:

- ✓ Strengthened national integrated disease, threat and vulnerability surveillance.
- ✓ Increased laboratory capacity for pathogen and genomic surveillance.
- ✓ Collaborative approaches for risk assessment, event detection and response monitoring.

Community protection

Outbreaks start and end in communities.

Community protection includes all co-created measures and interventions to protect communities, prevent epidemics from happening or reduce their impact. It includes a wide range of interventions such as risk communication, infodemic management, community engagement, public health and social measures (PHSM), vaccination and environmental measures. Health and other sector actions need to be based on local contexts and customs, ensure that community concerns are addressed, and that livelihoods and social welfare are protected.

PHSM refer to non-pharmaceutical interventions implemented by individuals, communities and governments to reduce the spread of infectious diseases with epidemic or pandemic potential by reducing transmission of the pathogen. They are crucial in all stages of the outbreak management cycle, alone or in combination with medical countermeasures. The implementation of PHSM during an infectious disease outbreak can decrease the number of cases and hence reduce pressure on the health care system, help keep businesses and essential services open, and buy time for the development and production of medical countermeasures. More information can be found in *Focus 5 Public health and social measures during epidemics and pandemics* (page 65).

Community protection means:

- ✓ Interventions that protect communities such as:
 - Vaccination
 - Environmental measures (vector control, water and sanitation, etc.)
 - PHSM
- ✓ Proactive risk communication and infodemic management to inform communities, identify their needs and build trust.
- ✓ Community engagement and empowerment to co-create mass population and environmental interventions based on local contexts and customs.
- ✓ Multi-sectoral action to address community concerns such as social welfare and livelihood protection.

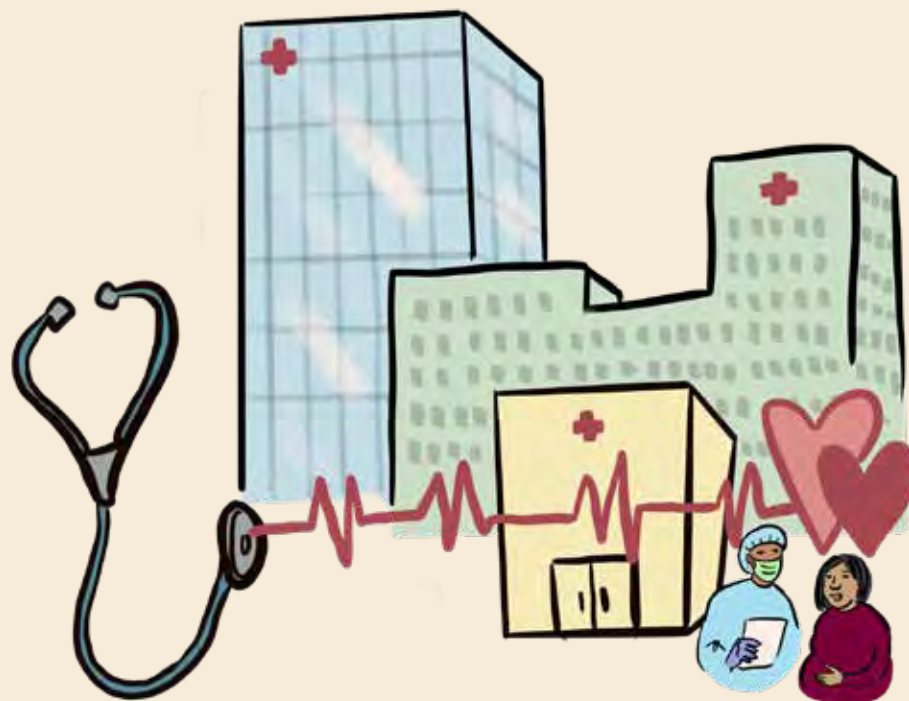


Clinical care

Lifesaving and scalable clinical care is crucial, as is protection of health care workers and patients, and health systems that can maintain essential health services. Each disease requires a different set of health interventions with the objectives of reducing transmission, severe morbidity and mortality, minimizing the impact on health systems and the political and social sector, amongst others. These interventions are made possible by creating adequate surge capacity, ensuring health workers are protected through appropriate IPC measures, and maintaining health services and systems functioning even during health emergencies.

Clinical care means:

- ✓ Safe and scalable emergency care.
- ✓ Protecting health workers and patients.
- ✓ Health systems that can maintain essential health services during emergencies.

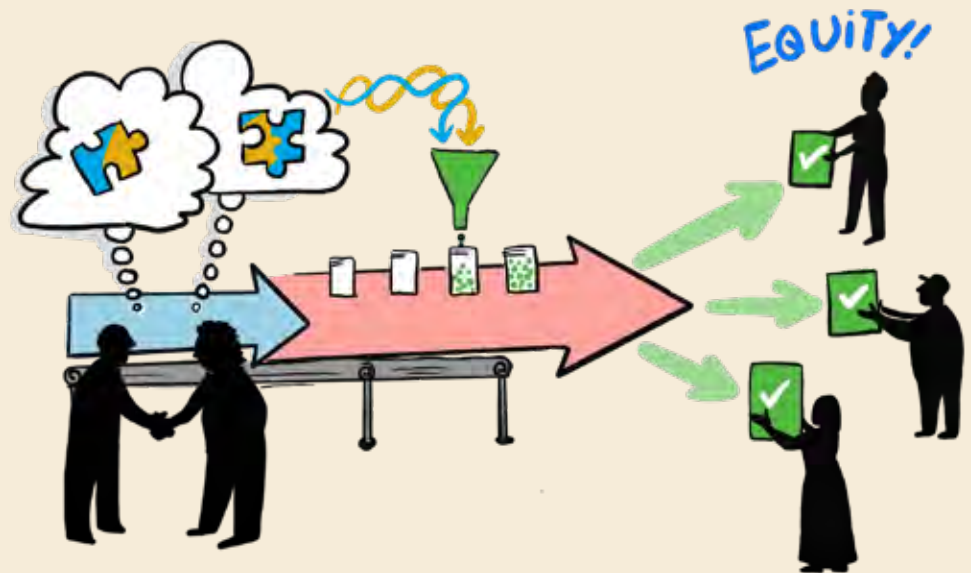


Access to countermeasures

Countermeasures should be accessible by all on an equitable and timely basis. Equitable access to countermeasures should be based on fast-tracked and prioritized R&D with pre-negotiated benefit-sharing agreements, scalable manufacturing platforms and agreements for technology transfer, as well as coordinated procurement and emergency supply chains.

Access to countermeasures means:

- ✓ Fast track R&D with pre-negotiated benefit sharing agreements.
- ✓ Scalable manufacturing platforms and agreements for technology transfer.
- ✓ Coordinated procurement and emergency supply chains to ensure equitable access.





Emergency coordination

Emergency coordination should draw on health emergency alert and response teams that are interoperable and rapidly deployable; coherent national action plans for preparedness, prevention, risk reduction and operational readiness; and scalable health emergency response coordination through a standardized and commonly applied emergency response framework.

An outbreak is, by definition, an exceptional event, which often requires extra human and financial resources and may also rely on additional partners, agencies and other sectors. Strong coordination is essential at all times to ensure that all those resources and partners are working effectively together to control the outbreak. WHO is often expected to lead the international response to support national health authorities.

Effective coordination requires a dedicated physical space (usually an emergency operation centre); various tools to ensure optimal organization of meetings and filing of documentation (such as a list of contacts and a meetings tracking system); a joint plan of action regularly updated as the situation evolves, to describe the interventions needed and the distribution of roles and responsibilities among stakeholders; and finally tools to ensure communication between the various stakeholders engaged in the response (phone numbers, a dashboard, maps and a directory).

Emergency coordination means:

- ✓ Strengthened health emergency alert and response teams that are interoperable and rapidly deployable.
- ✓ Coherent national action plans for preparedness, prevention, risk reduction and operational readiness.
- ✓ Scalable health emergency response coordination through standardized and commonly applied Emergency Response Framework (ERF).



For more information about emergency coordination:

- Public Health Emergency Operations Centre Network (EOC-NET)
<https://www.who.int/groups/eoc-net>
- Strengthening health emergency prevention, preparedness, response and resilience. Geneva: World Health Organization; 2023
<https://www.who.int/publications/m/item/strengthening-the-global-architecture-for-health-emergency-prevention--preparedness--response-and-resilience/>
- Emergency response framework – 2nd ed. Geneva: World Health Organization; 2017
<https://www.who.int/publications/i/item/9789241512299>

FOCUS 1

Community engagement during epidemics

Defining a community

Community is a broad term that can be applied to a variety of social groupings. It defines a distinct group of people who have a sense of belonging together. A community may be defined through the sharing of:

- A common geographical location
- A common geographical location
- Common values or interests
- Common identity.

With new technologies, a community may be totally virtual, for instance a group of people sharing interests and points of view on social media. Community identity and how



a community positions itself in relation to other communities can shape what information sources they trust and are shared. This can be shaped by many factors, including previous adverse experiences a community may have had with the health care system and government.

WHO has defined community engagement as a process of developing relationships that enable stakeholders to work together to address health-related issues and promote well-being to achieve positive health impact and outcomes.¹

Meaningful participation and sustained engagement of all communities and individuals are fundamental to an effective epidemic response as there is an established relationship built on trust, ownership over interventions and accountability between stakeholders.

¹ Community engagement: a health promotion guide for universal health coverage in the hands of the people. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO. <https://www.who.int/publications/i/item/9789240010529>



Why engage communities

People everywhere need to have timely access to the right information in the right format so that they can make decisions to protect their health and the health of their communities. This is important at all times, but critical during epidemics and pandemics.

Communities, when engaged, are integral to detecting and managing epidemics. Epidemics start in communities, communities will be the most affected by an epidemic and communities will make the greatest contribution to supporting mitigation measures as new diseases emerge or old ones re-emerge.

People live in unique and dynamic political, social and cultural contexts. These contexts influence a person's perception of risks, information-seeking behavior and acceptance of or compliance with health advice. Experience has shown that telling people what to do, even if the advice is based on the best evidence, is not effective in all situations. More effective strategies include engaging individuals and communities in dialogue, listening to and addressing their questions and concerns and building trust over time by delivering on promises made and incorporating their feedback. Consider the spectrum of engagement in WHO guidance on community engagement when planning activities.¹

¹ Community engagement: a health promotion guide for universal health coverage in the hands of the people. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO. <https://www.who.int/publications/i/item/9789240010529>

Three elements of community engagement

Disease outbreaks and epidemics are complex phenomena with several aspects that are intimately intertwined: public health, medical, social, environmental and political. Community engagement is an approach to account for the social, public health, environmental (and to some degree the political) aspects of epidemics. Community engagement is essential for the effective control of infectious diseases through high acceptance and adherence to public health interventions.

Community engagement is based on three elements:

1. Establishing a dialogue between responders and communities to understand the perceptions and beliefs about diseases and the public health response, as well as to identify the specific cultural and social patterns of transmission and vulnerability that exist at community level.
2. Building on trusted relationships with communities, health authorities can co-design and identify mitigation measures that are practical and acceptable to a community and find joint solutions to health challenges.
3. Health authorities play a key role in empowering communities, providing them with necessary medical and other supplies and skills to implement PHSM and promoting the use of sustained and safe interventions within the community.

Epidemic risk mitigation relies on people adopting health protective behaviors and adhering to PHSM. Given this, health authorities can partner with existing trusted community leaders and networks representing special interests such as youth organizations, faith-based organizations, business sector associations, unions and others. These partnerships can enable health authorities to better understand the concerns and information needs arising from within different communities and provide opportunities to co-develop and disseminate localized, relevant and implementable guidance.

A key community to empower during outbreaks are health care workers and volunteers who are often frontline responders. To the community, these frontline workers represent the face of the whole outbreak response. Their attitude towards community members and their collaboration in implementing health advice can have significant influence on how advice is perceived and accepted, or rejected, by community members.

Key components of epidemic response that require meaningful engagement of communities (affected populations as well as health care workers and frontline responders themselves) include:

- Detecting the start of an outbreak and newly infected people during an outbreak (case detection, contact tracing).

- Identifying and addressing questions, concerns, information voids and misinformation through consistent, accurate communication and proactive community engagement.
- Seeking and providing health care as advised (in the household, community and health facility).
- Minimizing practices (at individual and community levels) that can increase susceptibility and exposure and adopting protective practices (medical and non-medical).
- Reducing and addressing stigma associated with infection.



Ten things to know

1. Disease outbreaks can affect the social fabric of communities. A community is a social network and infectious diseases outbreaks are deeply linked to social behaviors. Disease outbreaks spread through personal and social contacts and links at home or during professional and recreational activities.
2. Disease creates fear, which often leads to practices that further amplify the epidemic. These can be both individual and collective. They can relate to the transmission of the disease, or the stigma and extreme stress on the ties that bind communities.
3. Epidemics are by nature rapidly evolving. It is particularly challenging to promote meaningful community engagement in this highly pressured context. For this reason, community engagement must be ongoing. Outbreak responses that build on existing community engagement mechanisms and work with trusted partners and community leaders are more likely to succeed. This is particularly important at the beginning of an outbreak when there is a very urgent need to break the chains of transmission and prevent the outbreak from becoming an epidemic. It is vital to acknowledge that in many settings there are communities that are vulnerable or have been marginalized. Concerted efforts are needed to include these communities, build trust with them, strengthen their ties to the health system and engage them in the outbreak response.
4. Communities are the main actors in preventing, identifying, responding to and recovering from the physical, psychological, social and economic impacts of epidemics. Communities are not passive subjects of interventions.
5. Community understanding of diseases and their spread is complex, context-dependent and culturally mediated. Thus, a one-size-fits-all approach is neither desirable nor effective and sociobehavioral insights may be needed to design contextualized and more effective interventions.
6. Communities are multi-layered and power dynamics exist between individuals, groups and networks. Social scientists can help foster understanding about these dynamics and work with specialists in health education, health promotion and local communities to inform behaviour change interventions. Together they can design the messages and interventions necessary to raise awareness, as well as inform behaviour adaptations or changes needed to meet the demands of a new infection. This work can be done using simple tools to assess relevant perceptions and beliefs for any outbreak response. Embedding social scientists in response teams will also help to monitor how people adapt public health measures to different social contexts and whether these are implemented in a way that respects social and cultural systems.
7. Community engagement helps to strengthen and ensure resilience to future outbreaks. When people have already learned how to implement their own solutions, they will be better able to deal with the next outbreak.
8. Information needs and communication messages will evolve as the epidemic evolves. The messages must also proactively detect misinformation and rumours. Effective community engagement promotes the sharing of accurate, credible information from trusted messengers and limits the opportunities for misunderstandings and the proliferation of rumours, as well as mitigating the spread of fear and anxiety.
9. Identify people that the community trusts and build relationships with them. Involve them in decision-making to ensure interventions are collaborative, contextually appropriate and that communication is shared through community channels and trusted messengers.
10. Two-way communication should be achieved through the most socially acceptable and effective channels. Messages must be translated into local language and context and to match the education levels and preferences of the target population (for example, visual, written or oral cultures). All communication with communities should be transparent, timely, easy-to-understand, acknowledge uncertainty, address affected populations, promote self-efficacy and be disseminated using multiple platforms, methods and channels.

Ensuring effective community engagement

To ensure effective community engagement, three elements are needed for communities and for field responders:

For communities:

- **Knowledge:** Communities must know what the disease is, how it is transmitted and how to protect against it (social mobilization messages).
- **Trust:** The most important determinant to ensuring communities heed public health advice is trust. Communities must be consulted, engaged and participate, whenever possible, in identifying and implementing response measures.
- **Self-efficacy:** Communities must be able to implement PHSM. For example, communities must be able to access soap and water, gloves, waste management services, transportation, safe burial teams, amongst others.

Field responders:

- **Understand:** Field responders need to understand local perceptions of the disease and of the response measures.
- **Listen:** Field responders need to listen to communities' fears and beliefs and adapt their own behaviours accordingly.
- **Support and empower:** Field responders need to support communities' participation, ownership and resilience.



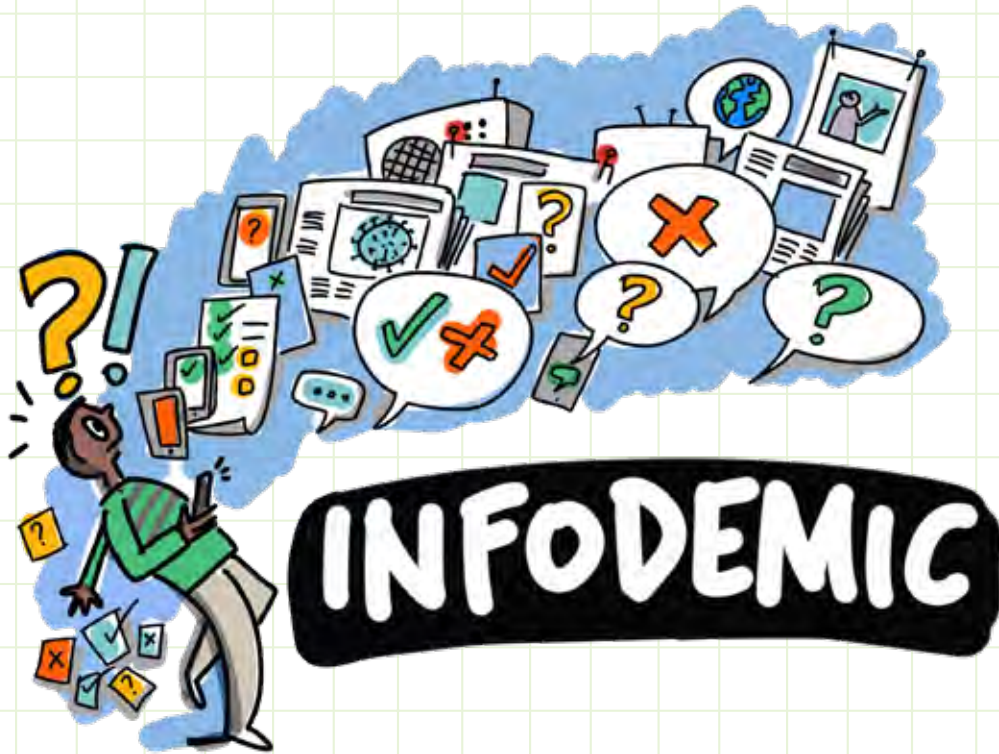


More information about community engagement:

- Risk communication and community engagement during emergencies. WHO EURO
<https://www.euro.who.int/en/health-topics/health-emergencies/pages/whos-work-in-emergencies/risk-communication-in-emergencies/emergency-risk-communications>
- Communicating risk in public health emergencies: a WHO guideline for emergency risk communication (ERC) policy and practice
<https://apps.who.int/iris/handle/10665/259807>
- 10 Steps to Community Readiness
<https://www.rcce-collective.net/rcce-10-steps/>
- Infodemic WHO webpage
https://www.who.int/health-topics/infodemic#tab=tab_1
- Communicating risk in public health emergencies
<https://www.who.int/publications/i/item/9789241550208>
- WHO competency framework: Building a response workforce to manage infodemics
<https://www.who.int/publications/i/item/9789240035287>
- Community engagement: a health promotion guide for universal health coverage in the hands of the people
<https://www.who.int/publications/i/item/9789240010529>

FOCUS 2

Managing an Infodemic



Understanding how information flows and affects behaviour in the 21st century

With ever increasing internet use and the development of social media platforms, the information ecosystem in which we live is drastically different than when the IHR (2005) were adopted. The production, transmission, analysis and amplification of health information has changed in step with technological advancements. People have access to enormous amounts of information from many different sources every day. Health institutions are no longer the primary source of health information as many people turn to the digital realm.

In every epidemic increasing case numbers are accompanied by increasing information, in both physical and virtual spaces, related to the disease, its prevention and treatment. The fear and uncertainty that characterize epidemics and pandemics drive information-seeking behavior. As people seek information and guidance on how to protect themselves and their communities they are exposed to information and advice from many sources. A vast amount of information, coupled with fear and doubts can make it difficult to objectively evaluate information. Rapidly evolving science related to the epidemic sets a dizzying pace, with new diagnostics, vaccines, and treatment creating even more information.

An infodemic is an overabundance of information, accurate or not, in the digital and physical space, accompanying an acute health event such as an outbreak or epidemic.

Infodemics are not a new phenomenon, but with changes in our societies brought about by the digital age they are reaching farther than ever and on a far greater scale. In turn, health authorities are increasingly challenged to respond to infodemics. The way people search, receive, interact with and discuss information has been changed as the online world has grown. Changes have been vast with the digitization of news and media, as well as the way we form our online and offline social identities and interactions. We are now living with and using a digitalized information environment. For example, people now seek health advice through online sources. News media is available around the clock, while citizen journalism and social media content have spurred the rise of personal opinion as news. Epidemics and the way they are managed capture media attention quickly, leading to intense coverage of events at local, national and international levels. Questions and concerns now travel across borders, often faster than the health authorities can react.

The psychology of crises means we tend to remember the first thing we hear, have trouble processing complex information, and look for additional information.

This creates the perfect storm for information overload and questions, concerns, information voids where people look for information but can't find it, and mis- and disinformation to spread. Infodemics cannot be eliminated, they can only be managed.

In response to a changing world, and the vast amounts of information produced, new

evidence-based tools and methods to address infodemics have been established. Indeed, infodemics, like epidemics, can be managed. Infodemic management uses many skillsets to prioritize and problem solve the issue of too much and inaccurate information. The science of managing infodemics is called 'infodemiology', which enables us to understand the infodemics of the 21st century and develop tools and interventions to better manage them. The advancement of infodemiology calls for the development of research agenda to determine priorities in epidemic response that can rapidly increase our capacity to tackle infodemics.

Emergency risk communication and community engagement have long been recognized as critical components of the public health response to a disease outbreak. Risk communication includes the interactive exchange of information between experts and the public about health risks and behaviors. Infodemic management is a framework that uses the same principles. It is a countermeasure equally as important as surveillance, laboratories or contact tracing. Infodemic management is the systematic use of risk- and evidence-based analysis and approaches to promote a healthier information environment and resilience against infodemic impacts on health behaviours during health emergencies. Infodemic management aims to ensure that people have the right information at the right time in the right format, so they are informed and empowered to adopt behavioral changes during epidemics to protect their health, their loved ones and their communities.



Infodemic management in practice

Infodemic management develops and implements multi-level evidence-based interventions that are aimed at changing people's behaviors. It includes:

1. Listening to the concerns of individuals and communities online and offline and triangulating social listening and other data sources into infodemic insights to have a better understanding of their evolving concerns and information and service needs. Social listening online requires new tools that can monitor the public conversation on social media and disaggregate data by categories such as topics discussed and frequency of sharing, but also understand the sentiment, perspectives, practices and attitudes of the population with regards to certain aspects of the pandemic (for example transmission, treatments, masks).

2. Communicate risk and translate science. The evolving nature of the COVID-19 pandemic has challenged risk communication. It is crucial to develop effective communication about risk in a timely manner and translate the science. This requires interactive exchange of information between experts and the public about health risks and behaviours. The amplification of risk communication messages through adequate channels is an essential step to ensure a two-way dialogue between various groups (for example media, experts, health authorities, civil society) involved in the response.

3. Promote resilience to negative impacts of the infodemic. The COVID-19 infodemic has highlighted new sensitivity to false information. Means to address false information involve adopting short-term measures such as providing high-quality health information and guidance in a timely manner and amplifying its spread. High-quality health information must be amplified not only through traditional communication channels but also through communities' leaders. In addition, evidence and facts must be used to debunk misinformation and disinformation that could have a negative health impact on people and communities, while respecting their freedom of expression. Long-term approaches include improving the health, media and digital literacy of individuals and their communities to overcome cognitive barriers in the perception of information and empowering people to adopt healthy behaviours.

4. Engage and empower communities. Community engagement includes involving, consulting, informing, as well as engaging and collaborating with diverse communities across different cultures and geographies (for example the 'World of Work', health care workers, faith-based communities, youth) and leveraging their experiences and perspectives. We should strive to build two-way communication where communities have a role to play in pandemic preparedness and response before, during and after outbreaks. Community empowerment is promoted by enabling communities to develop and implement their own solutions. To make a lasting impact, communities need to own their role in addressing the infodemic. Infodemic management pushes towards shared leadership and decision-making, as well as community-led solutions in emergency response.



Ten things to know and do

1. Engage communities

Identify people that the community trusts, build relationships with them and involve them in decision-making to ensure interventions are collaborative, contextually appropriate and that communication is community-owned. Community engagement is one important start for communicating risk and facilitating changes in behaviours and practices. For more information see *Focus 1 Community engagement during epidemics and pandemics* (page 45).

2. Provide clear messages in acceptable and accessible formats and channels

According to the latest evidence, risk should be explained in non-technical terms to promote understanding and risk mitigation behaviours. Consistent messages should come from different information sources and emerge early in the outbreak. Messages should promote specific actions people can realistically take to protect their health.

To effectively communicate risk, establish the SOCO – Single Overarching Communications Objective.

To do so, the following questions need to be addressed:

- What is the current behaviour of the target population?
- What is the desired behaviour of the target population that reduces risk to individuals and communities of adverse health, social or economic outcomes in this emergency?



- What are the messages that need to be communicated that support this behaviour?
- What channels or strategies can be used to reach this population?
- What information does the target population need to know to make the best choice they can to protect themselves and their families?
- Are tools in place to conduct social listening to monitor for questions, concerns, information voids and misinformation?
- Is there a platform for community and civil society engagement, and commitment to a community-led and co-created response?
- Have steps been taken to translate guidance and scientific information into lay language and format?

- Is there a plan to communicate regularly with the various audiences?
- Have all personnel and volunteers in the risk communication response been trained in risk communication approaches?

3. Establish coordination and information systems

Develop and build on agency and organizational networks across geographic, disciplinary and, where appropriate, national boundaries. Tailor information and communication systems to the needs of users and involve local stakeholders to guarantee the flow of information across sectors.

4. Leverage listening and feedback systems

Listening and feedback systems should be previously established and use multiple means to listen to the public and affected communities. Ways of listening to the public include surveys, focus group discussions,



community walk-throughs, key informants, feedback from front-line responders, partners' and stakeholders' feedback, social media, etc. Triangulate social listening with other data sources into infodemic insights to understand questions, concerns, information voids and circulating narratives in communities affected by the emergency. Perform a risk assessment and use infodemic insights to improve not only communications, but also engagement, improve access, delivery and quality of services, and mitigate unintended harms of epidemic mitigation measures.

5. Build trust

People must trust those responsible for managing and issuing information about the outbreak. Public confidence that a government or agency is acting first and



foremost to safeguard their health will influence compliance with recommended control measures, and thus hasten outbreak containment. Accountability is key to trust. Given this, communicators and outbreak managers must demonstrate that they are accountable for what they say, promise and do by delivering on promises made, communicating what is known and not known and updating the public on new science, guidance or information. Evidence shows that to build trust, risk communication interventions and messages should link to functioning and accessible services, be transparent, timely, easy-to-understand, acknowledge uncertainty, address affected populations, promote self-efficacy and be disseminated using multiple platforms, methods and channels.

The building blocks of trust include:

- Being perceived as credible experts by providing advice that is correct, accurate and consistent with other trusted agencies and entities.
- Being perceived as honest brokers of the truth, addressing issues around conflicting messages and advice, unsettled science, late breaking developments and updated policies that may conflict with old policies and messages.
- Being perceived as having a good character by telling the truth and not omitting important information and following through on promises.
- Identifying with the affected population as sharing the same concerns and holding their best interests at heart.

- Exhibiting good will and demonstrating empathy and caring in messages and their delivery.

Distrust is an outgrowth of perception that promises were broken and values were violated. In addresses to risk communication, ensure that services are delivered in ways acceptable to affected populations and aligned with their values, and that health guidance is clear and addresses also their questions and concerns.

6. Communicate uncertainty proactively

Communication by authorities to the public should include explicit information about uncertainties associated with risks, events and interventions and indicate what is known and not known at a given time. Announce the event as early as possible, even when the information is incomplete. This will establish you as the leader to communicate risk, build trust in you and the response, help enable changes in practice and behaviors to bring the outbreak under control and minimize misinformation and rumours.

A good template to communicate uncertainty is:

- State what is known, what is unknown, and what you/your institution is doing about the issue.
- Communicate early, be first to announce the event (if possible), communicate often and communicate regularly.
- Provide information on the risk/danger but supplement it with some advice on how people can protect themselves.

- Speak as a human being, using empathy appropriately.
- Do not over-reassure.
- Do not make promises that you cannot keep.

7. Risk communication operations requires resources

Risk communication in epidemics is a massive operational undertaking and requires people, logistics, material and funds. Different types of expertise in many areas are required including media communications, social media, spokespersons, social mobilization, health promotion, community engagement, behavioral change communication, stakeholder communication, communication related to travel and trade, social science methods, etc.

Set up an infodemic management team to rapidly generate infodemic insights and support infodemic management during an outbreak, and to leverage analysis of information ecosystem to plan and promote a healthier information environment.

8. Use social media as appropriate

Social media should be used to engage the public, facilitate peer-to-peer communication, create situational awareness, monitor and respond to rumours, public reactions and concerns during an emergency and to facilitate local level responses. Social media and traditional media should be part of an integrated strategy with other forms of communication to achieve convergence of verified, accurate information.

9. Treat emergency risk communication as a strategic role, not an add-on

Emergency risk communication should be a designated strategic role in global and national emergency preparedness and response leadership teams. The IHR (2005) require all Member States to build national capacity to communicate risk in two domains: 1) systems capacities and 2) people capacities.

The Joint External Evaluation (JEE) process championed by the Global Health Security Agenda measures national risk communication capacity in six domains:

- 1) National strategies, policies and plan;
- 2) Coordination;
- 3) Stakeholder communication;
- 4) Public communication (using mass media approaches);
- 5) Communicating and engaging with communities;
- 6) Dynamic listening (to misinformation, fears, concerns) and rumour management.

10. Build capacity for the next emergency

Preparation and training of personnel for emergency risk communication should be organized regularly and focus on coordination across agencies. Emergency risk communication requires a defined and sustained budget which should be a part of core budgeting for emergency preparedness and response.



Other factors to remember

Infodemic management must be adapted to each outbreak, taking into consideration:

- The infectious hazard, including its severity, lethality, modes of transmission, how it can be diagnosed, treated or managed.
- The geography of the outbreak including whether it is contained or widely distributed; national or international spread; affecting certain vulnerable communities or the general population; in a remote village or major city; amongst others.
- The levels of trust that exist between the affected or at-risk populations and their authorities and experts or the response teams.
- People's underlying beliefs, cultures, traditions, values and practices.
- Education, levels of awareness, access to understandable information and trusted channels of communication.
- Self-efficacy, including whether communities have the ability, resources and environment to follow health advice.

FOCUS 3

Treating patients and protecting the health workforce



Advances in medicine: antibiotics, antivirals, vaccines and new treatments

With the remarkable progress in medicine and related technologies, briefly mentioned at the beginning of this handbook, many infectious diseases can now be prevented and treated.

This is the result of a public health revolution sparked by advances in research that began in the 1940s with the discovery of antibiotics for bacterial diseases, and expanded with improvements in their safety, efficacy and acceptability.

¹ WHO data, 2016.

Similarly, research on and development of vaccines, particularly for infants and young children, has given global protection against many childhood killers. For example, WHO estimates that there is now 86% global coverage of the combined diphtheria-tetanus-pertussis vaccine for babies.¹ In recent decades, hundreds of millions of children all over the world have grown up free of the risk of deadly and disabling diseases. Adults have benefited likewise, with protection against a wide range of infections that can explode into epidemics – cholera, influenza and yellow fever, for example. For many deadly diseases, there are vaccines that ideally should be administered in routine, large-scale immunization to prevent the occurrence or minimize the severity of the disease. Some vaccines can also be used during a reactive campaign when there is an epidemic in which the immunity of the population is not high enough.

The COVID-19 pandemic has offered an example of scientific advances leading to the rapid development of several novel and effective vaccines against an emerging infectious disease. Key to this development was the WHO R&D Blueprint, a global strategy and preparedness plan that allows the rapid activation of R&D

activities during epidemics. Its aim is to fast-track the availability of effective tests, vaccines and medicines that can be used to save lives and avert large scale crisis. The R&D Blueprint was crucial to vaccine development early in the pandemic underscoring the importance of conducting robust research even during outbreaks. Despite these rapid advancements, vast global inequity in vaccine distribution remains a challenge to ending the pandemic.

Meanwhile, there have also been great strides forward in the fields of diagnostics and treatments. The discovery of antiretrovirals towards the end of the 20th century revolutionized HIV care. Other innovations include monoclonal antibodies, which are becoming more widely available. However, the price of some of these is still prohibitively high and they are not yet available for mass administration.

While such advances have completely changed the way infectious diseases are confronted today, this progress has not come without problems. We now face challenges including public health complacency and the emergence of antibiotic resistance.



Treating patients with supportive care

But whether the focus is on antibiotics, antivirals, vaccines or the range of other available treatments, the vital, universal fact is that these can only be beneficial when they are administered by skilled, qualified and dedicated health personnel, all across the spectrum of care. When, for example, no specific treatment is available for a given disease, adequate clinical management can still protect and save lives. This has been shown by a dramatic reduction in deaths from Ebola virus disease in West Africa in 2014 – from 75% to 33% mortality was achieved through the provision of better supportive care for patients.

Protecting frontline responders

The role of the health workforce should never be underestimated nor taken for granted. In general, much of their day-to-day work is routine, providing tried-and-tested care and treatment for familiar illnesses, disabilities and injuries.

But when an outbreak or epidemic strikes, health workers make a vital difference at all levels, whether as community health workers and volunteers, midwives, nurses or doctors. With little or no warning, they are transformed into frontline responders, thrust into immediate contact with infected communities and individuals. Family members also take on the role of caring for their relatives at home, often linking up with health staff in clinics, hospitals and emergency centres.

This transformation is double-edged and dangerous for frontline responders. First, their immediate priorities are to prevent the spread of an epidemic, protect those people who are most at risk, and to care by all possible means for those who are already infected. The related dangers are obvious: health workers are putting themselves at risk. They find



themselves in the most dangerous place at the most dangerous time.

Yet, because their job is to care for the sick and injured, health workers are often viewed as immune to injury or illness. Their patients come first. However, human-to-human transmission is a major factor in many infectious diseases that cause epidemics. Patients are highly contagious and can spread the disease at home, at work, in public spaces, but also in hospitals.

Thus, it is essential to protect frontline responders from infection – both for their own safety and for the wider protection of the affected community. It is here that emergency planning, preparation, training and coordination are so essential. Equally essential is the urgent provision of practical safeguards, especially the necessary PPE and knowledge of how to properly use it.

Confronting the human resources crisis

These measures may seem obvious, but the role of frontline responders is frequently constrained by a major disadvantage: there are not nearly enough of them. This unfortunate truth applies to the health workforce in general. It is a global problem, but it is most acute in low and middle income countries with the weakest health systems, where epidemics are most likely to erupt.

Protecting the occupational health of health workers is critical to ensuring an adequate workforce of trained and healthy health personnel. This is nowhere more true than at the heart of an infectious disease epidemic.

Around the world, health care facilities employ over 59 million workers.² Yet at the same time, there is a chronic shortage of them in more than 50 countries. This crisis in human resources for health has persisted for decades, despite numerous attempts to tackle it. While prior to COVID-19 actions had shown notable progress, the pandemic has had devastating impacts on the health workforce globally, deepening the human resource crisis.

It is not just a matter of numbers. While there has long been an exclusive focus on how many there are, against how many are needed, there

² WHO data – Occupational health webpage: <https://www.who.int/health-topics/occupational-health>



is growing public health agreement on giving equal importance to accessibility, acceptability, quality and performance of health workers in addition to availability.

These four factors are inter-related and inter-dependent. The absence, or inadequacy, of any one of them undermines all the others. Without sufficient availability, accessibility to health workers cannot be guaranteed. If they are available and accessible, without acceptability, the health services may not be used. When the quality of the health workforce is inadequate, improvements in health outcomes will not be satisfactory.

Elaboration of these complex issues at length goes beyond the scope of this handbook. But it is important that they are taken into account in the context of infectious disease prevention, treatment and control. Indeed, they lead to recognition that protecting health workers has the added benefit of contributing to quality patient care and health system strengthening.

If it is accepted that health begins with health workers, their empowerment is necessary on a general basis. Their voices, rights and responsibilities must play a central role in developing, implementing, and evaluating solid policies and strategies towards universal health coverage. This applies to the context of epidemic disease control as much as it does to other health issues more widely. The engagement of communities during epidemics, including the health workforce community, needs to be at the center of the epidemic response.

For more information about protecting the health workforce:

- WHO global health workforce network website
<https://www.who.int/teams/health-workforce/network>
- WHO Research & Development Blueprint
<http://www.who.int/blueprint/en/>

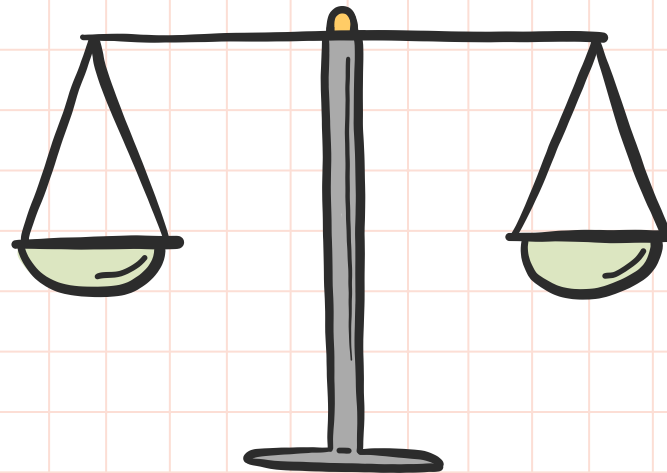
FOCUS 4

Managing ethical issues during epidemics and pandemics

Infectious disease outbreaks are periods of great uncertainty. As events unfold, resources and capacities that are often limited are stretched further, and decisions for a public health response must be made quickly even with scant evidence for decision-making. Furthermore, managing epidemics is about responding to human frailty and requires taking into consideration individuals' and communities' interests, perceptions, habits and practices.

Competing interests must often be weighed and balanced, and decisions made without unanimous support. In such situations, public health officials, policy-makers, funders, researchers, field epidemiologists, first responders, national ethics boards, health care workers and public health practitioners need a moral compass to guide their decision-making.

A variety of ethical principles must be taken into consideration and must be weighed when it is not possible to satisfy them all.



Ethical principles

Justice

Encompassing both fair distribution of resources, opportunities and outcomes, as well as fair processes for decision-making.

Beneficence

Acting for the benefit of others, for example society meeting the basic needs of individuals and communities.

Utility

Referring to actions that are right insofar as they promote the well being of individuals or communities; considerations of proportionality (balancing potential benefits against any risks of harm) and efficiency (achieving the greatest benefits at the lowest possible cost) are necessary to maximize utility.

Respect for persons

Treating individuals in ways that are fitting to and informed by a recognition of our common humanity, dignity, and inherent rights. It includes the notions of autonomy, informed consent, privacy and confidentiality, transparency, and respect for social, religious and cultural beliefs.

Liberty

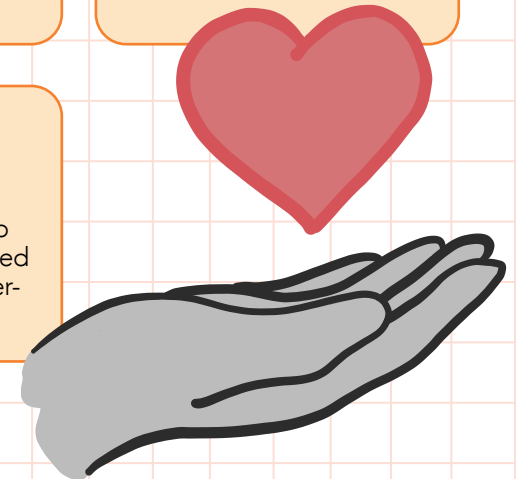
Involving a range of social, religious and political freedoms, and requiring respect for the freedom to make self-oriented decisions.

Reciprocity

Demonstrating respect for and making a “fitting and proportional return” for the sacrifices and contributions of others.

Solidarity

Standing together as a group, a community, a nation, or potentially a global community to justify collective action in the face of common threats and to overcome inequalities. This need not give rise to binary (us-them) relationships but rather encourage appreciation of our inter-relational interdependence.

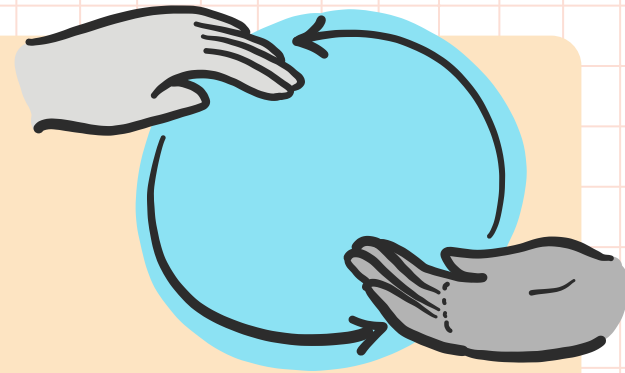


Based on these principles, decision-makers should take the following actions:

- **Affirm that governments respect their obligations**, ensuring the sufficiency of national public health laws, participating in ethical global surveillance¹, and providing financial, technical and scientific assistance.
- **Involve the local community** by respecting inclusiveness, openness to diverse perspectives, transparency and accountability.
- **Address situations of particular vulnerability**. For example, in the context of difficult access to services and resources, stigmatization and discrimination, and disproportionate burdens of outbreak response measures.
- **Address sex- and gender-based differences**, paying attention to social and cultural practices and implementing sex- and gender-inclusive prevention and control strategies.
- **Allocate scarce resources**, balancing considerations of effectiveness and equity, paying attention to the needs of vulnerable populations, and fulfilling reciprocity-based obligations to those who contribute to outbreak response efforts.
- **Ensure high-quality, ethically appropriate public health surveillance**, protecting the confidentiality of personal information.

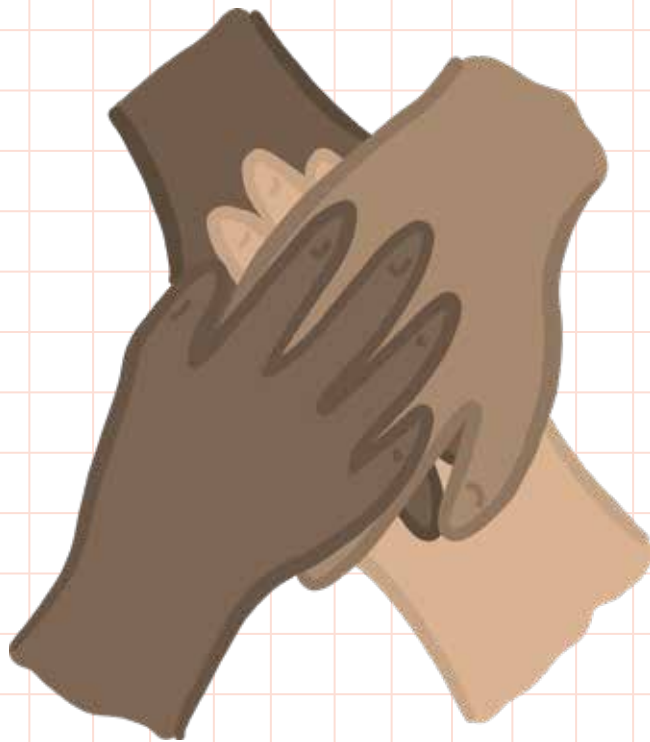
¹ WHO guidelines on ethical issues in public health surveillance, 2017. <https://www.who.int/publications/item/who-guidelines-on-ethical-issues-in-public-health-surveillance>

- **Implement restrictions on freedom of movement** only if less restrictive measures are unlikely to be as effective in achieving important public health objectives, and with the fewest constraints reasonably possible, ensuring humane conditions and equitable application.
- **Establish minimum standards in the care and treatment of patients affected by an outbreak**, taking into consideration the public health necessity of interventions, their feasibility, and the impact on community trust.
- **Integrate research during outbreaks**, involving local institutions and providing ethics reviews in time-sensitive circumstances, provided that research does not drain critical health-related resources, trust is gained and maintained, appropriate research methodologies are selected, data are rapidly shared and equitable access to the benefits of research is ensured.
- **Share public health and disease-related data rapidly**, protecting the confidentiality of personal information and addressing ownership issues.
- **Ensure ethical long-term storage of biological specimens collected during infectious disease outbreaks**, engaging communities, ensuring informed consent, and developing material transfer agreements and governance mechanisms for international sharing of biospecimens.
- **Guarantee frontline response workers' rights and clearly establish their obligations**, minimizing the risk of infection, ensuring priority access to health care, providing appropriate remuneration and supporting reintegration into the community.



- **Address ethical issues in deploying foreign humanitarian aid workers**, ensuring coordination with local officials, security and safety of aid workers, fairness in assigning foreign workers for deployment, clarity about conditions of deployment, provision of necessary training and resources, adherence to assigned roles and responsibilities, and attention to appropriate infection control practices.
- **Ensure that social listening and infodemic insights are collected**, analysed, generated and reported in a reproducible and transparent process, with protections for privacy, confidentiality, human rights and freedom of expression of communities whose questions, concerns and narratives they describe.

These considerations are important but may not be exhaustive. Preparation and early strategizing are the best ways to ensure that ethically justifiable decisions can be made if an outbreak occurs. These should consider and integrate local social, cultural and political contexts. WHO is committed to providing countries with technical assistance and tools in support of these efforts.

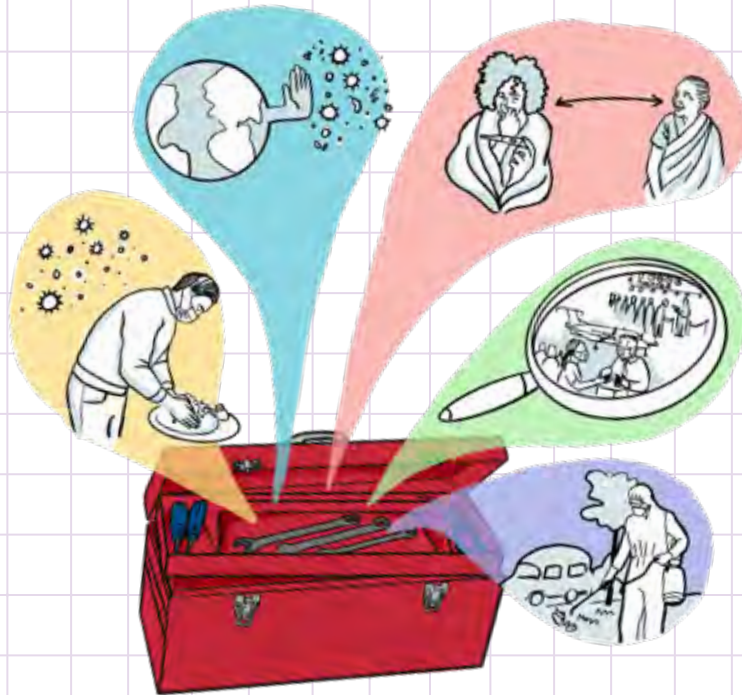


More information about protecting the health workforce:

- WHO webpage on global health ethics: outbreaks and emergencies
<https://www.who.int/teams/health-ethics-governance/emergencies-and-outbreaks>
- Guidance for managing ethical issues in infectious disease outbreaks, WHO, 2016
<https://apps.who.int/iris/handle/10665/250580>
- Ethics in epidemics, emergencies and disasters: Research, surveillance and patient care (training manual), WHO, 2015
<https://www.who.int/publications/i/item/ethics-in-epidemics-emergencies-and-disasters-research-surveillance-and-patient-care-training-manual>
- WHO guidelines on ethical issues in public health surveillance, 2017
<https://www.who.int/publications/i/item/who-guidelines-on-ethical-issues-in-public-health-surveillance>
- Bridging the gap between ethics and decision-making in pandemics: report of the WHO Pandemic Ethics and Policy Summit, 6 December 2021
<https://www.who.int/publications/i/item/9789240065086>

FOCUS 5

Public health and social measures during epidemics and pandemics



Public health and social measures (PHSM) refer to non-pharmaceutical interventions implemented by individuals, communities and governments to reduce the spread of infectious diseases with epidemic- or pandemic potential by reducing transmission of the pathogen. They are crucial in all stages of the outbreak management cycle, alone or in combination with medical countermeasures. The measures depend on the way the pathogen is transmitted.

The implementation of PHSM during an infectious disease outbreak can decrease the number of cases and hence reduce the pressure on the health care system, help to keep businesses and essential services open, and buy time for the development and production of medical countermeasures.

The implementation of PHSM has health and socio-economic impacts beyond the intended reduction of disease transmission. While implementing PHSM, decision-makers and health authorities have to take into account the available evidence and the benefits and

Non-exhaustive categorization of PHSM

Type of measures	Examples
Personal protective measures	Hand hygiene, respiratory etiquette, face masks, use of mosquito repellents/nets.
Environmental measures	Surface and object cleaning, ventilation, improving air/water quality, waste management, modifying humidity, human-animal interface measures, vector control measures.
Physical distancing measures	Screening, testing, contact tracing, isolation, quarantine, school/workplace measures and closure, avoiding crowding (for example bans of mass gatherings).
Travel-related measures (for reducing the geographic spread of the pathogen)	Travel advice, entry and exit screening, internal travel restrictions, border closures.

unintended negative consequences. For instance, school closures for long periods of time may have a substantial impact on education, while we know some pathogens have limited potential to cause severe disease in young age groups (for example COVID-19). Also, as some population subgroups may be more affected by those measures, it is important to understand the differentiated impacts (positive and negative) of PHSM among various population subgroups.

Mitigation measures should be introduced in parallel to PHSM to reduce their intervention burden and ensure a more equitable and acceptable implementation of PHSM, thus maximizing their health impact. This includes social protection policies ranging from paid sick leave to housing eviction bans or tax credit programmes as well as community-level interventions such as neighborhood support initiatives. Infodemic management and community engagement activities can further contribute to understanding the reasons behind communities' compliance, or lack thereof, with PHSM and inform agile, value-based, participatory and context-specific communication, mitigation measures and decision-making on PHSM.

Strategic implementation of PHSM needs to consider:

- The best timing to introduce, adapt, ease and lift measures.
- Tailored and evidence-informed combinations of different measures to maximize health gains.
- Adoption of mitigation measures to limit unintended negative consequences.
- Active engagement of various stakeholders (individuals, communities, local and national governments, international bodies).
- Conditions to foster community uptake of and adherence to measures.

This requires systematic, robust and timely research on the effectiveness of PHSM (including uptake and adherence) on broader health, social and economic systems.

As part of its pandemic and epidemic preparedness and prevention efforts, the WHO, together with its multidisciplinary partners, is working to develop evidence-informed tools to support countries in a more equitable, balanced and precise implementation of PHSM during future epidemics and pandemics.



More information about public health and social measures during epidemics and pandemics:

- Measuring the effectiveness and impact of public health and social measures
<https://www.who.int/activities/measuring-the-effectiveness-and-impact-of-public-health-and-social-measures>
- Report of the WHO global technical consultation on public health and social measures during health emergencies
<https://www.who.int/publications/i/item/9789240043213>
- Non-pharmaceutical public health measures for mitigating the risk and impact of epidemic and pandemic influenza
<https://www.who.int/publications/i/item/non-pharmaceutical-public-health-measures-for-mitigating-the-risk-and-impact-of-epidemic-and-pandemic-influenza>

Table: Primary modes of transmission and interventions per disease

DISEASE	MAJOR MODE OF TRANSMISSION	Clinical management		ENHANCED INFECTION PREVENTION & CONTROL	VACCINATION	SAFE & DIGNIFIED BURIALS	VECTOR CONTROL	WATER & SANITATION
		SPECIFIC	SUPPORTIVE					
Crimean-Congo haemorrhagic fever	Animals (mainly ticks) / contact	✓ ¹	✓	✓		✓	✓	
https://www.who.int/health-topics/cremean-congo-haemorrhagic-fever								
Chikungunya	Vector		✓				✓	
https://www.who.int/health-topics/chikungunya/#tab=tab_1								
Cholera	Fecal oral / water	✓	✓	✓	✓ ²			✓
https://www.who.int/health-topics/cholera#tab=tab_1								
COVID-19	Respiratory	✓	✓	✓	✓	✓		
https://www.who.int/emergencies/diseases/novel-coronavirus-2019								
Dengue	Vector		✓		✓ ³		✓	
https://www.who.int/health-topics/dengue-and-severe-dengue#tab=tab_1								
Ebola virus disease	Animals / contact	✓	✓	✓	✓	✓		
https://www.who.int/health-topics/ebola/#tab=tab_1								
Hepatitis E	Fecal oral / water		✓		✓			✓
https://www.who.int/en/news-room/fact-sheets/detail/hepatitis-e								
Influenza	Respiratory	✓	✓	✓	✓ ⁴	✓ ⁵		
https://www.who.int/health-topics/influenza-avian-and-other-zoonotic#tab=tab_1								
Lassa fever	Rodent / contact	✓	✓	✓			✓	
https://www.who.int/health-topics/lassa-fever/								
Leptospirosis	Rodent	✓	✓				✓	
https://apps.who.int/iris/handle/10665/205437								
Malaria	Vector	✓	✓		✓		✓	
https://www.who.int/health-topics/malaria#tab=tab_1								
Marburg virus disease	Animals / contact		✓	✓	✓			
https://www.who.int/health-topics/marburg-virus-disease#tab=tab_1								

¹ Ribavirin use currently under review by WHO.

² Oral vaccines.

³ There is a vaccine (Dengvaxia®) currently under assessment.

⁴ Intramuscular and intranasal vaccines.

⁵ Follow safe and dignified burials or IPC and safe management of a dead body for highly pathogenic non-human influenza.

DISEASE	MAJOR MODE OF TRANSMISSION	Clinical management		ENHANCED INFECTION PREVENTION & CONTROL	VACCINATION	SAFE & DIGNIFIED BURIALS	VECTOR CONTROL	WATER & SANITATION
		SPECIFIC	SUPPORTIVE					
Measles	Respiratory		✓	✓	✓			
https://www.who.int/health-topics/measles								
Meningitis	Respiratory	✓	✓	✓				
https://www.who.int/health-topics/meningitis#tab=tab_1								
MERS / SARS*	Respiratory / Animals		✓	✓		✓		
https://www.who.int/health-topics/middle-east-respiratory-syndrome-coronavirus-mers				https://www.who.int/health-topics/severe-acute-respiratory-syndrome#tab=tab_1				
Mpox	Animals / contact	✓	✓	✓	✓	✓		
https://www.who.int/health-topics/monkeypox#tab=tab_1								
Plague (pneumonic)	Respiratory	✓	✓	✓		✓		
https://www.who.int/health-topics/plague#tab=tab_1								
Plague (bubonic)	Rodent	✓	✓	✓		✓	✓	
https://www.who.int/health-topics/plague#tab=tab_1								
Poliomyelitis	Faecal oral		✓	✓	✓ ⁶			
https://www.who.int/health-topics/poliomyelitis#tab=tab_1								
Rickettsia	Vector	✓	✓				✓	
Rift Valley	Animals / vector		✓	✓			✓	
https://www.who.int/health-topics/rift-valley-fever#tab=tab_1								
Shigellosis	Faecal oral / food	✓	✓					✓
https://www.who.int/publications/i/item/9241592330								
Smallpox	Respiratory	✓	✓	✓	✓ ⁷			
https://www.who.int/health-topics/smallpox#tab=tab_1								
Typhoid fever	Food	✓	✓		✓			✓
https://www.who.int/health-topics/typhoid#tab=tab_1								
West Nile fever	Vector		✓				✓	
https://www.who.int/news-room/fact-sheets/detail/west-nile-virus								
Yellow fever	Vector		✓		✓ ⁸		✓	
https://www.who.int/health-topics/yellow-fever#tab=tab_1								
Zika	Vector		✓				✓	
https://www.who.int/health-topics/zika-virus-disease#tab=tab_1								

⁶ Oral and intramuscular/subcutaneous polio vaccines.

⁸ Intramuscular/subcutaneous vaccines.

* For SARS no evidence of direct animal-human transmission has been documented.

⁷ Intramuscular and scarification vaccines.

PART II

Be in the know

10 KEY FACTS ABOUT 19 DEADLY DISEASES

EBOLA DISEASE

LASSA FEVER

CRIMEAN-CONGO HAEMORRHAGIC FEVER (CCHF)

YELLOW FEVER (YF)

ZIKA

CHIKUNGUNYA

DENGUE

MALARIA

ANIMAL INFLUENZA

SEASONAL INFLUENZA

PANDEMIC INFLUENZA

MIDDLE EAST RESPIRATORY SYNDROME (MERS)

COVID-19

CHOLERA

MPOX (previously known as monkeypox)

PLAGUE

LEPTOSPIROSIS

MENINGOCOCCAL MENINGITIS

POLIOMYELITIS

Ebola disease

10 THINGS YOU SHOULD KNOW

1. Ebola disease (EBOD) is a group of viral diseases caused by different viruses from the Ebolavirus genera
2. EBOD can transmit from person to person through close contact with the body fluids of a sick or deceased person
3. EBOD are difficult to distinguish from other diseases with haemorrhagic presentations; laboratory testing is necessary to confirm Ebola infection
4. Health workers, mourners and family members are most at risk for infection
5. At-risk persons should be informed about IPC measures and provided with appropriate PPE
6. Outbreaks can be controlled through community engagement, active case finding and contact tracing, ring vaccination when recommended, laboratory support, early supportive care and safe and dignified burials are key to controlling outbreaks
7. A vaccine is effective and has been prequalified by WHO for responding to Ebola virus disease (EVD) outbreaks
8. Early intensive supportive care improves survival, and monoclonal antibody therapeutics have been shown to significantly reduce mortality from EVD
9. The virus can persist in people recovering from the disease for several months and survivors may suffer from stigma and sequelae
10. Research is continuing to develop and evaluate vaccines, diagnostics and therapeutics



Ebola disease response tips

Collaborative surveillance

- Conduct surveillance, contact identification and contact tracing.
- Set up laboratory capacities to support surveillance activities and patient management.
- Ensure early laboratory confirmation of suspected cases.
- Notify cases to WHO under the IHR (2005).

Community protection

- Support community engagement, health promotion and social science.
- Encourage health authorities to:
 - Implement active case finding and contact tracing.
 - Ensure protection of frontline workers through adequate IPC measures and vaccination as per SAGE recommendations.
 - Communicate early and frequently.
- Key messages are:
 - Ebola viruses are transmitted through contact with the body fluids of humans who are sick with EBOD or who have died from EBOD.
 - The bodies of deceased patients are contagious and it is possible to bury deceased people in a dignified way while minimizing body handling.
 - People in contact with sick or dead patients should apply strict IPC measures to protect themselves.
 - People cannot transmit Ebola viruses if they do not show symptoms.
 - People with symptoms should seek early medical care as intensive supportive care significantly increases chances of survivals, as do EVD specific therapeutics.
 - Contacts and contacts of contacts of EVD patients and frontline workers involved in EVD outbreak response should be vaccinated with Ervebo® using a ring vaccination strategy (Note: Ervebo® is for Zaire Ebolavirus only).

Clinical care

- Provide clinical management and ensure IPC:
 - Isolate EBOD patients in adapted health facilities.
 - Provide early intensive supportive care to patients and for EVD, treat with one of the two monoclonal antibodies (Ebanga or Inmazeb).
 - Implement adequate IPC measures for all patients in all health care facilities to reduce transmission in health care settings.

Access to countermeasures

- In response to EVD outbreak, proceed with ring vaccination with Ervebo®, a vaccine prequalified by WHO, per SAGE recommendations (Note: Ervebo® is for Zaire ebolavirus only).
- Ensure implementation of safe and dignified burials.

Emergency coordination

- Engage with religious, community, youth group and women's group leaders, and relevant local, subnational and national authorities.
- Ensure ongoing engagement with teams responsible for community engagement, surveillance, laboratory, clinical management, safe and dignified burials, IPC, vaccination against EVD and others as needed.

1

Ebola disease (EBOD) is a group of viral diseases caused by different viruses from the Ebolavirus genera

- EBOD, formerly known as Ebola haemorrhagic fever, are zoonotic diseases transmittable from wild animals to humans.
- Filovirus disease classification and nomenclature were incorporated into the WHO's ICD-11 framework (The International Classification of Diseases Revision 11). According to this classification:
 - EVD is caused by Ebola virus (EBOV) from Zaire Ebolavirus species;
 - Bundibugyo virus disease (BVD) is caused by Bundibugyo virus (BDBV); and
 - Sudan virus disease (SVD) is caused by Sudan virus (SUDV).
- The most frequent Ebola disease is EVD caused by EBOV from Zaire Ebolavirus species.
- The reservoir of these diseases is believed to be fruit bats, but other reservoirs have been identified.
- Ebola, Sudan and Bundibugyo viruses are first introduced into the human population through close contact with the blood, secretions, organs or other body fluids of infected animals such as fruit bats, chimpanzees, gorillas, monkeys, forest antelopes and porcupines found ill or dead, often in the rainforest. Ebola diseases should be suspected if any of these animals is found ill or dead in the rainforest.

- Ebola, Sudan and Bundibugyo viruses then spread through human-to-human transmission via direct contact (through broken skin or mucous membranes) with the blood, secretions, organs or other body fluids of infected people.
- The first introduction of the virus into the human population often occurs in rural settings but can spread to more densely populated areas along with movement of people.



2

EBOD can transmit from person to person through close contact with the body fluids of a sick or deceased person

- EBOD are severe illness in humans.
- The average case-fatality rate is around 50%, varying from 25–90% in past outbreaks.
- The incubation period ranges from 2–21 days.
- Humans are not infectious as long as they do not develop symptoms.
- During the course of the disease, those with symptoms remain infectious as long as their blood contains the virus.
- Infection can also occur if broken skin or mucous membranes of a healthy person come into contact with items or environments contaminated with body fluids from an infected person. These may include soiled clothing, bed linen, gloves and protective equipment. Medical waste, such as used syringes and needles, should be disposed of safely, as they could be a source of nosocomial infection.
- Ebola, Sudan and Bundibugyo viruses have not been reported to be transmitted by aerosols. They are not airborne.

*contact with
bodily fluids*



3

EBOD are difficult to distinguish from other diseases with haemorrhagic presentations; laboratory testing is necessary to confirm Ebola infection

- The first symptoms are nonspecific and common to many other diseases. They include sudden onset of fever, fatigue, muscle pain, headache and sore throat.
- These first symptoms are usually followed by vomiting, diarrhoea, rash, symptoms of impaired kidney and liver function and in some cases both internal and external bleeding (for example oozing from the gums, blood in the stools).
- Ebola virus infection should be confirmed using laboratory diagnostics including:
 - RT-PCR assay
 - ELISA
 - Antigen-capture detection test
 - Serum neutralization test
 - Electron microscopy
 - Virus isolation by cell culture.
- Current WHO recommended tests include:
 - NAT for routine diagnostic management.
 - Rapid antigen detection tests for use on oral fluid specimens for safe and dignified burials.
- All tests should be confirmed with NAT.

- The preferred specimens for diagnosis include:
 - Whole blood collected from live patients exhibiting symptoms.
 - Oral fluid specimens stored in universal transport medium collected from deceased patients or when blood collection is not possible (swab for dead bodies).
- In the absence of NAT capacities, specimen collection and transportation to a WHO Collaborating Centre is critical and must be set up in advance of an outbreak.
- Refer to recommended WHO case definitions for EVD. During an outbreak, case definitions are likely to be adapted to new clinical presentation(s) or different modes of transmission related to the local event.

4

Health workers, mourners and family members are most at risk for infection

- Populations at high risk of being infected with Ebola viruses include:
 - Health care workers, if IPC measures are not in place or not well followed during patient care;
 - Mourners, as levels of Ebola virus remain high in body fluids after death and if burial practices involve direct contact (for example washing, touching) with the body or body fluids of the deceased; and
 - Family members or others in close contact with infected people and who provide care that might involve contact with body fluids or contaminated items.



5

At-risk persons should be informed about IPC measures and provided with appropriate PPE

- All health care providers working at all levels of the health system, and family members caring for the sick, should be fully informed about the disease and its mode of transmission and should strictly follow the recommended IPC measures for Ebola.
- They should be provided with appropriate PPE.
- Standard precautions should be applied with all Ebola patients. These include hand hygiene; use of gloves before contact with body fluids, mucous membranes, non-intact skin and contaminated items; gown and eye protection before procedures and patient-care activities likely to involve contact with or projection of blood or body fluids; injection safety practices; safe cleaning, disinfection and waste management; and isolation of cases and appropriate flow of patients.



6

Outbreaks can be controlled through community engagement, active case finding, contact tracing, ring vaccination when recommended, laboratory support, early supportive care and safe and dignified burials

- The aim of Ebola outbreak response is to stop human-to-human transmission as early as possible. Ebola virus transmission is stopped by:
 - Community engagement:
 - Communities are essential for implementing appropriate control measures during Ebola outbreaks.
 - Communities play the most important role in accepting and implementing recommended health interventions.
 - Communities should be engaged in the response from the early stages and provided with the necessary information so that public health interventions can be adapted to their sociocultural beliefs and their compliance ensured.
 - Active case finding:
 - This refers to actively searching for new Ebola patients (for example going from house to house in the community, asking if people are sick or have died).
 - Suspected patients should be rapidly and safely referred to treatment centres for initiation of supportive care and treatment.



- Contact tracing:
 - This refers to the follow up of persons who have come into contact with a person infected with the Ebola virus (or their body fluids or an exposed environment such as linens, a dead animal, etc.).
 - Contacts should be followed for 21 days after the last exposure, looking for symptoms such as fever, and referred to a treatment centre if they become develop symptoms.
- Ring vaccination:
 - In response to EVD and following SAGE recommendations, contacts of confirmed cases, and their contacts should be offered vaccination with Ervebo®, along with frontline workers responding to the outbreak.
- Laboratory testing:
 - Laboratory testing is crucial for diagnosis of patients (EVD confirmed or not), to streamline surveillance, for patient triage and management, and to support research and development.

- In response to Ebola virus disease, a close-to-patient automated PCR platform has proven effective in offering timely support for diagnostic and patient management.
- Early intensive supportive care and treatment:
 - Providing intensive care to patients as early as possible has been shown to improve survival chances.
 - For EVD, two monoclonal antibody therapeutics (Inmazeb and Ebanga) should be provided to patients as early as possible, as treatment significantly reduces mortality.
- Safe and dignified burials:
 - Safe and dignified burials teams are necessary to facilitate mourning by affected families and communities and to avoid transmission of Ebola virus from deceased patients.
- Other key elements to control outbreaks are:
 - Psychosocial support to patients and their families.
 - Follow-up and care for Ebola survivors as the virus may persist in some body fluids that can in rare cases lead to secondary infections.
 - Public health emergency plans and standard operating procedures at designated points of entry, in accordance with the IHR (2005).

- After 42 days (two times 21-day maximum incubation period for Ebola virus) with no new cases, human-to-human transmission is considered controlled and the outbreak can be declared over.



7

A vaccine is effective and has been prequalified by WHO for responding to Ebola virus disease (EVD) outbreaks

- The Ervebo® vaccine, has been shown to be effective in protecting people against Ebola virus belonging to Zaire Ebola virus species, and is recommended by the Strategic Advisory Group of Experts on Immunization (SAGE) as part of a broader set of Ebola outbreak response tools.
- Ervebo® was licensed in November 2019 by the European Medicines Agency and in December 2019 by the US Food and Drug Administration and prequalified by WHO.
- As per SAGE recommendations, this vaccine should be delivered through a ring vaccination strategy to contacts and contacts of contacts of confirmed cases, and to frontline workers responding to the outbreak.
- A global stockpile (ICG-EboVax) managed under the ICG of vaccine provision was established in January 2020. Countries reporting laboratory confirmed case of EVD can access doses from the stockpile.

8

Early intensive supportive care improves survival, and monoclonal antibody therapeutics have been shown to significantly reduce mortality from EVD

- For all EBOD, early intensive supportive care, including close and regular monitoring of patient's vital signs, fluids and electrolytes balance with careful oral or intravenous rehydration, and treatment of specific symptoms and possible co-infections, improves chances of survival.
- Field laboratories providing biochemistry and haematology testing help improve patient supportive care and management.
- It is important that health workers have the trust of patients and families to facilitate acceptance of care in dedicated treatment facilities.
- Care should be patient-centered and respect patients' preferences.
- In 2020, two monoclonal antibodies (Inmazeb and Ebanga) have been approved for the treatment of patients confirmed with EVD. Confirmed cases should be treated, as early as possible with one of the two monoclonal antibodies.

**INTENSIVE
SUPPORTIVE
CARE**



9

The virus can persist in people recovering from the disease for several months and survivors may suffer from stigma and sequelae

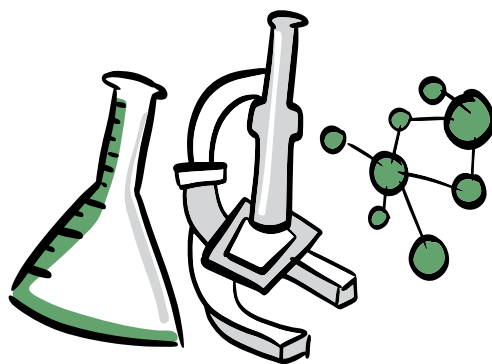
- With increasing capacities to provide care and treatment, patients are at increased chance of survival from EBOD.
- Ebola, Sudan and Bundibugyo viruses are known to persist in immune-privileged sites in some people who have recovered from the disease.
 - These sites include the testicles, the inside of the eye and the central nervous system.
 - In women who have been infected while pregnant, the virus may persist in the placenta, amniotic fluid and fetus.
 - In women who have been infected while breastfeeding, the virus may persist in breast milk.
- Several cases of sexual transmission have been reported from a male survivor to his partner.
- All Ebola survivors and their sex partners should receive counselling to ensure safer sex practices, be provided with condoms when discharged from an Ebola treatment unit and enrolled in a national semen and body fluid testing programme.
- Male Ebola survivors should be offered semen testing when discharged from an Ebola treatment unit until they receive two consecutive negative results by RT-PCR at one month apart.
- Relapse-symptomatic illness has been documented in very few patients who recovered from EVD.
 - These occurrences of EVD recrudescence have manifested as uveitis from Ebola virus in the aqueous humour of a survivor and meningitis caused by virus detected in a survivor's cerebrospinal fluid months after recovering from the initial infection.
 - Disease recrudescence can be associated with changes in a patient's immune status, but reasons for this phenomenon are not yet fully understood.
- Survivors may suffer from physical sequelae and should receive care. The most common physical sequelae are musculoskeletal, ocular, auditory, abdominal, neurological and sexual issues.
- Survivors may suffer from psychological conditions such as post-traumatic stress disorder and need to be offered adequate support.
- Survivors may suffer from stigma. They may be rejected from their community and should be followed and assisted, if needed, regarding employment, living conditions, family, social support, etc. They should receive counselling regarding possible sequelae and psychosocial challenges.
- Specific follow-up considerations should be applied for children and pregnant women who survived.

10

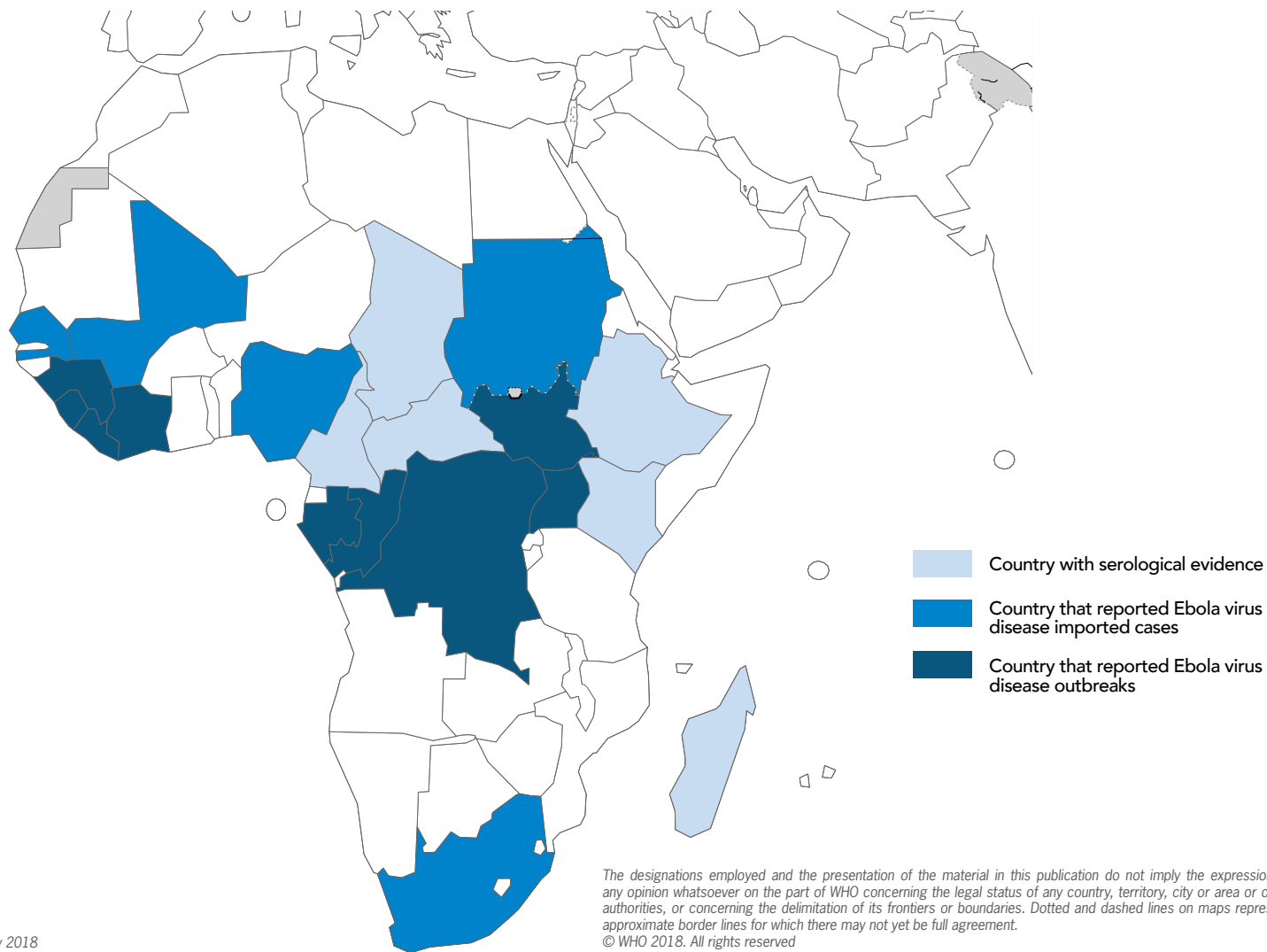


Research is continuing to develop and evaluate vaccines, diagnostics and therapeutics

- WHO continues to work with partners toward an internationally coordinated governing mechanism to ensure fair access to vaccines according to risk criteria and to manage supplies and stockpiles, especially as supplies will remain limited until full manufacturing capacity is established or other vaccines are licensed.
- For EVD, four NATs and three RDTs were approved for emergency use during the Ebola crisis in 2014–2016.
- Building on these, during the 2018–2020 EVD outbreak, the government of the Democratic Republic of the Congo chose to use semi-automated RT-PCR with Expert Ebola (Cepheid) as the standard diagnostic method, allowing deployment of up to 11 field national laboratories close to treatment centres. Diagnostic confirmation was available in less than 24 hours of sample reception, allowing close patient monitoring throughout their disease.
- Further research is on-going to develop additional specific diagnostic products and therapeutics for Bundibugyo virus disease, Sudan virus disease and new emerging EBOD.



Geographic distribution of Ebola virus disease outbreaks (1976-2018)



Source: WHO/IHM, as of 15 February 2018



More information on Ebola disease:

- Ebola WHO webpage
<http://www.who.int/ebola/en/>
- Ebola WHO fact sheet
<http://www.who.int/mediacentre/factsheets/fs103/en/>
- EboVax ICG
<https://www.who.int/groups/icg/ebola-virus-disease/ebola-stockpiles>
- OpenWHO course on Ebola
<https://openwho.org/courses/pandemic-epidemic-diseases>
- Ebola and Marburg virus disease epidemics: preparedness, alert, control and evaluation
<https://www.who.int/publications/i/item/WHO-HSE-PED-CED-2014.05>
- Case definitions
<https://www.who.int/publications/i/item/WHO-EVD-CaseDef-14.1>
- Implementation and management of contact tracing for Ebola virus disease
<https://www.who.int/publications/i/item/WHO-EVD-Guidance-Contact-15.1>
- Case management and IPC
<https://www.who.int/publications/i/item/WHO-HIS-SDS-2014.4-Rev.1>
- Clinical care for survivors of EVD
<https://www.who.int/publications/i/item/WHO-EVD-OHE-PED-16.1>
- Safe and dignified burials
<https://www.who.int/publications/i/item/WHO-EVD-Guidance-Burials-14.2>

Lassa fever

10 THINGS YOU SHOULD KNOW

1. Lassa fever is a viral haemorrhagic fever that occurs in West Africa
2. The reservoir of Lassa fever is a rat
3. Humans are primarily infected through exposure to rats' urine or faeces
4. Human-to-human transmission then occurs through direct contact with body fluids of infected persons
5. Lassa fever disease varies in severity and some population groups such as pregnant women and infants may experience more severe disease
6. Lassa fever is hard to distinguish from other viral diseases
7. Hygiene and rodent control are the best prevention in communities
8. Strict implementation of IPC measures in health care settings is critical to prevent the spread of the disease
9. Early supportive treatment reduces mortality
10. Outbreaks can be controlled through community engagement, active case finding, early case recognition and laboratory confirmation, early supportive care, IPC measures in health facilities, community hygiene and rodent control



Lassa fever response tips

Collaborative surveillance

- Conduct surveillance, contact identification and contact tracing.
- Ensure early laboratory confirmation of suspected cases.
- Notify cases to WHO, under the IHR (2005).

Community protection

- Support community engagement, health promotion and social science.
- Encourage health authorities to:
 - Implement active case finding.
 - Ensure protection of health workers through IPC measures.
 - Communicate and train health workers on how to protect themselves from becoming infected.
 - Provide targeted communication to at-risk groups such as pregnant women.
- Key messages to the general public:
 - Humans are primarily infected through exposure to rats' urine or faeces.
 - Avoid contact with body fluids of sick people.
 - Seek health advice rapidly if you show symptoms.
 - Wash your hands regularly.
 - Implement measures to reduce contact with rodents.

Clinical care

- Case management and IPC:
 - Isolation of cases.
 - Early supportive treatment.
 - Protect health workers.

Access to countermeasures

- To prevent infection, people should follow basic hygiene practices including hand washing and thoroughly cooking food.
- In communities, measures should be put in place to reduce human-rodent interactions.

Emergency coordination

- Engage with partners involved in the response (surveillance, laboratory, case management, IPC and community engagement).
- Engage with religious and community leaders.

1

Lassa fever is a viral haemorrhagic fever that occurs in West Africa

- Lassa fever is a viral haemorrhagic illness of 1–4 weeks duration that occurs in West Africa.
- Lassa fever has been reported in Benin, Burkina Faso, Côte-d'Ivoire, Ghana, Guinea, Liberia, Mali, Nigeria, Sierra Leone and Togo, but should be considered endemic in other West African countries.
- The overall case fatality rate is 1%.
- Observed case fatality rate among patients hospitalized with severe presentation of Lassa fever is 15%.

2

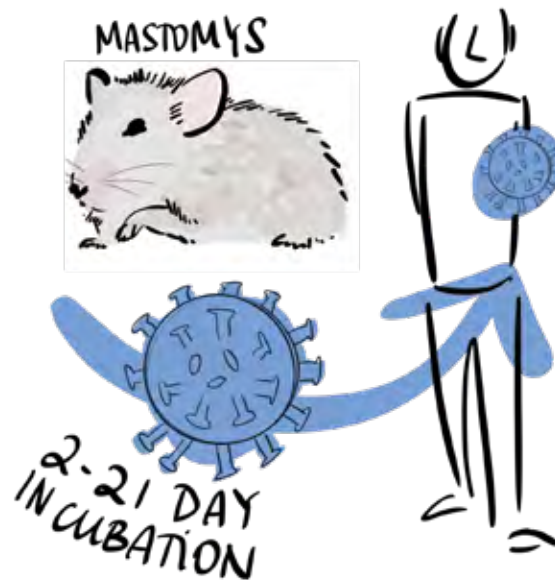
The reservoir of Lassa fever is a rat

- The animal reservoir of Lassa virus is a rodent: the *Mastomys* rat, commonly known as the "multimammate rat".
- *Mastomys* rats are infected at birth and are chronic asymptomatic carriers of Lassa virus.
- The infected rats do not become ill but can shed the virus in their urine and faeces.
- The virus is present in excreta, particularly urine.

3

Humans are primarily infected through exposure to rats' urine or faeces

- Humans usually become infected with Lassa virus from exposure to urine or faeces of infected rats.
- 85–90% of humans are infected through:
 - Direct contact by catching, handling and preparing *Mastomys* as a food source.
 - Ingestion of food contaminated by infected rodent excreta;
 - Direct contact with objects and surfaces contaminated by rats' urine and faeces; or
 - Inhalation of aerosolized virus (rare).
- Transmission of Lassa fever virus from rats to humans is common, since these rodents scavenge on human food items and readily colonize areas where humans live.
- People at high risk of being infected, through rat-to-human transmission, are:
 - Persons living in rural areas where *Mastomys* are usually found, especially in communities with poor sanitation or crowded living conditions; and/or
 - Persons hunting and consuming rodent products.



4

Human-to-human transmission then occurs through direct contact with body fluids of infected persons

- 15–10% of human infections are acquired through secondary human-to-human transmission. Lassa virus may spread from human to human through direct contact with the blood, urine, faeces or other body secretions of a person infected with Lassa fever.
- Human-to-human and laboratory transmission also occur, particularly in health care settings lacking adequate IPC measures (for example the virus may be spread by contaminated medical equipment, such as re-used needles).
- People most at risk of being infected through human-to-human transmission, are:
 - Health workers or anyone caring for Lassa fever patients in the absence of proper IPC practices; and
 - People handling dead bodies of infected patients (for example during funerals).
- There is no evidence supporting airborne spread between humans.

contact with
bodily fluids



5

Lassa fever disease varies in severity and some population groups such as pregnant women and infants may experience more severe disease

- The incubation period of Lassa fever ranges from 2–21 days.
- About 80% of infected people do not show symptoms or experience a mild disease.
- The onset of the disease is usually gradual. Symptoms start with fever, general weakness and malaise and can then be followed by headache, sore throat, muscle pain, chest pain, nausea, vomiting, diarrhoea, cough and abdominal pain.
- In mild cases, the patient usually recovers rapidly.
- Severe cases (20%) may develop facial swelling, fluid in the lung cavity, bleeding from the mouth, nose, vagina or gastrointestinal tract and low blood pressure. Severe cases require hospitalization. Shock, seizures, tremor, disorientation, and coma may also be seen in the later stages.
- Death usually occurs within 14 days of onset in fatal cases. Fatal cases represent 1–2% of total infected symptomatic cases.
- Various degrees of deafness occur in 25% of severe cases who survive the disease. In half of these cases, hearing returns partially after 1–3 months. Transient hair loss and gait disturbance may occur during recovery.

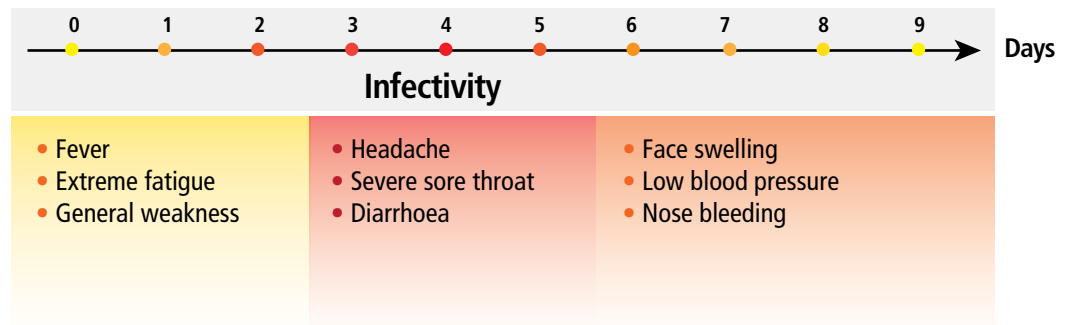
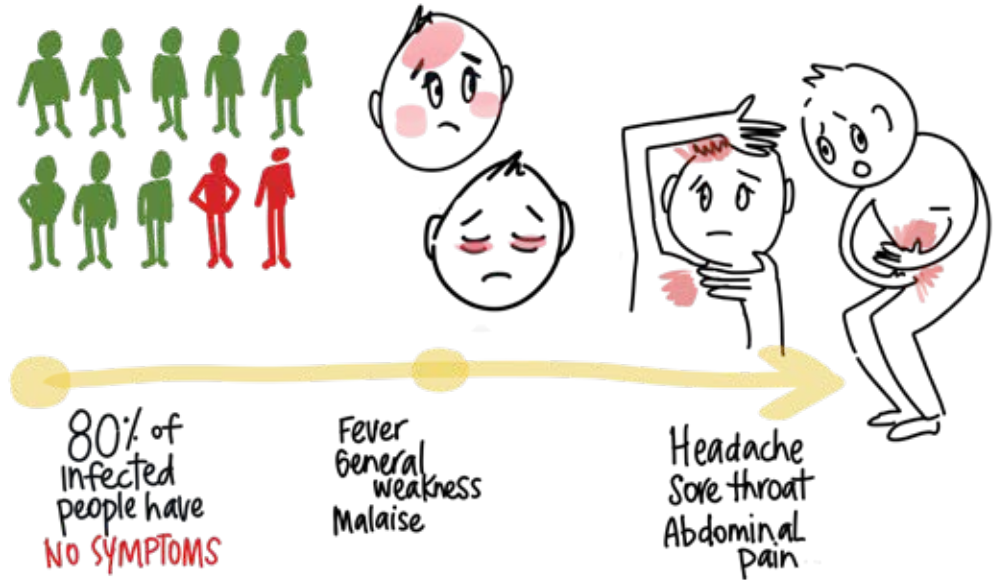
- The disease is especially severe late in pregnancy:
 - Maternal mortality can be greater than 30% in third trimester and 50% in the last month.
 - Fetal loss occurs in more than 80% of cases during the third trimester.
 - Pregnant women show increased level of viraemia (virus levels in the blood).
 - Infection in infants is also associated with a very high case fatality rate. Infants (up to 2 years old) can present with swollen baby syndrome (oedema, abdominal distension and bleeding, often leading to death). Older children experience similar symptoms as adults.



6

Lassa fever is hard to distinguish from other viral diseases

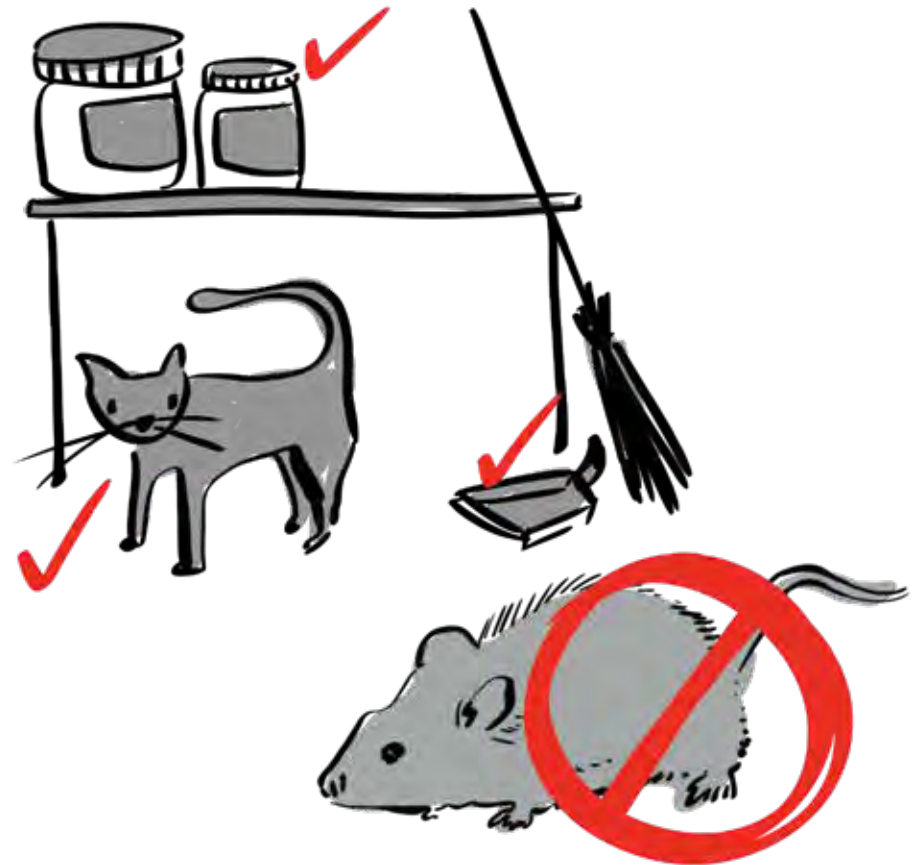
- Symptoms of Lassa fever are non-specific, which makes clinical diagnosis difficult, especially early in the course of the disease. Lassa fever can be difficult to distinguish from other viral haemorrhagic fevers (for example Ebola virus disease) as well as from other diseases that cause fever such as malaria, typhoid fever, yellow fever, influenza, measles, shigellosis, cholera, leptospirosis, rickettsial infections, relapsing fever, meningitis, bacterial sepsis and hepatitis.
- Patient history is essential to guide diagnosis and should include exposure to rodents, residence or travel to area/village endemic for Lassa and/or contact with Lassa cases.
- Lassa virus infections can only be diagnosed definitively in the laboratory using the following tests:
 - RT-PCR
 - ELISA
 - Antigen detection tests
 - Virus isolation by cell culture
- Laboratory specimens may be hazardous and must be handled with extreme care. Handling specimens with live virus requires BSL 4 facilities. If samples have been inactivated, they can be manipulated in a basic biosafety environment.



7

Hygiene and rodent control are the best prevention in communities

- Engaging with communities is the first step to empower them in taking adequate actions to reduce the risk of infection.
- To prevent infection, people should follow basic hygiene practices:
 - Wash their hands regularly and
 - Cook food thoroughly.
- At the community level, to reduce human-rodent contacts, people are advised to:
 - Store food in covered rodent-proof containers.
 - Keep homes clean and clear away any rubbish in or around the house.
 - Keep a cat.
 - Implement measures to reduce rodent populations. This would require strong political commitment and sustained efforts. Techniques that could be used include:
 - Trapping and poisoning
 - Using non-lethal, non-toxic alternatives to chemical rodenticides (research ongoing)
 - Reducing reproduction (fertility control).



8

Strict implementation of IPC measures in health care settings is critical to prevent the spread of the disease

- In health care settings, staff should always apply standard IPC precautions when caring for patients, regardless of their presumed diagnosis. These include:
 - Hand hygiene
 - Respiratory hygiene
 - Use of PPE to block splashes or other contact with infected materials)
 - Safe injection practices
 - Safe and dignified burial practices.
- Health workers caring for patients with suspected or confirmed Lassa fever should apply extra IPC measures to prevent contact with the patient's blood, body fluids and contaminated surfaces or materials such as clothing and bedding.
- When in close contact (within 1 metre) of patients with Lassa fever, health workers should wear face protection (a face shield or a medical mask and goggles), a clean, non-sterile long-sleeved gown and gloves (sterile gloves for some procedures).
- Health workers should remember that maternity wards are potential sites of amplification as miscarriage and natural abortion with massive bleeding may conclude from women with Lassa fever.



9

Early supportive intensive care improves chance of survival

- Treatment is supportive and includes symptomatic treatment of symptoms or other concurrent diseases or conditions, rehydration, monitoring fluid and electrolyte balance and renal function.
- Biological monitoring (hematology and biochemistry) along with viral load monitoring are needed to improve supportive care.
- The antiviral drug ribavirin seems to be effective if given early in course of the disease, however further research is needed on its use.
- There is currently no licensed or commercially available vaccine. New candidate vaccines are under development.
- Candidate drugs are being evaluated.



10

Outbreaks can be controlled through community engagement, active case finding, early case recognition and laboratory confirmation, early supportive care, IPC measures in health facilities, community hygiene and rodent control.

- The transmission of the disease can be stopped through:
 - Community engagement:
 - Communities are essential for controlling Lassa fever outbreaks.
 - Communities have a role to play in the detection of new cases and reduction of transmission through safe caring of the sick at home.
 - Communities should be engaged in the response since the early stage and be provided with the necessary information and PPE so that they can adapt public health measures to their socio-cultural beliefs and ensure compliance of community members.
 - Support communities to implement some rodent control measures as needed and feasible.
 - Active case finding, rapid isolation of patients and early laboratory confirmation of suspected cases.
 - Active case finding refers to actively searching for new cases (for instance, going from house to house in the community asking if people are sick or if people have died).



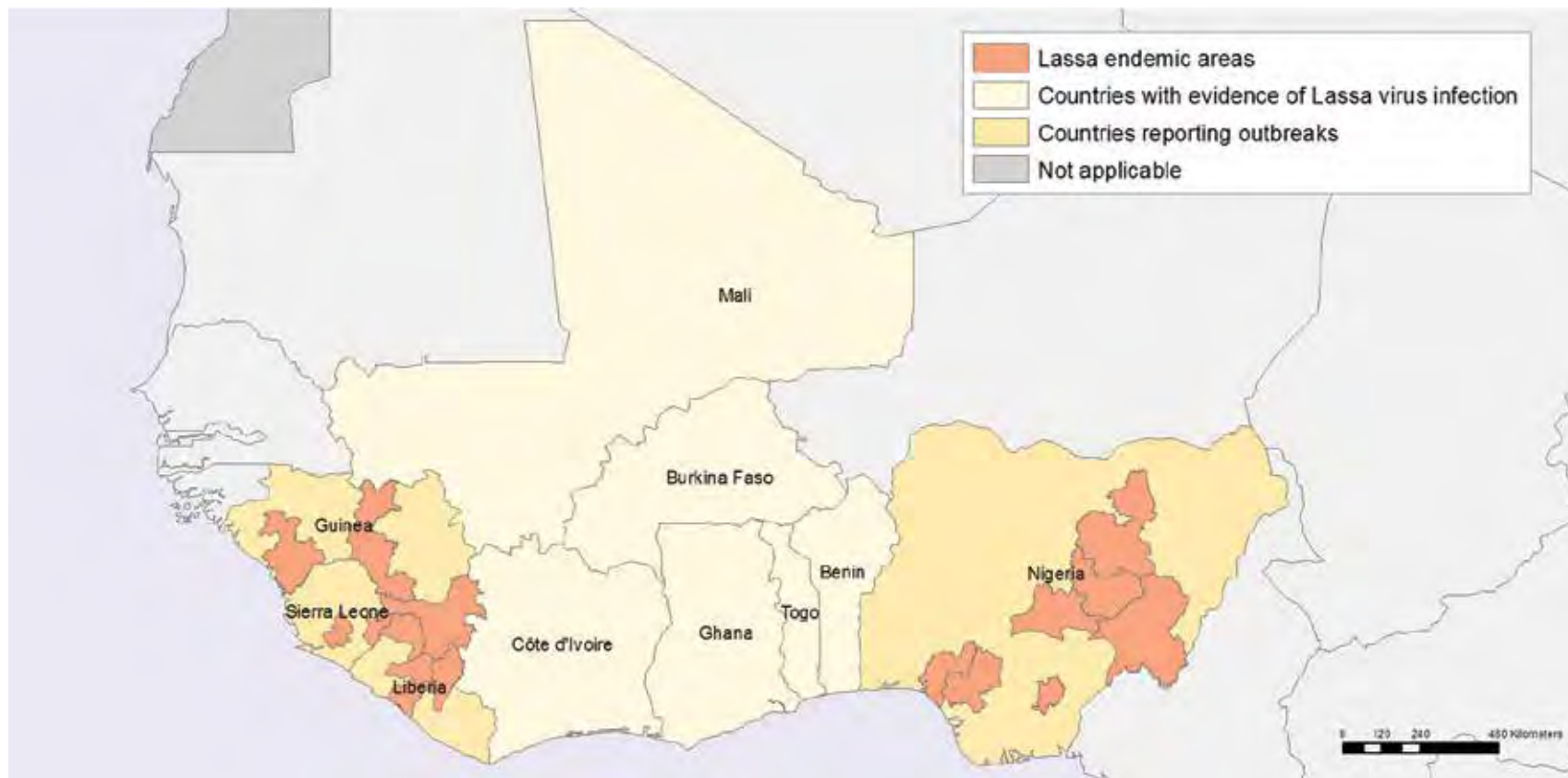
- New (suspected) cases should be rapidly and safely referred to treatment centres for isolation and treatment.
- Support clinical staff in endemic areas to improve early recognition of Lassa fever so that care can be initiated timely.
- Ensuring strong laboratory set-up to ensure timely confirmation and patients' biological monitoring.
- Provide early supportive care (rehydration and pain relief) to patients as early as possible as it reduces mortality (see point 6).
 - In hyperendemic areas, it is advisable that dedicated a Lassa ward be set-

up with specialized staff and specific equipment.

- Strengthen IPC measures in health care facilities that may receive Lassa fever patients to protect health workers and limit the risk of transmission in health care facilities.



Geographic distribution of Lassa fever in West African affected countries, 1969–2018



The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

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More information about Lassa fever:

- Lassa fever WHO webpage
https://www.who.int/health-topics/lassa-fever/#tab=tab_1
- Lassa fever WHO fact sheet
<http://www.who.int/mediacentre/factsheets/fs179/en/>
- WHO generic presentation – Introduction to Lassa fever
https://cdn.who.int/media/docs/default-source/documents/emergencies/health-topics---lassa-fever/lassa-fever-introduction.pdf?sfvrsn=b1b96509_2&download=true
- OpenWHO course on Lassa fever
<https://openwho.org/courses/pandemic-epidemic-diseases>



Crimean-congo haemorrhagic fever (CCHF)

10 THINGS YOU SHOULD KNOW



1. CCHF disease is a viral zoonotic disease that is transmitted by ticks, generally those living on livestock
2. Humans are primarily infected through tick bite, although there are other modes of transmission
3. Infected livestock animals do not develop apparent disease
4. CCHF is a severe disease with a high case fatality ratio
5. CCHF can be misdiagnosed as other viral haemorrhagic fevers and early laboratory confirmation of suspected cases is critical
6. Early supportive care improves chances of survival
7. IPC measures are critical to control the infection when caring for patients
8. Raising awareness on risk factors and preventive measures is key to reduce infection in people, especially among at-risk groups in CCHF endemic areas
9. Efficient vector control measures are currently lacking
10. CCHF is one of the priority diseases for research and development of countermeasures

Crimean-Congo haemorrhagic fever (CCHF) response tips

Collaborative surveillance

- Ensure early laboratory confirmation of suspected cases.
- Laboratory system for case confirmation and patient management.
- Notify cases to WHO, under the IHR (2005).
- Conduct surveillance, contact identification and contact tracing.

Community protection

- Support community engagement, health promotion and social science, particularly targeting groups most at-risk.
- Raise awareness of the risk factors for CCHF.
- Inform people about measures to reduce tick-to-human transmission, animal-to-human transmission and human-to-human transmission.
- Encourage health authorities to:
 - Implement active case finding and contact tracing.
 - Ensure protection of health workers through implementation of IPC measures.
 - Communicate about how to protect from becoming infected.
- Key messages are:
 - CCHF is transmitted by ticks or through contact with body fluids of infected animals and humans.
 - Apply IPC measures when in contact with sick or dead patients.
 - People with symptoms should seek medical advice as early supportive care increases chances of survival.

Clinical care

- Case management and IPC:
 - Isolation of cases.
 - Early supportive care supported by biological monitoring.
 - Protect health workers through implementation of adequate IPC measures and prevent transmission in health care facilities.

Access to countermeasures

- Vector control measures are currently lacking, raising awareness and engaging communities is key.

Emergency coordination

- Engage with partners involved in the response (community engagement, surveillance, laboratory, case management, IPC and vector control).
- Engage with the animal health and food production sectors.

1

CCHF disease is a viral zoonotic disease that is transmitted by ticks, generally those living on livestock

- Ticks of the genus *Hyalomma* are the principal vector of the disease, although a number of other ticks are capable of becoming infected with CCHF virus.
- Domestic and wild animals become infected by the bite of infected ticks and the virus remains in their bloodstream for about one week after infection, allowing the tick-animal-tick cycle to continue when another tick bites.
- The hosts of the CCHF virus include a wide range of wild and domestic animals such as cattle, sheep and goats. Many birds are resistant to infection, but ostriches are susceptible and may show a high prevalence of infection in endemic areas (for example South Africa).
- CCHF is endemic where the tick vector is present, including Africa, the Balkans, the Middle East and Asian countries south of the 50th parallel north – the geographical limit of the principal tick vector.



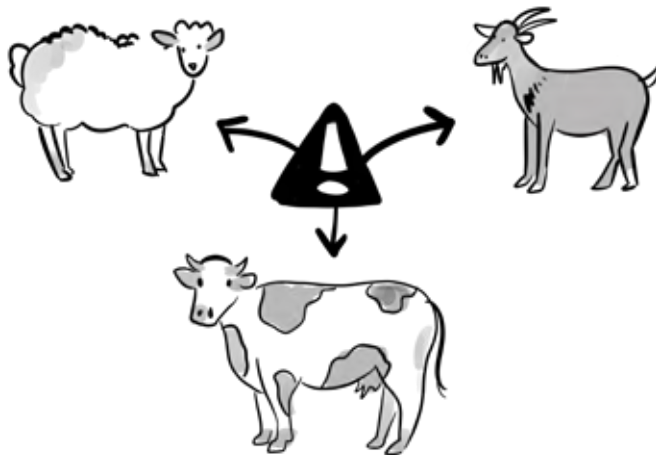
2

Humans are primarily infected through tick bite, although there are other modes of transmission

- CCHF can cause severe outbreaks in humans.
- 80–90% of human cases are infected either by tick bites or through direct contact with blood or tissues of infected ticks or infected wild animals and livestock.
- Most people at risk of animal-to-human transmission are those involved in the livestock industry, including both formal and informal agricultural workers, slaughterhouse workers, as well as veterinarians.
- 10–20% of human cases are infected through secondary human-to-human transmission that occurs through direct contact with the blood, secretions, organs or other body fluids of infected persons.

- There is high human-to-human transmission risk when providing direct patient care or handling bodies of deceased individuals.
- Hospital-acquired (nosocomial) infections can also occur due to lack of appropriate IPC measures.

contact with
bodily fluids

3

Infected livestock animals do not develop apparent disease, which makes it difficult to anticipate and prevent infection in humans

- CCHF-infected livestock animals do not show any symptoms.
- This allows the virus to maintain itself in unnoticed enzootic tick-vertebrate-ticks cycles.
- This makes it difficult to anticipate and prevent potential infection in humans.

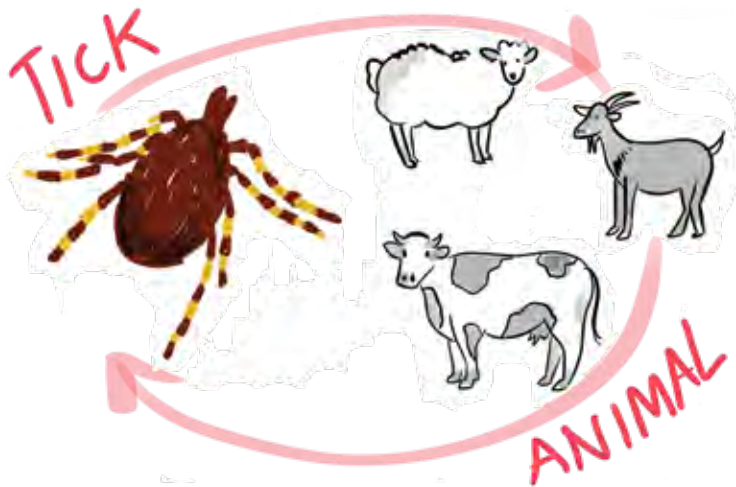
4

CCHF is a severe disease with a high case fatality ratio

- The case fatality ratio from CCHF is approximately 30% (it ranges from 10–50%), with death occurring in the second week of illness. In patients who recover, improvement generally begins on day nine or 10 after the onset of illness.
- The length of the incubation period depends on the mode of acquisition of the virus. Following infection by a tick bite, the incubation period is usually 1–3 days, with a maximum of nine days. The incubation period following contact with infected blood or tissues is usually 5–7 days, with a documented maximum of 13 days.
- Onset of symptoms is sudden, with fever, myalgia (muscle ache), dizziness, neck pain and stiffness, backache, headache, sore eyes and photophobia (sensitivity to light). There may be nausea, vomiting, diarrhoea, abdominal pain and sore throat early on, followed by sharp

mood swings and confusion. After 2–4 days, the agitation may be replaced by sleepiness, depression and lassitude, and the abdominal pain may localize to the upper right quadrant, with detectable hepatomegaly (liver enlargement).

- Other clinical signs include tachycardia (fast heart rate), lymphadenopathy (enlarged lymph nodes) and a petechial rash (a rash caused by bleeding into the skin) on internal mucosal surfaces, such as in the mouth and throat, and on the skin. The petechiae may give way to larger rashes called ecchymoses, and other haemorrhagic phenomena. There is usually evidence of hepatitis, and severely ill patients may experience rapid kidney and liver failure or pulmonary failure after the fifth day of illness.



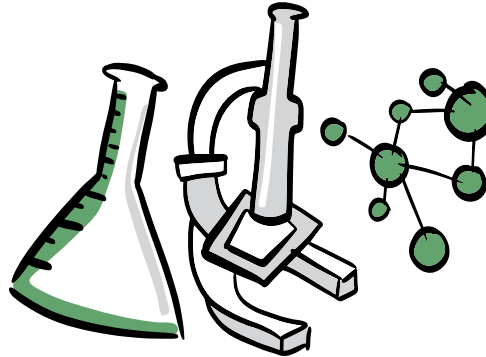
**SEVERE DISEASE
WITH HIGH CASE
FATALITY RATIO**

5

CCHF can be misdiagnosed as other viral haemorrhagic fevers and early laboratory confirmation of suspected cases is critical

- Symptoms are non-specific so clinical diagnosis may be difficult.
- Differential diagnosis includes other viral haemorrhagic fevers, malaria, typhoid fever, shigellosis and other viral and bacterial diseases.
- Patient history is essential and should include exposure to ticks; or exposure to wild animals and livestock; and/or area/village endemic for CCHF; and/or contact with CCHF cases.
- Early laboratory confirmation of suspected cases is critical to mount the response.
- Samples taken from people with suspected CCHF should be handled by trained staff working in suitably equipped laboratories.
- CCHF virus infection can be diagnosed by several different laboratory tests:
 - ELISA
 - Antigen detection
 - Serum neutralization
 - RT-PCR
 - Virus isolation by cell culture.

- Tests on patient samples present an extreme biohazard risk and should only be conducted under maximum biological containment conditions (BSL4). However, if samples have been inactivated, they can be manipulated in a basic biosafety environment.



6

Early supportive care improves chances of survival

- Intensive supportive care with treatment of symptoms is the main approach to managing CCHF in people
- This includes monitoring of fluids, electrolytes balance, renal function, blood pressure, oxygenation and rehydration as needed. Supportive drug therapy should be considered.
- Biological monitoring (hematology and biochemistry) along with viral load monitoring are needed to improve supportive care.
- The antiviral drug ribavirin has been used to treat CCHF infection and may be beneficial if used early in the course of the illness. Both oral and intravenous formulations exist and seem to be effective. Currently, WHO is reviewing evidence for ribavirin use for the treatment of CCHF.

- There is currently no licensed or commercially available vaccine against CCHF for humans and the animal hosts.



7

IPC measures are critical to control the infection when caring for patients

- Health workers should implement Standard Precautions with all patients, regardless of their diagnosis, in all work practices at all times including safe injection practices.
- While treating patients with CCHF they should apply extra infection control measures to prevent contact with the patient's blood and body fluids and contaminated surfaces or materials such as clothing and bedding.



PRECAUTIONS TO BE TAKEN		
When caring for patients	Standard IPC precautions regardless of the diagnosis	<ul style="list-style-type: none"> • Hand hygiene • Respiratory hygiene • Use of PPE to block splashed or contact with infected material • Safe injection practices
	Health workers caring for patients with suspected or confirmed CCHF virus infection	<ul style="list-style-type: none"> • Extra infection control measures to prevent contact with patient's blood and body fluids and contaminated surface or material, in particular clothing or bedding • Face protection (a face shield or a medical mask and goggles), a clean, non-sterile long-sleeved gown, and gloves (sterile gloves for some procedures) should be worn when in close contact (within 1 metre) of patients with CCHF

8

Raising awareness on risk factors and preventive measures is key to reduce infection in people, especially among at-risk groups in CCHF endemic areas.

- In the absence of a vaccine, the best way to reduce infection in people is by raising awareness of the risk factors and informing people about the measures they can take to reduce exposure to the virus. People should be informed about:
 - Measures to reduce the risk of tick-to-human transmission include:
 - Wearing protective clothing (long sleeves, long trousers).
 - Wearing light coloured clothing to allow easy detection of ticks on the clothes.
 - Using approved acaricides (chemicals intended to kill ticks) on clothing.



- Using approved repellent on the skin and clothing.
- Regularly examining clothing and skin for ticks, if found, removing them safely.
- Seeking to eliminate or control tick infestations on animals or in stables and barns.
- Avoiding areas where ticks are abundant and seasons when they are most active.

- Measures to reduce the risk of animal-to-human transmission include:

- Wearing gloves and other protective clothing while handling animals or their tissues in endemic areas, notably during slaughtering, butchering and culling procedures in slaughterhouses or at home.
- Quarantining animals before they enter slaughterhouses or routinely treating animals with approved acaricides two weeks prior to slaughter.

- Measures to reduce the risk of human-to-human transmission in the community include:

- Avoiding close physical contact with people infected with CCHF.
- Wearing gloves and protective equipment if taking care of ill people.
- Washing hands regularly after caring for or visiting ill people.

9

Efficient vector control measures are currently lacking

- Current vector control measures are not fully satisfactory
 - Chemicals produce resistant ticks, food contamination and environmental pollution. Furthermore, the tick vectors are numerous and widespread, so tick control with acaricides (chemicals intended to kill ticks) is only a realistic option for well-managed livestock production facilities.
 - Physical measures (heavy grazing, burning of grasslands) have an important negative impact on the environment.
 - Biological measures (for example using hormones and growth regulators, predators, bacteria, nematodes and fungi) have not demonstrated full efficacy.
- An animal vaccine effective against *Hyalomma* ticks that prevent the tick-animal-tick cycle would decrease the tick population, decrease CCHF prevalence in animals, and therefore decrease human exposure, and as such be a cost-effective CCHF prevention measure.

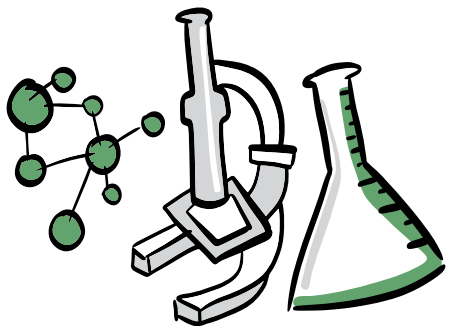


A VACCINE EFFECTIVE
AGAINST HYALOMMA
— TICKS? —

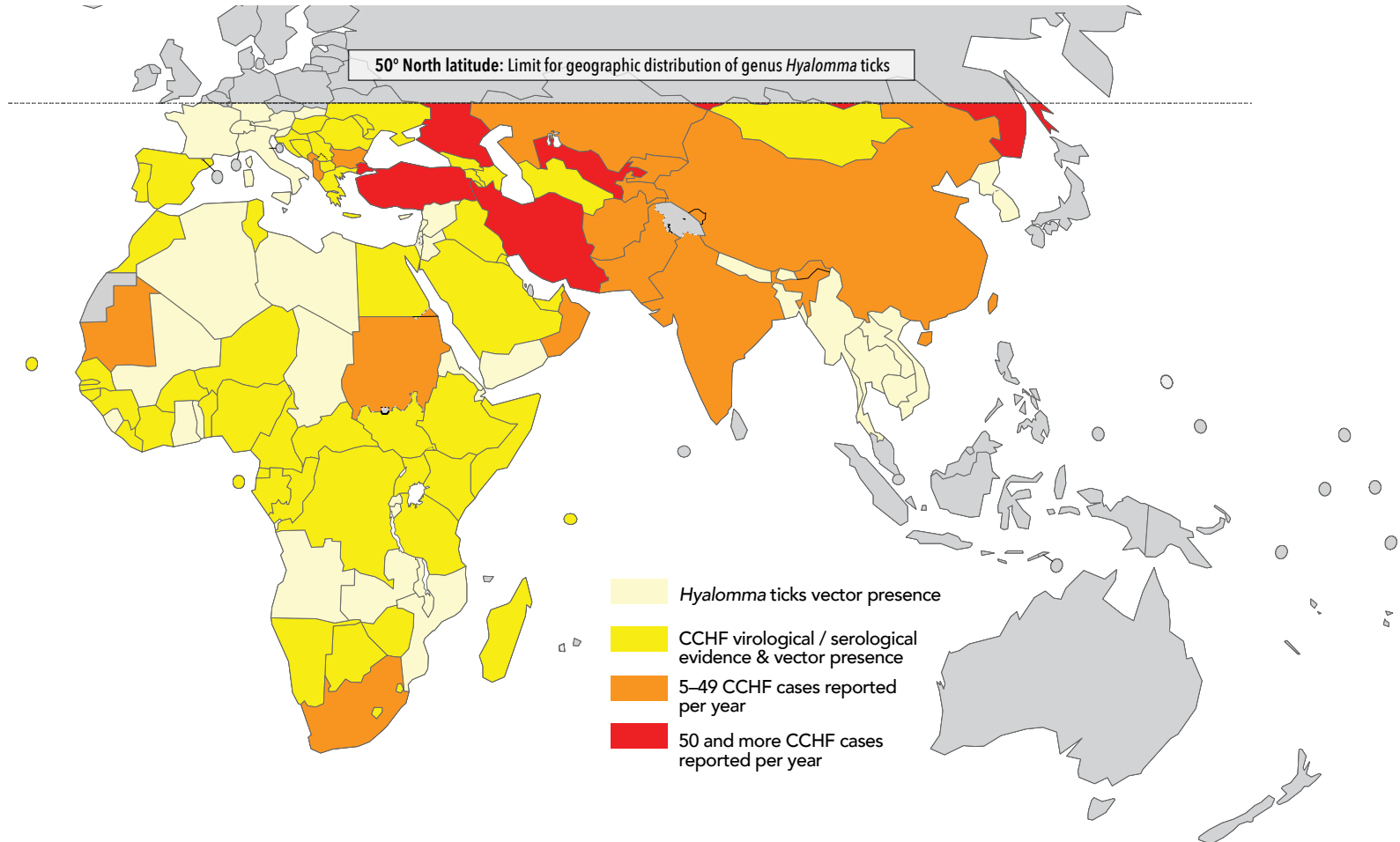
10

CCHF is one of the priority diseases for research and development of countermeasures

- R&D roadmaps and target product profiles are being developed in consultation with experts and stakeholders (as part of the R&D Blueprint).
- Research is ongoing for therapeutics (ribavirin, favipiravir, intravenous immunoglobulin, monoclonal antibodies), for rapid diagnostics and for an animal anti-tick vaccine effective against *Hyalomma* ticks.
- Given the epidemiology of CCHF, with a limited number of cases reported yearly, a human vaccine might not be the most cost-effective and viable control measure.



Geographic distribution of Crimean-Congo haemorrhagic fever



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More information about Crimean-Congo haemorrhagic fever (CCHF):

- CCHF WHO webpage
https://www.who.int/health-topics/crimean-congo-haemorrhagic-fever/#tab=tab_1
- CCHF WHO fact sheet
<http://www.who.int/mediacentre/factsheets/fs208/en/>
- WHO Introduction to Crimean-Congo Haemorrhagic fever
<https://www.who.int/publications/i/item/introduction-to-crimean-congo-haemorrhagic-fever>
- R&D Blueprint
<http://www.who.int/blueprint/en/>



Yellow fever (YF)

10 THINGS YOU SHOULD KNOW

1. YF is a mosquito-borne disease
2. Urban outbreaks can be devastating
3. YF is difficult to distinguish from other diseases causing febrile jaundice and/or haemorrhagic signs
4. Early clinical management improves survival rates
5. YF vaccine is efficient, safe and provides lifelong immunity
6. Vaccine production is limited, but there is a global emergency stockpile
7. Routine immunization in children is the key to long-term epidemic prevention
8. Emergency mass vaccination and vector control are two key pillars of YF outbreak response in urban settings
9. The risk of international spread of YF exists but can be prevented
10. Endemic countries are committed to eliminating YF epidemics



Yellow fever response tips

Collaborative surveillance

- Laboratory confirmation may be difficult (serological tests cross-react with dengue and other flaviviruses); think of differential diagnosis of febrile jaundice.
- Distribute vaccination cards.
- Notify cases to WHO, under the IHR (2005).

Community protection

- Support community engagement, health promotion and social science.
- Encourage health authorities to:
 - Engage communities for vector control.
 - Work with partners for social mobilization for vaccination campaigns.
 - Ensure vector control in health facilities.
- Key messages are:
 - YF is transmitted by mosquitoes.
 - YF vaccine is efficient, safe and provides lifelong immunity.
 - Seek medical care early to increase chances of survival.

Clinical care

- Provide supportive care to patients.
- Use insecticide-treated bed nets (especially during the day).

Access to countermeasures

- Implement emergency mass vaccination.
- Control vectors, especially in urban settings.
- Control YF vaccination status at borders (airports, seaports, land borders).

Emergency coordination

- Contact the ICG for emergency vaccines.
- Engage partners and communities for vector control around cases, particularly in urban settings.
- Organize emergency mass vaccination campaigns, including social mobilization, cold chain management, waste management, monitoring of adverse events following immunization and conducting a post-campaign coverage survey.

1

YF is a mosquito-borne disease

- The YF virus is transmitted to humans through the bites of infected mosquitoes, most commonly the *Aedes* species in Africa and *Haemagogus* species in the Americas.
- Urban YF, the most threatening form of YF epidemics, is spread through the *Aedes aegypti* mosquito in tropical and subtropical regions.
- *Ae. aegypti*, is the same mosquito species that spreads chikungunya, dengue, and Zika viruses.
- *Aedes* mosquitoes are present on all continents except Antarctica. Mosquito-transmitted disease are amplified by urbanization, which increases human population densities and enhances manmade habitats for mosquito breeding.
- *Aedes* mosquitoes usually bite during the day, peaking in the hours around sunrise and sunset. *Ae. aegypti* will bite indoors as well as outdoors.

2

Outbreaks of YF in urban areas can be devastating

- YF outbreaks in urban settings can be devastating as they have the potential to amplify rapidly and spread widely, especially to other countries, because of:
 - Increased human population densities that lead to rapid amplification of the disease.
 - Increased density of the *Ae. aegypti* mosquito vector of urban YF epidemics that breeds in man-made containers of water, feeds predominantly on human blood, bites multiple individuals in a single blood meal, and lives in close association with human dwellings.

- Ease and speed of population movements, as well as easy access to airports, that facilitate spread of the disease and its exportation to other countries.
- Difficulties in assessing target populations and in mounting reactive interventions in informal urban settings or in cross-border areas.
- There are three types of transmission cycles, as illustrated below. However, with climate and demographic change in endemic settings, their dynamic may evolve.

Jungle YF

- *Haemagogus* and *Sabethes* (Am.) and *Aedes* (Afr.) mosquitoes
- Human are sporadically infected



Intermediate YF

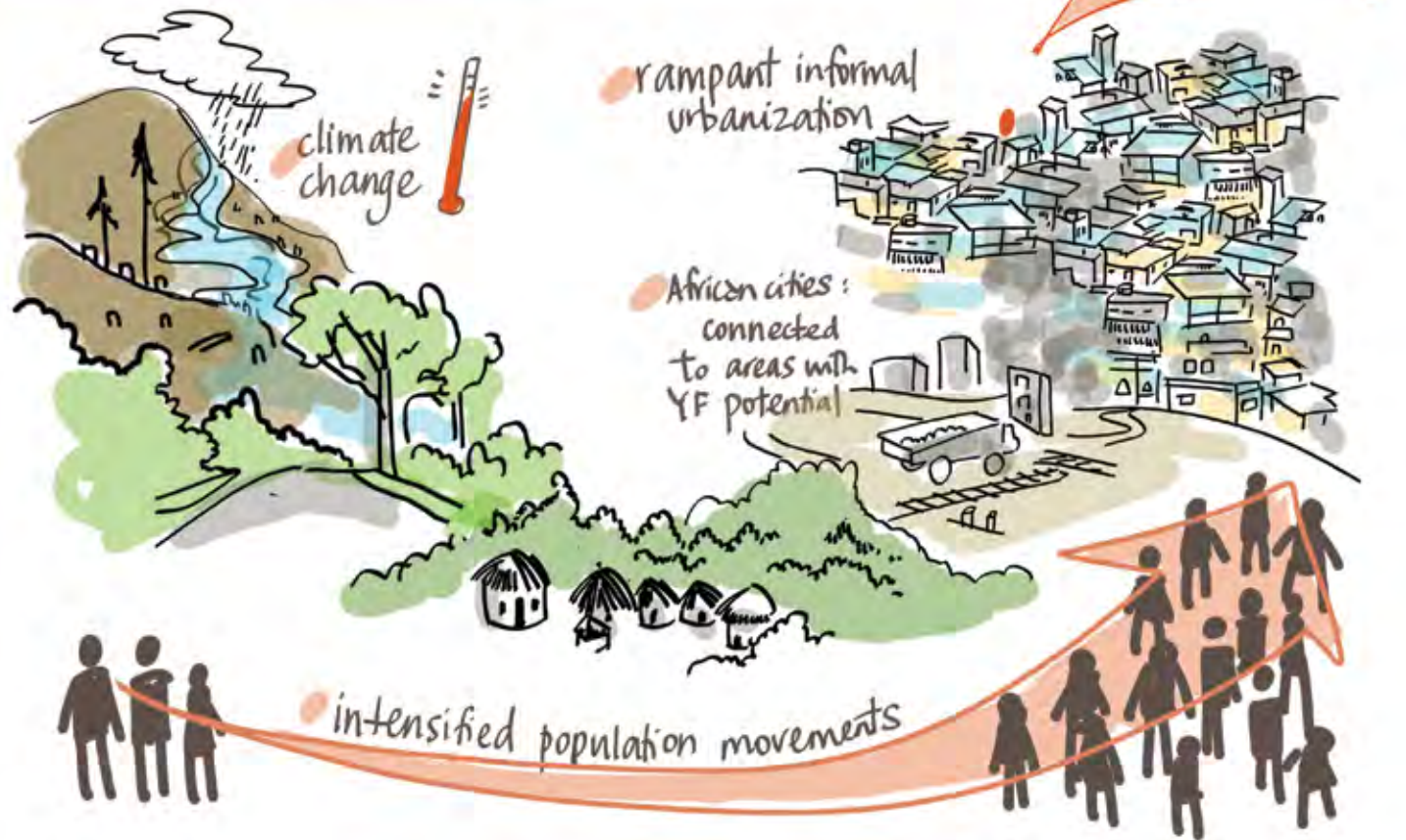
- Various *Aedes* species
- Small-scale epidemics in moist savannah areas
- "Zone of emergence"

Urban YF

- *Aedes aegypti*
- Human-to-human transmission
- Risk of large outbreak and international spread



INCREASED RISK OF URBAN OUTBREAK WITH INTERNATIONAL SPREAD



3

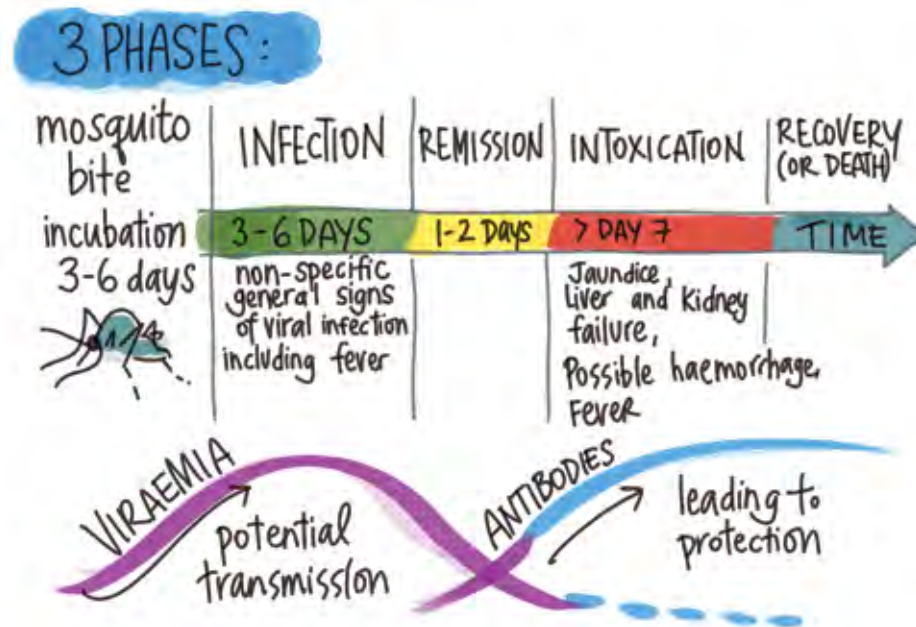
YF is difficult to distinguish from other diseases causing febrile jaundice and/or haemorrhagic signs

- YF is difficult to diagnose (especially during the early stages) because its symptoms are not specific and can be confused with other common diseases such as malaria, viral hepatitis (when jaundice), dengue, leptospirosis (when jaundice), other arboviral diseases and Ebola virus disease (when haemorrhagic), as well as poisoning.
- Once contracted, the YF virus incubates in the body for 3–6 days.
- Most people (about 88% of those infected) do not experience symptoms.
- Symptoms usually develop in two phases:
 - First to occur are common nonspecific symptoms, including fever, muscle pain with prominent backache, headache, loss of appetite, and nausea or vomiting. In most cases, symptoms disappear after 3–4 days.
 - A small percentage of patients (about 2–3% of infected people) will enter a second, more toxic, phase within 24 hours of recovering from initial symptoms. High fever returns and several body systems are affected, usually the liver and the kidneys, with the characteristic jaundice that gives YF its name, dark urine and abdominal pain with vomiting. Bleeding can occur from the mouth, nose, eyes or stomach. Half of patients who enter the toxic phase die within 7–10 days. The others recover without significant organ damage.

- Laboratory tests are necessary to confirm YF and gain access to the global emergency stockpile of vaccines.
- In the first phase, blood is collected for RT-PCR to confirm the presence of the virus (viraemia).
- In later stages of the disease, serology testing to identify antibodies is needed: ELISA and plaque reduction neutralization test (PRNT) for neutralizing antibodies. Detection of antibodies indicates that the person has been either infected or vaccinated, but it cannot distinguish between the two. The level of antibody titres and their evolution over time, on a second sample, can provide indication of

how acute the infection might be.

- Whenever YF is suspected, there should also be systematic testing by serology and PCR for other arboviruses (such as dengue, Zika, chikungunya, West Nile and Rift Valley fever), and for viral haemorrhagic fevers (such as Ebola, Lassa and Crimean-Congo haemorrhagic fevers) in case of haemorrhagic symptoms.
- YF tests should be conducted in laboratories with appropriate capacity to test for both YF and the differential diagnosis.



4

Early clinical management improves survival rates

- Good and early supportive treatment in hospitals improves survival rates.
- There is currently no specific antiviral drug for YF, but specific care to treat dehydration, liver and kidney failure, fever and associated infections improves outcomes.
- Patients need to stay under insecticide-treated bed nets during the day to limit the risk of spread to others through mosquito bites.



5

YF vaccine is efficient, safe and provides lifelong immunity

- There is a good vaccine against YF. It has been used for many decades and is safe and affordable, providing effective immunity against YF within 10 days for more than 90% of persons vaccinated and within 30 days for 99% of persons vaccinated. A single dose provides lifelong protection. A booster dose of YF vaccine is not needed. The YF vaccination card is valid for life.
- Adverse effects of the YF vaccine are generally mild and may include headaches, muscle aches and low-grade fevers. Serious adverse effects are rare. All adverse events need to be monitored, and management kits should be readily available in immunization posts.
- In YF-endemic countries, WHO strongly recommends routine vaccination for everyone older than 9 months. People over 60 years of age should be given the vaccine after a careful risk-benefit assessment. Some people should not be routinely vaccinated, including:
 - Infants aged less than 9 months.
 - Pregnant women (unless during an outbreak if the risk of disease outweighs the potential adverse effects of the vaccine).
 - People with severe allergies to egg protein.
 - People with severe immunodeficiency.



6

Vaccine production is limited, but there is a global emergency stockpile

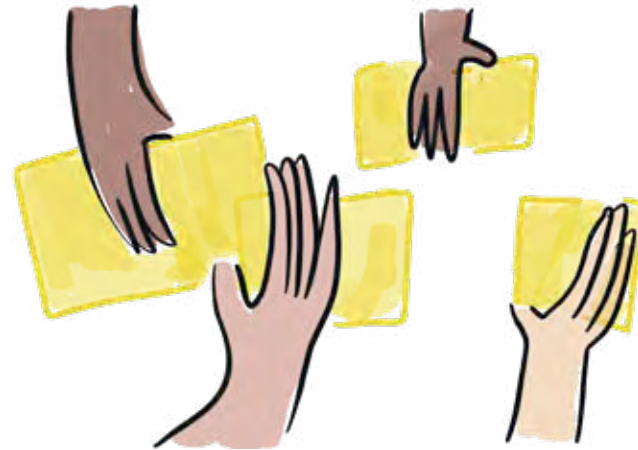
- There are four prequalified vaccine manufacturers, but global production is limited. Any country facing an outbreak can gain access to the global emergency stockpile of 6 million vaccine doses through a request to the ICG.
- For outbreak response in the event of a global shortage of vaccine and acute demand surge, it is possible to use a fraction of the vaccine dose (1/2–1/5) to rapidly increase population immunity and stop human-to-human transmission. This exceptional decision should be taken in close consultation with WHO technical experts.
 - Children under the age of age 2 years, pregnant women and lactating mothers should be offered a full dose of vaccine.
 - There is no evidence of increased serious adverse effects when using a fractional dose.
 - Vaccination with fractional doses should be recorded using personal registries for effectiveness and safety monitoring.
 - A specific community engagement approach should be implemented to ensure that appropriate messages are conveyed to health care workers and the population on the efficiency of fractional immunization. Rumor tracking, including on social media platforms, is also important.



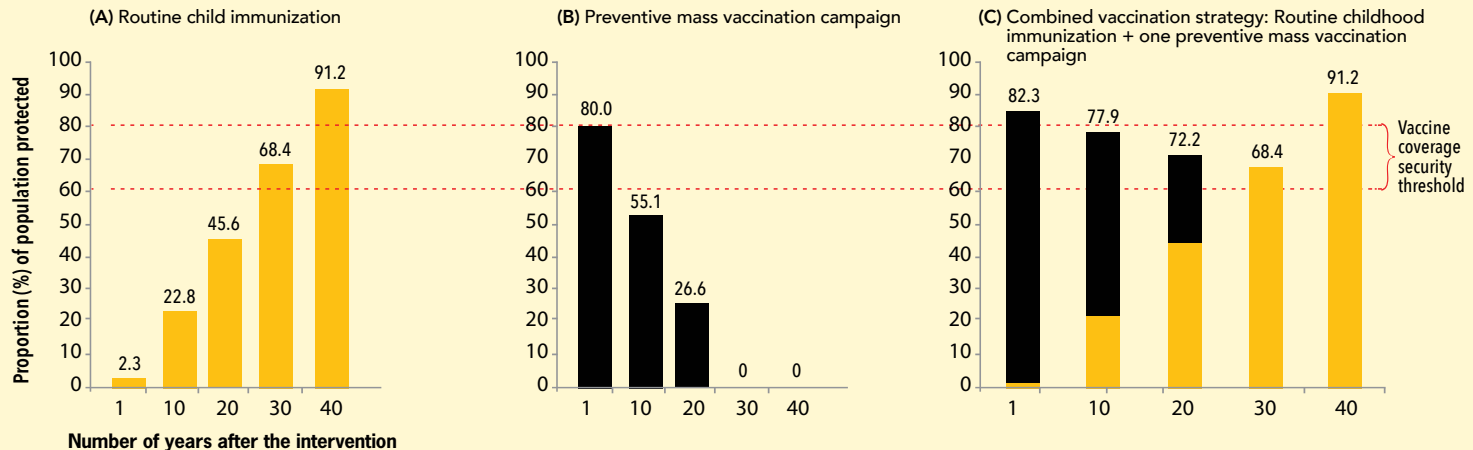
7

Routine immunization in children is the key to long-term epidemic prevention

- Vaccination is the single most important measure for preventing YF. Prevention of outbreaks can be achieved only if the majority of the population is immunized.
- Routine YF immunization in the Expanded Programme on Immunization (EPI) can provide sufficient population immunity. However, it takes about 30 years of well-performing EPI programmes to build population immunity to adequate levels to stop potentially large-scale outbreaks. Mass preventive vaccination campaigns for other age groups accelerate the building of population immunity through what is called the YF combined vaccination strategy.



Population protected by routine immunization, preventive mass campaigns and combined vaccination strategy



8

Emergency mass vaccination and vector control are two key pillars of YF outbreak response in urban settings

• Emergency mass vaccination:

- Reactive mass vaccination campaigns reduce the possibility of transmission of the virus by rapidly increasing immunity in the population. Vaccine coverage greater than 80%, with a 60–80% security threshold, is necessary to interrupt autochthonous transmission (human-mosquito-human transmission) of YF virus within a community and ensure that sporadic unvaccinated cases do not generate secondary cases.
- Access to the YF global emergency stockpile is coordinated by the ICG upon receiving a request based on a detailed investigation.
- A post-campaign coverage survey is important to assess the campaign performance.



• Vector control:

- Vector-control strategies should address all life stages of the *Aedes* mosquito - from egg to larva and adult. Community engagement is essential for these interventions:
 - Elimination of breeding sites as well as eggs, larvae and pupae in standing water (for example cleaning roof gutters, clean up campaigns, cover containers with stagnant water).
 - Targeted residual spraying of adult mosquitoes (in areas known to be resting sites for *Aedes* mosquitoes) and space spraying during outbreaks.
 - Mosquito control programmes targeting wild mosquitoes in forested areas are not practical and not recommended for preventing jungle (or sylvatic) YF transmission.
- Personal preventive measures to avoid mosquito bites include clothing that minimizes skin exposure, and use of repellents, window screens and air conditioning. The use of insecticide-treated bed nets is limited by the fact that *Aedes* mosquitoes bite during daytime.
- Houses with solid floors and roofs, window screens and air conditioning can reduce the chance of mosquito-borne virus transmission.



- Mosquito surveillance is part of vector control and helps improve the timeliness of decisions to control mosquito populations and prevent epidemic amplification, particularly in urban settings. Both larval and adult vector populations should be targeted for surveillance.
- Mosquito vector surveillance is important for the prevention and control of a number of diseases including chikungunya, dengue, malaria and Zika.



9

The risk of international spread of YF exists but can be prevented

- With the increasing occurrence of urban YF outbreaks comes an increased risk of international spread because big cities are transport hubs with frequent transport connections. A particularly concerning scenario would be exportation of the disease to a country where the vector is present and population immunity levels are low, which could potentially lead to local transmission.



- Exportation of cases to Asia is especially worrisome as favorable conditions for local transmission (vector such as *Ae. aegypti*, non-immune populations) are present, as demonstrated by dengue activity.
- Sectors that recruit international workers with potential sylvatic exposure (for example extractive, mining, construction and forestry industries) should take measures to ensure that staff and families are vaccinated.
- To prevent international spread, it is essential to apply the IHR (2005) requirements and to ensure that travellers present YF vaccination certificates. Under IHR (2005), it is also essential to notify YF cases that have a serious public health impact and/or are unusual or unexpected, and/or could lead to international spread and/or present a significant risk of travel or trade restrictions.
- Vector-control measures may be applied in various forms of transport, in accordance with IHR (2005).



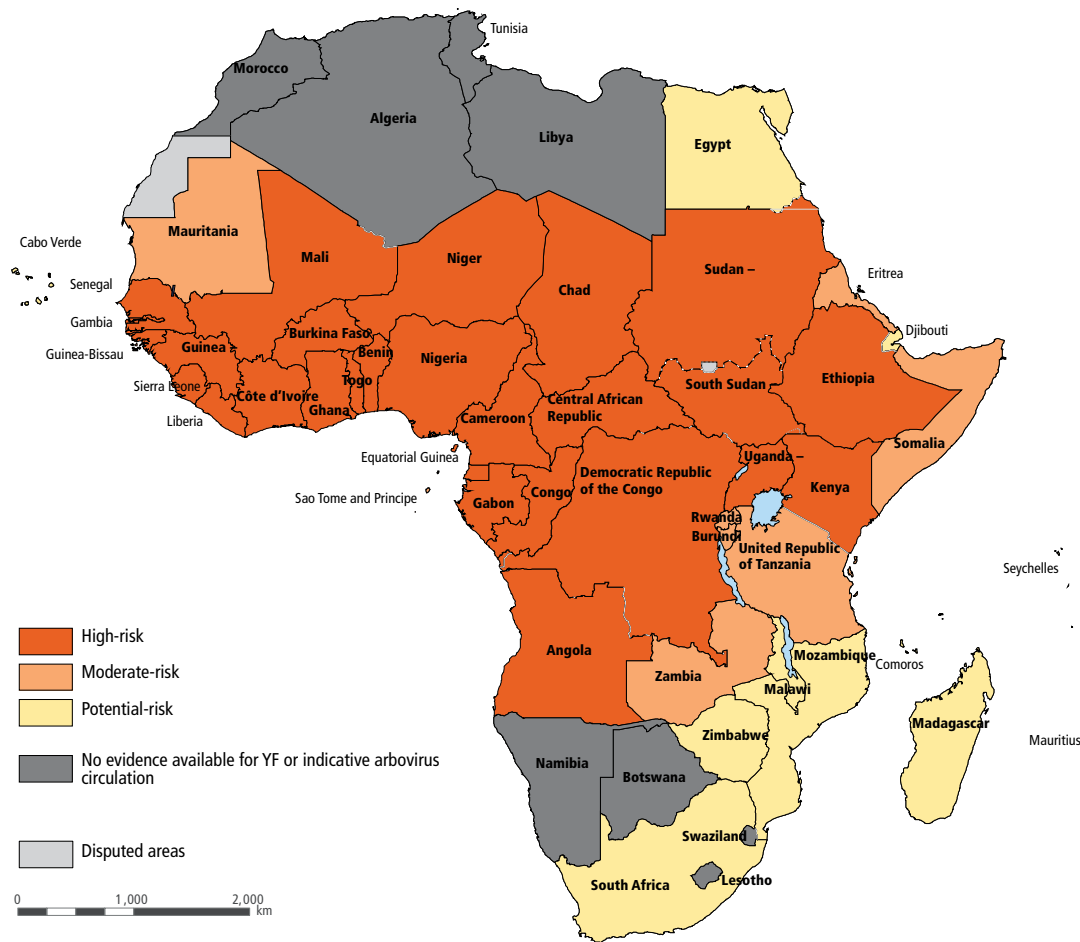
10

Endemic countries are committed to eliminating YF epidemics

- YF is an acute viral haemorrhagic disease. The virus is endemic in tropical areas of Africa and the Americas. Susceptible nonhuman primates are the animal reservoirs and maintain endemicity. YF cannot be eradicated because we cannot eradicate the disease in the primate populations.
- Of the 47 YF-at risk countries, 40 have been identified as priority countries by the Eliminate Yellow Fever Epidemics (EYE) Strategy. The updated Strategy was developed by a coalition of countries and partners to respond to the disease's changing epidemiology, resurgence of mosquitoes and increased risk of urban outbreaks and international spread.
- African Member States endorsed the EYE Strategy in 2017 and agreed on ten priority actions to guide countries to the elimination of YF epidemics by 2026.

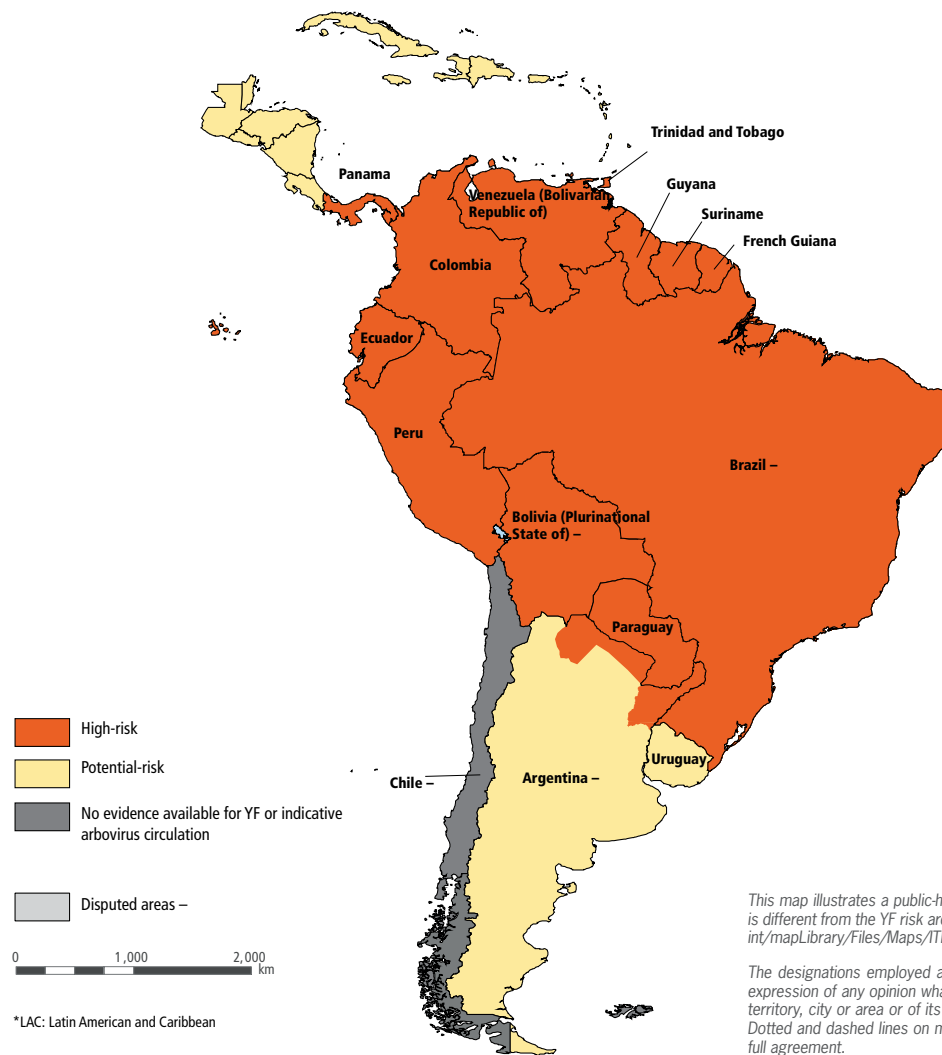


Yellow fever (YF) risk classification, by country - Africa, 2016



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Yellow fever (YF) risk classification, by country – LAC* countries, 2016



This map illustrates a public-health-intervention oriented YF risk approach at country level. Its purpose is different from the YF risk area maps for travellers in the context of IHR, eg. http://gamapservr.who.int/mapLibrary/Files/Maps/1TH_YF_vaccination_americas.png

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More information about Yellow fever (YF):

- Yellow fever WHO webpage
<https://www.who.int/health-topics/yellow-fever>
- Yellow fever WHO fact sheet:
<https://www.who.int/news-room/fact-sheets/detail/yellow-fever>
- EYE Strategy
<https://www.who.int/initiatives/eye-strategy>
- OpenWHO course on Yellow fever
<https://openwho.org/courses/pandemic-epidemic-diseases>
- WHO standard case definitions
<https://www.who.int/publications/m/item/case-definitions-for-public-health-surveillance>
- International Coordinating Group (ICG) on vaccine provision for yellow fever
<https://www.who.int/groups/icg/yellow-fever>



Zika

10 THINGS YOU SHOULD KNOW



1. Zika virus disease is a mosquito-borne disease
2. Zika virus can also be transmitted from women to their child during pregnancy, through sexual contact, blood transfusions and unprotected laboratory exposure
3. Zika virus infection is usually asymptomatic but can lead to severe complications
4. Zika virus infection during pregnancy may lead to adverse outcomes, including pregnancy loss and congenital Zika syndrome in the child
5. In some individuals, Zika virus infection can cause Guillain-Barré syndrome and other neurological complications
6. There is no vaccine or specific treatment for Zika virus infection, however there are several in development
7. Strong integrated surveillance, including adequate testing, mosquito vector surveillance and control strategies are important for prevention and control of Zika and several vector-borne diseases
8. Individuals should protect themselves from mosquito bites to reduce exposure from Zika virus
9. Access to counselling and laboratory testing is critical for pregnant women if they are likely to have been infected with Zika virus during pregnancy
10. WHO guidelines are available to prevent exposure to Zika virus in the general population, couples of reproductive age, pregnant women and their partners

Zika response tips

Collaborative surveillance

- Ensure and strengthen capacity for early detection, diagnosis, reporting and monitoring of cases.
- Implement and strengthen mosquito surveillance to maintain timely data on vector distribution and risk of transmission in communities.
- Provide access to reliable laboratory testing. Laboratory diagnosis of Zika virus infection may, however, be difficult; serological tests cross-react with dengue and other flaviviruses, and antibodies may be detected for prolonged periods following infection. In pregnant women this may reflect infection prior to pregnancy.

Community protection

- Support community engagement, health promotion and social science.
- Prevent Zika virus infection by preventing mosquito bites, particularly for pregnant women.
- Prevent sexual transmission of Zika virus.
- Encourage health authorities to:
 - Identify and engage populations at-risk for Zika virus exposure with tailored information delivered through trusted sources on how to protect themselves from infection and prevent transmission.
 - Advise high-risk groups to seek health care if symptomatic.
 - Engage communities in eliminating mosquito breeding sites.
- Key messages are:
 - Zika virus is transmitted to humans through mosquito bites, which mostly occur during the day, peaking in the hours around sunrise and sunset.
 - Zika virus infection can be sexually transmitted.
 - Infants born to women who were infected with Zika virus during pregnancy are at risk for adverse outcomes including congenital Zika syndrome.
 - Women of reproductive age who live in or travel to areas with Zika virus transmission should seek trusted medical advice before getting pregnant and if they become pregnant.
 - Couples of reproductive age should follow recommendations to prevent sexual transmission of Zika virus.
 - People can protect themselves from infection with personal preventive measures against mosquito bites such as wearing clothing that minimizes skin exposure, using mosquito repellents and using window screens and air conditioning if available.

Clinical care

- Provide clinical supportive care to patients with Guillain-Barré syndrome and other severe symptoms.
- Provide support to infants born with congenital Zika syndrome and their families.
- Provide counseling to women of reproductive age and pregnant women about Zika virus infection prevention, testing and potential adverse outcomes from infection.
- Provide psychosocial counselling and support in communities experiencing outbreaks, particularly for women of reproductive age and their families.

Access to countermeasures

- Prevent Zika disease by preventing mosquito bites.
- Personal preventive measures to avoid mosquito bites include clothing that minimizes skin exposure, and use of repellents, window screens and air conditioning.
- Reduce breeding sites of *Aedes* mosquitoes around dwellings by cleaning roof gutters, clean up campaigns, cover containers with stagnant water.

Emergency coordination

- Ensure coordination between public health, maternal and child health, vector-control, clinical, and psychosocial services for effective surveillance, diagnosis, risk assessment, outbreak investigation and response, as well as research, development and implementation of control measures and supportive services.
- Ensure availability of social services to support affected mothers, children and families.

1

Zika virus disease is a mosquito-borne disease

- Zika virus is transmitted to humans by infected mosquitoes, most commonly *Aedes* species mosquitoes.
- Two types of *Aedes* mosquitoes are known to be capable of transmitting Zika virus:
 - In most cases, Zika is spread through the *Aedes aegypti* mosquito in tropical and subtropical regions. *Ae. aegypti*, is the same mosquito species that spreads urban yellow fever, chikungunya and dengue viruses.
 - *Aedes albopictus* mosquitoes can also transmit Zika virus. This species, commonly known as the 'tiger mosquito', can tolerate cooler temperatures than *Ae. aegypti*, which may expand the potential range of regions at risk of Zika virus transmission. *Ae. albopictus* is also responsible for some transmission of chikungunya and dengue viruses.
- *Aedes* mosquitoes usually bite during the day, peaking in the hours around sunrise and sunset. Both *Aedes* species are found biting outdoors, but *Ae. aegypti* will also bite indoors.
- Outbreaks usually occur in areas where mosquitoes breed.

- *Aedes* mosquitoes are present on all continents except Antarctica. Mosquito-transmitted disease are amplified by urbanization, which increases human population densities and enhances manmade habitats for mosquito breeding.
- Local transmission of Zika virus by *Aedes* mosquitoes has been reported in Africa, the Americas, Europe, South-East Asia and the Western Pacific.



2

Zika virus can also be transmitted from pregnant women to their child during pregnancy, through sexual contact, blood transfusions, and unprotected laboratory exposure

- In pregnant women, Zika virus can be transmitted from mother to child (congenital infection).
- Zika virus can be transmitted through sexual intercourse.
- In regions with active Zika virus transmission, health programmes should ensure that:
 - All people with Zika virus infection and their sex partners (particularly pregnant women) receive information about the risks of sexual transmission of Zika virus.
 - Sexually active men and women are counselled on safer sexual practices and offered a full range of contraceptive methods to make informed choices about whether and when to become pregnant, to prevent unintended pregnancies, and to prevent possible adverse pregnancy outcomes.
 - Pregnant women are advised not to travel to areas where there is Zika virus transmission, particularly during outbreaks.
- Other modes of person-to-person Zika transmission include blood transfusion and laboratory or other bloodborne exposure. Transmission through organ transplantation has not been documented but is theoretically possible based on experience with related flavivirus infections.

3

Zika virus infection is usually asymptomatic but can lead to severe complications

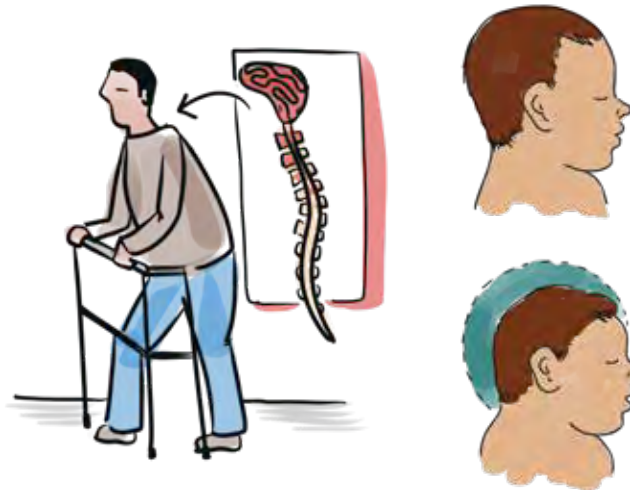
- The incubation period may range from 3–14 days.
- Approximately 50–80% of infected people do not develop symptoms.
- People with symptoms usually present with rash, conjunctivitis, mild fever, muscle and joint pain, malaise, and headache.
- Symptoms normally last from 2–7 days.
- In pregnant women, Zika virus infection can cause miscarriage and stillbirth, as well as cause some infants to be born with microcephaly and other congenital malformations, known as congenital Zika syndrome.¹
- Investigations are ongoing on the links between Zika virus infection and other adverse outcomes from congenital infection.
- In a relatively small proportion of people, Zika virus infection can also lead to Guillain-Barré syndrome, a neurological complication that occurs in adults.
- Zika virus can be classified into two main ancestral lineages: Asian and African. The Asian lineage strain was responsible for the recent 2015/2016 epidemics. It is not known whether the African lineage strains would produce neurological symptoms and congenital Zika syndrome with similar, lesser, or worse severity than those observed in the 2015/2016 epidemics.

¹ Fetal/infant congenital infections occur for 20–30% of mothers with infection during pregnancy; among those, 5–14% are microcephaly (source: Musso 2019, N Engl J Med. Zika after the Pandemic)

4

Zika virus infection during pregnancy may lead to adverse outcomes, including pregnancy loss and congenital Zika syndrome in the child

- Infants born to women who were infected with Zika virus during pregnancy should be evaluated for neurodevelopmental disorders associated with congenital Zika syndrome:
 - Microcephaly is a condition in which the infant's head is smaller than those of other babies of the same age and sex (more than three standard deviations below average for gestational age). Infants born with microcephaly are at risk for severe intellectual disability and may also develop convulsions and physical disabilities as they grow older. There is no specific treatment for microcephaly.



- Diagnosis of microcephaly is often made at birth. All infants should have head circumference measured and recorded within 24 hours of birth. Early diagnosis of microcephaly can sometimes be made by fetal ultrasound. Prenatal diagnosis by ultrasound is more accurate in the second and third trimesters.
- Other newborn complications associated with congenital Zika infection include brain calcifications, seizures, irritability, brainstem dysfunction such as swallowing problems, limb contractures, developmental delays, hearing and sight abnormalities and other brain abnormalities.
- Support services for affected infants and families are an important component of Zika programmes.
- Other adverse pregnancy outcomes associated with Zika virus infection include miscarriage and stillbirth. Infection passed from mother to child immediately before, during or soon after birth has also been described but is generally associated with self-limited illness.
- Zika virus has been identified in breast milk but transmission by breastfeeding has not yet been confirmed. Evidence suggests that the benefits of breastfeeding outweigh the theoretical risk of Zika virus transmission through breast milk.
- More information is needed on the long-term outcomes of infants infected during pregnancy, delivery and the early postpartum period.

5

In some individuals, Zika virus infection can cause Guillain-Barré syndrome and other neurological complications

- Guillain-Barré syndrome is a rare neurological complication in which a person's immune system attacks the peripheral nerves after Zika infection. It is hard to estimate, but approximately 0.5–1.23% of Zika infections lead to Guillain-Barré syndrome.^{2,3}
 - People of all ages can be affected, but it is more common in adults and in males.
 - Symptoms of Guillain-Barré syndrome typically last few weeks and if supported through the early stages of disease, most individuals can recover without long-term complications.
- The first symptoms of Guillain-Barré syndrome include weakness or tingling, usually starting in the legs and sometimes spreading to the arms and face.
- Some patients develop paralysis of the legs, arms or face muscles. In 20–30% of people, the chest muscles are affected, making it difficult to breathe and requiring hospitalization and respiratory support in ICU.

² Muñoz LS, Barreras P, Pardo CA. Zika Virus-Associated Neurological Disease in the Adult: Guillain-Barré Syndrome, Encephalitis, and Myelitis. *Semin Reprod Med.* 2016 Sep;34(5):273-279. doi: 10.1055/s-0036-1592066. Epub 2016 Sep 9. PMID: 27612158.

³ Coelho, A.V.C., Alencar, L.C.A.D. and Crovella, S., 2018. Prevalence of Guillain-Barré syndrome among Zika virus infected cases: a systematic review and meta-analysis. *Brazilian Journal of Infectious Diseases*, 22, pp.137-141



- The ability to speak and swallow may become affected in severe cases of Guillain-Barré syndrome.
- Severe cases of Guillain-Barré syndrome are rare but can result in near-total paralysis.
- Guillain-Barré syndrome is potentially life threatening. People with Guillain-Barré syndrome should receive medical attention and be closely monitored for life-threatening complications. Severe cases may require ICU including ventilatory respiratory support. Treatment includes supportive care and some immunological therapies.

Approximately 3–5% of Guillain-Barré syndrome patients die from complications, including paralysis of the muscles that control breathing, infection, sepsis or cardiac arrest.

6

There is no vaccine or specific treatment for Zika virus infection, however there are several in development

- Currently, there are no antiviral drugs or specific treatments for people with Zika virus infections. Zika virus disease in individuals including non-pregnant women is usually mild and requires no specific treatment. Individuals with more severe symptoms should receive supportive care including rest, fluids and management of pain and fever. In areas with co-circulation of dengue, non-steroidal anti-inflammatory drugs should be avoided in the acute phase of infection until dengue virus infection has been ruled out.
- Research is ongoing to develop potential therapies and vaccines to treat or prevent Zika virus infection and congenital Zika syndrome. Research to develop more diagnostic tests for congenital Zika syndrome is ongoing.



7

Strong integrated surveillance, including adequate testing, mosquito vector surveillance and control strategies are important for prevention and control of Zika and several vector-borne diseases

- It is important to provide access to validated laboratory testing for Zika virus infection.
- Groups prioritized for diagnostic testing should be symptomatic individuals and asymptomatic pregnant women with possible exposure to Zika virus.
- Molecular diagnosis (RT-PCR) of Zika virus infection may, however, be challenging; serological tests cross-react with dengue and other flaviviruses, and antibodies may be detected for prolonged periods following infection. In pregnant women this may reflect infection prior to pregnancy.
- Adequate testing is also important to support surveillance activities.
- Vector-control strategies should address all life stages of the *Aedes* mosquito from the egg to larva and adult. Community engagement is essential for these interventions:



- Elimination of breeding sites as well as eggs, larvae and pupae in standing water (for example cleaning roof gutters, conducting clean up campaigns, covering containers with stagnant water).



- Targeted residual spraying of adult mosquitoes (in areas known to be resting sites for *Aedes* mosquitoes) and space spraying during outbreaks.
- Standard WHO recommendations regarding vector control at airports should be implemented in accordance with the IHR (2005). Refer to WHO aircraft disinsection methods and procedures: <https://www.who.int/publications/i/item/9789240014459>
- Mosquito surveillance is key to guide vector control and helps improve the timeliness of decisions to control mosquito populations and prevent disease. Both larval and adult vector populations should be targeted for surveillance.
- Data from mosquito surveillance can enable the selection and use of the most appropriate vector-control tools and can be used to monitor their effectiveness. Communities should be engaged to develop, implement, and evaluate mosquito surveillance activities.
- Mosquito vector surveillance is important for the prevention and control of arboviruses including Zika, chikungunya, dengue and yellow fever, and other mosquito-borne diseases like malaria.

8

Individuals should protect themselves from mosquito bites to reduce exposure from Zika virus

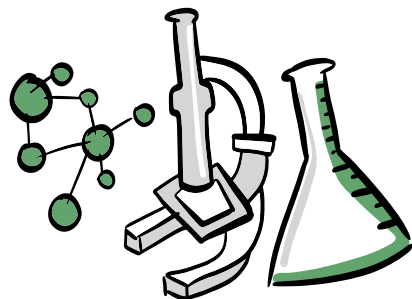
- Community members, particularly pregnant women, women of reproductive age, and couples considering pregnancy should be educated about the risk of transmission and how to minimize this risk of Zika and other arboviruses by reducing contact with mosquitoes and eliminating mosquito breeding sites.
- Personal preventive measures to avoid mosquito bites include clothing that minimizes skin exposure, and use of repellents, window screens and air conditioning.
- The use of insecticide-treated bed nets is limited by the fact that *Aedes* mosquitoes bite primarily during daytime. However, these may be useful to prevent some mosquito bites at night and in populations likely to be in bed during the day (such as the ill, elderly, infants and young children).
- Houses with solid floors and roofs, window screens, and air conditioning can reduce the chance of mosquito-borne virus transmission.



9

Access to counselling and laboratory testing is critical for pregnant women if they are likely to have been infected with Zika virus during pregnancy

- Because of the association between Zika virus infection and adverse pregnancy and infant outcomes, it is important that women be provided with accurate information on risks and have access to reliable laboratory testing in accordance with local and national guidelines. Women (and their partners as desired) should be offered non-directive counselling so that they, in consultation with their health care providers, can make a fully informed choice about the next steps in pregnancy management.
- Laboratories should have the capacity to test for Zika virus infection. Laboratory tests are done RT-PCR during the acute phase of the disease.



- Nucleic acid amplification tests (e.g., RT-PCR) and serological (IgM) testing with PRNT; infection with Zika virus is difficult to confirm retrospectively because serological tests cross-react with other flaviviruses, in particular dengue virus.

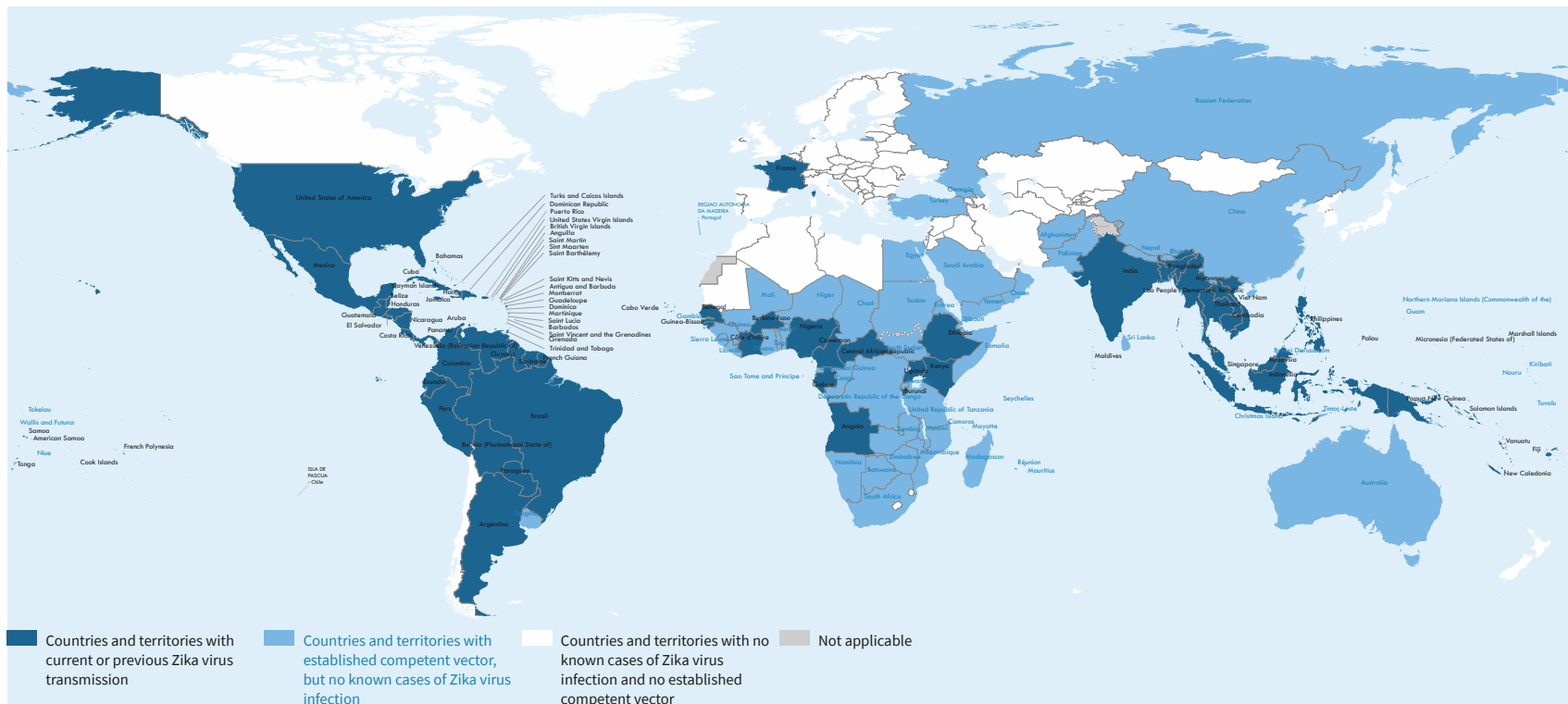
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Guidelines from WHO are available to prevent exposure to Zika virus for the general population, couples of reproductive age, pregnant women and their partners

- There are no general restrictions on travel or trade with countries, areas and territories with Zika virus transmission.
- However, WHO advises pregnant women to avoid traveling to areas with Zika virus transmission, particularly during outbreaks. Women who may become pregnant within two months of travel and male travellers whose partner may become pregnant within three months of travel are advised to check with their health care providers and carefully consider the risks and possible consequences of Zika virus infection before traveling to areas where there may be Zika virus transmission.
- National health authorities are responsible for advising travellers on risks and preventive measures.



Countries and territories with current or previous Zika virus transmission



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Map date: February 2022
 Data Source: World Health Organization
 Map Production: WHO Health Emergencies Programme

Zika virus country classification tables available at:
<https://www.who.int/emergencies/diseases/zika/countries-with-zika-and-vectors-table.pdf>





More information about Zika:

- Zika WHO webpage
https://www.who.int/health-topics/zika-virus-disease#tab=tab_1
- Zika virus WHO fact sheet
<https://www.who.int/news-room/fact-sheets/detail/zika-virus>
- OpenWHO course on Zika
<https://openwho.org/courses?utf8=%E2%9C%93&q=zika>

Chikungunya

10 THINGS YOU SHOULD KNOW



1. Chikungunya is a mosquito-borne disease
2. Chikungunya is emerging as a global disease and outbreaks typically occur in urban settings and crowded environments
3. Chikungunya virus can cause an acute febrile illness, usually accompanied by severe joint pains
4. Complete recovery from chikungunya virus infection may take a long time
5. Chikungunya virus infection is often misdiagnosed as dengue or other diseases
6. Treatment is directed primarily at relieving symptoms
7. Strong surveillance including adequate patient testing, mosquito vector surveillance and control strategies are important for prevention and control of chikungunya
8. Individuals should protect themselves from mosquito bites to reduce exposure to chikungunya virus
9. Although causing significant outbreaks and spreading globally, research is ongoing as much is still unknown about chikungunya
10. Rehabilitation and counselling support should be provided for people with chronic symptoms

Chikungunya response tips

Collaborative surveillance

- Ensure and strengthen capacity for early detection, diagnosis, reporting and monitoring of cases.
- Ensure adequate laboratory capacity for diagnosis and surveillance; reagent availability is often limited, which hampers detection and reporting.
- Implement and strengthen mosquito surveillance to maintain timely data on vector distribution and risk of transmission in communities.

Community protection

- Support community engagement, health promotion and social science.
- Encourage health authorities to:
 - Identify and engage populations at-risk for chikungunya virus exposure with tailored information delivered through trusted sources on how to protect themselves from infection and prevent transmission.
 - Advise high-risk groups to seek health care if symptomatic.
 - Engage communities in eliminating mosquito breeding sites.
- Key messages are:
 - Chikungunya is transmitted through mosquito bites, which mostly occur during the day.
 - Chikungunya can be transmitted from mother to child during delivery (or around the time of delivery) and can cause severe disease in the newborn that can lead to death
 - Chikungunya virus causes debilitating acute illness and, in some cases, long term sequelae that can last for years.
 - People can protect themselves from infection by taking personal preventive measures against mosquito bites, such as wearing clothing that minimizes skin exposure, using mosquito repellents, and using windows screens and air conditioning if available.
 - Newborns and young infants should be protected from mosquito bites through the use of screen covers over bassinets/cribs.

Clinical care

- Provide clinical supportive care for infected people and those experiencing prolonged/chronic chikungunya disease.
- Provide psychosocial support to infected people, those experiencing prolonged/chronic chikungunya disease and their families.

Access to countermeasures

- Prevent chikungunya disease by preventing mosquito bites.
- Reduce breeding sites of *Aedes* mosquitoes around dwellings.
- Encourage the use of insecticide-treated bed nets for infected people during the day and at night.

Emergency coordination

- Ensure coordination between public health, environmental, clinical and vector control services for effective surveillance, diagnosis, risk assessment, outbreak investigation and response, as well as research, development and implementation of control measures and supportive services.

1

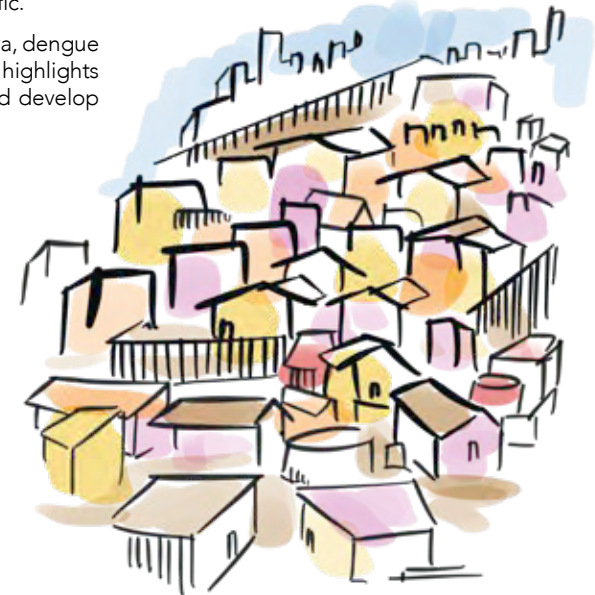
Chikungunya is a mosquito-borne disease

- Chikungunya virus is transmitted to humans by infected mosquitoes.
- Two types of *Aedes* mosquitoes are known to be capable of transmitting chikungunya virus:
 - In most cases, chikungunya is spread through the *Aedes aegypti* mosquito in tropical and subtropical regions. *Ae. aegypti*, is the same mosquito species that spreads urban yellow fever, Zika virus, and dengue viruses.
 - *Aedes albopictus* mosquitoes can also transmit chikungunya virus. This species commonly known as the 'tiger mosquito' can tolerate cooler temperatures than *Ae. aegypti*, which may expand the potential range of regions at risk of chikungunya virus transmission. *Ae. albopictus* can transmit dengue and Zika viruses. *Aedes* mosquitoes are present on all continents except Antarctica.
- *Aedes* mosquitoes usually bite during the day, peaking in the hours around sunrise and sunset. Both *Aedes* species are found biting outdoors, but *Ae. aegypti* will also bite indoors.
- Theoretically, transmission of the virus can occur through blood transfusion and laboratory and other bloodborne exposures. There is a risk of intrapartum transmission that would potentially lead to severe disease in the newborn. Maternal-fetal transmission is seen in outbreaks and occurs mostly during intrapartum (up to 49% probability of infection during delivery).

2

Chikungunya is emerging as a global disease and outbreaks typically occur in urban settings and crowded environments

- Mosquito-transmitted disease are amplified by urbanization, which increases human population densities and enhances manmade habitats for mosquito larvae. Humans serve as the main reservoir for chikungunya virus during epidemic periods.
- Increasingly dense urban settings, in addition to human travel, viral adaption, lack of effective control measures and spread of new vectors likely have contributed to the recent re-emergence of chikungunya virus.
- Local transmission of chikungunya virus by *Aedes* mosquitoes has been reported in Africa, the Americas, Europe, South-East Asia and the Western Pacific.
- The rapid spread of chikungunya, dengue and Zika viruses in recent years highlights the urgent need to identify and develop new *Aedes* control strategies.



3

Chikungunya virus can cause an acute febrile illness, usually accompanied by severe joint pains

- Chikungunya virus causes an acute febrile illness typically accompanied by severe joint pain. Other common signs and symptoms include muscle pain, headache, nausea, fatigue and rash.
- Newborns, the elderly and people with chronic underlying medical conditions are at greater risk of severe chikungunya disease.
- The joint pain from chikungunya infection is often debilitating. Usually, this joint pain lasts a few days but, in some cases, may be prolonged to months and even years.
- Newborns are at risk for severe chikungunya virus disease and may require hospitalization for monitoring and care.
- In rare cases, adults and children may experience severe symptoms of chikungunya including neurological manifestations.
- Chikungunya virus disease is generally not fatal, but symptoms can be debilitating. Supportive treatment is based on symptoms.
- The incubation period is usually between 4–8 days but can range from 2–12 days.
- Approximately 20% of infections are asymptomatic.

4

Complete recovery from chikungunya virus infection may be long

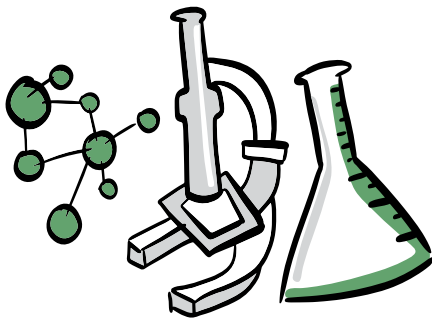
- The acute phase of chikungunya infection typically lasts for 3–10 days.
- In some cases, convalescence (recovery from) from chikungunya infection can be prolonged.
- Some patients have reported debilitating joint pain or arthritis, which may last for months or years.
- In rare cases, chikungunya virus disease may cause neurological, haemorrhagic and ocular symptoms, as well as severe multiple organ-system involvement.



5

Chikungunya virus infection is often misdiagnosed as dengue or other diseases

- Chikungunya patients may present with non-specific symptoms that can be confused with many other diseases such as dengue, malaria, Zika virus disease, leptospirosis, meningitis and rheumatic fever. Laboratory diagnosis is critical to establish the cause of infection and initiate a specific public health response.
- Dengue needs to be ruled out to be able to safely use NSAIDs in people with chikungunya symptoms in areas where both viruses are co-circulating.
- Methods used for diagnosis include:
 - Molecular technique: RT-PCR.
 - Serological tests, such as ELISA, may confirm the presence of IgM and IgG anti-chikungunya antibodies. IgM antibody levels are first detected within a week after illness onset, concentrations peak at 3–5 weeks after the onset of illness and remain detectable in the majority of patients for at least three months.



- Ensuring adequate laboratory capacity for diagnosis and surveillance is challenging due to limited availability of adequate RT-PCR and serologic tests. In addition, in some regions with circulating related arthritogenic alphaviruses, cross-reaction of serological tests could complicate the interpretation of serologic test results.

6

Treatment is directed primarily at relieving symptoms

- There is currently no specific antiviral drug treatment for chikungunya.
- Treatment is directed primarily at relieving symptoms using antipyretics (for example paracetamol), optimal analgesics and fluids. Applying cold compresses has been reported to lessen joint symptoms.
- Paracetamol may be used for symptom relief. NSAIDs can be used once the diagnosis of dengue has been ruled out.
- Patients with prolonged convalescence may require long-term anti-inflammatory therapy.
- All suspected and confirmed cases should use insecticide-treated bed nets during the febrile period.
- Patients with severe clinical manifestations and their families should be provided with psychosocial support, if needed.
- There is currently no chikungunya vaccine approved, although some candidate vaccines are currently in different stages of development.



7

Strong surveillance including adequate patient testing, mosquito vector surveillance and control strategies are important for prevention and control of chikungunya

- It is important to provide access to reliable laboratory testing for chikungunya virus infection and adequate testing is also important for surveillance activities.
- Vector-control strategies should address all life stages of the *Aedes* mosquito from the egg to larva and adult. Community engagement is essential for these interventions:
 - Elimination of breeding sites as well as eggs, larvae and pupae in standing water (for example cleaning roof gutters, conducting clean up campaigns, covering containers with stagnant water).
 - Targeted residual spraying of adult mosquitoes (in areas known to be resting sites for *Aedes* mosquitoes) and space spraying during outbreaks.
- Standard WHO recommendations regarding vector control at airports should be implemented in keeping with the IHR (2005). Countries should consider disinsection of aircraft.

- Mosquito surveillance is key to guide vector control activities and helps improve the timeliness of decisions to control mosquito

populations and prevent disease. Both larval and adult vector populations should be targeted for surveillance.

- Data from mosquito surveillance can enable the selection and use of the most appropriate vector-control tools and can be used to monitor their effectiveness. Communities should be engaged to develop, implement, and evaluate mosquito surveillance activities.
- Mosquito vector surveillance is important for the prevention and control of arboviruses including Zika, chikungunya, dengue and YF, as well as other mosquito-borne diseases like malaria.



8

Individuals can and should protect themselves from mosquito bites to reduce exposure from chikungunya virus

- Community members should be educated about the risk of transmission of chikungunya and other arboviruses and how to minimize this risk by reducing contact with mosquitoes and eliminating mosquito breeding sites.
- Personal preventive measures to avoid mosquito bites include clothing that minimizes skin exposure, and use of repellents, window screens and air conditioning.
- The use of insecticide-treated bed nets is limited by the fact that *Aedes* mosquitoes bite primarily during daytime. However, these may be useful to prevent some mosquito bites at night and in populations likely to be in bed during the day (such as the ill, elderly, infants and young children).
- Houses with solid floors and roofs, window screens and air conditioning can reduce the chance of mosquito-borne virus transmission.



9

Although causing significant outbreaks and spreading globally, research is ongoing as much is still unknown about chikungunya

- Since the early 2000s there have been multiple outbreaks of chikungunya, infecting millions globally.
- However, there are still a lot of unknowns about chikungunya, and research is ongoing to fill scientific gaps in understanding of the disease.
- Further studies are needed to understand the reasons underlying large outbreaks interspersed by periods of prolonged absence, virus survival in nature and factors triggering outbreaks.
- Research needs to focus on diagnostics tests, treatments and vaccines for chikungunya. Several vaccines are in late stages of development.
- Research is ongoing about the long-lasting protective immunity conferred by chikungunya infection.

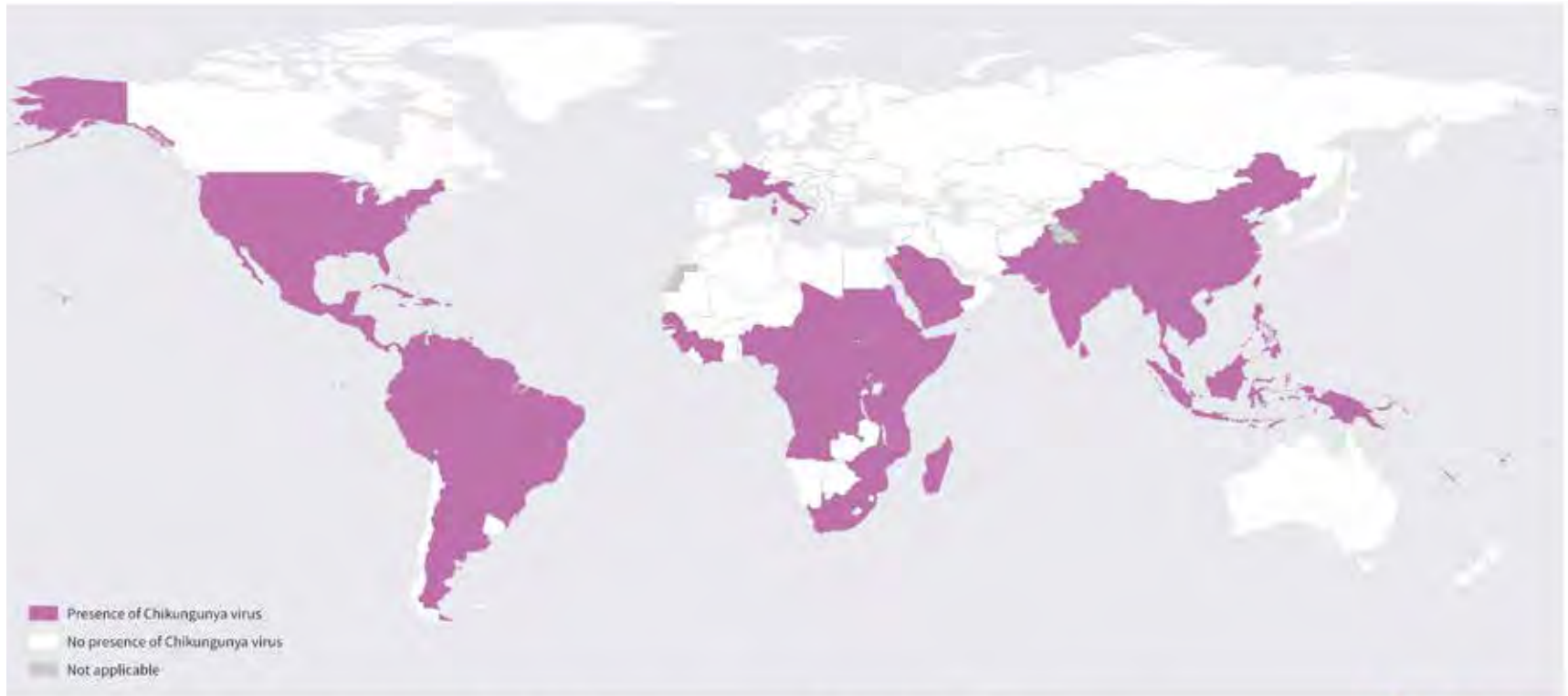
10

Rehabilitation and counselling support should be provided for people with chronic symptoms

- Patients with a long convalescence that includes chronic arthritis require appropriate and timely, pain management and physiotherapy as well as instructions on the safely doing non-weightbearing exercises and other rehabilitative counselling.
- Amongst those patients with chronic symptoms, culturally appropriate emotional and psychosocial support should be offered, including timely information on chikungunya.
- A plan should be made with patients for arranging adequate support in the community, including occupation and social rehabilitation.



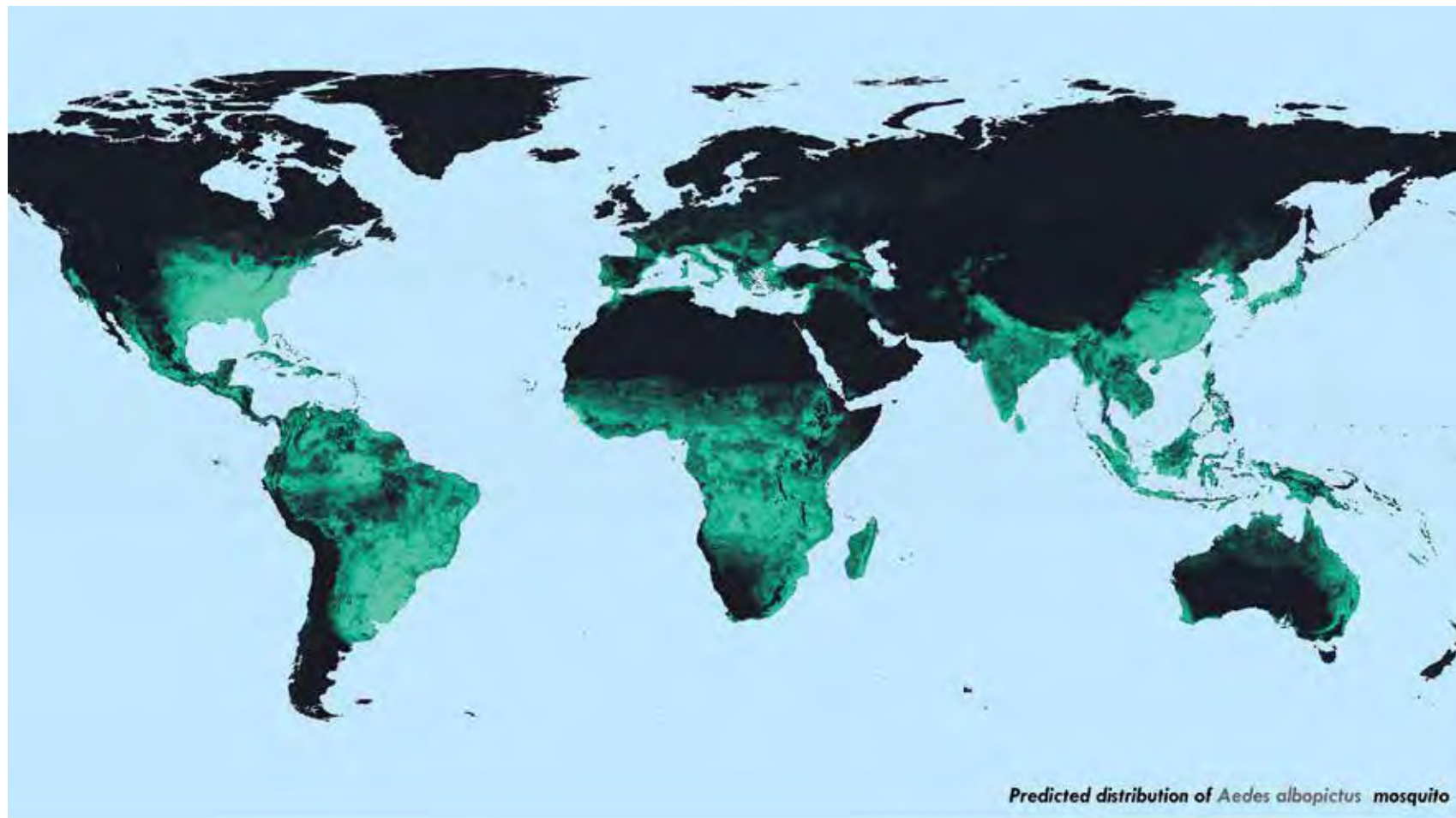
Predicted distribution of the *Aedes aegypti* mosquito



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Data Source: World Health Organization
Map Production: WHO Health Emergencies Programme
Request ID: RITM00065

Predicted distribution of the *Aedes Albopictus* mosquito



High Low

Map redrawn using satellite layers from <http://silholence.org/content/1/v08247/73>, Krouse MJO et al. eLife (Published June 30, 2013)

The geographical names shown and the designations used on this map are not the responsibility of any specific Government or the staff of the World Health Organization. The names of the countries, territories, cities and towns, and the names of the countries, are necessary for the purposes of the present report. The World Health Organization is not responsible for any errors or omissions in the text or in the map.



More information about chikungunya:

- Chikungunya WHO webpage
https://www.who.int/health-topics/chikungunya/#tab=tab_1
- Chikungunya WHO fact sheet
<https://www.who.int/en/news-room/fact-sheets/detail/chikungunya>
- WHO Chikungunya: case definitions for acute, atypical and chronic cases
<https://apps.who.int/iris/handle/10665/242406>



Dengue

10 THINGS YOU SHOULD KNOW



1. Dengue is a mosquito-borne disease
2. Approximately 4 billion people are at risk of dengue infection
3. Diagnosing dengue is important for clinical care, surveillance and outbreak control
4. Dengue virus infection is often asymptomatic but can also causes flu-like or more severe illness
5. Warning signs of severe dengue should be identified early so patients are referred to hospital care
6. Symptomatic treatment can reduce mortality
7. There is a vaccine for dengue virus that requires pre-vaccination screening
8. Prevention and control require strong surveillance including adequate diagnostic testing, mosquito vector surveillance and control strategies
9. Individuals can and should protect themselves from mosquito bites to reduce exposure
10. There is a global strategy that aims to reduce the burden of dengue and prevent deaths

Dengue response tips

Collaborative surveillance

- Ensure and strengthen capacity for early detection, diagnosis, reporting and monitoring of cases.
- Implement and strengthen mosquito surveillance to maintain timely data on vector distribution and risk of transmission in communities.
- Provide access to reliable laboratory testing and ensure adequate laboratory capacity for diagnosis and surveillance. An appropriate referral system should be in place for managing severe dengue cases.
- Report cases to WHO, under the IHR (2005).

Community protection

- Support community engagement, health promotion and social science.
- Encourage health authorities to:
 - Identify and engage populations at-risk for dengue or other arbovirus exposure with tailored information delivered through trusted sources on how to protect themselves from infection and prevent transmission.
 - Advise high-risk groups to seek health care if symptomatic.
 - Engage communities in eliminating mosquito breeding sites at least once a week.
- Key messages are:
 - Dengue virus is transmitted to humans through mosquito bites, which mostly occur during the day, peaking in the hours around sunrise and sunset.
 - People can protect themselves from infection with personal preventive measures against mosquito bites such as wearing clothing that minimizes skin exposure, using mosquito repellents, and using windows screens and air conditioning if available.
 - People should protect themselves in places of work or study since the mosquitos that carry dengue virus bite during the daytime.

Clinical care

- Treatment is directed primarily at relieving symptoms, maintaining body fluid volume and monitoring for warning signs of severe dengue.
- Depending on the clinical manifestations and other circumstances, patients may be sent home, be referred for in-hospital management or require emergency treatment and urgent referral.

Access to countermeasures

- Prevent dengue by preventing mosquito bites.
- Reduce breeding sites of *Aedes* mosquitoes around dwellings.
- Vaccination should be considered as part of an integrated dengue prevention and control strategy.

Emergency coordination

- Ensure coordination between public health, maternal and child health, vector-control, clinical and psychosocial services for effective surveillance, diagnosis, risk assessment, outbreak investigation and response, as well as research, development and implementation of appropriate control measures and supportive services.

1

Dengue is a mosquito-borne disease

- Dengue is caused by a virus of the Flaviviridae family. There are four distinct, but closely related, serotypes of the virus that cause dengue (DEN-1, DEN-2, DEN-3 and DEN-4).
- Dengue virus is transmitted to humans by infected mosquitoes, most commonly *Aedes* species mosquitoes.
- Two types of *Aedes* mosquitoes are known to be capable of transmitting dengue virus:

- In most cases, dengue is spread through the *Aedes aegypti* mosquito in tropical and subtropical regions. *Ae. aegypti*, is the same mosquito species that spreads urban yellow fever, chikungunya, and Zika viruses.

- *Aedes albopictus* mosquitoes can also transmit dengue virus. This species commonly known as the 'tiger mosquito' can tolerate cooler temperatures than *Ae. aegypti*, which may expand the potential range of regions at risk of dengue virus transmission. *Ae. albopictus* can transmit chikungunya and Zika viruses. *Aedes* mosquitoes are present on all continents except Antarctica.



- *Aedes* mosquitoes usually bite during the day, peaking in the hours around sunrise and sunset. Both *Aedes* species are found biting outdoors, but *Ae. aegypti* will also bite indoors.
- Outbreaks usually occur in areas where mosquitoes breed.
- Mosquito-transmitted diseases are amplified by urbanization, which increases human population densities and enhances manmade habitats for mosquito breeding.

2

Approximately 4 billion people are at risk of dengue infection

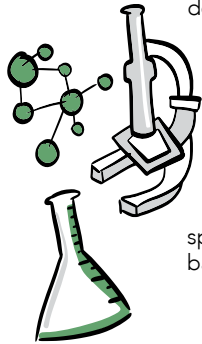
- Dengue is found in tropical and subtropical climates worldwide, mostly in urban and semi-urban areas, with local variations in risk influenced by rainfall, temperature, humidity and unplanned rapid urbanization.
- Over 40% of the world's population, approximately 4 billion people in 129 countries, live in areas with risk of dengue.
- The disease is endemic in more than 100 countries in the Caribbean, Central and South America, Africa, Southeast Asia, Western Pacific and the Pacific Islands.
- Each year, up to 400 million people get infected with dengue. Approximately 100 million people get sick from infection and 22,000 die from severe dengue.
- Travellers play an essential role in the global spread of dengue infections.



3

Diagnosing dengue is important for clinical care, surveillance and outbreak control

- The choice of diagnostic method depends on the purpose for which the testing is done (for example clinical diagnosis, epidemiological survey, vaccine development and roll out), the type of laboratory facilities and technical expertise available, costs and the time of sample collection.
- Before day five of illness, during the febrile period, dengue infections may be diagnosed by:
 - Virus isolation in cell culture.
 - Detection of viral RNA by NAAT.
 - Detection of viral antigens by ELISA or rapid tests.
- After day five, dengue viruses and antigens disappear from the blood coincident with the appearance of specific antibodies. If specimens are collected after day five of illness, commercial IgM ELISA or sensitive dengue IgM rapid tests may suggest a dengue outbreak.



- During outbreak investigations, the rapidity and specificity of diagnostic tests is more important than test sensitivity. Samples collected from febrile patients could be tested by nucleic acid methods in a well-equipped laboratory or broader spectrum of laboratories using an ELISA-based dengue antigen detection kit.

- Dengue surveillance systems aim to detect the circulation of specific viruses in the human or mosquito populations. The diagnostic tools used should be sensitive, specific and affordable for the country.
- Platelets and hematocrit values are commonly measured during acute stages of dengue infection to evaluate the severity of the disease.
- Infected symptomatic or asymptomatic humans are the main carriers and multipliers of the virus, serving as a source of the virus for uninfected mosquitoes. Infected patients can transmit the infection via *Aedes* mosquitoes after their first symptoms appear, usually during day 4–5 (maximum 12). Thus, it is important to identify cases to ensure adequate clinical care, surveillance and outbreak control.



4

Dengue virus infection is often asymptomatic but can also cause flu-like or more severe illness

- Over 80% of cases are asymptomatic with potential to transmit the virus to the vector.
- Symptomatic cases of dengue virus infection present with a severe, flu-like illness that affects infants, young children and adults, but seldom causes death.
- Symptoms usually last for 2–7 days, after an incubation period of 4–10 days after the bite from an infected mosquito. After the incubation period, the illness starts abruptly and is followed by the three phases: febrile, critical and recovery (see page 143).
- Dengue should be suspected when a high fever (40 °C/104 °F) is accompanied by two of the following symptoms: severe headache, pain behind the eyes, muscle and joint pains, nausea, vomiting, swollen glands or rash.
- Recovery from infection by one dengue virus provides lifelong immunity against that particular virus serotype. However, this immunity confers only partial and transient protection against subsequent infection by the other three serotypes of the virus. Evidence points to the fact that secondary infection increases the risk of developing severe dengue.

5

Warning signs of severe dengue should be identified early so patients are referred to hospital care

- Severe dengue is a potentially deadly complication and is defined by one or more of the following:
 - 1) Plasma leaking that may lead to shock and/or fluid accumulation, with or without respiratory distress, and/or
 - 2) Severe bleeding and/or
 - 3) Severe organ impairment.
- Warning signs occur 3–7 days after the first symptoms in conjunction with a decrease in temperature (below 38 °C/100 °F).
- Individual risk factors such as secondary infection, age, ethnicity and possibly chronic diseases may determine the severity of the disease.
- Young children are at higher risk of severe dengue due to a lesser ability than adults to compensate for capillary leakage.



6

Symptomatic treatment can reduce mortality

- Treatment is directed primarily at relieving symptoms, maintaining body fluid volume and monitoring for warning signs of severe dengue.
- There is currently no specific antiviral drug treatment for dengue virus infection, but mortality can be drastically reduced by implementing timely appropriate clinical management (for severe dengue, mortality rates decrease from more than 20% to less than 1%).
- Patients should seek medical advice, rest and drink plenty of fluids.

- Paracetamol can be taken to bring down fever and reduce joint pains. However, aspirin or ibuprofen should not be taken as these can increase the risk of bleeding.
- Depending on the clinical manifestations and other circumstances, patients may be sent home, be referred for in-hospital management or require emergency treatment and urgent referral.
- Intravenous fluid resuscitation with isotonic crystalloid solutions is essential and required for the management of severe dengue.
- The triage of dengue patients is as follows:

Group A (Home care)

- Patients able to tolerate adequate volumes of oral fluids and pass urine at least once every six hours and who do not have any of the warning signs of severe dengue, particularly when fever subsides.

Group B (In-hospital care)

- Patients with warning signs of severe dengue;
- Those coexisting conditions that may make dengue management more complicated (pregnancy, infancy, old age, obesity, diabetes mellitus, renal failure, chronic haemolytic diseases) and;
- Those with certain social circumstances (living alone or living far from a health facility without reliable means of transport, remote islands).

Group C (Emergency treatment or urgent referral)

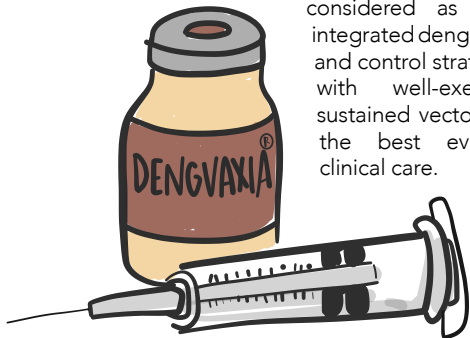
- Patients who require emergency treatment and urgent referral when they have severe dengue.

7

There is a vaccine for dengue virus that requires pre-vaccination screening

- A vaccine exists, *Dengvaxia*[®] (CYD-TDV), which in 2015 became the first dengue vaccine to be licensed. It is now licensed in 20 countries.
- It is a live recombinant vaccine given as a three-dose series on a 0/6/12-month schedule.
- WHO recommends that for countries considering vaccination as part of their dengue control programme, a pre-vaccination screening strategy would be the preferred option, in which only dengue-seropositive persons are vaccinated. People who receive the vaccine and have not been previously infected with a dengue virus may be at risk of developing severe dengue if they get dengue after being vaccinated. Serological testing for past dengue infection could be used to identify persons who have had previous dengue infections before vaccination.

- Vaccination should be considered as part of an integrated dengue prevention and control strategy together with well-executed and sustained vector control and the best evidence-based clinical care.



8

Prevention and control require strong surveillance including adequate diagnostic testing, mosquito vector surveillance and control strategies

- It is important to provide access to reliable laboratory testing for dengue virus infection and adequate testing is also important to surveillance activities.
- Vector-control strategies should address all life stages of the *Aedes* mosquito from the egg to larva and adult. Community engagement is essential for these interventions:
 - Elimination of breeding sites as well as eggs, larvae and pupae in standing water (for example cleaning roof gutters, clean up campaigns, cover containers with stagnant water).



- Targeted residual spraying of adult mosquitoes (in areas known to be resting sites for *Aedes* mosquitoes) and space spraying during outbreaks.
- Safe water supply and storage will further enhance vector control.
- Standard WHO recommendations regarding vector control at airports should be implemented in accordance with the IHR (2005). should consider disinfection of aircraft.
- Mosquito surveillance is key to guide vector control and helps improve the timeliness of decisions to control mosquito populations and prevent disease. Both larval and adult vector populations should be targeted for surveillance.
- Data from mosquito surveillance can enable the selection and use of the most appropriate vector-control tools and can be used to monitor their effectiveness. Communities should be engaged to develop, implement and evaluate mosquito surveillance activities.
- Mosquito vector surveillance is important for the prevention and control of arboviruses including dengue, chikungunya, YF, Zika, as well as other mosquito-borne diseases such as malaria.

9

Individuals can and should protect themselves from mosquito bites to reduce exposure

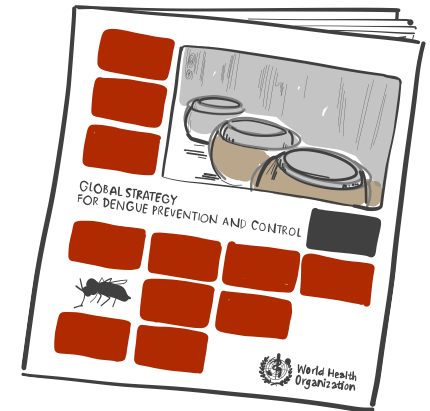
- Community members should be educated about the risk of transmission and how to minimize this risk by reducing contact with mosquitoes and eliminating mosquito breeding sites.
- Personal preventive measures to avoid mosquito bites include clothing that minimizes skin exposure, and use of repellents, window screens and air conditioning.
- The use of insecticide-treated bed nets has limited impact due to the fact that *Aedes* mosquitoes bite primarily during daytime. However, these may be useful to prevent some mosquito bites at night and in populations likely to be in bed during the day (such as the sick, elderly, infants and young children).
- Houses with solid floors and roofs, window screens and air conditioning can reduce the chance of mosquito-borne virus transmission.



10

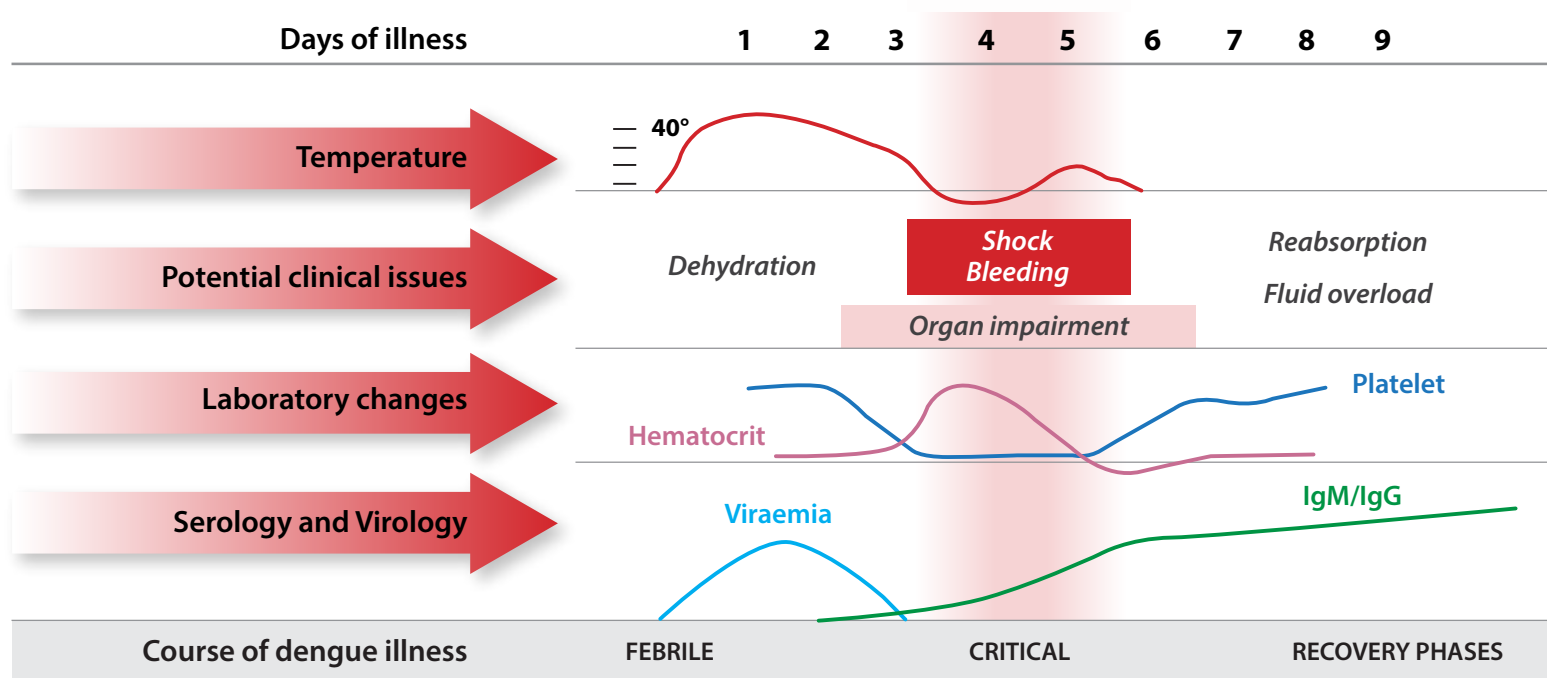
There is a global strategy that aims to reduce the burden of dengue and prevent deaths

- Oriented by the main goal of reducing the burden of dengue, the global strategy for dengue prevention and control, 2012–2020 was developed. Its specific objectives are:
 - To reduce dengue mortality by at least 50% by 2020.
 - To reduce dengue morbidity by at least 25% by 2020.
- This strategy promotes coordination and collaboration among multisectoral partners, an integrated vector management approach and sustained control measures at all levels.
- The two major components of the emergency response to a dengue outbreak are:
 1. Emergency vector control to reduce transmission of the dengue virus as rapidly as possible.
 2. Early diagnosis and appropriate clinical case management of severe dengue to minimize the number of dengue associated deaths.



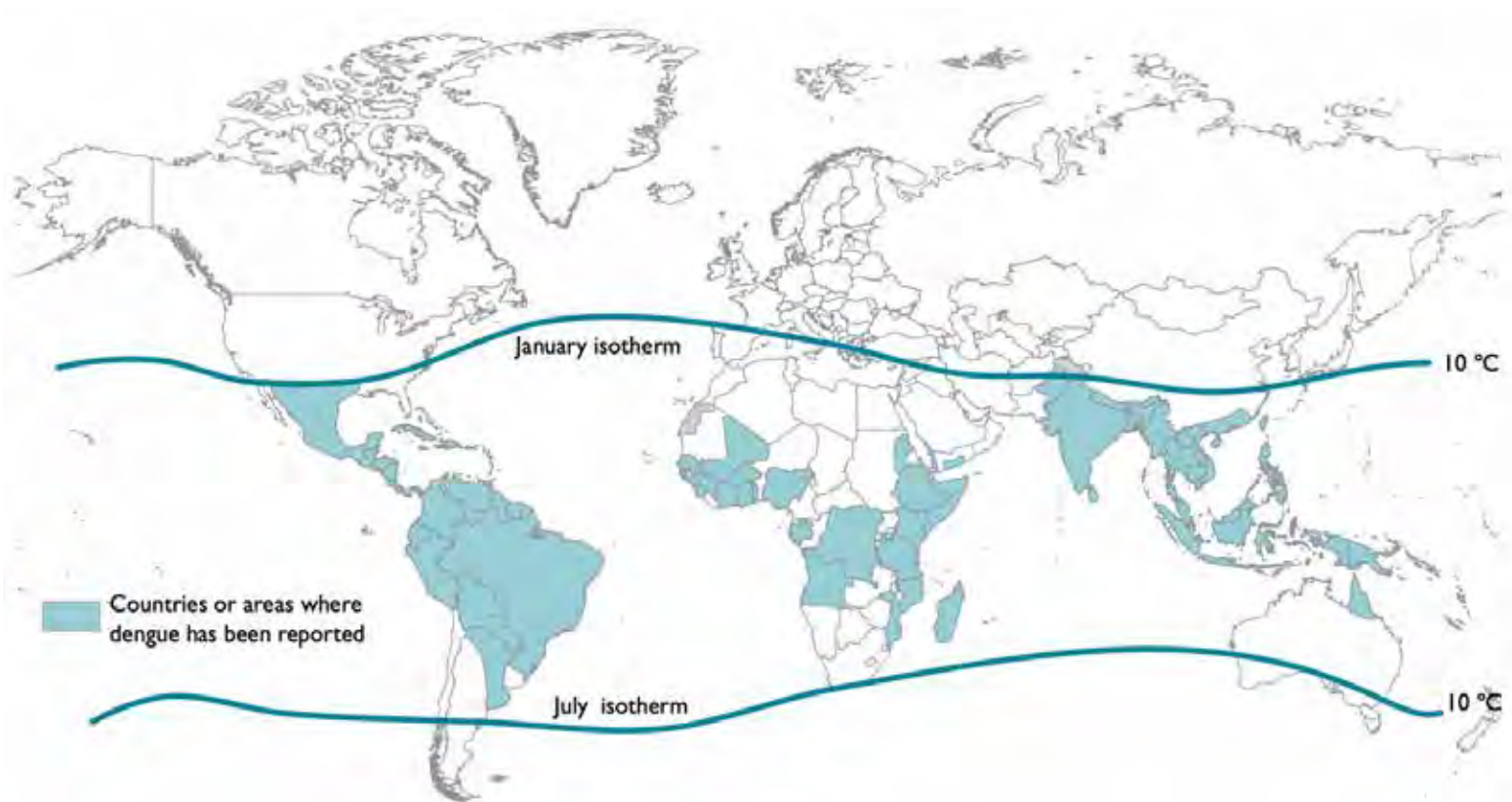
- However, major research gaps in integrated surveillance and vector control still exist.
- There is an urgent need for the development of highly specific and sensitive RDTs for determination of dengue serostatus.
- The development of safe, effective and affordable dengue vaccines for use irrespective of serostatus remains a high priority. Research is also needed to evaluate vaccine schedules with fewer doses, and to assess the need for booster doses.

The course of dengue illness



Source: Dengue guidelines for diagnosis, treatment, prevention and control, 2009

Dengue, countries or areas at risk, 2011



The contour lines of the January and July isotherms indicate areas at risk, defined by the geographical limits of the northern and southern hemispheres for year-round survival of *Aedes aegypti*, the principal mosquito vector of dengue viruses. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

More information about dengue:

- Dengue and severe dengue WHO webpage
https://www.who.int/health-topics/dengue-and-severe-dengue#tab=tab_1
- Dengue and severe dengue WHO fact sheet
<https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue>
- Global Strategy for dengue prevention and control, 2012-2020
<https://www.who.int/publications/i/item/9789241504034>



Malaria

- Malaria is a life-threatening disease caused by parasites that are transmitted to people through the bites of infected female *Anopheles* mosquitoes. It is preventable and curable.
- In 2020, there were an estimated 241 million cases of malaria and 627 000 deaths caused by malaria worldwide.
- The WHO African Region carries a disproportionately high share of the global malaria burden. In 2020, the region was home to 95% of malaria cases and 96% of malaria deaths. Children under 5 years of age accounted for an estimated 80% of all malaria deaths in the region.
- For the latest recommendations and guidance please refer to the WHO Guidelines for malaria: <https://app.magicapp.org/#/guideline/6832>

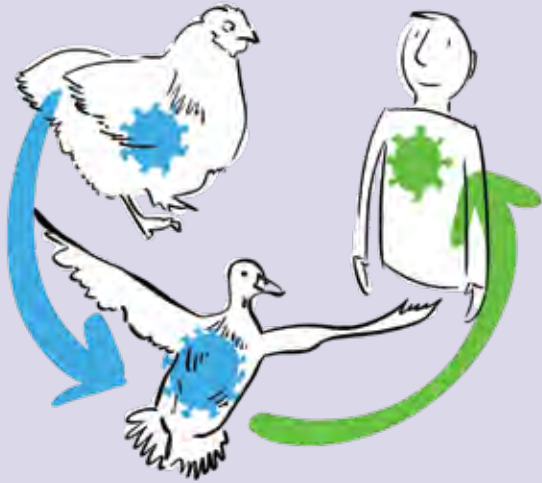


More information about malaria:

- **Malaria fact sheet**
<https://www.who.int/news-room/fact-sheets/detail/malaria>
- **World Malaria report 2021**
<https://www.who.int/publications/i/item/9789240040496>
- **Global technical strategy for malaria 2016-2030, 2021 update**
<https://www.who.int/publications/i/item/9789240031357>

Animal influenza

10 THINGS YOU SHOULD KNOW



1. Animal influenza viruses (avian, swine and other zoonotic influenza viruses) have occasionally infected humans (zoonotic influenza)
2. Multisectoral coordination and communication are essential in outbreak response
3. All persons with exposure to occupational or other risks associated with animal influenza should be alerted to potential zoonotic infection
4. Eggs, meat and meat products can be safely consumed if they are properly cooked and properly handled during food preparation
5. Public health management, including actions in animal and human populations, is crucial to preventing and managing animal influenza epidemics
6. Timely detection of human infections with animal influenza and assessment of the risk of animal-to-human and human-to-human transmission are critical
7. Collection of appropriate samples, rapid detection and thorough characterization of the virus are essential for management of patients and triggering of countermeasures
8. Health care facilities need to be ready to manage patients with animal influenza virus infections particularly by strengthening IPC
9. The animal health and food security sectors are charged with preventing and controlling outbreaks of disease in animals
10. Vaccines for avian and other zoonotic influenza viruses for use in humans are not widely available, and the decision to use them depends on the risk of infection

Animal influenza response tips

Collaborative surveillance

- Collect appropriate specimens for confirmation of infection.
- Monitor contacts.
- Ensure information sharing from the animal health sector to the human health sector to support preventive action in affected areas.
- Ensure information sharing on human cases with the animal health sector to target response activities.
- To encourage early reporting, urge health authorities to have a way to compensate owners/farmers for the loss of sick animals.
- Ensure sharing of viruses from human cases with WHO Collaborating Centres of the Global Influenza Surveillance and Response System (GISRS).
- Investigate cases and enhance surveillance.
- Report cases to WHO, under the IHR (2005) and assess the risk of further human cases or sustained human-to-human transmission.

Community protection

- Encourage proper personal hygiene, especially frequent handwashing and instruct people to seek medical help if illness develops.
- Encourage health authorities to have a multisector communications strategy in place.
- Key messages are:
 - Zoonotic influenza is transmitted primarily from infected animals to humans through direct contact; the risk of further transmission should be assessed on a case-by-case basis.
 - Sustained human-to-human transmission of avian or other zoonotic viruses is rare; its occurrence marks the start of a potential influenza pandemic.
 - Promote good personal hygiene including using PPE and handwashing.
 - Promote proper food safety.
 - Report sick animals to the authorities, including the handling of dead animal carcasses.

Clinical care

- Provide case-patients with antiviral and supportive treatment.
- Ensure adherence to IPC and use of PPE to prevent health care associated infections.
- Depending on the clinical manifestations and other circumstances, patients may be sent home, be referred for in-hospital management or require emergency treatment and urgent referral.

Access to countermeasures

- Vaccines for avian and other zoonotic influenza viruses for use in humans are not widely available, and the decision to use them depends on the risk of infection.

Emergency coordination

- Ensure a multisectoral response: collaboration between the animal health, food and agriculture, environment and public health sectors is key for surveillance, risk assessment, response and prevention activities.

1

Animal influenza viruses (avian, swine and other zoonotic influenza viruses) have occasionally infected humans (zoonotic influenza)

- When animal influenza viruses infect their natural animal host, they are named for that host, as with avian influenza viruses, swine influenza viruses, equine influenza viruses, etc.
- Avian influenza is a disease of domestic and wild birds. Domesticated populations (poultry such as chickens, ducks, turkeys and ostriches) can become infected by contact with wild birds. Avian influenza viruses are categorized as low pathogenic or highly pathogenic viruses. The two terms do not refer to the disease severity in humans infected with the viruses.
- When swine influenza viruses of certain subtypes (e.g., A(H1N1), A(H3N2)) infect people, they are labeled “variant” (with a “v” placed after the name of the virus) to distinguish them from seasonal human viruses of the same subtype.
- Humans can be infected with animal influenza viruses that can cause disease ranging from mild conjunctivitis to severe pneumonia and even death.
- Zoonotic influenza A viruses are distinct from human influenza viruses and do not easily transmit between humans. Human infections are acquired primarily through direct contact with infected animals or contaminated environments but rarely result in further transmission between people.

2

Multisectoral coordination and communication are essential in outbreak response

- Animal influenza outbreaks have the potential to be significant to public health and can have social and economic impacts.
- Effective communication with all stakeholders is an essential part of any outbreak response.
- Strong coordination between animal and human health sectors is needed for surveillance, risk communication and intervention monitoring.



3

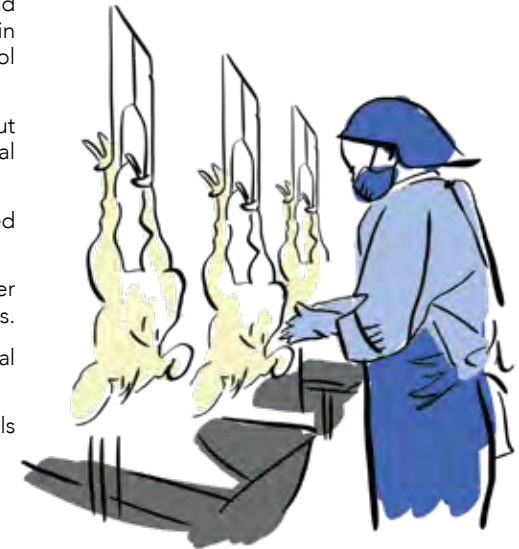
All persons with exposure to occupational or other risks associated with animal influenza should be alerted to potential zoonotic infection

- People involved in high-risk tasks such as sampling sick birds, culling and disposing of infected birds and cleaning of contaminated premises should be protected, including by provision of appropriate PPE and training on proper use.
- All persons involved in these tasks should be registered and monitored closely by local health authorities for 7–10 days (or longer depending on the incubation period) following the last day of exposure of risks, for example sick birds or their environments.
- Symptomatic persons should be treated with influenza-specific antivirals according to WHO guidelines.
- If sufficient antivirals are available, antiviral chemoprophylaxis can be considered.
- Seasonal influenza vaccination is recommended for persons with potential for exposure to animal influenza viruses. Although seasonal influenza vaccines do not protect against animal influenza viruses, the vaccine will protect workers from seasonal influenza viruses and reduce the potential reassortment of seasonal and animal influenza viruses.

4

Eggs, meat and meat products can be safely consumed if they are properly cooked and properly handled during food preparation

- The public should be informed about ways to promote safe food consumption:
 - Thoroughly cook poultry and poultry products.
 - Handle and store meat properly.
 - Separate raw meat from cooked and ready-to-eat foods.
 - Keep clean and practice hand hygiene.
- Hygiene and biosecurity in live animal markets should be assessed and improved where possible.
- National food safety authorities and meat producers should develop and implement quality assurance schemes in line with Hazard Analysis Critical Control Point principles and steps.
- The public should also be informed about potential risks from water and animal waste:
 - Carefully treat drinking water supplied from open surface water.
 - Be aware that properly treated wastewater seems to pose only a small risk for humans.
 - Be aware that, in some cases, recreational water might be contaminated.
 - Consider that faeces from infected animals can be infectious.



5

Public health management, including actions in animal and human populations, is crucial to preventing and managing animal influenza epidemics

- Minimize exposure of the public to potentially infected animals and other sources of contamination; encourage proper personal hygiene, especially frequent handwashing; and instruct people to seek medical help if illness develops.
- When animal influenza viruses circulate in an area, all people who are exposed to infected animals (for example birds) are at risk, especially persons who do the following:
 - Keep live poultry in their backyards or homes or purchase live poultry or birds at markets.
 - Slaughter, de-feather or butcher poultry.
 - Handle and prepare raw meat for cooking and consumption.
 - Transport or sell live animals or carcasses.
 - Perform culling/depoulling/disposing of poultry.



- Perform other work in the poultry industry, including by farmers and veterinarians.
- Have contact with poultry or meat by-products (for example viscera, manure, feathers) or water contaminated with these by-products (for example wastewater from a live bird market or slaughtering facility).
- Consume raw meat products.
- The general public should minimize contact with infected animals and avoid areas where infected animals are housed, slaughtered or prepared. They should also:
 - Keep children away from potentially infected animals and their waste, including bird feathers and manure; children should neither collect eggs nor assist with slaughtering or food preparation.
 - Report sick or unexpectedly dead animals to the authorities immediately.
 - Comply with all official prevention measures (for example animal movement restrictions).
 - Do not slaughter and/or consume animals that are showing signs of disease or that have died unexpectedly.

6

Timely detection of human infections with animal influenza and assessment of the risk of animal-to-human and human-to-human transmission is critical

- Animal influenza viruses are not easily transmitted from animals to humans or sustained human-to-human transmission.
- However, it is important to investigate suspected human cases to ensure appropriate treatment, identify and monitor other potential human contacts and determine if there is human-to-human transmission.
- The most important goal for investigations of human cases of infections with animal influenza viruses is to assess the extent of potential human-to-human transmission, especially in clusters of human cases and contacts of confirmed cases.
- Enhanced surveillance should consider the health care-seeking behaviour of the population and can include active and passive approaches that are health care and/or community-based.
- Persons with exposure to known risks of zoonotic (or animal) influenza virus infection should monitor their health for the duration of the known exposure period plus an additional 7–10 days (or longer depending on the incubation period). This will facilitate early detection

of illness and timely commencement of antiviral treatment and isolation precautions. They should report any relevant health problems to a health care facility.

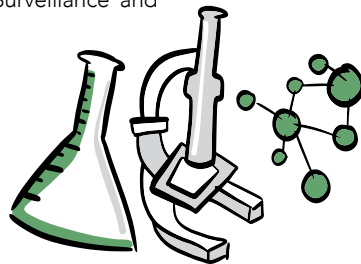
- The risk of virus transmission from animal-to-human and human-to-human should be assessed and updated as information becomes available. Risk assessment can inform mitigation measures.
- Following a risk assessment, Member States should use the Annex 2 decision instrument of the IHR (2005) to decide if an acute public health event requires formal notification to WHO. The effective use of Annex 2 depends on each national authority and its IHR (2005) National Focal Point to carry out risk assessments on public health events occurring within their territories.



7

Collection of appropriate samples and rapid detection and thorough characterization of the virus are essential for management of patients and triggering of countermeasures

- Collection of appropriate specimens from suspected human cases for virus detection by a qualified laboratory, together with thorough characterization of the virus at a specialized reference laboratory, are essential for early detection of cases, proper management of patients, and understanding of the epidemiology of the disease.
- In addition, appropriate specimen collection and subsequent laboratory analysis are important for evaluation for antiviral susceptibility, monitoring the development of resistance to antivirals, producing effective vaccines and evaluating testing and diagnostic methods.
- Ensure that specimen collection materials are available and that collection of specimens is done safely, correctly, and in a timely manner.
- Promote regular and timely virus/sample sharing with WHO Collaborating Centres of the Global Influenza Surveillance and Response System (GISRS).



8

Health care facilities need to be ready to manage patients with animal influenza virus infections particularly by strengthening IPC

- Health care facilities should strengthen early infection control precautions to prevent health care-associated (originating in a hospital) spread of the disease.
- Health workers should manage cases properly to prevent severe illness and death:
 - Administer neuraminidase inhibitor treatment as the primary choice of antiviral treatment, using the standard regimen for seasonal influenza virus infection, as soon as possible (ideally, within 48 hours following symptom onset) to maximize therapeutic benefits.
 - Monitor patients and viruses for indications of antiviral resistance.
- Many countries, regions and WHO have antiviral stockpiles in varying sizes and with varying conditions for triggering use.
- Employ other supportive therapies based on clinical presentation, including oxygen therapy and advanced respiratory interventions, such as non-invasive and invasive mechanical ventilation.
- Laboratory-confirmed cases should be reported to WHO, under IHR (2005).



9

The animal health and food security sectors are charged with preventing and controlling outbreaks of disease in animals

- Controlling disease in the animal source is critical to decreasing risk to humans.
- Reporting new and ongoing outbreaks in animals is important for focusing human health prevention action in affected areas and raising awareness among professionals working with potentially infected animals, as well as the public. The sharing of information on human cases with the animal health sector is equally important for targeting of response activities.
- The Food and Agriculture Organization (FAO) of the United Nations promotes food security and good nutrition by providing access to knowledge, policy advice and technical assistance to Member Countries. FAO publishes information and guidance on avian

influenza, provides direct technical assistance to countries, and works closely with many stakeholders.

- The World Organization for Animal Health (OIE) sets international standards for animal health and zoonoses through the 'OIE Code' and 'OIE Manual' and is responsible for collecting and disseminating official animal disease information from OIE Member Countries. It collaborates with National Veterinary Services as well as with FAO at national, regional, and global levels to provide technical assistance to countries (for example laboratory support).
- National Veterinary Services, often located within the Ministry of Agriculture, are responsible for implementation of national animal influenza measures to control and prevent the spread of the disease in animals.

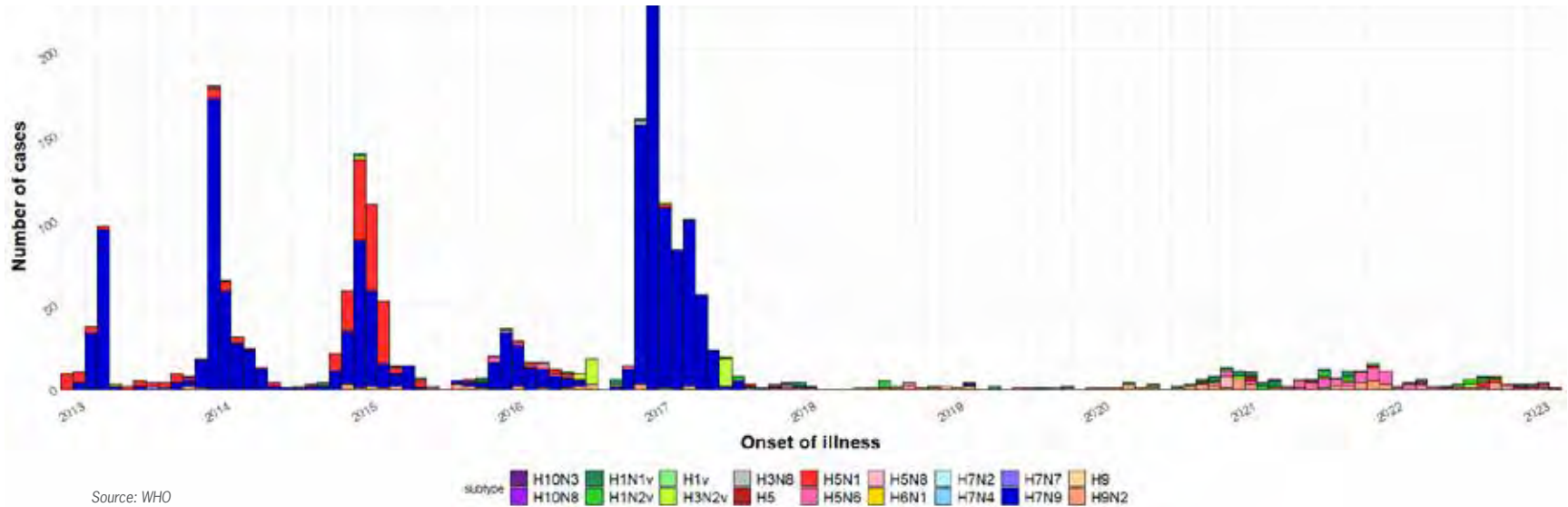


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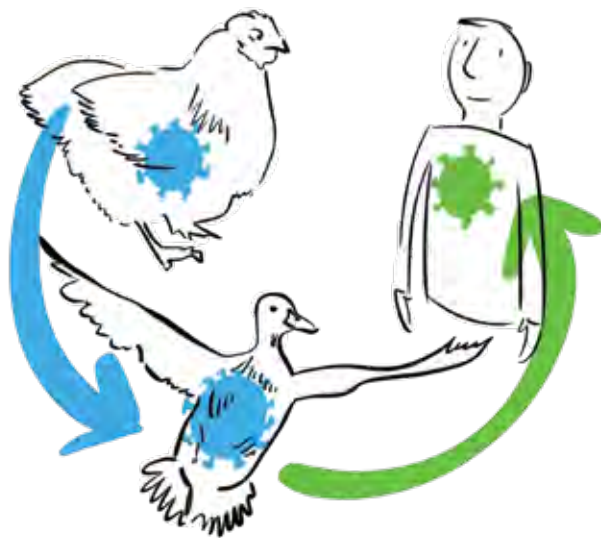
Vaccines for avian and other zoonotic influenza viruses for use in humans are not widely available, and the decision to use them depends on the risk of infection

- WHO recommends vaccination against seasonal influenza infection to personnel at increased risk of exposure to avian or other zoonotic influenza viruses as one of several measures for reducing opportunities for co-infection with zoonotic and human influenza viruses.
- Vaccines of several subtypes of avian influenza viruses including A(H5N1) and A(H7N9) for human use have been developed. These are based on candidate vaccine viruses developed by Global Influenza Surveillance and Response System (GISRS) and licensed in several countries. They are not widely available. WHO has no stockpile of zoonotic influenza vaccines.
- Animal influenza vaccination in humans should be based on risk assessment and decided by countries. Considerations of timing (for example immediately after an outbreak is detected or before) and priority groups (for example a laboratory technician handling the zoonotic virus, first responders to zoonotic outbreaks in humans or animals and health workers who evaluate or manage patients with suspected or confirmed zoonotic influenza infection) should be made carefully.
- High-growth reassortant viruses for animal influenza vaccine development for human use are reviewed and updated by the GISRS at least twice a year.

Monthly incidence of zoonotic influenza cases, 2013 to present



Source: WHO



More information about animal influenza:

- Influenza (avian and other zoonotic) WHO webpage
<https://www.who.int/health-topics/influenza-avian-and-other-zoonotic>
- Avian and other zoonotic influenza WHO fact sheet
[https://www.who.int/news-room/fact-sheets/detail/influenza-\(avian-and-other-zoonotic\)](https://www.who.int/news-room/fact-sheets/detail/influenza-(avian-and-other-zoonotic))
- OpenWHO course on Avian and other influenza
<https://openwho.org/courses/avian-and-other-zoonotic-influenza-introduction>
- WHO summary of key information practical to countries experiencing outbreaks of A(H5N1) and other subtypes of avian influenza, July 2016
<http://apps.who.int/iris/bitstream/10665/246251/1/WHO-OHE-PED-GIP-EPI-2016.1-eng.pdf?ua=1>
- Case definitions for the four diseases requiring notification to WHO in all circumstances under the IHR (2005)
[https://www.who.int/publications/m/item/case-definitions-for-the-four-diseases-requiring-notification-to-who-in-all-circumstances-under-the-ihp-\(2005\)](https://www.who.int/publications/m/item/case-definitions-for-the-four-diseases-requiring-notification-to-who-in-all-circumstances-under-the-ihp-(2005))
- Pandemic Influenza Preparedness Framework for sharing of influenza virus and access to vaccines and other benefits
<https://www.who.int/initiatives/pandemic-influenza-preparedness-framework>
- Human-animal interface, WHO Global Influenza Programme
<https://www.who.int/teams/global-influenza-programme/avian-influenza>
- Rapid risk assessment of acute public health events
<https://www.who.int/publications/i/item/rapid-risk-assessment-of-acute-public-health-events>
- Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases
<https://www.who.int/publications/i/item/WHO-WHE-IHM-GIP-2018.2>

Seasonal influenza

10 THINGS YOU SHOULD KNOW



1. Seasonal influenza is an acute viral respiratory disease transmitted from person to person
2. Influenza A and B viruses cause seasonal influenza disease
3. Outbreaks and seasonal epidemics of influenza disease can be very disruptive
4. Influenza disease ranges from mild to severe and can be fatal
5. Seasonal influenza disease and other respiratory diseases that cause similar symptoms are hardly distinguishable
6. PHSM can reduce transmission and prevent disease outbreaks
7. Early treatment with influenza antiviral drugs may reduce complications and deaths
8. Annual seasonal influenza vaccination is the best way to prevent infection and reduce disease severity
9. Border closures and entry and exit screening of travellers are not recommended to reduce seasonal influenza virus transmission
10. Monitoring influenza activity through regular surveillance and sharing of data and viruses is critical

Seasonal influenza response tips

Collaborative surveillance

- Regular and timely sharing of data on the epidemic situation, including the severity of influenza illnesses as well as the circulating influenza viruses, helps authorities develop policies to target interventions and countermeasures, including vaccines, to reduce the burden of influenza disease.

Community protection

- PHSM:
 - Personal protection measures (for example respiratory etiquette, mask-wearing, hand hygiene, voluntary self-isolation).
 - Environmental measures (for example cleaning and frequent, effective ventilation).
 - Physical distancing (for example avoiding overcrowding, maintaining distance in public or workplaces).
- Encourage health authorities to:
 - Educate on recommended PHSM (for example personal protective measures, environmental measures and physical distancing).
 - Communicate about influenza vaccine effectiveness and safety, especially for high-risk groups.
- Promote respiratory etiquette, hand hygiene and staying at home when sick.
- Key messages are:
 - Seasonal influenza viruses are highly contagious.
 - The influenza virus spreads efficiently from person to person.
 - Annual seasonal influenza vaccinations are safe and are the best way to prevent infection and reduce disease severity and death.
 - High-risk groups, such as older adults, people with underlying conditions, pregnant women, young children under 5 years old and particularly those under 2 years old are most at risk for complications and should seek medical care when sick.

Clinical care

- Pharmaceutical interventions:
 - Influenza antiviral drugs.
- IPC measures in health care facilities.

Access to countermeasures

- Pharmaceutical interventions: Vaccines (annual vaccination) and antiviral drugs.

Emergency coordination

- WHO's GISRS monitors influenza virus evolution globally, assesses associated risks, and provides recommendations in areas including laboratory diagnostics, vaccines, antiviral susceptibility and risk assessment.

1

Seasonal influenza is an acute viral respiratory disease transmitted from person to person

- Seasonal influenza (or “flu”) is an acute (sudden-onset) respiratory disease caused by influenza viruses and characterized by fever, headache, cough, muscle and joint pain, general malaise and a runny nose.
- The influenza virus is highly contagious. It can spread easily from person to person through respiratory droplets when an infected individual coughs or sneezes.
- Transmission can also be airborne, especially when aerosol-generating medical procedures are performed.
- It can also be transmitted by direct contact (for example kissing or shaking hands) or indirect contact (for example touching contaminated surfaces or objects and then touching the nose or eyes).



- Rapid transmission can occur in crowded areas (for example schools or nursing homes).
- Influenza viruses circulate in all parts of the world.
- Tools for prevention and control of influenza disease include pharmaceutical measures (vaccines and antiviral medications) and PHSM, previously known as non-pharmaceutical measures.

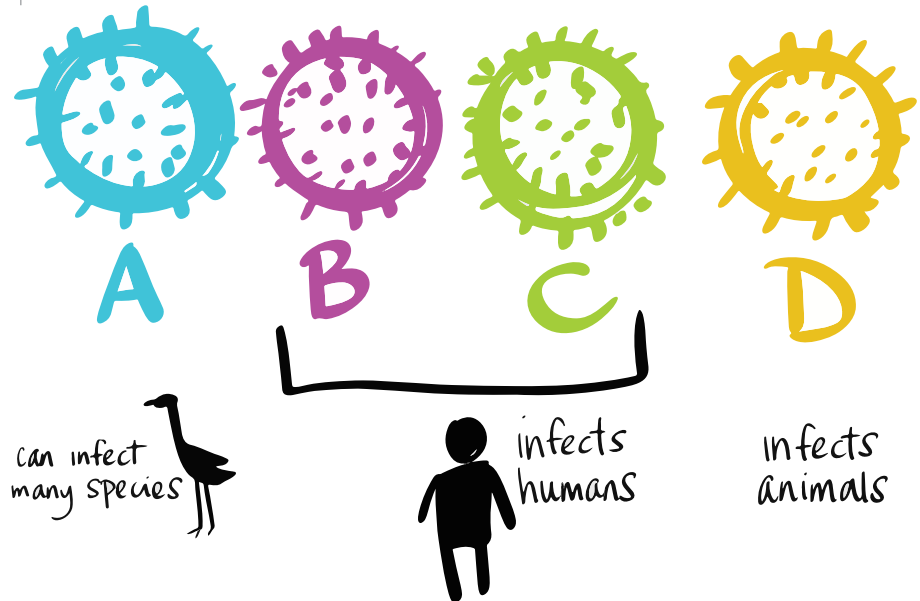
2

Influenza A and B viruses cause seasonal influenza disease

- There are four types of influenza viruses – A, B, C and D – but only influenza A and B cause epidemics of disease in humans. Influenza A can infect many species (for example birds, humans, pigs, horses). Influenza B and C infect mainly humans. Influenza type C virus is less frequent, usually causes only mild infections, and thus presents less significant public health implications. Influenza D has been detected in several animal species.
- Influenza A viruses are further classified in subtypes based on their surface proteins. There are 18 different haemagglutinin

(H) types and 11 different neuraminidase (N) types. Different combinations are possible. Currently, H3N2 and H1N1 are circulating in humans as seasonal influenza A viruses.

- Influenza B viruses are not classified into subtypes, but rather, they are broken down into lineages. Currently circulating influenza B viruses belong to either the B/Yamagata or B/Victoria lineages.
- Influenza viruses are constantly evolving. This change in viruses leads to antigenic drift, which makes people susceptible to getting infected every year as the immunity against the drifted viruses is weak in people.



3

Outbreaks and seasonal epidemics of influenza disease can be very disruptive

- In temperate climates, seasonal epidemics occur mainly during winter months. The epidemics generally last from 8–10 weeks in temperate areas.
- In tropical regions, the pattern of influenza epidemics is not always as regular. Some countries regularly have two epidemics in a year, whereas others can have epidemics throughout the year with no regular pattern.
- The burden of seasonal epidemics is substantial. It is estimated that between 3 million–5 million cases of severe respiratory illness and between 290 000–650 000 respiratory-related deaths due to influenza occur each year. The total number of influenza-related deaths is likely much higher.
- Influenza epidemics can have a high economic burden every year due to work and school absenteeism, productivity losses and direct and indirect medical costs.

4

Influenza disease ranges from mild to severe and can be fatal

- Influenza can cause severe illness or death in any person, although most hospitalizations and deaths related to influenza occur in people in high-risk groups.
- People at higher risk of developing complications and severe seasonal influenza are:
 - People older than 65 years;
 - People with chronic medical or immunosuppressive conditions such as HIV/AIDS, asthma, heart and lung diseases and diabetes; and
 - Children younger than 5 years;
 - Pregnant women.
- Flu can also make chronic medical problems worse. For example, people with asthma may experience asthma attacks while they have flu or are recovering from the flu, and people with chronic heart disease may experience a worsening of this condition triggered by flu.
- A wide range of complications can be caused by influenza virus infection of the upper respiratory tract (nasal passages, throat) and lower respiratory tract (lungs). Sinus and ear infections are examples of moderate complications from flu, whereas pneumonia is a serious flu complication that people with chronic lung disease are at higher risk of developing.

- Other possible serious complications triggered by flu can include inflammation of the heart (myocarditis), brain (encephalitis) or muscle (myositis, rhabdomyolysis) tissues, and multi-organ failure (for example respiratory and kidney failure). Flu virus infection of the respiratory tract can trigger an extreme inflammatory response in the body, leading to sepsis.

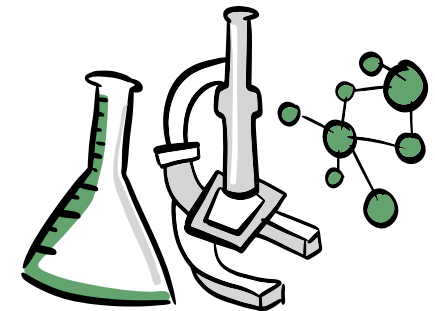
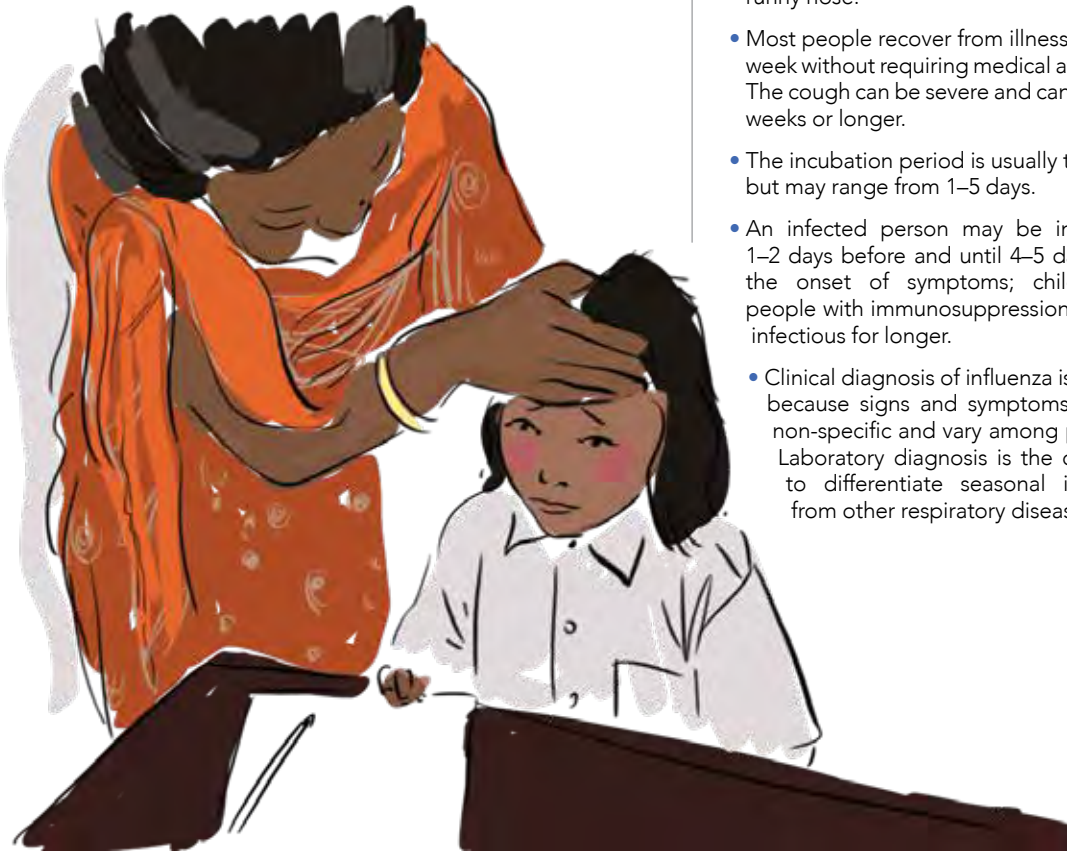


5

Seasonal influenza disease and other respiratory diseases that cause similar symptoms are hardly distinguishable

- People with seasonal influenza usually show non-specific symptoms. These include fever, headache, cough, muscle and joint pain, general malaise and a runny nose.
- Most people recover from illness within a week without requiring medical attention. The cough can be severe and can last two weeks or longer.
- The incubation period is usually two days but may range from 1–5 days.
- An infected person may be infectious 1–2 days before and until 4–5 days after the onset of symptoms; children or people with immunosuppression may be infectious for longer.
- Clinical diagnosis of influenza is difficult because signs and symptoms can be non-specific and vary among patients. Laboratory diagnosis is the only way to differentiate seasonal influenza from other respiratory diseases.

- While RT-PCR is the gold standard for influenza diagnosis, it does require testing at specialized laboratories and turnaround times for results may not be timely to inform clinical management decisions. Rapid influenza diagnostic tests (RIDTs) are used in clinical settings, but they often have lower sensitivity compared to RT-PCR methods, and their reliability depends largely on the conditions under which they are used.
- Other laboratory techniques are available, including virus isolation in cell culture and identification of viral antigens (fluorescent antibodies test or ELISA). Single serum sample analysis is not ideal for diagnosis of an acute infection.
- The most appropriate specimens for the diagnosis of influenza are upper respiratory tract specimens. Samples should be taken from the deep nostrils (nasal swab), throat (oropharyngeal swab) and nasopharynx (nasopharyngeal swab). Nasopharyngeal and bronchial aspirates are also useful.



6

PHSM can reduce transmission and prevent disease outbreaks

- Pharmaceutical measures include vaccination and treatment with antiviral medications but should be complemented by other measures.
- The goal of PHSM is to slow the spread of influenza in a population by reducing transmission.
- Recommended PHSM to reduce transmission and prevent seasonal influenza epidemics include:
 - Personal protection measures (for example respiratory etiquette, mask-wearing, hand hygiene, voluntary self-isolation).
 - Environmental measures (for example cleaning and frequent, effective ventilation).
 - Physical distancing (for example avoiding overcrowding, maintaining distance in public or workplaces).
- Before an epidemic, to reduce the potential disruptive effects of seasonal influenza, it is critical that:
 - There is effective health planning in place to ensure implementation of health education and immunization for at-risk patients, their close contacts and health workers.
 - Increased demand for medical care and possible absenteeism of health workers during the epidemic period are anticipated.
- To reduce transmission during a seasonal influenza epidemic, the following measures should be considered:

- Continued health education.

- Respiratory etiquette (for example covering mouth and nose with a tissue when coughing and then disposing of the tissue and washing hands) and hand hygiene (for example washing hands).

- Well-fitted masks should be worn by symptomatic individuals when in contact with other individuals.

- Cleaning surfaces and objects with safe cleaning products in all settings.

- Voluntary isolation at home of sick individuals with uncomplicated illness (for example individuals not seeking medical attention) until major symptoms disappear.

- School and workplace measures and closures, and avoiding overcrowding, are conditionally recommended depending on the severity of the epidemic. The benefits and timing of the interventions need to be considered against the adverse effects on the community.

- Recommended interventions should be adapted to the local context and risk communication and community engagement should be implemented to share the rationale for the recommended interventions, encourage active engagement of the population and empower people with information.



7

Early treatment with influenza antiviral drugs may reduce complications and deaths

- Most people with influenza disease that are not from a high-risk group can be managed with supportive care. Medical advice should be sought if the symptoms are rapidly progressing or if an individual is at high risk for complications.
- People with seasonal influenza disease should always hydrate properly, rest and stay at home to reduce transmission to others.
- Antiviral drugs may reduce severe complications and deaths. Ideally, they need to be administered early in the disease (within 48 hours of onset of symptoms). For severe cases presenting symptoms suggesting active virus replication, antiviral drugs can be administered later in the course of disease based on clinical evaluation. If the clinical presentation suggests secondary or concomitant bacterial infection (for example secondary bacterial pneumonia), appropriate antimicrobials should be added adhering to the local treatment regimen for community acquired pneumonia.

- They are three major classes of influenza antiviral drugs: neuraminidase inhibitors (oseltamivir), M2 inhibitors (adamantanes), and polymerase inhibitors (baloxavir marboxil, favipiravir). Currently, the majority of circulating influenza viruses are resistant to adamantanes, limiting their effectiveness. Therefore, neuraminidase inhibitors are the recommended first-line treatment. Baloxavir marboxil is the newest influenza antiviral drug and has been licensed in some countries in recent years. For more information about the use of influenza antivirals, please refer to WHO Guidelines for the clinical management of severe illness from influenza virus infections¹.



¹ Guidelines for the clinical management of severe illness from influenza virus infections: <https://www.who.int/publications/i/item/9789240040816>

8

Annual seasonal influenza vaccination is the best way to prevent infection and reduce disease severity

- The most effective way to prevent the disease and reduce disease severity is by getting vaccinated every year.
- WHO recommends that all countries should consider implementing seasonal influenza vaccination programmes based on disease epidemiology, burden of disease, cost-effectiveness, and competing public health priorities. Certain groups should be prioritized for vaccination, such as pregnant women, children aged between 6 months and 5 years, people aged 65 years and above, people with chronic medical conditions and health workers and people who live with or care for those at high risk.
- For the most effective coverage, people should get vaccinated just before the influenza season begins but getting vaccinated at any time during the influenza season can still help prevent infections.
- Influenza viruses evolve constantly, and in preparation for each hemisphere's influenza season, WHO makes recommendations to update the vaccine compositions based on the monitoring done through Global Influenza Surveillance and Response System (GISRS). This maximizes the effectiveness of the vaccines to match circulating viruses. A number of inactivated influenza vaccines and recombinant influenza

vaccines are available in injectable form. Live attenuated influenza vaccines are available as a nasal spray.

- Influenza vaccines are safe and have been used for more than 60 years. Severe side effects are extremely rare. Influenza vaccines do not cause influenza disease.



9

Border closures and entry and exit screening of travellers are not recommended to reduce seasonal influenza virus transmission

- Border closures and entry and exit screening and quarantining of travellers crossing international borders are not recommended.
- Border closures and exit and entry screening to detect people with fever might be inefficient as:
 - Infected people may travel during the incubation period, during which they will not show symptoms but will already be able to transmit the disease.
 - People may be using fever-reducing medications.

- Implementing border closures may be very expensive and disruptive and have other social and political implications.
- Providing travel advice to citizens before their travel (for example to get vaccinated and to avoid potential exposure) is highly recommended.

10

Monitoring influenza activity through regular surveillance and sharing of data and viruses is critical

- Strong local and national surveillance capacities are vital to the regular monitoring of seasonal influenza activity and contribute to an enhanced global understanding of the impact and burden of influenza.
- Regular monitoring of epidemiological information is important to assess the severity of current epidemics, anticipate severe epidemics and plan health care services, and implement control measures. Monitoring includes trends of Influenza-like illness (ILI) and severe disease (severe acute respiratory disease hospitalizations) and deaths, as well as virological information (for example characteristics of circulating viruses).
- Since 1952, WHO has been coordinating the GISRS, which now has more than 150 laboratories in more than 125 countries and which monitors and analyses the global disease dynamics and evolution of influenza viruses and recommends the seasonal influenza vaccine composition and other risk mitigation measures.



More information about seasonal influenza:

- Influenza (seasonal) WHO webpage
<https://www.who.int/health-topics/influenza-seasonal>
- Seasonal influenza WHO fact sheet
[https://www.who.int/news-room/fact-sheets/detail/influenza-\(seasonal\)](https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal))
- OpenWHO course on Seasonal influenza
<https://openwho.org/courses/seasonal-influenza-introduction>
- Global Influenza Surveillance and Response System (GISRS)
<https://www.who.int/initiatives/global-influenza-surveillance-and-response-system>
- WHO biweekly seasonal influenza updates and maps
<https://www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/influenza-updates>
- Global Influenza Strategy 2019-2030
<https://apps.who.int/iris/handle/10665/311184>



Pandemic influenza

10 THINGS YOU SHOULD KNOW



1. Another influenza pandemic is inevitable but unpredictable
2. A pandemic happens when an influenza virus emerges to which most people have little or no immunity
3. Influenza pandemics are global and may be mild, moderate or severe, and destructive
4. Risk groups and symptoms might be different from seasonal influenza epidemics or past pandemics
5. Pandemic response requires concerted global actions and a whole-of-society approach
6. Early treatment with influenza antiviral drugs and other medical support are expected to reduce severe complications and deaths
7. Vaccines will probably not be available in the first months of a pandemic
8. PHSM may be the only initial measures in most countries
9. Empower communities to communicate risk, develop and implement control measures to reduce the impact of pandemic influenza
10. Pandemic response capacities can be built, tested and strengthened through seasonal influenza programmes

Pandemic influenza response tips

Collaborative surveillance

- Report initial cases to WHO under the IHR (2005) and follow other WHO guidance as the pandemic progresses.
- Share viruses and information with WHO's Global Influenza Surveillance and Response System (GISRS).
- Consult WHO technical guidance, especially on pandemic surveillance and severity assessments.
- Share information and communicate with other sectors.

Community protection

- PHSM:
 - Personal protective measures (for example hand hygiene and respiratory etiquette, masks).
 - Environmental measures (for example cleaning and infection control in health care facilities).
 - Physical distancing (for example voluntary self-isolation, school and workplace interventions, avoiding overcrowding, good ventilation of rooms).
- Encourage health authorities to:
 - Operationalize preparedness plans covering all aspects of response (for example plan for use of diagnostics, antiviral drugs and vaccines, multisectoral risk communication plan) and communicate the response details in advance of a pandemic.
 - Communicate early and frequently about how to protect from the disease.
- Engage communities and individuals to practice good respiratory and hand hygiene.
- Key messages are:
 - Pandemic influenza is caused by a new virus to which people have little or no immunity.
 - Protect yourself by using proper respiratory etiquette and hand hygiene (for example effective handwashing) and by distancing yourself from others if you become sick (for example voluntary self-isolation).
 - Stay at home, and drink plenty of fluids.
 - Seek medical advice if you have severe symptoms or other medical conditions that may put you at risk of severe disease.
 - Take the new pandemic influenza vaccine when it becomes available if you are encouraged to do so.

Clinical care

- Antiviral drugs are an important tool to prevent the spread of the disease and severe outcomes and complications.

Access to countermeasures

- Vaccines are one of the most effective ways to protect people during influenza epidemics and pandemics but will probably not be available during the first months of a pandemic.

Emergency coordination

- Ensure global coordination.
- Ensure multisectoral coordination and collaboration.
- Ensure a whole-of-society approach.

1

Another influenza pandemic is inevitable but unpredictable

- Currently, it is not possible to predict when or where the next influenza pandemic will start, what subtype will cause it and what morbidity and mortality impact it will have, but it is certain that there will be one.
- History has shown that pandemics occur at 10–50-year intervals, with varying severity and impact. During the 20th century, there were three influenza pandemics (1918, 1957 and 1968). Since 2000, there has been one influenza pandemic (2009).
- Influenza viruses are very unstable and constantly mutating. They undergo small mutations (antigenic drift) and cause seasonal influenza epidemics and out-of-season outbreaks. But a substantial change (antigenic shift) can occur at any time. This will result in a new virus (different subtype) that may lead to a pandemic. This antigenic shift can be the reassortment of human influenza viruses with avian or swine viruses, or significant point mutations of avian or swine viruses.



2

A pandemic happens when an influenza virus emerges to which most people have little or no immunity

- Three factors are necessary for the emergence of pandemic influenza:
 - A new influenza virus emerges and causes illness in humans.
 - This virus has the ability to transmit from person to person efficiently.
 - The human population has little or no immunity to the virus.
- Because it is a new virus to which people have not yet been exposed, the population has no or little immunity and

the virus, once emerged, is able to spread quickly in human population and cause illness in people.

- A pandemic influenza virus may arise when:
 - Genes from animal and human influenza viruses mix to create an influenza reassortant virus (genetic reassortment); and/or
 - Genes in an animal influenza virus change, allowing the virus to infect humans and transmit easily among them (genetic mutation).
- It is mandatory to notify a human influenza case caused by a new subtype to WHO, under the IHR (2005).

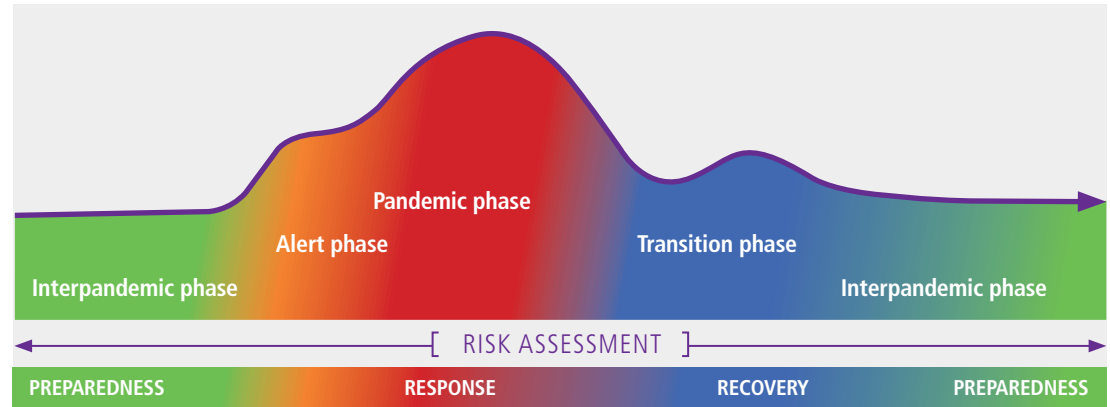


3

Influenza pandemics are global and may be mild, moderate or severe, and destructive

- Influenza pandemics have various levels of severity and impact:
- It is difficult to predict the characteristics, including the level of severity, of the next pandemic.
- During an influenza pandemic, severity assessments should be conducted regularly at local, national and global levels to inform public health decisions (for example vaccine production and use, antiviral use, school closures, social distancing strategies).
- Key elements to take into consideration are the transmissibility of the disease, its seriousness (for example complications, affected groups), and the impact on the health sector.
- Because historical data on seasonal influenza epidemics serve as a baseline for assessing the severity of pandemics, it is critical to support routine influenza surveillance during the interpandemic period.

The continuum of pandemic phases



Characteristics of the past four influenza pandemics

Pandemic year of emergence and common name	Area of origin	Influenza A virus sub-type (type of animal genetic introduction / recombination event)	Estimated reproductive number	Estimated case fatality	Estimated attributable excess mortality worldwide	Age groups most affected
1918 "Spanish flu"	Unclear	H1N1 (unknown)	1.2–3.0	2–3%	20–50 million	Young adults
1957–1958 "Asian flu"	Southern China	H2N2 (avian)	1.2–3.0	<0.2%	1–4 million	All age groups
1968–1969 "Hong Kong flu"	Southern China	H3N2 (avian)	1.3–1.6	<0.2%	1–4 million	All age groups
2009–2010 "influenza A(H1N1)	North America	H1N1 (swine)	1.1–1.8	0.02%	100 000–400 000	Children and young adults

Source: *Pandemics of the 20th–21st centuries*. Stockholm, European Centre for Disease Prevention and Control.

4

Risk groups and symptoms might be different from seasonal influenza epidemics or past pandemics

- Although the risk groups for infection and severe outcomes are likely the same as for seasonal influenza, there might be differences, as was seen during the 2009 H1N1 influenza pandemic, which disproportionately affected younger age groups.
 - Historical knowledge from the 1918 and 2009 pandemics indicates that healthy young adults can be disproportionately and more severely affected.
 - Pandemic influenza might present differently from seasonal influenza, and symptoms may be more severe and complications more frequent.
- People with influenza will usually develop the following symptoms: sudden onset of fever, headache, cough (usually dry), muscle and joint pain, fatigue, sore throat and runny nose.
- Complications can include pneumonia, sepsis and inflammation of the heart (myocarditis), brain (encephalitis) or muscle (myositis).
- The incubation period is usually two days but may range from 1–5 days, although the exact range is uncertain.

5

Pandemics require concerted global actions and a whole-of-society approach

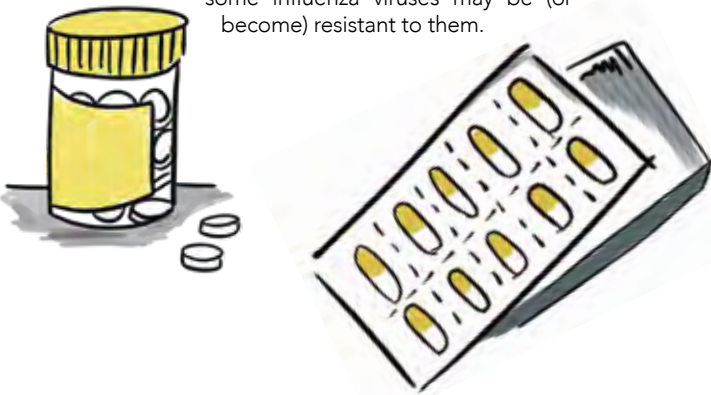
- Influenza pandemics are very disruptive events that can cause severe social, economic and political stress.
- Preparedness requires a whole-of-society approach to ensure that when the next pandemic strikes, the world will be able to respond rapidly and effectively to reduce morbidity and mortality.
- The health sector and all other sectors, individuals, families and communities have a role to play in mitigating the effects of a pandemic.



6

Early treatment with influenza antiviral drugs and other medical support are expected to reduce complications and deaths

- Pharmaceutical interventions typically encompass the application of antiviral drugs and other drug treatment (for example antibiotics for secondary bacterial infections).
- Antiviral drugs may reduce severe complications and deaths. Ideally, they need to be administered early in the disease (within 48 hours of onset of symptoms). They are especially important for high-risk groups.
- During an influenza pandemic, antiviral drugs are an important tool to prevent the spread of the disease and severe outcomes and complications, as vaccines will most likely not be available at an early stage.
- Effectiveness of the drugs on the pandemic virus must be monitored, as some influenza viruses may be (or become) resistant to them.



7

Vaccines will probably not be available in the first months of a pandemic

- Vaccines are one of the most effective ways to protect people during influenza epidemics and pandemics.
- However, the availability of a pandemic vaccine may be delayed by several months because of the requirements for vaccine formulation and production lead-time. It is expected that it takes about 24 weeks (almost six months) for a vaccine to be available after the identification of the pandemic virus.
- It is probable that the worldwide production capacity will still be insufficient and restrict global access to the vaccine, at least during the first phase of the pandemic. Pandemic influenza vaccine production may also be challenged by co-circulation with seasonal influenza and the use of some available capacity to continue seasonal influenza vaccine production.
- In 2019, it was estimated that in the best-case scenario over a 12-month period global pandemic influenza vaccine production capacity could reach about 8.31 billion doses. This is still insufficient to cover the world population because two doses of vaccines will probably be needed to fully protect against the virus. Furthermore, it is challenging to maintain this production capacity.¹

¹ Sparrow E, Wood JG, Chadwick C, Newall AT, Torvaldsen S, Moen A, et al. Global production capacity of seasonal and pandemic influenza vaccines in 2019. *Vaccine*. Volume 39, Issue 3. 2021. <https://doi.org/10.1016/j.vaccine.2020.12.018>

- Vaccination should target individuals most at risk of exposure (for example health workers, people living in crowded areas) and those most at risk of complications.
- Antigen-sparing strategies can be used to increase vaccine availability.
- Some countries are stockpiling pre-pandemic vaccines against some avian influenza viruses.

8

PHSM may be the only initial measures in most countries

- Vaccination is the primary intervention to prevent infection and severe outcomes caused by influenza virus. However, at the beginning of a pandemic, vaccines that match the new virus will most likely not be available.
- In addition to antiviral drugs (which might also be in short supply), PHSM should be put in place at the early stage of a pandemic to slow transmission and reduce its impact. PHSM include (but are not limited to):
 - Personal protective measures (for example respiratory etiquette, face masks hand hygiene).
 - Environmental measures (for example cleaning and frequent, effective ventilation).
 - Physical-distancing measures (for example self-isolation, school and workplace interventions, avoiding overcrowding, good ventilation of rooms). School and workplace measures and closures and avoiding overcrowding are conditionally recommended depending on the severity of the pandemic. The benefits of the interventions need to be considered against the adverse effects on the community.
 - Travel-related measures. Internal travel restrictions are conditionally recommended during an early stage of a localized and extraordinarily severe pandemic for a limited time.
- PHSM will help to reduce the number of people who are exposed and then infected and reduce the impact on health care systems.
- IPC measures in health care facilities.



9

Empower communities to communicate risk, develop and implement control measures to reduce the impact of pandemic influenza

- Communities should be empowered, enabled and engaged to participate in pandemic influenza risk communication and control measures.
- An infodemic is an overabundance of information, accurate or not, in the digital and physical space, accompanying an acute health event such as an outbreak or epidemic. Infodemics make it difficult for people to make decisions for their health. Questions and concerns that go unaddressed, unfilled information voids, and mis- and disinformation narratives can harm public health, loosen social cohesion, and erode trust in health authorities, emergency responders and emergency response itself.

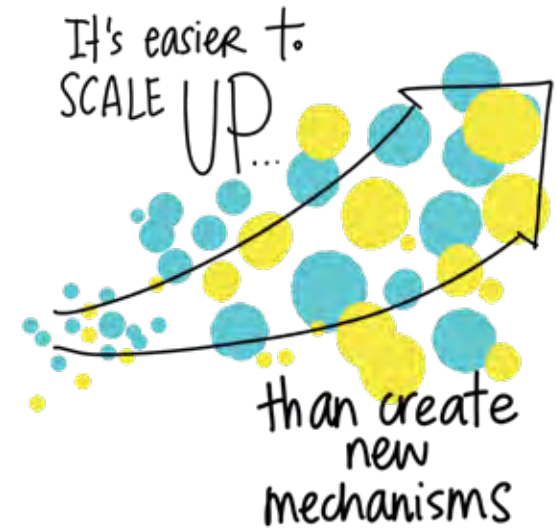


- Infodemic management is the systematic use of risk- and evidence-based analysis and approaches to promote a healthier information environment and resilience against infodemic impacts on health behaviours during health emergencies.
- Engage communities (particularly those made most vulnerable and at risk from influenza) early and often to develop infodemic management plans, partnerships, and secure access to relevant data sources.
- Infodemic management plans should include an infodemic insights function, and a monitoring and evaluation component to ensure they can adapt to changing information and the evolving situation.
- Information should be developed with and tailored to communities, settings, and different groups depending on their needs and should address questions and concerns and narratives of highest risk to public health.
- See more information in *Focus 2 Managing an Infodemic* (page 51).

10

Pandemic response capacity capacities can be built, tested and strengthened through seasonal influenza programmes

- The response to an influenza pandemic will require implementation of the same control measures used during seasonal influenza, but on a larger scale: surveillance, IPC, hand hygiene, health education, vaccination, early treatment, social distancing, risk communication and community engagement.
- The development and strengthening of national capacities in these areas before a pandemic occurs are essential to enhance local, national and global preparedness and mitigate the impact of the next pandemic.



Highlight: the PIP Framework

- The Pandemic Influenza Preparedness Framework or PIP Framework is an innovative public health instrument that seeks to better prepare the world to respond to pandemic influenza.
- It brings together Member States, industry, other stakeholders and WHO to implement a global approach to pandemic influenza preparedness and response.
- The objective of the PIP Framework is to improve pandemic influenza preparedness and response and strengthen protection against pandemic influenza by improving and strengthening the WHO Global Influenza Surveillance and Response System (GISRS), with the objective of a fair, transparent, equitable, efficient and effective system for, on an equal footing:
 - The sharing of H5N1 and other influenza viruses with human pandemic potential; and
 - Access to vaccines and sharing of other benefits, including diagnostics, antivirals and other medical supplies.
- The Framework, developed by Member States, came into effect on 24 May 2011, unanimously adopted by the World Health Assembly.



More information about pandemic influenza:

- Influenza (seasonal) WHO webpage
<https://www.who.int/health-topics/influenza-seasonal>
- Influenza (avian and other zoonotic) WHO webpage
<https://www.who.int/health-topics/influenza-avian-and-other-zoonotic>
- Global Influenza Strategy
<https://apps.who.int/iris/handle/10665/311184>
- OpenWHO course on Pandemic influenza
<https://openwho.org/courses/pandemic-influenza-introduction>
- WHO Global Epidemiological Surveillance Standards for Influenza
<https://www.who.int/publications/i/item/9789241506601>
- WHO surveillance case definitions for influenza-like illness (ILI) and severe acute respiratory infections (SARI)
<https://www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/case-definitions-for-ili-and-sari>
- WHO guidance for surveillance during an influenza pandemic, 2017 update
<https://apps.who.int/iris/handle/10665/259886>
- Pandemic influenza risk management: a WHO guide to inform and harmonize national and international pandemic preparedness and response, 2017
<https://apps.who.int/iris/handle/10665/259893>
- WHO Checklist for Pandemic Influenza Risk and Impact Management
<https://www.who.int/publications/i/item/9789241513623>
- WHO Pandemic Influenza Severity Assessment (PISA)
<https://www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/pandemic-influenza-severity-assessment>
- Pandemic Influenza Preparedness Framework
<https://www.who.int/initiatives/pandemic-influenza-preparedness-framework>



Middle East Respiratory Syndrome (MERS)

10 THINGS YOU SHOULD KNOW



1. MERS is a respiratory disease caused by a coronavirus
2. Humans can be infected through unprotected contact with infected dromedary camels and potentially from camel products, as well as from close contact with an infected person
3. MERS coronavirus (MERS-CoV) infection can be asymptomatic or cause a range of disease from mild symptoms to severe pneumonia and death
4. People with weakened immune systems and chronic underlying medical conditions are at higher risk of severe disease and death
5. Early identification and supportive clinical management reduce mortality
6. IPC measures are critical to prevent human-to-human transmission, particularly in health care settings
7. Laboratory diagnostics are available for MERS-CoV infection
8. Early case identification and isolation, comprehensive contact tracing, supported quarantine of contacts and thorough outbreak investigations can prevent human-to-human transmission of MERS-CoV
9. Research is ongoing for MERS-specific treatments for humans and vaccines for both camels and humans
10. MERS-CoV infection is a notifiable disease under the IHR (2005)

MERS response tips

Collaborative surveillance

- Implement active case finding and contact tracing, including testing of all contacts, regardless of the development of symptoms. Cases should be isolated, and contacts should be in supported quarantine. This means individuals in quarantine receiving adequate food, water, protection, hygiene, and communication provisions, including access to education for children and paid leave or remote work options from jobs. During quarantine period, adequate ventilation and IPC measures are implemented and maintained and the requirements for monitoring the health of quarantined persons can be met.
- Report cases to WHO, under the IHR (2005).
- Refer to WHO's global risk assessments for MERS-CoV.
- Refer to WHO's standard case reporting forms to facilitate data analysis and guide actions.

Community protection

- Encourage health authorities to:
 - Identify and target populations at-risk for MERS-CoV infection with tailored information on how to protect themselves from infection and prevent transmission from dromedary camels to humans, as well as between humans.
 - Develop and activate a multisectoral risk communication plan.
- Key messages are:
 - People at high risk of infection due to increased exposure, as well as those at high risk of developing severe disease should follow several precautions to prevent against infection from dromedary camels:
 - Practice good personal hygiene.
 - Avoid unprotected contact with dromedary camels.
 - Do not drink raw camel milk or camel urine.
 - Do not eat camel meat that has not been thoroughly cooked.
 - Seek health care early if MERS-CoV is suspected and follow medical advice.

Clinical care

- Provide early supportive case management for those who are infected.
- Enhance IPC in health care facilities and adhere to standard IPC measures at all times to prevent infections in health workers.
- Enhance IPC among infected people who are cared for at home, to reduce human-to-human transmission of MERS-CoV.

Access to countermeasures

- There are no specific countermeasures against MERS-CoV and research is ongoing.
- Risk communication, personal hygiene and IPC are important actions to prevent the spread of MERS-CoV.

Emergency coordination

- Ensure coordination between the animal and human health sectors for effective surveillance, risk assessment, outbreak investigation, as well as research, development and implementation of control measures.

1

MERS (Middle East respiratory syndrome) is a respiratory disease caused by a coronavirus

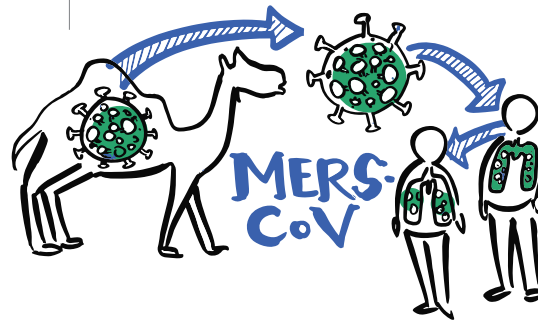
- MERS is a viral respiratory illness caused by a coronavirus (Middle East respiratory syndrome coronavirus, or MERS-CoV) that was first identified in humans in Saudi Arabia in 2012.
- Coronaviruses are a large family of viruses that can cause diseases in humans, ranging from the common cold to severe acute respiratory syndrome (SARS) and coronavirus disease 2019 (COVID-19).
- Dromedary camels (one-humped camels) are an animal reservoir for MERS-CoV.
- Since 2012, MERS has been reported in 27 countries. Approximately 80% of human cases have been reported by the Kingdom of Saudi Arabia. Cases identified outside the Middle East are people who were infected in the Middle East and then travelled elsewhere. Outbreaks have occurred in areas outside the Middle East and tend to be limited in size, however, some have resulted in a large number of infections (for example the 2015 outbreak in Republic of Korea.)



2

Humans can be infected through unprotected contact with infected dromedary camels and potentially camel products, as well as from close contact with an infected person

- MERS-CoV is a zoonotic virus: it is transmitted between animals and people.
- Dromedary camels are the main source of infection in humans. Humans are infected through direct or indirect contact with infected dromedary camels or with close contact with an infected person.
- Groups at risk for infection because they are in contact with dromedary camels include camel farm workers, slaughterhouse workers, market workers, veterinarians,



and anyone handling dromedary camels or dromedary camels' products (for example when cooking). Health workers without adequate PPE or strict adherence to standard IPC measures who provide care for people infected with MERS-CoV are also at high risk of infection.

- Those at higher risk for infection due to increased exposure to the virus should practice good personal hygiene, including

frequent hand hygiene. Hands should be washed with soap and water and/or alcohol gel after every contact with a dromedary camel. Camel workers should wear facial protection where feasible and protective clothing. Protective clothing should be removed after work (followed by hand hygiene) and washed daily.

- Consumption of raw or undercooked animal products, including milk, urine and meat carries a potential risk. Animal products that are processed through cooking or pasteurization are safe for consumption. Properly cooked products should be handled with care to avoid cross contamination with uncooked foods.
- As a general precaution, anyone visiting farms, markets, barns or other places where dromedary camels and other animals are present should practice general hygiene measures, including regular handwashing before and after touching animals, and should avoid contact with sick animals. People should avoid unprotected direct contact with any animal that has been confirmed positive for MERS-CoV infection.
- There has not been sustained human-to-human transmission; that is, the virus does not pass easily from person to person unless there is close and unprotected contact. There have been outbreaks that have occurred, and human-to-human transmission has been relatively limited among family or household members and between patients and health workers. Human-to-human transmission can be amplified in health care settings, especially when IPC measures are inadequate. This can cause large scale outbreaks, which has repeatedly occurred.

3

MERS-CoV infection can be asymptomatic or cause a range of disease from mild symptoms to severe pneumonia and death

- The clinical spectrum of MERS-CoV infection ranges from no symptoms (asymptomatic) or mild respiratory symptoms to severe acute respiratory disease and death.
- MERS symptoms are non-specific and can mimic other respiratory infections. They can include headache, tiredness,

feverishness, mild cough, sore throat and runny nose. Some patients may present with gastrointestinal symptoms such as diarrhoea, nausea and vomiting. Pneumonia is a common occurrence but is not always present.

- Severe illness can cause respiratory failure that requires mechanical ventilation and support in an intensive-care unit.
- The average incubation period is estimated to be approximately five days but may range from 2–14 days.
- It is not always easy to detect cases early because symptoms are nonspecific, and this may lead to human-to-human transmission in health care settings.

MERS-CoV infection symptoms



4

People with weakened immune systems and chronic underlying medical conditions are at higher risk of severe disease and death

- The virus causes more severe disease in older people, people with weakened immune systems and those with chronic underlying medical conditions such as renal disease, cancer, chronic lung disease, blood disease and diabetes. These people are also at increased risk of infection.
- People at high risk of developing severe disease (people with underlying medical conditions) should avoid contact with dromedary camels.

5

Early identification and supportive clinical management reduce mortality

- Supportive therapies prevent complications and increase chances of survival of those with MERS. Therapies include oxygen support, antimicrobials and specific treatment for underlying medical conditions such as diabetes and kidney failure.
- Treatment is based on a person's clinical condition.
- Currently there is no specific treatment or vaccine for MERS, but several MERS-specific therapeutics are under investigation. Human and camel MERS vaccines are in development.



6

IPC measures are critical to prevent human-to-human transmission, particularly in health care settings

- Standard precautions should be routinely applied by health workers to all patients at all times. They include hand hygiene, respiratory hygiene, use of PPE, safe waste management, cleaning and disinfection of equipment and cleaning of the environment.
- Droplet precautions should be added to standard precautions when providing care to any patient with symptoms of acute respiratory infection (ARI). These include use of a mask and eye protection when working within 1–2 metres of the patient and patient isolation. Patient isolation is organization of the space and processes to allow separation of at least 1–2 metres between a patient with ARI and other individuals not wearing PPE.
- Triage policies should be implemented to rapidly detect potential MERS patients and all individuals with acute respiratory symptoms. Health workers should apply droplet and contact precautions when MERS-CoV infection is suspected.

- Triage areas, waiting areas and patient rooms should be adequately ventilated.
- Health workers involved in aerosol-generating procedures, or those working in areas where aerosol generating procedures are conducted, are at greater risk of infection.
 - When performing aerosol-generating procedures for a patient with ARI, or when working in an area in which aerosol-generating procedures are conducted, airborne precautions should be used by health workers. These include appropriate PPE and ventilation, as well as exclusion of unnecessary persons from the room.
 - Health workers should be educated and trained in IPC and should be given opportunities to refresh these skills regularly.
 - Hospital cleaning staff should be informed of and trained to take proper precautions when cleaning rooms of MERS patients.

IPC when caring for patients with known or suspected MERS-CoV infection

All patients	Standard precautions; triage procedures
Patients with ARI	Droplet and contact precautions
When performing or working in an area where aerosol-generating procedures for patients with ARI are performed	Airborne precautions

7

Laboratory diagnostics are available for MERS-CoV infection

- Laboratory confirmation of MERS-CoV infection requires proper sample collection, high levels of biosafety and good laboratory capacities.
- A case of MERS-CoV infection can be laboratory confirmed by detection of viral nucleic acid.
- The presence of viral nucleic acid can be confirmed by either:
 - A positive real-time RT-PCR result on at least two specific genomic targets (a patient with a positive RT-PCR result for a single specific target without further testing but with a history of potential exposure and consistent clinical signs is considered a probable case); or
 - A single positive target with sequencing.
- If initial testing is negative in a patient who is strongly suspected to have MERS-CoV infection, resampling should be conducted using lower respiratory specimens from the patient. To confirm clearance of the virus, respiratory samples should continue to be collected until there are two consecutive negative results at least 24 hours apart in clinically recovered persons.

- It is strongly recommended to collect lower respiratory specimens such as sputum, endotracheal aspirate or broncho-alveolar lavage for MERS-CoV. If not possible, upper respiratory tract specimens such as nasopharyngeal aspirate or combined nasopharyngeal and oropharyngeal swab should be collected.
- Molecular testing for MERS-CoV should be conducted under BSL-2 conditions; virus culture requires BSL-3 conditions.

- Paired serum samples can also be used for serological testing in the absence of molecular testing. The initial samples should be collected in the first week of illness and the second ideally collected 3–4 weeks later.



8

Early case identification and isolation, comprehensive contact tracing, supported quarantine of contacts and thorough, multi-disciplinary outbreak investigations can prevent human-to-human transmission of MERS-CoV

- Each human case of MERS-CoV infection requires thorough investigation to understand how they were infected (the source of infection) and the potential for human-to-human transmission to their contacts.
- Thorough case investigation includes investigation of potential human, animal and/or environmental sources of exposure(s) and risk factors for infection.
- Patients (confirmed or suspected cases) and family members should be interviewed to collect essential basic information, exposure information and travel history, and clinical information.
- WHO has generated case report forms identifying the minimum amount of information that should be collected for each case of MERS-CoV infection.



- Once a case has been confirmed, to prevent further transmission of the virus, active case finding should be implemented in the community and in health care settings.
- All cases should be isolated in a health care facility.
- All close contacts should be identified, monitored for the presence of symptoms for 14 days and supported in quarantine to prevent potential onward transmission of the virus if infected. A contact is any person who has cared for or lived with a person confirmed to have MERS (confirmed case), or had unprotected contact with that person's respiratory secretions, body fluids and/or excretions when that person was symptomatic.
- Contacts should be placed under active surveillance for 14 days after last exposure to the confirmed or probable case, with monitoring for respiratory symptoms (a health worker should visit or call them on a daily basis) and, ideally, contacts should be tested for MERS-CoV infection by molecular testing (RT-PCR).

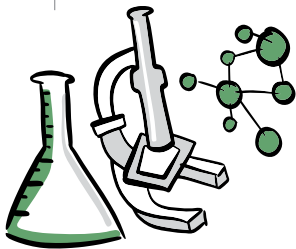
- As a minimum precaution, any contacts who develop symptoms should be quarantined in a health care facility and tested for MERS-CoV infection to prevent potential onward spread.
- Health care workers with direct contact with a MERS patient should be closely monitored and tested for MERS-CoV infection. Health care workers tend to be younger and healthier than MERS patients and can have infection without developing disease (asymptomatic).
- Trained individuals should provide health education and training, including basic information about MERS, how to prevent MERS-CoV infection for different groups (contacts of confirmed patients, health workers caring for MERS patients, occupational groups who work with dromedary camels, and populations at higher risk of severe disease) and what people should do if they suspect they have MERS-CoV infection.



9

Research is ongoing for MERS-specific treatments for humans and vaccines for both camels and humans

- WHO has developed a MERS-CoV research agenda to address key unknowns for this virus focusing on five major areas of research: virus origin and characteristics, epidemiology and transmission, clinical management and IPC measures, product development and implementation, and impact of interventions and operational research.
- WHO's R&D Blueprint is working to accelerate the development of medical interventions for MERS.
- Currently, there are no licensed treatments for MERS.
- Currently, a dozen vaccine candidates for both humans and dromedary camels are in preclinical or clinical development.



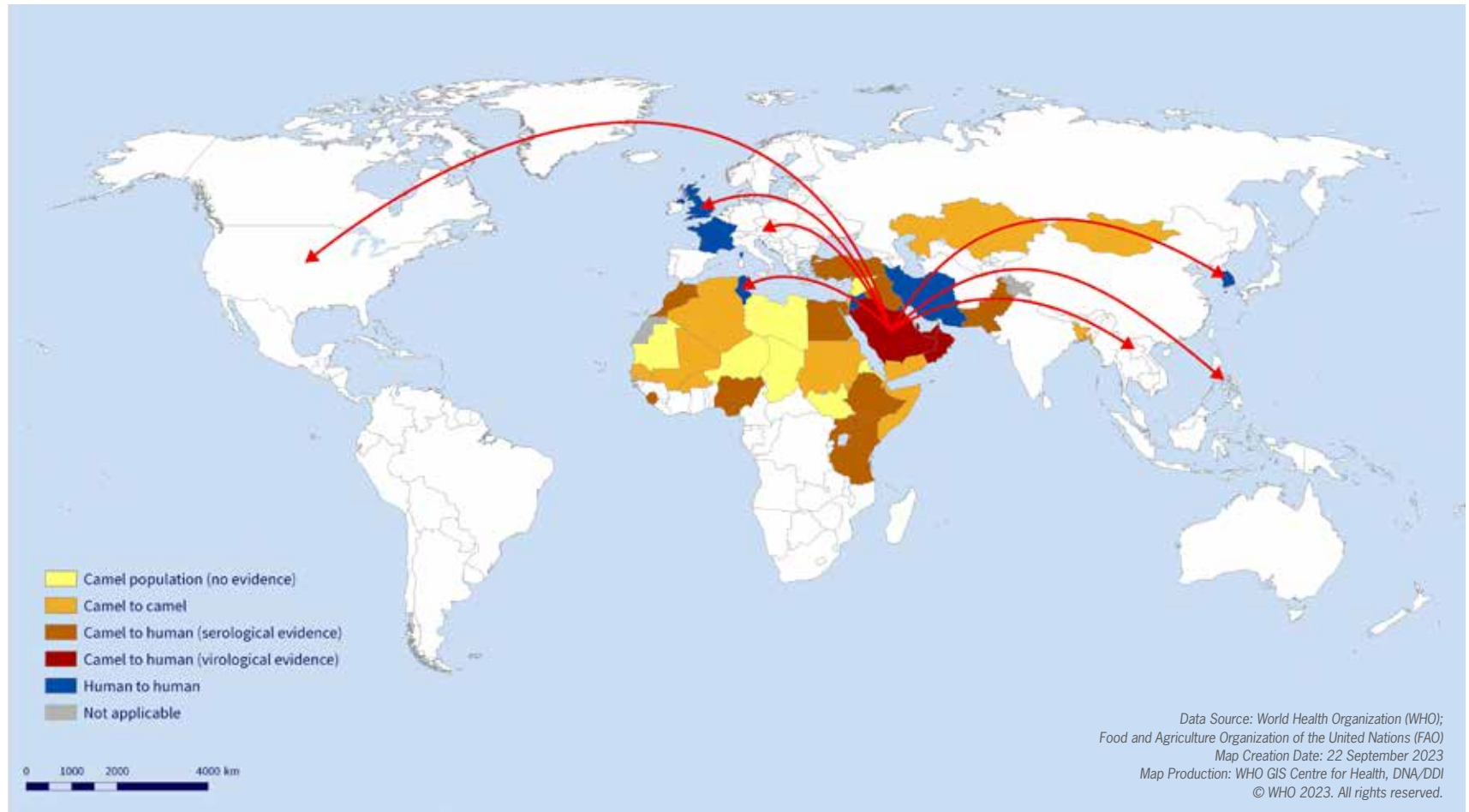
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MERS-CoV infection is a notifiable disease under the IHR (2005)

- Probable and confirmed MERS cases must be reported within 24 hours of classification with information about exposure, testing and clinical course. Refer to MERS case definitions for reporting to WHO.



Zoonotic and human-to-human transmission of MERS-CoV

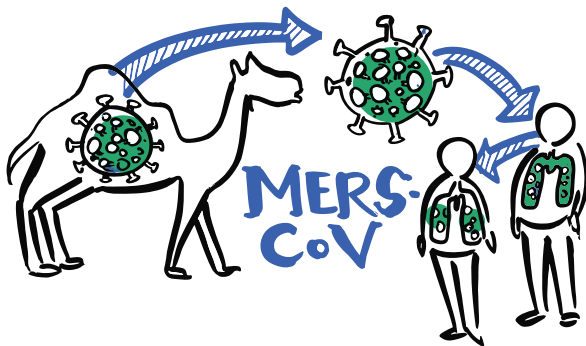


The red arrows highlight exportation of human cases with exposure in the Middle East, but detection in other countries. Within this map, they illustrate the global nature of MERS-CoV risk, beyond areas where there are dromedary camels with history of MERS-CoV infection.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

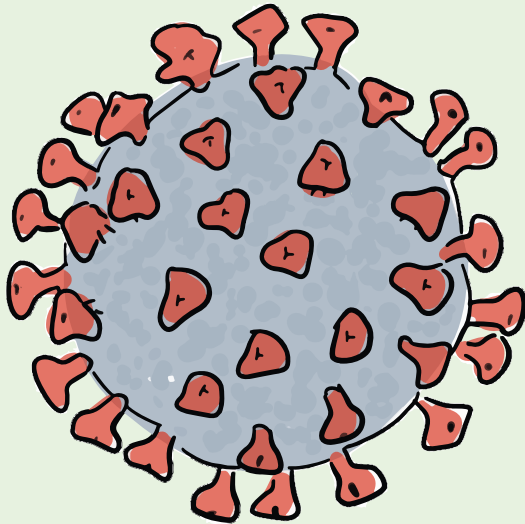
More information about MERS:

- MERS-CoV WHO website
https://www.who.int/health-topics/middle-east-respiratory-syndrome-coronavirus-mers#tab=tab_1
- OpenWHO courses on MERS
<https://openwho.org/courses?q=mers>
- MERS outbreak toolbox
<https://www.who.int/emergencies/outbreak-toolkit/disease-outbreak-toolboxes/mers-outbreak-toolbox>
- Information about MERS-CoV research and development
<http://www.who.int/blueprint/priority-diseases/key-action/mers-cov/en/>



COVID-19

10 THINGS YOU SHOULD KNOW



1. Coronavirus disease 2019 (COVID-19) is an acute respiratory infectious disease caused by a coronavirus that led to a pandemic in 2020
2. The disease is characterized mostly by respiratory symptoms but affects many organs of the human body
3. COVID-19 spreads easily in crowded places, close-contact settings and confined spaces (3Cs)
4. There are several therapies that have been approved and recommended in the treatment of COVID-19
5. Several COVID-19 vaccines are currently available and are effective in reducing the risk of severe disease and death from COVID-19
6. PHSM are crucial to preventing and limiting COVID-19 transmission within communities
7. IPC measures are critical to maintain safe health care services
8. Empowered, enabled and engaged communities are essential to develop and implement control measures
9. The severe acute respiratory syndrome virus 2 (or SARS-CoV-2 virus) has been evolving and this has an impact on diagnostic and control measures
10. The global scientific and research community has come together to rapidly accelerate research related to COVID-19, however, there are still unknowns and more research on COVID-19 is needed

COVID-19 response tips

Collaborative surveillance

- Reduce mortality and morbidity from COVID-19 by ensuring early diagnosis and appropriate treatment for cases.
- Monitor the spread of the virus through the monitoring of influenza-like illness (ILI) and in at risk populations using appropriate testing and sequencing strategies.
- Monitor the severity of diseases through severe acute respiratory infection (SARI) surveillance.
- Implement surveillance at the human-animal interface when needed to detect spill over early on and better understand possibility of spillback of SARS-CoV-2 into animals.
- Maintain an alert system in place to detect new SARS-CoV-2 variants and ensure that capacity to rapidly analyse and adjust control measures (for example contact tracing, quarantine of contacts).
- Implement mechanisms to monitor impact on the health system to guide surge efforts.
- Ensure genomic sequencing is conducted on representative samples to monitor the evolution of the virus and detect the emergence of variants of concern (VOC). Upload results to open access platforms for more robust global analyses.
- Share experiences and report cases hospitalizations and deaths/epidemiological situation to WHO, under the IHR (2005), as per WHO guidance.

Community protection

- Listen to communities to address their concerns in a timely manner and to counter misinformation.
- Engage pro-actively with communities that are at risk for severe disease (for example older adults living in nursing homes, people with underlying conditions) to co-develop and implement appropriate control and mitigation measures.
- Reduce or slow down transmission by implementing PHSM that are contextual, time-bound, adjusted to the level of transmission and population immunity (natural or vaccination-derived).
- Encourage health authorities to develop and implement an infodemic management plan.
- Key messages are:
 - Responding to COVID-19 involves a multisectoral all government approach using a comprehensive set of evidence-based measures to be implemented and adjusted to local levels. It is important to follow several precautions to prevent transmission:
 - Avoid crowded indoor settings in times of high transmission.
 - Maintain physical distance (of at least 1 metre, preferably more) from others.

- Ensure adequate ventilation indoors by opening windows, where possible.
- Wear a well fitted mask, where appropriate.
- Regularly and thoroughly clean your hands with either an alcohol-based hand rub or soap and water.
- Cough and sneeze into a bent elbow or tissue, throw used tissues into a closed bin right away.
- Stay home when sick.
- Get vaccinated when it is your turn, follow local guidance and recommendations about vaccination and boosters.
- Follow all PHSM that are in place in your community.

Clinical care

- A number of treatments for COVID-19 exist and a number are under study. Currently, treatment of COVID-19 includes antivirals, monoclonal antibodies and dexamethasone for severe forms of the disease.
- Enhance IPC measures to reduce SARS-CoV-2 transmission in health facilities, care homes and for infected people who are cared for at home and their caretakers.
- During times of surge, minimize disruption to the broader health system by reorganizing health care resources, deploying emergency assets and protecting the health workforce, while ensuring ongoing access to acute and essential health services.

Access to countermeasures

- Vaccinate people, with priority to groups at high-risk of severe disease or exposure and ensure equitable access to COVID-19 vaccines.
- Encourage research on additional medical control measures (for example new vaccines preventing infection, new antivirals, better PPE).

Emergency coordination

- Ensure multisectoral coordination across the health sector, and other relevant sectors, for effective surveillance, public health actions (including, strategic testing, comprehensive contact tracing, supported quarantine, early clinical care provided by trained and protected health workers), maintaining health system capacities and implementing PHSM.
- Whole-of-society approaches include actively involving civil-society actors, community members, multidisciplinary experts, individuals, as well as government stakeholders in developing and implementing response measures.

1

Coronavirus disease 2019 (COVID-19) is an acute respiratory infectious disease caused by a coronavirus that led to a pandemic in 2020

- Coronaviruses are a large family of viruses that can cause diseases in humans, ranging from the common cold to SARS and MERS. Coronaviruses widely circulate in the animal kingdom.
- COVID-19 is a disease caused by a coronavirus called severe acute respiratory syndrome coronavirus 2 or SARS-CoV-2, which was first reported in December 2019 in Wuhan, China.
- On 30 January 2020, the WHO Director-General declared that COVID-19 constituted a PHEIC. This event was characterized as a pandemic in March 2020.
- As of January 2023, the pandemic is still causing large-scale disruptions with high levels of transmission, severe disease and death. Recent estimates suggest 14.83 million excess deaths globally due to COVID-19.¹ Variants of the virus with increased transmissibility and/or properties of immune escape have emerged, posing a challenge to control efforts. As of January 2023, WHO has designated five variants as variants of concern (VOC): Alpha, Beta, Gamma, Delta and Omicron. For more information about VOC, please see section 2.

¹ Msemburi, W., Karlinsky, A., Knutson, V. et al. The WHO estimates of excess mortality associated with the COVID-19 pandemic. *Nature* (2022). <https://doi.org/10.1038/s41586-022-05522-2>

- In addition to significant health impacts, the COVID-19 pandemic has had significant and variable socio-economic effects across the world that directly impact communities. At the time of publication, it is estimated that the pandemic has resulted in over \$13 trillion dollars in economic losses.
- WHO is continuing its investigations into the origin of the SARS-CoV-2 virus. In 2021, the Scientific Advisory Group for the Origins of Novel Pathogens (SAGO) was created to outline the types of studies and investigations that needed to understand the source of the virus' spread into the human population. At this time, WHO and SAGO are unable to make any definite conclusions about the origins of COVID-19 – neither the origin or the

reservoirs are confirmed. Key information needed to confirm the origins pathway is not yet available from recommended studies. WHO reiterates the critical importance of conducting and sharing findings of key studies on the origins of SARS-CoV-2.



2

The severe acute respiratory syndrome virus 2 (or SARS-CoV-2 virus) continues to evolve and this has an impact on diagnostic and control measures

- The SARS-CoV-2 virus has been evolving since its emergence and variants have been identified as Variants of Interest (VOIs) and VOCs.²

- VOIs are defined as a SARS-CoV-2 variant:

- with genetic changes that are predicted or known to affect virus characteristics such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape; AND
- identified to cause significant community transmission or multiple COVID-19 clusters, in multiple countries with increasing relative prevalence alongside increasing number of cases over time, or other apparent epidemiological impacts to suggest an emerging risk to global public health.

- VOCs are defined as a SARS-CoV-2 variant that meets the definition of a VOI (see above) and, through a comparative assessment, has been demonstrated to be associated with one or more of the following changes at a degree of global public health significance:

- Increase in transmissibility or detrimental change in COVID-19 epidemiology; OR

- Increase in virulence or change in clinical disease presentation; OR

- Decrease in effectiveness of PHSM or available diagnostics, vaccines, therapeutics.

- At the time of publication, WHO has identified five VOCs named after the Greek alphabet letters to facilitate communication, avoid stigmatization of certain geographies and harmonize various scientific classifications.

- The variants, called Alpha, Beta, Gamma, Delta and Omicron, have been circulating in different parts of the world a different time producing epidemic waves. Since the discovery of Omicron in November 2021, hundreds of sub-lineages have been detected (BA.1, 2,3,4,5; XBB; BF7; BQ1; and so on).

- The Technical Advisory Group on SARS-CoV-2 Virus Evolution (TAG-VE) is an expert group that periodically monitors and evaluates the evolution of SARS-CoV-2 and assess if specific mutations and combinations of mutations alter the behaviour of the virus. The group assesses the variants of SARS-CoV-2 and defines if they are VOCs or VOIs.

- Anyone with symptoms should be tested for SARS-CoV-2, wherever possible, to receive appropriate care and also to detect new variants.

- Testing strategies and associated measures (treatment, isolation of cases, quarantine of contacts, contact tracing) will depend on context.

- There are three different types of tests: nucleic acid testing, antigen testing and antibody testing. (See page 201.)

- Enhancing laboratory capacities worldwide, including capacities for genomic sequencing, beginning at the local level with close links to national and global levels surveillance and data sharing platforms, is critical to monitor and understand changes in SARS-CoV-2 and thereby support better decision making during an evolving situation.



² Tracking SARS-CoV-2 variants: <https://www.who.int/activities/tracking-SARS-CoV-2-variants/>

3

The disease is characterized mostly by respiratory symptoms, however can affect several organs in the human body

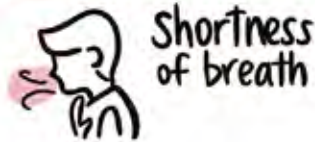
- Most people with COVID-19 experience mild or moderate illness. From the initial clinical assessment in 2020 with the ancestral strain: 80% of cases are mild, 20% are severe and requiring hospitalization, 5% are critical requiring care in an ICU. With Omicron it seems that the proportion of severe illness is reduced yet there are still significant geographic variations depending on immunity in the population from prior infection and/or vaccination and the quality of the health care system.
- Regardless of VOC, the risk of severe disease increases with age, in those with underlying medical conditions such as diabetes, cardiovascular disease, immunosuppression, cancer and obesity.
- Common symptoms of COVID-19 are fever, cough, fatigue, sputum production, shortness of breath, muscle and/or joint pain, sore throat and headache. Some cases of COVID-19 also report loss of smell and/or loss of taste.
- Severe disease is characterized by pneumonia or sepsis.
- Cardiovascular complications such as myocardial injury, thromboembolic events, arrhythmia and heart failure have been observed. They are either due to direct viral invasion, inflammation or the decompensation of pre-existing conditions.
- The incubation period ranges between 1–14 days but most people show symptoms 2–6 days after being in contact with someone infected.
- Typically, most people recover from COVID-19 after 2–6 weeks. However, some people can have symptoms that last for weeks or even months after recovery from acute illness.
- Long-term effects may impact pulmonary, cardiovascular and nervous systems, as well as psychological effects. These effects appear to occur irrespective of the initial severity of infection, but occur more frequently in women, middle aged people and in those with more symptoms initially.
- This persistent state of ill health is known as post COVID-19 condition or long COVID. The current WHO case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021.³



³ A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021 <https://apps.who.int/iris/handle/10665/345824>

COMMON COVID-19 SYMPTOMS

SERIOUS SYMPTOMS: IMMEDIATE MEDICAL CARE NEEDED



MOST COMMON:



LESS COMMON SYMPTOMS:



4

COVID-19 spreads easily between people in crowded places, close-contact settings and confined spaces (3Cs)

- SARS-CoV-2 spreads mainly between people who are in close contact with each other, for example at a conversational distance. The virus can spread from an infected person's mouth or nose in small liquid particles when they cough, sneeze, speak, sing or breathe. Another person can then contract the virus when infectious particles that pass through the air are inhaled at short range (this is often called short-range aerosol or short-range airborne transmission) or if infectious particles come into direct contact with the eyes, nose or mouth (droplet transmission).
- The virus can also spread in poorly ventilated and/or crowded indoor settings, where people tend to spend longer periods of time. This is because aerosols can remain suspended in the air or travel farther than conversational distance (this is often called long-range aerosol or long-range airborne transmission).
- Infected people can transmit the virus to others, whether they have symptoms or not, although patients who exhibit symptoms are estimated to be 3–18 times more likely to infect others than those who are asymptomatic. Infected people appear to be most infectious approximately two days before they develop symptoms and early in their illness.

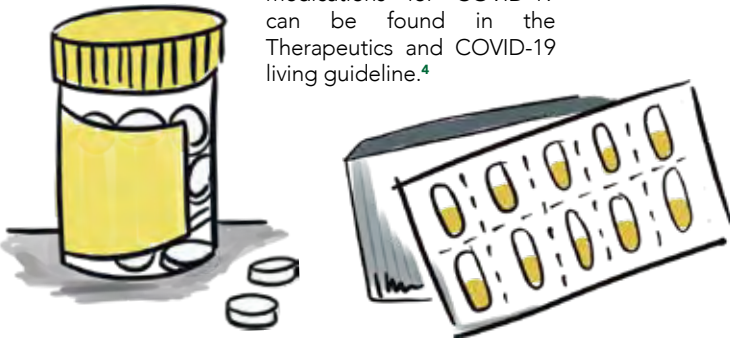
- A person can be infected when aerosols or droplets containing the virus are inhaled or come directly into contact with the mucosal membranes of the eyes, nose or mouth.
- The virus spreads mainly between people who are in close contact with each other, typically within 1 metre (short-range). The virus can also spread beyond 1 metre, or typical conversational distances, in poorly ventilated and/or crowded indoor settings, where people may spend longer periods of time together.
- Settings where transmission of the COVID-19 virus spreads more easily are called the 3Cs:
 - Crowded places
 - Close-contact settings (especially where people have conversations very near each other)
 - Confined and enclosed spaces with poor ventilation
- The risk of COVID-19 spreading is especially high in places where these 3Cs overlap.



5

There are several therapies that have been approved and recommended in the treatment of COVID-19

- Different treatments exist for patients with mild, severe and critical disease. Care (supportive and specific) is the main factor to reduce mortality.
- Early treatment of people at risk of severe disease is essential to prevent severe outcomes.
- Research is ongoing to develop new therapies, but already significant progress has been made with the development of antivirals, immunotherapies (casirivimab and imdevimab, Sotrovimab) and corticosteroids (dexamethasone, hydrocortisone or prednisolone) with IL-6 receptor blockers (tocilizumab or sarilumab) or JAK-inhibitors (Baricitinib).
- The latest WHO recommendations on medications for COVID-19 can be found in the Therapeutics and COVID-19 living guideline.⁴



⁴ Therapeutics and COVID-19 living guideline <https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2022.1>

6

Several COVID-19 vaccines are currently available and are effective in reducing the risk of severe disease and death from COVID-19

- Many safe and effective COVID-19 vaccines have been developed through an accelerated process, but all safety requirements were, and still are, the same as for any other vaccine.
- Several COVID-19 vaccines have received WHO Emergency Use Listing and the first mass nationwide vaccination programmes started in December 2020.
- COVID-19 vaccines are very effective at protecting those vaccinated from serious illness and death but are less effective in preventing infection and transmission. This is why even vaccinated people can get infected with SARS-CoV-2 virus but when vaccinated they are less likely to develop severe disease.
- When vaccines are scarce, vaccination programmes should prioritize health workers and groups with high occupation-related exposure, as well as populations at risk of severe disease (older individuals and those with underlying medical conditions). Vaccination programmes should work with communities to ensure equitable vaccine distribution based on needs, including providing tailored information designed in partnership with communities.
- Global solidarity to ensure equitable access to a vaccine, based on public health needs,

is the only way to mitigate the public health, social and economic impact of the pandemic, prioritizing those at higher risk of developing severe disease or at higher exposure risk in every country.

- COVAX is a worldwide initiative co-led by Gavi The Vaccine Alliance, CEPI and WHO. COVAX aims to accelerate the development and manufacture of COVID-19 vaccines, and to guarantee fair and equitable access for every country in the world.
- The evolution of the virus is reducing the effectiveness of current vaccines. Therefore, WHO established the Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) to provide recommendations on vaccine composition and ensure that the best vaccine is available. TAG-CO-VAC is an independent group of experts that periodically reviews the evidence and analyses the implications of emerging VOCs on the performance of COVID-19 vaccines.



7

PHSM are crucial to preventing and limiting COVID-19 transmission within communities

- PHSM should be introduced, adapted or lifted based primarily on an ongoing situational assessment of the intensity of transmission at sub-national levels and the capacity of the health system to respond, while also considering the effects that PHSM may have on the general welfare of society, individuals and families.

- PHSM include a comprehensive set of individual and population level measures, including:

- Personal protective measures including physical distancing of at least 1 metre, avoiding crowded settings, ensuring adequate ventilation when indoors, wearing of a well-fitted mask, hand hygiene and respiratory etiquette.
- Containment measures (in absence of sustained community transmission): strategic testing of suspected cases, contact tracing, isolation of cases and quarantine of contacts.

- Physical distancing measures to reduce community transmission by regulating the number and flow of people attending gatherings, maintaining distance in public or workplaces, school closure or class suspensions, encouraging remote working options and online education.

- Environmental measures including cleaning, disinfection and adequate ventilation.

- Travel-related measures to reduce geographic spread through both domestic and international travel.

- PHSM introduction and adaptation should be a part of a multi-sectoral and "whole-of-society" approach that engages government, civil-society and community members (and especially those made most vulnerable by the introduction of such measures) to develop a response that aims to reduce vulnerability, limit community transmission while also limiting the social and economic hardship in communities while adhering to control measures.

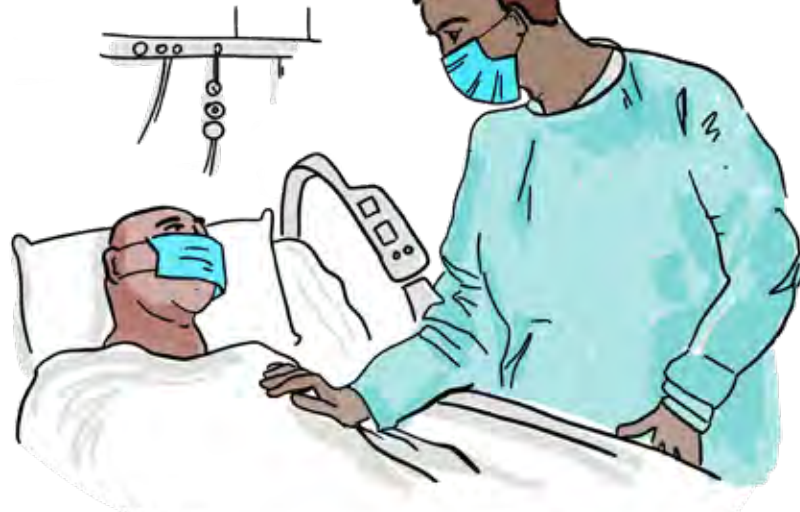


8

IPC measures are critical to maintain safe health care services

- Given the high transmissibility of the virus, especially the Omicron VOC, IPC strategies and measures are required to prevent and/or limit SARS-CoV-2 transmission in health facilities among health care personnel and to and from patients and visitors.
- Standard precautions should be routinely applied by health workers to all patients at all times. These include, but are not limited to, hand hygiene, respiratory hygiene, use of appropriate PPE as per risk assessment, environmental cleaning, safe handling of linen and laundry, safe waste management, injection safety and safe handling, cleaning and disinfection of medical equipment.
- Screening and triage areas should display information on signs and symptoms of COVID-19, have hand hygiene dispensers and masks available, be well-ventilated, require personnel and patients to maintain at least 1 metre distance (for example waiting room chairs to be distanced, implementing the use of physical barriers such as glass between health workers and patients).
- Maintain a one-way flow of patients and staff. Those screened as having symptoms should have a separate, well-ventilated waiting area until they can be moved to an isolation room and tested as soon as possible. Those who screen negative can follow the routine health services pathway.

- In areas of widespread community transmission, universal masking with a well-fitted medical mask is recommended within health care facilities in settings when caring for non-COVID-19 patients, by all health workers, other staff, visitors, outpatients and service providers. Inpatients are not required to wear a medical mask unless physical distancing of at least 1 metre cannot be maintained (for example during examinations or bedside visits) or when outside of their care area (for example when being transported), provided the patient is able to tolerate the mask and there are no contraindications.
- Appropriate isolation for suspect or confirmed COVID-19 patients includes applying contact and droplet precautions in addition to standard precautions when assessing or providing care to any suspected or confirmed COVID-19 patient.
- In light of the Omicron VOC, it is recommended that health workers wear respirators when caring for suspected or confirmed COVID-19 patients in areas where ventilation is insufficient or cannot be assessed and based on availability and preference of the health worker.
- Health workers involved in aerosol-generating procedures (for example intubation), or those working in areas where aerosol generating procedures are conducted (such as intensive care units, semi-intensive care units or emergency departments) on patients with suspected or confirmed COVID-19, are at increased infection risk and therefore require airborne precautions in addition to contact and droplet precautions.



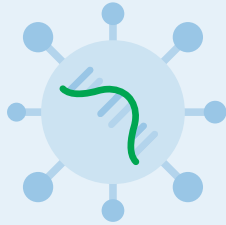
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Empowered, enabled and engaged communities are essential to develop and implement control measures

- Engaging communities is essential to ensure proper adaptation and optimal implementation of control measures to the local conditions. Community engagement can also ensure community compliance with the interventions. Co-development with the community to create local guidance, tools or interventions has proven to be more effective and more agile (for example co-development of guidance with faith-based organization to ensure safe religious gatherings). See more information in *Focus 1: Community engagement during epidemics* (page 45).
- The COVID-19 pandemic has been accompanied by a massive and far-reaching infodemic. An infodemic is an overabundance of information, accurate or not, in the digital and physical space, accompanying an acute health event such as an outbreak or epidemic.
- Infodemic management is the systematic use of risk- and evidence-based analysis and approaches to promote a healthier information environment and resilience against infodemic impacts on health behaviours during health emergencies.
- It is important to engage communities (particularly those vulnerable to severe disease) early and often to co-develop infodemic management plans, which should include a monitoring and evaluation component to ensure they can adapt to changing information and the evolving situation.
- Information should be developed with, and tailored to, communities, settings and different groups depending on their needs and should address misinformation, disinformation and stigma.
- See more information in *Focus 2: Managing an Infodemic* (page 51).



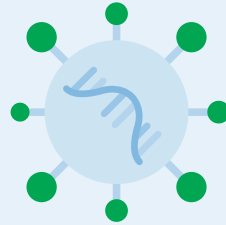
Tests for diagnosing infection:



Nucleic Acid Amplification Testing

Detects **genetic material** of the virus

- Uses **upper respiratory specimens*** to diagnose **current SARS-CoV-2 infection**.
- Nucleic acid amplification tests (NAAT), for example RT-PCR, are the **reference method** for detection of current SARS-CoV-2 infection.
- **Results: usually available within 24 hours.** Testing takes 30 minutes to 4 hours (depending on the test), but transport to the testing laboratory can add hours to days.



Antigen Testing

Detects **viral protein(s)**(e.g. nucleocapsid)

- Uses **upper respiratory specimens*** to diagnose **current SARS-CoV-2 infection**. Most often in a lateral flow format, termed antigen-detection rapid diagnostic tests (Ag-RDTs).
- Available for professional use or self-testing.
- Performance is best within first 5-7 days of symptoms.
- **Results: within 15-30 minutes**, not requiring laboratory infrastructure.

Tests to detect immunity:



Antibody Testing

Detects **antibodies** against the virus from prior infection or vaccination

- Uses **serum/plasma or whole blood specimens** to detect antibodies generated by **prior SARS-CoV-2 infection or vaccination**.
- SARS-CoV-2 antibodies are usually detectable 1-2 weeks after infection or vaccination. Antibody testing should not be used as a standalone test to identify current SARS-CoV-2 infection.
- **Results: within 24 hours**; point of care tests within 10-30 minutes.

* NAATs and Ag-RDTs are designed to work using upper respiratory tract samples or saliva
For more information: https://www.youtube.com/watch?v=PhdSdJu_QXI

10

The global scientific and research community has come together to rapidly accelerate research related to COVID-19, however, there are still many unknowns and more research on COVID-19 is needed

- The COVID-19 pandemic has demonstrated unprecedented mobilization of the research and development community through the collaborative and high-quality work of thousands of researchers and research institutions.
- The WHO R&D Blueprint for epidemics plays a convening role for global research efforts and provides a standard research protocol for randomized clinical trials to ensure comparability of results between countries.



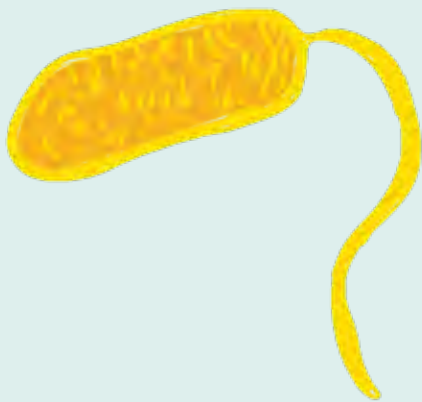
- Partnerships and mechanisms to prioritize and advance research are in place in many areas including:
 - The origin of the virus, including potential animal reservoirs.
 - The extent to which people who have no symptoms can spread the virus. While someone who does not develop symptoms can pass the virus to others, it is not clear how frequently this occurs.
 - The prevalence of different modes of transmission.
 - The development of additional medical countermeasures (vaccine treatment).
 - The prevalence, characteristics, risk factors for and treatment of post COVID-19 condition.
 - The efficacy and effectiveness of PHSM, both individual and combined measures, including questions about which PHSM to use, in which combination, for how long, and their impact across many dimensions of health, social and economic well-being.
 - Research is ongoing to determine the duration of protection of COVID-19 vaccines and the impact of variants on the effectiveness of current vaccines.
 - The development of infodemiology.
 - Behavioural science and ethics.

More information about COVID-19:

- **COVID-19 WHO Webpage**
<https://www.who.int/emergencies/diseases/novel-coronavirus-2019>
- **OpenWHO courses on COVID-19**
<https://openwho.org/channels/covid-19>
- **WHO COVID-19 Strategic Preparedness and Response Plan (SPRP 2021)**
<https://www.who.int/publications/i/item/WHO-WHE-2021.02>
- **Living guidance for clinical management of COVID-19**
<https://www.who.int/publications/i/item/WHO-2019-nCoV-Clinical-2022.2>
- **Infection prevention and control in the context of coronavirus disease (COVID-19): a living guideline**
<https://www.who.int/publications/i/item/WHO-2019-nCoV-ipc-guideline-2022.2>
- **COVID-19 Contact tracing information**
<https://www.who.int/publications/i/item/contact-tracing-in-the-context-of-covid-19>
- **EPI-WIN: WHO Information Network for Epidemics**
<https://www.who.int/teams/risk-communication>
- **COVID-19 PHSM information**
<https://www.who.int/publications/i/item/considerations-in-adjusting-public-health-and-social-measures-in-the-context-of-covid-19-interim-guidance>
- **COVID-19 Vaccine information**
<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines>
- **The Access to COVID-19 Tools (ACT) Accelerator and COVAX**
<https://www.who.int/initiatives/act-accelerator>
- **COVID-19 Information for health workers and administrators**
<https://www.who.int/teams/risk-communication/health-workers-and-administrators#infection%20prevention%20and%20control>
- **Therapeutics and COVID-19: living guideline**
<https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2022.4>
- **WHO R&D Blueprint**
<https://apps.who.int/blueprint-brochure/>
- **WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC)**
[https://www.who.int/groups/technical-advisory-group-on-covid-19-vaccine-composition-\(tag-co-vac\)](https://www.who.int/groups/technical-advisory-group-on-covid-19-vaccine-composition-(tag-co-vac))
- **WHO The Technical Advisory Group on SARS-CoV-2 Virus Evolution (TAG-VE)**
<https://www.who.int/groups/technical-advisory-group-on-sars-cov-2-virus-evolution>

Cholera

10 THINGS YOU SHOULD KNOW



1. Cholera is closely linked to inadequate access to safe water and sanitation
2. Cholera is caused by the bacterium *Vibrio cholerae* and is transmitted by faecally contaminated water and food or through inadequate hand hygiene (faecal-oral route)
3. Cholera outbreaks can spread rapidly
4. At the start of an outbreak, rapid detection of suspected cases and their laboratory confirmation are essential
5. People with cholera experience acute watery diarrhoea with no fever and they may also have profuse vomiting
6. Cholera is an easily treated disease, severe forms can kill within hours if left untreated, early rehydration is critical
7. Oral cholera vaccines (OCVs) are safe and should be used with other prevention and control strategies
8. Populations at risk should be provided with safe water and adequate sanitation
9. Mapping the origin of cases is critical to target control activities
10. WHO can provide countries with cholera kits

Cholera outbreak response tips

Collaborative surveillance

- Investigate the source of the outbreak.
- Once the epidemic strain of *Vibrio cholerae*, the cholera-causing bacterium, is confirmed, the WHO clinical case definition is sufficient to identify cases.
 - Before outbreak confirmation: Age 2 or above, with severe dehydration or dying from acute watery diarrhoea (AWD).
 - After outbreak confirmation: any person of any age presenting with AWD.
- Carry out systematic, periodic and representative sampling and testing of stool samples from suspected cases throughout the epidemic to monitor antimicrobial sensitivity and the level of on-going transmission.
- Collect epidemiological data on the origin of cases to drive a multisectoral response.
- Monitor water quality at point of distribution and point of use (free residual chlorine or faecal coliforms).

Community protection

- Provide populations with safe water and sanitation.
- Encourage health authorities to:
 - Engage communities to enhance hygiene and food safety practices, discourage open defecation.
 - Set up facilities for treatment, and let the public know how to access them.
 - Make sure oral rehydration solution (ORS) is available, even at the community level.
- Key messages are:
 - Cholera is transmitted through contaminated water or food and inadequate hand hygiene.
 - Severe cholera can rapidly lead to severe dehydration and death if left untreated, seek treatment quickly.
 - Start drinking ORS as soon as symptoms appear and seek treatment quickly.
 - Breastfeeding should be encouraged.
 - Wash hands at critical moments:
 - Before, during, and after preparing food.
 - Before and after eating food.
 - Before and after caring for someone at home who is sick with vomiting or diarrhoea.

- After using the toilet.
- After changing diapers or cleaning up a child who has used the toilet.
- Mild cases can be treated with ORS.
- Take the cholera vaccine if advised to do so if there is a cholera outbreak, or the risk of one in the future, in your area.

Clinical care

- Implement IPC practices in all health facilities
- Treat early (rehydration):
 - Oral rehydration points in the community facilitate early access to treatment.
 - Cholera treatment centres provide 24-hour care for patients with more severe forms of cholera.

Access to countermeasures

- Vaccinate with OCV in humanitarian emergencies and to prevent the spread of epidemics.
- Obtain and preposition cholera kits in advance where there is risk for outbreaks to be prepared for immediate outbreak response.

Emergency coordination

- Ensure intersectoral coordination at national and local levels, including between water, sanitation, hygiene (WASH), health and surveillance.
- Contact the ICG for emergency oral cholera vaccines and the Global Task Force on Cholera Control (GTFCC)

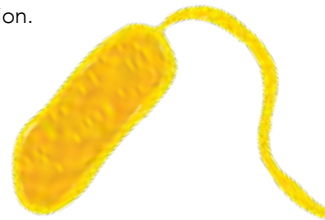
1

Cholera is closely linked to inadequate access to safe water and sanitation

- The long-term solution for cholera control is economic development that prioritizes universal access to safe drinking water and adequate sanitation. These measures prevent both epidemic and endemic cholera as well as other faeco-orally transmitted and waterborne diseases. They may require substantial long-term investments.
- Cholera is closely linked to poor environmental conditions. The absence or shortage of safe water and proper sanitation are the main contributors to the spread of the disease. Typical at-risk areas are peri-urban slums with precarious basic infrastructure, as well as camps for internally displaced people or refugees, or more rural areas where open defecation is more common and rivers used as water sources.



- Actions to reduce the transmission of cholera include:
 - Implementation of adapted long-term and sustainable WASH solutions to ensure use of safe water and basic sanitation and good hygiene practices for populations at risk of cholera:
 - Interventions at the household level include water filtration; chemical, thermal (boiling) or solar disinfection of water; safe water storage; construction of systems for safe sewage disposal, including latrines.
 - Adoption of basic hygiene practices.
 - Access to safe water and sanitation in public areas such as health facilities and schools.
 - Adapted water quality monitoring and remedial action (for example bulk chlorination or chlorination at point of use) when required.
 - Rapid access to treatment.
 - Implementation of adapted IPC in treatment structures.
 - Vaccination.



2

Cholera is caused by the bacterium *Vibrio cholerae* and is transmitted by faecally contaminated water and food or through inadequate hand hygiene (faecal-oral route)

- A person can become infected by drinking water or eating food contaminated by the bacterium *Vibrio cholerae*.
- Bacteria present in the faeces of an infected person are the main source of contamination.
- Food may be contaminated by soiled hands during food preparation, while eating or by some irrigation practices.
- During funeral ceremonies for people dying from cholera, transmission can occur through consumption of food and beverages contaminated by inadequate hygienic practices. Customary practices such as washing the body before funerals, if not properly done, can also be a source of contamination. In any case, large gatherings in an area where cholera transmission is occurring may constitute a risk for cholera spread.
- Beverages prepared with contaminated water and sold by street vendors are vehicles of cholera transmission, as are vegetables and fruits freshened with contaminated water and raw or undercooked seafood. Prepared food sold by street vendors may also transmit the disease.
- The bacterium can persist in water for a variable period of time (or is continually re-introduced by repeated faecal contamination) and may multiply in moist leftover food.



3

Cholera outbreaks can spread rapidly

- The incubation period is very short. It ranges from two hours to five days, usually 1–2 days.
- This can lead to explosive epidemics as the number of cases can rise extremely quickly.
- Early detection and treatment of cases and rapid initiation of control activities are critical.
- Asymptomatic carriers can transmit the infection. As long as stools contain *V. cholerae*, infected people can transmit the disease. Even among asymptomatic carriers, the pathogen stays in faeces for seven days (up to 14 days in some cases) and is shed back into the environment, possibly infecting other people.
- Epidemic cholera contexts are those areas that may have a cholera outbreak every 3–5 years, sometimes with an explosive onset. There may be a season of risk (rainy season), but not reliably frequent to fully anticipate. All age groups are affected equally as, without vaccination, durable immunity from repeated exposure is not present.
- A cholera-endemic area is one where confirmed cholera cases, resulting from local transmission, have been detected in the last three years. An area can be defined as any subnational administrative unit including state, district or smaller localities. The cholera pattern tends to

be seasonal and at least once per year. Some endemic contexts report suspect cases year-round and outbreaks may be signaled by an increase in cases above a threshold. Children under the age of 5 affected may be more affected as immunity from repeated exposure has not yet occurred.

- Epidemics can occur in endemic countries. Epidemic countries can become endemic over time with repeated outbreaks.



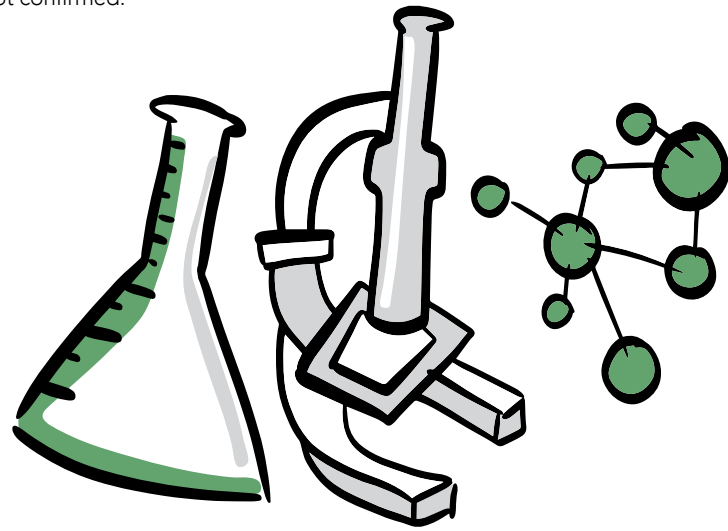
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At the start of an outbreak, rapid detection of suspected cases and their laboratory confirmation are essential

- When an outbreak is suspected, a multidisciplinary team should be sent to the field to confirm the outbreak and take the first measures to control the spread of disease. These teams should carry sampling materials, RDTs, the means to make clean water, and ORS at a minimum. More medical materials should be carried if a treatment facility is visited.
- RDTs should be used to reinforce suspicion of cholera. RDTs allow quick testing without the need for a laboratory and are frequently used to increase suspicion during outbreak investigations. While the sensitivity of cholera RDTs is sufficient (negative predictive value > 90%), their specificity is not adequate for use as individual diagnostic tests. RDT-positive stool samples should be sent to the laboratory for confirmation.
- Cholera is confirmed by identifying *V. cholerae* O1 (or O139) in stool samples from affected patients using culture (including a seroagglutination test) or sometimes PCR for confirmation. Antibiotic sensitivity testing should be performed to inform case-management. Whole-genome sequencing can be used to identify global transmission patterns.
- Laboratory confirmation is essential to verify a cholera outbreak. Once an outbreak is confirmed, a clinical diagnosis using the WHO standard case definition is sufficient. Laboratory confirmation should

be carried out in each new area (district or region) reporting cases to confirm extension of the outbreak.

- Systematic, periodic and representative sampling and testing of stool from suspected cases should be performed throughout an outbreak to monitor the outbreak, determine antibiotic sensitivity and monitor the strain.
- An outbreak is considered over when all samples from suspected patients test negative by RDT, culture or PCR for four weeks.
- Do not wait for laboratory confirmation before starting control activities. Access to clean water and basic sanitation, hygiene promotion and access to treatment are important public health interventions even if the outbreak is not confirmed.



5

People with cholera experience acute watery diarrhoea with no fever and they may also have profuse vomiting

- Most people infected with cholera (approximately 80%) do not develop any symptoms even though the bacteria are present in their faeces for up to 14 days after infection.
- Among people who develop symptoms, approximately 80% present with mild to moderate watery diarrhoea resulting in no or only minor signs of dehydration. The remaining 20% will have severe cholera and rapidly develop profuse watery diarrhoea with or without vomiting that can lead to severe dehydration and to death if not treated.
- Other signs and symptoms may include profuse vomiting, abdominal or muscle cramps, hypoglycemia (low blood sugar, <70 mg/dL) or hypokalaemia (low blood potassium level <3.5 mmol/L).
- There is a high risk of fetal loss in pregnant woman with cholera.
- Fever is not a symptom of cholera but may be a result of comorbidity in patients with cholera.



6

Cholera is an easily treated disease, severe forms can kill within hours if left untreated, early rehydration is critical

- The most important treatment is rehydration, which consists of prompt replacement of fluids and salts lost through severe diarrhoea and vomiting. Early rehydration can save the lives of nearly all cholera patients. With early and proper treatment, the case-fatality rate should remain below 1%.
- Good assessment of the state of dehydration is key to appropriate treatment.
- Patients (adults and children) with no signs or some signs of dehydration (approximately 80% of patients) can be rehydrated quickly and easily by following standard protocols for treatment of dehydration with ORS. ORS should be given as early as possible, including at home, by volunteers and family members to avert delays in rehydration and potentially death.
- Patients who become severely dehydrated need to receive fluids intravenously (Ringer's lactate solution).
- Antibiotics are recommended for patients with severe dehydration, women who are pregnant, the elderly and children with severe acute malnutrition to reduce the duration and severity of diarrhoea. Doxycycline is the first line of treatment for all patient groups, but local antibiotic sensitivity should be verified.



- Patients should be offered food as soon as capable of drinking ORS without vomiting.
- Continued breastfeeding of infants and young children with cholera is encouraged.
- Zinc is also an important adjunctive therapy for children under 5 years old. It reduces the duration of diarrhoea and may prevent future episodes of other causes of acute watery diarrhoea.
- It is important to reinforce IPC measures and ensure basic levels of water and sanitation in all treatment structures to reduce the risk of transmission of cholera within and from treatment centres.

7

Oral cholera vaccines (OCVs) are safe and should be used with other prevention and control strategies

- There are two OCVs:
 - Euvichol®: One dose can be used to contain epidemics (protection for at least six months). Two doses are required for longer protection (the vaccine provides sustained protection of >65% for at least three years after two doses). The two doses can be administered to all persons over the age of 1 year with a minimum two-week interval between doses.
 - A second vaccine, Dukoral®, is used primarily for travellers. It also confers significant short-term protection against Enterotoxigenic Escherichia coli (ETEC). The vaccine is administered with a buffer solution. It can be given to all persons over the age of 2 years with a minimum of a week between doses. Children aged 2–5 years require a third dose of vaccine.
- Oral cholera vaccines are considered safe for pregnant women.
- OCV can be used for emergencies:
 - In humanitarian crises, OCV can be used to prevent cholera, even before any suspected cases are reported.
 - For outbreak response, OCV is used to prevent further spread of cholera. It should be used as early as possible to prevent the greatest number of cases.
 - All OCVs currently require cold chain (2–8 °C).
 - For emergency use of OCV, there is a global emergency stockpile of doses (Euvichol®) managed by the ICG.
- In endemic settings, OCVs are used as part of a longer-term cholera control plan that includes reinforcement of surveillance and laboratory diagnostic capacity and improvements in water, sanitation and hygiene conditions. OCV

is used to provide mid-term protection to the population while longer term water, sanitation and hygiene solutions are being implemented. OCV for endemic use is available via a global stockpile.

ORAL CHOLERA VACCINE



8

Populations at risk should be provided with safe water and adequate sanitation

- During outbreaks:
 - Provide people with safe water or the means to prepare and store safe water at home.
 - When possible, implement measures to improve excreta disposal in affected communities.
 - Organize awareness campaigns and provide information to the community about the potential risks and symptoms of cholera, precautions to avoid cholera, when and where to report cases and to seek immediate treatment when symptoms appear. The location of appropriate treatment sites should also be shared.



- There is a high risk of cholera transmission within households and with close neighbours of patients with cholera. Preventive measures, including access to clean water, disinfection of key areas in the households of patients and protective hygiene measures should be reinforced.
- Community engagement is critical so that communities adopt preventive behaviors to avert contamination:
 - Implement health education campaigns to promote adoption of appropriate hygiene practices such as handwashing with soap, safe preparation and storage of food and safe disposal of faeces.
 - Promote handwashing at key times.
 - Continue to promote breastfeeding.
 - Adapt health campaigns to local culture and beliefs.
 - Adapt funeral practices for individuals who die from cholera to prevent infection among funeral attendees.



9

Mapping the origin of cases and engaging in the hotspot identification process are critical to target control activities

- Mapping the origin of cases can help identify priority areas for water and sanitation activities and hygiene promotion. The more precise the mapping, the more effective the targeting of interventions.
- Hotspot mapping requires a country-led analysis of historical data of annual incidence and persistence at the smallest administrative level for which these data are available (usually district-level). A judicious use of cut-off points will permit describing cholera risk level (high, medium and low) with which priority interventions and timelines can be assigned. A tool is available from the GTFCC.
- Access to treatment for people living in priority areas should also be ensured.
- Oral rehydration points in key areas and transport services to cholera treatment centres can save lives.
- Active case finding should also be carried out in these areas.
- In areas with community health programmes, community health workers or volunteers can be trained to identify and report suspected cholera cases, safely make and give ORS, and refer patients for treatment.

10

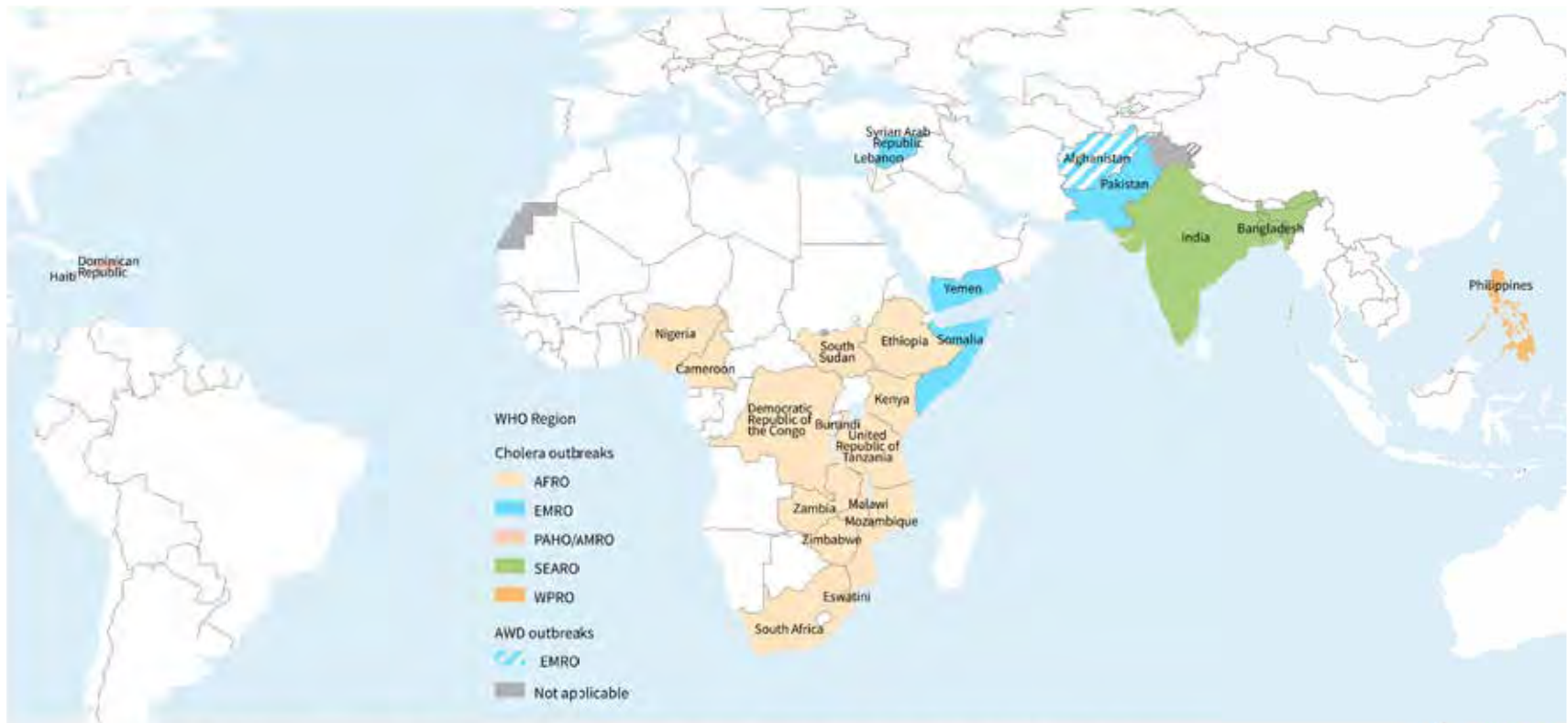
WHO can provide countries with cholera kits

- WHO hosts the secretariat of the GTFCC.
- WHO can provide materials for investigation and confirmation of cholera outbreaks, as well as for treatment of cholera patients.
- Cholera kits are designed to help prepare for a potential cholera outbreak and to support the first month of the initial response.
- Six kits are available:
 - One kit provides materials for investigation of cholera outbreaks.
 - One kit provides supplies for laboratory confirmation of suspected cholera cases (Note: triple packaging for sample transport is NOT included, but guidance on preparing, packaging, and shipping samples is available (in French and English) on the GTFCC website.
 - Three kits are designed for treatment of cholera patients within existing structures at the central, peripheral and community levels.
 - One kit provides materials to set up a provisional structure for patient care when no such structure is in place.
- A tool for quickly estimating needs for cholera kits is also available.

- Partners of the GTFCC launched Ending Cholera: A Global Roadmap to 2030 in October 2017. The Roadmap targets a 90% reduction in cholera deaths by 2030 and elimination of cholera in at least 20 countries of the 47 currently affected. The Roadmap is based on three strategic axes:
 - Early detection and response to contain outbreaks
 - Multisectoral interventions in cholera hotspots
 - Effective coordination at country, regional and global levels
- Based on the Roadmap, countries are now developing National Cholera Plans aligned with their health and development priorities with the support of the GTFCC, and integrating multisectoral interventions on WASH, OCV, early warning systems, health care and community engagement.



Global situation of active epidemics of cholera and acute watery diarrhoea as of April 2023



The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

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Data Source: World Health Organization
Map Production: WHO Health Emergencies Programme
Map Date: 18 April 2023



More information about cholera:

- Cholera WHO webpage
<http://who.int/cholera/en/>
- Cholera WHO factsheet
<http://who.int/mediacentre/factsheets/fs107/en/>
- Ending Cholera: a global roadmap to 2030
<http://www.who.int/cholera/publications/global-roadmap/en/>
- Cholera kits
<http://who.int/cholera/kit/en/>
- GTFCC Cholera Outbreak Field Manual
<https://www.gtfcc.org/wp-content/uploads/2020/05/gtfcc-cholera-outbreak-response-field-manual.pdf>
- First steps for managing an outbreak of acute diarrhoea, GTFCC
<https://apps.who.int/iris/handle/10665/70538>
- Technical guidance, Job aids, Fact sheets for laboratories including for sample collection and transport, proper use of RDT, confirmation through culture and environmental surveillance of cholera, GTFCC Laboratory Working Group
https://www.gtfcc.org/resources/?r_intervention=laboratory
- Oral cholera vaccines position paper, WHO
<http://apps.who.int/iris/bitstream/10665/258763/1/WER9234.pdf?ua=1>
- International Coordinating Group (ICG) on vaccine provision for cholera
<https://www.who.int/groups/icg/cholera/stockpiles>
- OpenWHO course on Cholera Outbreaks: Emergency Preparedness and Response
<https://openwho.org/courses/cholera-eprep>
- OpenWHO course on Cholera Introduction
<https://openwho.org/courses/cholera-introduction-en>

Mpox (previously known as monkeypox)

10 THINGS YOU SHOULD KNOW



1. Mpox is an infectious disease caused by the mpox virus; it is usually characterized by fever, swollen lymph nodes and skin rash
2. Mpox emerged as a zoonotic disease which also spreads from person to person
3. Human-to-human transmission occurs mainly through skin-to-skin or mucosal contact
4. A global outbreak of mpox with human-to-human transmission began in 2022
5. Surveillance, isolation of cases and contact-tracing are essential for outbreak control
6. The preferred laboratory diagnostic test for mpox is PCR testing of skin lesions or affected mucosa
7. Supportive patient care can help prevent serious medical complications
8. IPC measures are essential to prevent onward transmission in health facilities, households and communities
9. Risk communication and community engagement (RCCE) are key to controlling outbreaks
10. There are licensed vaccines and antiviral therapeutics for mpox

Mpox response tips

Collaborative surveillance

- Develop a case definition and case investigation form.
- Test all suspected cases for mpox.
- Conduct contact-tracing and health monitoring for close contacts.
- Describe the outbreak in terms of person, place and time using epidemiological maps and charts.
- Ensure laboratory and surveillance databases are linked.
- Notify WHO, under the IHR (2005).

Community protection

- Raise awareness of the risk of mpox, how it spreads and how to protect yourself and others using locally adapted, transparent, timely information using trusted channels.
- Engage at-risk communities and involve them in the outbreak response.
- Develop strategies for preventing and responding to stigma and discrimination to mpox (including for people with symptoms, health workers and families/close contacts).
- Adapt community strategies and approaches to the local context depending on the drivers of transmission, socio-behavioral and social listening data and community input.

Clinical care

- Symptoms include rash, fever, headache, muscle aches, back pain, low energy and swollen lymph nodes. Disease can be self-limiting or severe.
- Optimal supportive care reduces the risk of complications and long-term sequelae.
- Patients may require hospitalization for severe pain, secondary infection or other complications.
- Integrate mpox prevention and care with other health services, such as immunization, sexual health and HIV prevention and care.
- Offer specific antiviral therapy according to national protocol.
- Ensure IPC measures are in place in the hospital or congregate setting or at home.

Access to countermeasures

- Diagnostic tests should be used to confirm mpox infection.
- Vaccines are recommended for persons at risk and for post-exposure protection.
- Specific antiviral medications may be available in some locations.

Emergency coordination

- Ensure coordination of partners for all aspects of prevention and response.
- Ensure public health and animal health specialists engage in coordinated outbreak response in a One Health approach.

1

Mpox is an infectious disease caused by the mpox virus; it is usually characterized by fever, swollen lymph nodes and skin rash

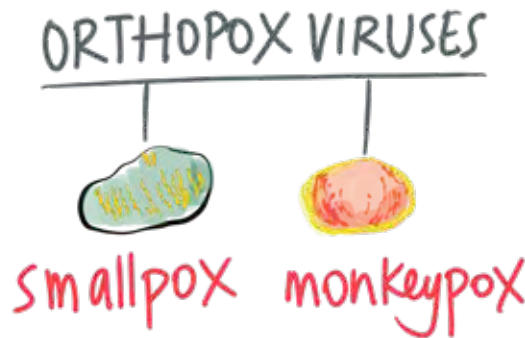
- Mpox originated as a viral zoonosis caused by the mpox virus, an orthopoxvirus.
- There are two distinct clades of mpox virus: Clade I (formerly known as the Congo Basin or Central African clade) and Clade II (formerly known as the West African clade), which has two sub clades (Clade IIa and Clade IIb).
- Clade I was historically noted to cause severe disease with a case-fatality ratio of up to 10%, whereas the case fatality for Clade II in West Africa was and continues to be approximately 1%. Conversely, during the global outbreak linked to Clade IIb that began in 2022, fewer than 0.1% of patients died.
- Spill-over zoonotic infection occurs in areas where the virus circulates among wildlife.

- The incubation period of mpox is usually 6–13 days but can range from 2–21 days.
- Patients with mpox usually present with fever, headache, malaise, lymphadenopathy (swelling of the lymph nodes) and rash. Clinical features can range from no symptoms to severe disease.
- Mpox is usually self-limited, lasting a few weeks and can also cause severe illness.
- Persons with weakened immune systems, such as those with uncontrolled HIV infection or on immuno-suppressive therapy for other conditions, are at risk for more severe disease. Infants and children are at higher risk for severe disease.
- Infection in pregnancy can lead to complications including fetal loss or congenital infections.

- The severity of disease can be related to the extent of exposure to the virus, the patient's overall health and the complications experienced.
- During the 2022-2023 global outbreak, patients often had few lesions or lesions concentrated in the genital or peri-anal areas.
- The rash which develops may resemble features from other infectious diseases or conditions. It is therefore critically important to consider the differential diagnosis and seek laboratory testing in order to ensure appropriate treatment and support for patients
- Mpox symptoms are similar to those seen in smallpox, which was eradicated in 1980. Smallpox was more severe and led to death in one third of cases.
- Smallpox vaccines were cross-protective against other diseases caused by orthopoxviruses, including mpox.

The clinical course of mpox typically evolves over two periods

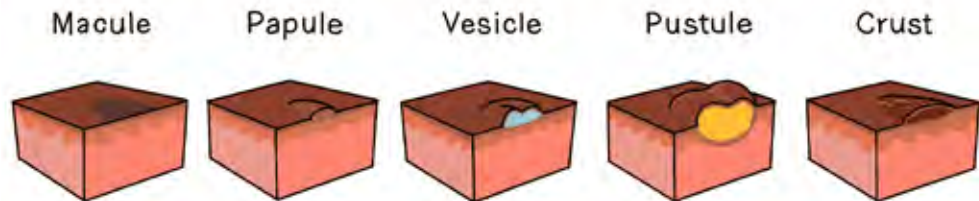
The viral invasion period (Up to the first five days)	The skin eruption period (1–3 days after appearance of fever)
<ul style="list-style-type: none">• Characterized by fever, intense headache, lymphadenopathy, especially around the neck, armpits and inguinal areas, back pain, myalgia (muscle ache) and an intense asthenia (lack of energy).	<ul style="list-style-type: none">• A rash appears in stages, often beginning on the face and then spreading elsewhere on the body, and to palms of the hands and soles of the feet.• The rash evolves from macules (lesions with flat bases) and papules (firm raised lesions) to vesicles (small fluid-filled blisters), pustules, and crusts in approximately 10 days. Complete disappearance of the skin lesions or sores might take 3–4 weeks.• The rash can affect the face, palms of the hands, soles of the feet, groin, genital and/or anal regions. It may also be found in the mouth, throat, anus or vagina, or on the eyes. The number of lesions or sores can range from one to several thousand.



Clinical presentation and differential diagnosis between mpox, chickenpox, measles and smallpox

	Mpox	Chickenpox	Measles	Smallpox*
Fever	1-3 days before rash	1-2 days before rash	3-5 days before rash	2-4 days before rash
Rash appearance	Macules, papules, vesicles, pustules, crusts Lesions are firm, deep, well circumscribed and umbilicated, may coalesce	Macules, papules, vesicles, crusts Lesions are superficial with irregular borders	Macules, papules Lesions are blotchy red spots and raised bumps which then fade, may coalesce	Macules, papules, vesicles, pustules, crusts Lesions are firm, deep, well circumscribed and umbilicated, may coalesce
Rash development and distribution	Slow All lesions at the same stage More dense on face and extremities Present on palms and soles	Rapid Lesions in different stages More dense on body Rare on palms and soles	Rapid Lesions in different stages Start on face and spreads downwards Sometimes reaching hands and feet	Slow All lesions at the same stage More dense on face and extremities Present on palms and soles
Rash duration	14-28 days	6-14 days	5-6 days	14-28 days
Other distinctive features	Lymphadenopathy (swollen lymph nodes) before appearance of rash	Itchy rash looks like 'a dew drop on a rose petal'	Cough, coryza (runny nose), conjunctivitis, and Koplik spots (small white spots) inside the mouth	No lymphadenopathy
Death	Up to 10%	Rare	Up to 10%	Up to 30%

*Note: Smallpox has been eradicated. Information in this table was gathered before 1980.



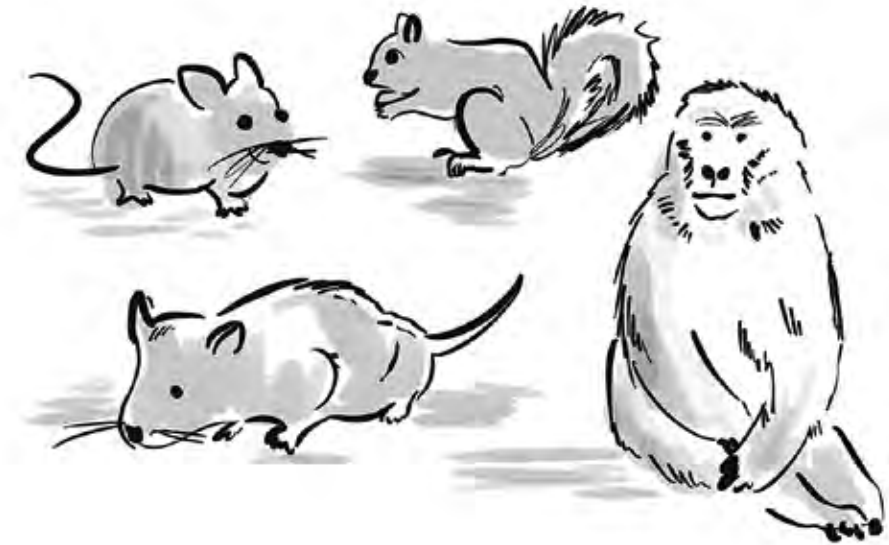
2

Mpox emerged as a zoonotic disease which also spreads from person to person

- The monkeypox virus has been identified in small mammals, including rope squirrels, tree squirrels, giant pouched rats, dormice and different species of monkeys. Some species, such as monkeys and great apes, develop the classic monkeypox skin rash.
- The ecology of the virus is largely unknown and the animal reservoir has not been identified.
- As previously reported in East Central and West Africa, human mpox typically occurs in areas close to tropical rainforests where people have frequent contact with wild animals.
- Mpox can spread to people when they come into physical contact with an infected animal – for example through bites or scratches, or during activities such as hunting, skinning, trapping, cooking or playing with carcasses.
- In areas where mpox occurs in wild animals, the risk of mpox can be reduced by avoiding contact with animals, especially those that are sick or dead and by using gloves and protective clothing when slaughtering animals or handling animal products.
- The virus can be caught through infected meat if not cooked thoroughly. In regions where animals can carry the monkeypox virus, any foods containing animal parts or meat should be cooked thoroughly before eating.

- People living in or near forested areas in enzootic regions may have indirect or low-level exposure, possibly leading to subclinical (asymptomatic) infection and immunity.
- In recent years, and as population immunity to smallpox has waned over time, human-to-human transmission has been increasingly documented, including in urban areas.
- Outbreaks have occurred in congregate settings, such as prisons and camps for internally displaced persons or refugees. In these settings further spread can occur by zoonotic or human-to-human transmission, or both.

- People with mpox should maintain physical distance from domestic pets or livestock and proper waste management is critical to prevent spillback from infected humans to susceptible animals. Precautions should be taken around health facilities, at home (including pets), in zoos and wildlife reserves and to peri-domestic animals, especially rodents.



3

Human-to-human transmission occurs mainly through skin-to-skin or mucosal contact

- Mpox spreads from person-to-person primarily through skin-to-skin or mucosal contact. Other forms of close contact that can lead to transmission include face-to-face (such as talking or breathing close to one another, which can generate droplets or short-range aerosols); mouth-to-mouth (such as kissing); or mouth-to-skin contact (such as oral sex or kissing the skin). Skin-to-skin contact includes intimate contact and sexual activity such as oral, vaginal or anal sex.
- Infection can occur from materials (such as bedding, clothing, surfaces and objects) that carry infectious viruses.
- Infection can also occur from contaminated sharps, such as from a needle stick injury or tattoo.
- Environments can become contaminated with the mpox virus. Someone else who touches these items may become infected if they have any cuts or abrasions or they accidentally touch their eyes, nose mouth or other mucous membranes. This is known as fomite transmission.
- Cleaning hands after touching objects that may be contaminated can help prevent infection.
- It is also possible to become infected from breathing in skin flakes or virus from clothing, bedding or towels. For these reasons, it is important to wear appropriate PPE including a respirator mask when caring for a patient or cleaning their room.

- Other possible mechanisms of transmission through the air for mpox are not well understood and studies are underway to learn more.
- Mpox during pregnancy can put mother and child at risk. Transmission of mpox to a fetus occurs during pregnancy which can lead to congenital infection, fetal loss or stillbirth. The virus can also spread to an infant during or after birth or during breastfeeding through skin-to-skin contact, or from a parent with mpox to an infant or child in the household.
- The mpox virus has been found in a range of body fluids during and following infection. More information is needed

to better understand various modes of transmission via contact with other bodily fluids (such as breastmilk, semen, vaginal fluid, amniotic fluid or blood) and to better understand transmission by respiratory droplets and aerosols.

- Until more is understood about transmission through sexual fluids, condoms are recommended as a precaution during sexual contact for a period of 12 weeks after recovery to reduce the risk of transmission. It is important to note that condoms alone are not sufficient to prevent mpox.



4

A global outbreak of mpox with human-to-human transmission began in 2022

- Prior to the 2022-2023 global outbreak, smaller outbreaks had occurred outside of areas of known virus circulation:
- A mpox outbreak occurred in the United States of America in 2003 following importation of small mammals from Ghana from which mpox spread to pet prairie dogs, which resulted in zoonotic cases in people across six states.
- Mpox has been diagnosed in travellers in regions outside of its usual ecological niche: Benin (1972), South Sudan (2005), Israel (2018), Singapore (2018), the United Kingdom (2018 and 2021) and the United States of America (2021).
- The geographic areas in which outbreaks have occurred in Africa have been extending over time since the eradication of smallpox.
- During the 2022-2023 global outbreak:
- Cases of mpox were reported to WHO from over 110 Member States across all six WHO regions.
- Most cases were reported from countries without previously documented mpox transmission.
- Most cases were reported in gay, bisexual and other men who have sex with men who had reported recent intimate contact with one or more casual partners.
- Patients commonly experienced rash, fever and headache. Severe

manifestations of disease included widespread and disseminated rash, secondary bacterial infections, abscesses, airway obstruction, ocular lesions, severe pain, anal involvement with proctitis, balanitis, urethritis and urinary retention, encephalitis, myocarditis and sepsis.

- Whereas case fatality was below 0.2% overall, it remained around 1% or higher in the African setting. Causes of death included encephalitis, sepsis and bronchopeumonia.

5

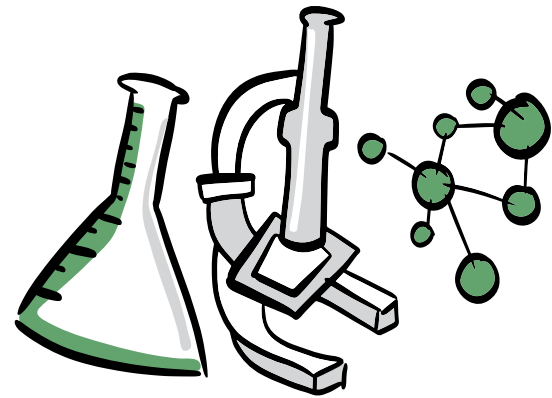
Surveillance, isolation of cases, and contact tracing are essential for outbreak control

- Surveillance should be included in national integrated surveillance systems.
- Once a case is suspected or confirmed, enhanced surveillance should be put in place to ensure early detection of cases and effective response and control measures.
- All cases should be notified to national health authorities.
- At the beginning of an outbreak investigation, a laboratory and surveillance database should be developed to record the information collected in case report forms. Alternatively, care should be taken to ensure databases are linked through unique case identification numbers.
- Contact-tracing should be conducted for all suspected, probable and confirmed cases.
- Cases should be isolated for the duration of the infectious period, that is until lesions have healed, crusts have fallen off and new skin has formed underneath.
- Laboratory confirmation of mpox is important, in order to distinguish it from other rash illnesses, such as chickenpox, measles, scabies, bacterial skin infections, syphilis, herpes or medication-associated allergies.
- Lymphadenopathy (swollen lymph nodes) is a distinctive feature of mpox and in some patients may occur before a rash appears.

6

The preferred laboratory diagnostic test for mpox is RT-PCR testing of skin lesion material

- Collecting material from skin lesions for RT-PCR testing is the preferred diagnostic and laboratory method, given its accuracy.
 - Specimens should be taken from skin lesions – the roof, vesicular fluid, or crusts or by skin biopsy where feasible. Lesion fluid can be sampled with a dry polyester swab.
 - Other sample types may be collected, including oropharyngeal swabs or anal swabs, particularly if patients present without lesions, but it is not clear how sensitive these methods are so they should not be used to rule out infection.
 - Store specimens in a dry, sterile tube (without viral transport media) and keep cold during storage and transport (between 2–8 °C) for up to seven days.
- The presence of monkeypox virus material in skin can also be confirmed through genomic sequencing of specimens, or virus isolation in cell culture.
 - Serology can be useful to confirm infection retrospectively, or as part of epidemiological studies.
 - Although orthopoxviruses are visible by electron microscopy as a classic large brick shape, this technique is now rarely used.
 - If for any reason smallpox is suspected, the health authorities must be contacted immediately in accordance with IHR (2005).



7

Supportive patient care can help prevent serious medical complications

- Patients should be treated symptomatically with optimal supportive care with:
 - Antipyretics for fever.
 - Oral and topical analgesics for pain management.
 - Localized care to keep skin lesions clean and prevent bacterial infection.
 - Adequate nutrition and hydration. Ensuring nutritional support is especially important for children.
- The risk of complications, long-term sequelae and death can be reduced with good clinical care.
- Patients at risk for complications (young children, pregnant women and those who are immunosuppressed) should be admitted to hospital where possible. Infection during pregnancy requires close monitoring of mother and fetus.
- Some patients will require hospitalization for further management.
- Patients not at risk for complications can be isolated at home during the infectious period if IPC measures are in place.

- Patients who are cared for at home and their families should be counselled on when to contact their health care provider, such as worsening pain, persistent fever, nausea or vomiting, difficulty eating or drinking fluids, visual symptoms, difficulty breathing or dizziness or confusion.
- Specific antiviral agents can be offered where appropriate and available according to national protocols to slow disease progression or treat severe infections.



8

IPC measures are essential to prevent onward transmission in health facilities, households and communities

- Appropriate IPC measures are essential to reduce the risk of transmission of mpox in health care and community settings.
- Health workers should be trained to recognize mpox symptoms and ensure that samples are collected for testing. Most importantly, they should be trained on how to provide appropriate isolation and IPC procedures in a stigma-free way.
- Health workers should apply standard precautions including:
 - Regular handwashing before and after caring for the patient
 - Respiratory hygiene and cough etiquette
 - PPE
 - Aseptic technique
 - Safe injections and sharps injury prevention
 - Environmental cleaning and disinfection
 - Proper handling of laundry and linen
 - Decontamination and reprocessing or reusable patient care items and equipment
 - Waste management
- In health facilities, it is critical to ensure that basic IPC standards are put in place to ensure protection of patients, health workers, caregivers and visitors. Patients should wear a medical mask in the presence of others. Anyone caring for a person with mpox at home should also take the necessary precautions, including wearing a mask (respirator).
- Patients should be isolated in a health facility setting or at home. Close physical contact should be avoided until the person has fully recovered.
- A decision to isolate and monitor a patient at home should be made according to their ability to isolate, clinical severity, presence of complications, care needs, risk factors for severe disease and access to referral for hospitalization if condition deteriorates.
- In case of death from mpox, conduct safe and dignified preparation, funeral and burial or cremation.
- Ensure measures are in place to prevent introduction of monkeypox virus into community and congregate settings such as residences, camps and prisons, and identify cases early. These measures include:
 - Exposure risk assessment for possible infection and transmission.
 - Training for facility staff on case identification and response action.
 - Provision of appropriate PPE for staff.
- Isolation of suspected and confirmed cases (staff or residents).
- Environmental decontamination, especially of potentially contaminated spaces.
- Avoid sharing personal spaces, clothing and eating utensils.
- Proper handling of waste from persons with mpox as infectious.
- Consideration for pre-exposure and post-exposure vaccination.
- Assessment of capacity for case detection and isolation.



9

Risk communication and community engagement (RCCE) are key to controlling the transmission of mpox

- The key objectives are to engage affected populations in the outbreak response, raise awareness of the risk, symptoms and protective measures, manage risk perception, maintain trust in health authorities and proactively communicate to support people at risk to make informed decisions to protect themselves and others from infection and severe disease.
- Communities may be affected in different ways and will require tailored information and engagement through trusted sources.

- RCCE strategies and activities should be locally targeted and informed by local epidemiology, socio-behavioural data, social listening, community feedback, demographic data (such as literacy rates, local languages, etc.) and personal factors such as higher risk of exposure or serious symptoms.
- Stigma and discrimination must be addressed through active strategies to support people to access health services (including testing, vaccination and care) and create an enabling environment where people feel able to report their symptoms.
- Health workers are often a trusted voice in the community who raise awareness, prevent stigma and discrimination and support uptake of protective behaviours.

- Key messages for communities include:
 - Mpox is caused by a virus.
 - Symptoms can include a rash, fever or body aches, among others.
 - Mpox can spread through touching, kissing, and oral, vaginal and anal sex.
 - It can also spread through contact with infected animals (such as monkeys, squirrels, etc.) in places where there is animal to human transmission of the virus.
 - To protect yourself and others:
 - Know the symptoms and check yourself regularly.
 - Have open conversations with close contacts.
 - Avoid close contact with someone who has mpox.
 - Seek health advice and get tested if you have been exposed or have symptoms.
 - Isolate if you have mpox, whenever possible.
 - Wear a medical mask when possible, especially when outside of your home.
 - Get vaccinated if it is available to you.
 - Having or being exposed to mpox is nothing to be ashamed of. Anyone can get mpox. Let's take care of each other.



10

There are licensed vaccines and antiviral therapeutics for mpox

- Three smallpox vaccines (MVA-BN, LC16-KMB, and OrthopoxVac) have been approved for prevention of mpox.
- Given similarities among orthopoxviruses, smallpox vaccines offer some protection against mpox. Persons vaccinated against smallpox before 1980 may continue to have some protection against mpox but the duration of immunity in most people is not known.
- During the global outbreak some studies provided early estimates of the effectiveness, against mpox, of vaccines approved for smallpox and mpox (at approximately 80%). Studies on vaccine safety and effectiveness for mpox are ongoing.
- In the context of the global outbreak, primary preventive vaccination (PPV) is recommended for persons at high risk of exposure, including but not limited to gay or bisexual men who have sex with men or other persons with multiple sex partners, health workers at risk, laboratory personnel working with orthopoxviruses, clinical laboratory staff performing diagnostic testing for mpox and others who may be at risk, as per national policy. Vaccination of animal handlers may be considered.
- Post-exposure vaccination (PEPV) should also be offered to contacts of a confirmed or probable case of mpox, including household contacts, sexual partners and health workers without adequate PPE.
- Vaccination programmes must be a part of a comprehensive approach, backed by thorough surveillance and contact-tracing, and accompanied by a strong information campaign and robust vaccine safety monitoring.
- Research is ongoing on the use of treatments against mpox. Tecovirimat is one antiviral drug approved by regulatory authorities for treatment of orthopoxvirus-associated infections, including mpox. It has been developed in oral and intravenous formulations for 14 days of treatment.

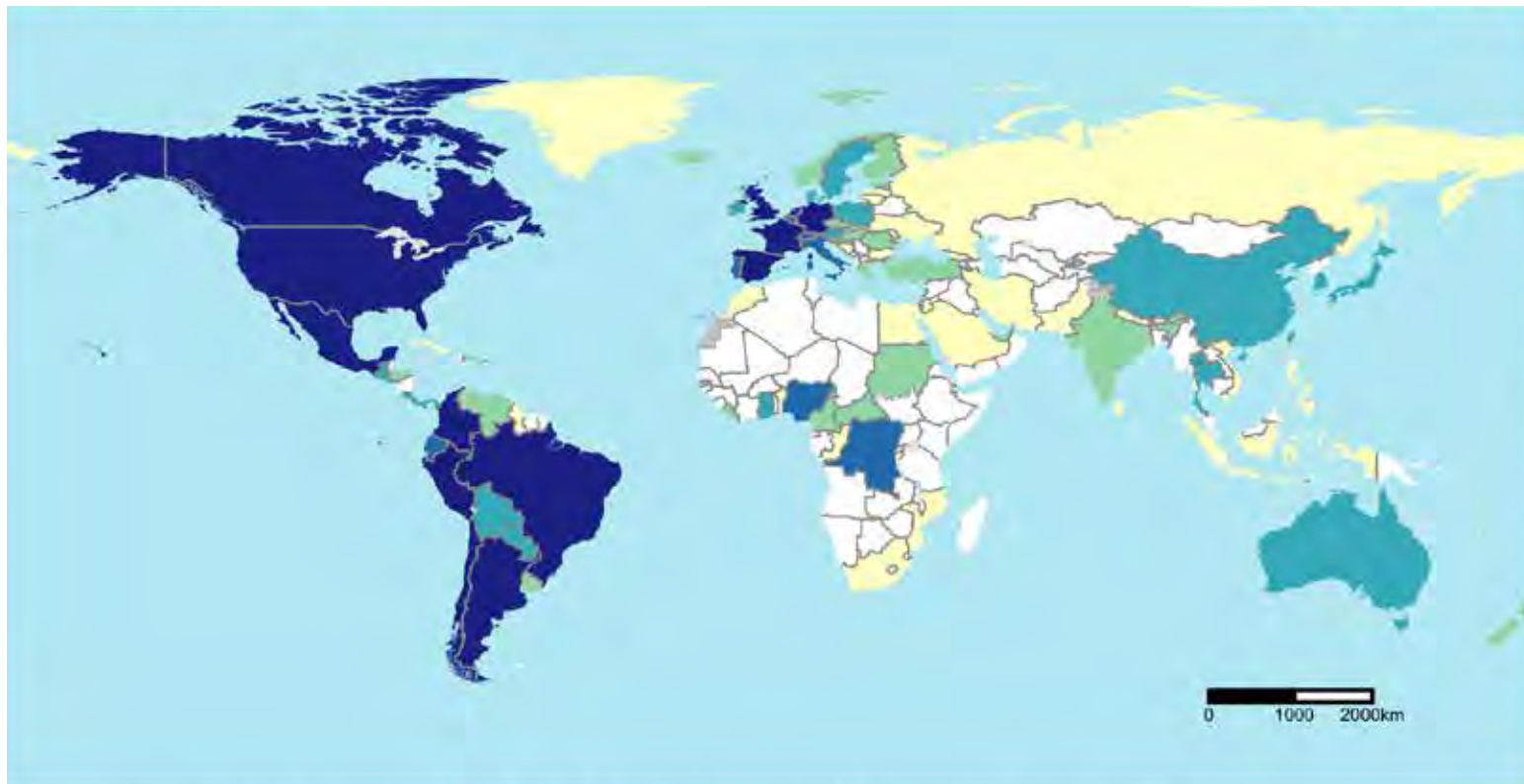


Countries in Africa reporting confirmed human cases of monkeypox from 1970–2021



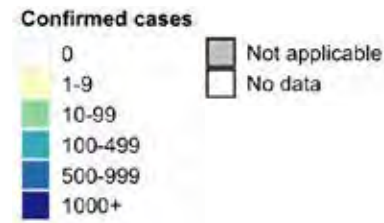
The designations employed on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2021. All rights reserved

Confirmed cases of mpox from 01 January 2022, as of 18 July 2023



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Data source: World Health Organization
 Map production: WHO Health Emergencies Programme
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More information about mpox:

- **Health Topics: Mpox**
https://www.who.int/health-topics/monkeypox/#tab=tab_1
- **Mpox outbreak page**
<https://www.who.int/emergencies/situations/monkeypox-oubreak-2022>
- **Mpox outbreak toolbox**
<https://www.who.int/emergencies/outbreak-toolkit/disease-outbreak-toolboxes/mpox-outbreak-toolbox>
- **Surveillance, investigation and contact-tracing for mpox**
<https://www.who.int/publications/i/item/WHO-MPX-Surveillance-2022.3>
- **Laboratory testing for the mpox virus. Interim Guidance, 2022**
<https://www.who.int/publications/i/item/WHO-MPX-laboratory-2022.1>
- **Vaccines and immunization for mpox. Interim Guidance, 2022**
<https://www.who.int/publications/i/item/WHO-MPX-Immunization-2022.2-eng>
- **Clinical management and infection prevention and control for mpox: Interim rapid response guidance, 2022**
<https://www.who.int/publications/i/item/WHO-MPX-Clinical-and-IPC-2022.1>
- **Risk communication and community engagement for mpox outbreaks. Interim guidance. 2022**
<https://www.who.int/publications/i/item/WHO-MPX-RCCE-2022.1>
- **OpenWHO course on Mpox introduction**
<https://openwho.org/courses/monkeypox-introduction>
- **La variole du singe: introduction. Formation en ligne OpenWHO 2020**
<https://openwho.org/courses/variole-du-singe-introduction>
- **OpenWHO course on Mpox: intermediate training**
<https://openwho.org/courses/monkeypox-intermediate>
- **La variole du singe: formation intermédiaire. Formation en ligne OpenWHO 2020**
<https://openwho.org/courses/variole-du-singe-intermediaire>
- **OpenWHO course on Mpox and the 2022-2023 global outbreak**
<https://openwho.org/courses/mpox-global-outbreak-2022-2023>

Plague

10 THINGS YOU SHOULD KNOW



1. Plague is a zoonotic disease caused by bacteria usually found in small mammals (mostly rodents)
2. Potential natural foci are distributed worldwide and are extending
3. Bubonic plague, the most common form of the disease, is not transmittable from human to human
4. Pneumonic plague can cause widespread epidemics and is difficult to control
5. Septicaemic plague occurs when plague-causing bacteria circulate in the bloodstream
6. Initial symptoms of plague are nonspecific and difficult to distinguish from symptoms of other acute febrile diseases
7. Plague is treatable and early treatment is essential for survival
8. Rapid diagnosis is essential and easy-to-use point of care tests are available
9. Health education, IPC, safe and dignified burial, and vector and rodent control are critical to prevent and manage epidemics
10. Plague usually disproportionately affects vulnerable populations

Plague response tips

Collaborative surveillance

- A robust and sensitive rapid diagnostic test is available for bubonic plague.
- Find the source of infection to target control measures.
- Depending on circumstances, plague cases are notifiable to WHO, under the IHR (2005).
- For pneumonic plague, follow close contacts.

Community protection

- Encourage health authorities to:
 - Initiate health education on the disease, its symptoms and modes of transmission.
 - Engage populations at-risk for plague with tailored information delivered through trusted sources on how to protect themselves from infection and prevent transmission.
 - Engage communities in vector control in endemic areas.
- Key messages are:
 - Plague is treatable. People who have symptoms or exposure to the disease should receive treatment immediately.
 - Bubonic and pneumonic plague are transmitted in different ways.
 - Pneumonic plague is contagious and human-to-human transmission of pneumonic plague occurs through respiratory droplets.
 - Bubonic plague is not contagious in or within the general population, although there may be a risk to health workers providing care to patients with bubonic plague.
 - To prevent bubonic plague, take precautions against flea bites and do not handle animal carcasses.

Clinical care

- Treat both suspected and confirmed cases early with antibiotics.
- For pneumonic plague provide close contacts with chemoprophylaxis for seven days.
- For pneumonic plague practice IPC standard precautions and use PPE appropriate for droplet precautions.
- For bubonic plague, depending on circumstances, people exposed to the same risk (for example people living in the same house as the patient) can receive chemoprophylaxis.
- For bubonic plague, practice IPC standard precautions

Access to countermeasures

- Ensure safe and dignified burials.
- For bubonic plague, implement vector and rodent control.
- People in plague affected areas should be advised to avoid flea bites and wear insect repellent.

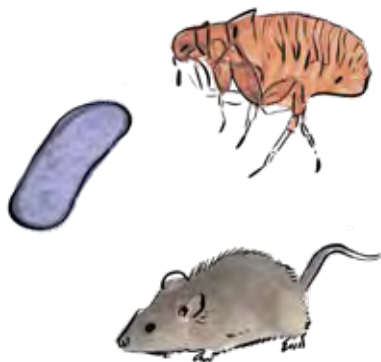
Emergency coordination

- Engage with partners in the agricultural sector and with communities for vector control in endemic areas.
- Ensure coordination between the animal and human health sectors for effective prevention and control, as well as outbreak investigation and management.

1

Plague is a zoonotic disease caused by bacteria usually found in small mammals (mostly rodents)

- Plague is a zoonotic disease caused by the bacteria *Yersinia pestis*, usually found in small mammals (mostly rodents).
- It is transmitted between animals by their fleas.
- Humans can become infected by the bite of infected fleas, by direct contact with infected materials, or by inhalation of infectious respiratory particles from a sick person with pneumonic plague.
- There are three main forms of plague, depending on the clinical presentation of infection: Bubonic, septicaemic and pneumonic.



2

Potential natural foci are distributed worldwide and are extending

- Plague natural foci include the bacteria (*Y. pestis*), an animal reservoir (such as a rodent), and a vector (a flea).
- There is a risk of human plague wherever the presence of plague natural foci and human populations coexist.
- Plague natural foci are distributed worldwide, and the range of the natural foci are also expanding. This could be due to:
 - Environmental modifications (for example deforestation).
 - Ongoing colonization of the black rat (one of the reservoirs).
 - Increased national and international trade which may potentially transport rodents to new environments
 - Increasing and widespread urbanization.

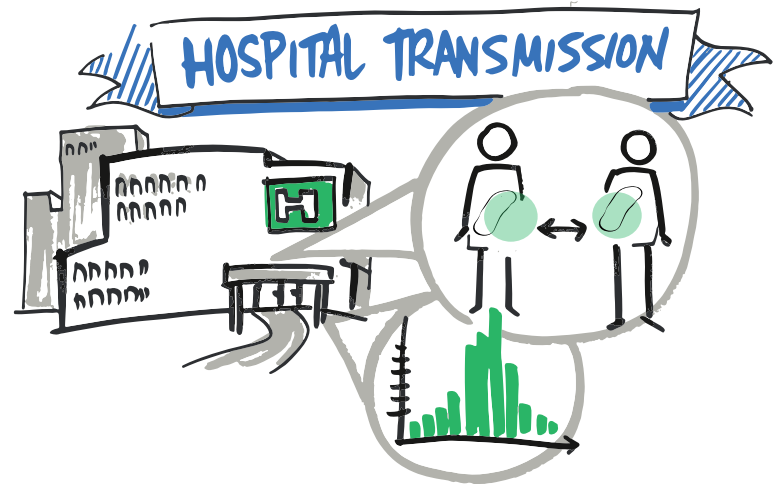
- There is currently a global re-emergence of the plague in some places where it had disappeared and its emergence in other places where it has never occurred.
- Plague epidemics have occurred in Africa, Asia and South America. Since the 1990s, most human cases have occurred in Africa. The three most endemic countries are Madagascar, the Democratic Republic of the Congo and Peru.
- In endemic countries, entomological and zoological surveillance activities are expensive and complicated to maintain. They are very often neglected in the absence of any human cases, and it is hard to obtain detailed knowledge about the status or development of natural foci.



3

Bubonic plague, the most common form of the disease, is not transmittable from human-to-human

- Bubonic plague results from flea bites or direct contamination of an open skin lesion by plague-infected materials or body fluids.
 - Infection can occur when handling dead animals without appropriate protective measures. However, transmission can also occur in health care settings (nosocomial infections).
 - The incubation period for bubonic plague is 2–6 days followed by sudden onset of illness, with symptoms such as headache, chills, fever, malaise and pain in the affected regional lymph nodes (neck, groin, etc.).
 - The infection spreads via the lymphatic system to the nearest lymph node where it replicates itself. The lymph node then becomes inflamed, tense and painful and is called a bubo. At advanced stages of the infection, inflamed lymph nodes can turn into suppurating (open pus-filled) sores.
- Bubonic plague cannot be transmitted from human-to-human unless there is contact with pus from suppurating buboes, most often occurring as nosocomial transmission.
 - Measures to control an epidemic of bubonic plague include early treatment of patients, vector, and rodent control, and depending on the circumstances, chemoprophylaxis for people exposed to the same environment where there is a common risk of contamination (for example shared living space with exposure to fleas).



4

Pneumonic plague can cause widespread epidemics and is difficult to control

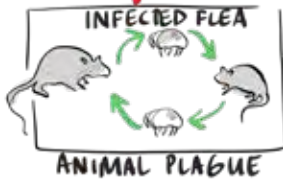
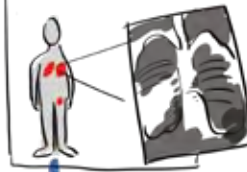
- Around 10% of people with bubonic plague will develop pneumonic plague.
- Pneumonic plague is the most virulent form of plague. The incubation period can be as short as 24 hours and untreated pneumonic plague is always fatal.
- Pneumonic plague is transmitted from person to person via respiratory droplets (coughing), so it has high epidemic potential and is the most difficult form of plague to control.
- Pneumonic plague occurs when the plague-causing bacteria infect the lungs. It can occur from the evolution of advanced bubonic plague, through the bloodstream or directly from inhalation of infected respiratory droplets.

- In cases of human-to-human transmission, the incubation period of pneumonic plague is usually 1–3 days, followed by sudden onset of fever, headache, chills, pain, weakness, chest discomfort, shortness of breath, cough and sometimes bloody or mucous secretions.
- There is a great risk of nosocomial infection, especially for the pneumonic form.
- Patients with pneumonic plague should be isolated so they do not infect others via respiratory droplets and should be cared for by trained medical staff.
- Medical staff should wear PPE and potentially receive chemoprophylaxis to prevent nosocomial transmission.
- Close contacts must be kept under medical surveillance and must receive chemoprophylaxis with antibiotics for seven days.

BUBONIC PLAGUE



PNEUMONIC PLAGUE



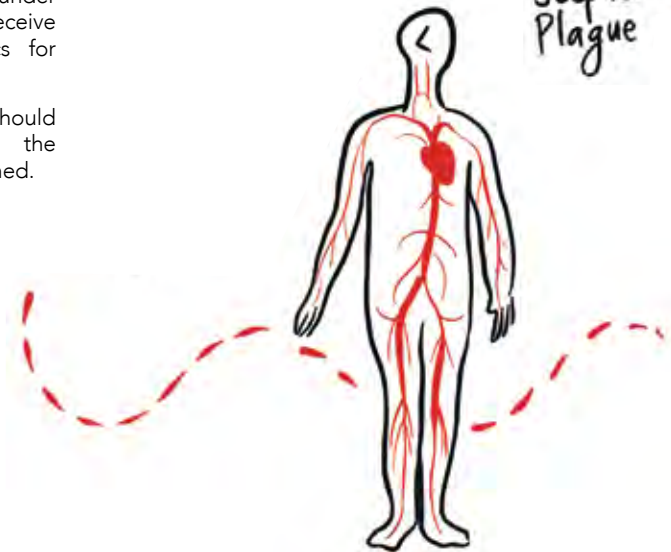
- Any suspect case should be treated until the diagnosis is confirmed.

5

Septicaemic plague occurs when the plague-causing bacteria circulate in the bloodstream

- Septicaemic plague occurs when the infection spreads through the bloodstream.
- Septicaemic plague may result from flea bites, from direct contact with infective materials through cracks in the skin or following bubonic plague.
- Septicaemic could also result in pneumonic plague.

Scepticemic Plague



6

Initial symptoms of plague are nonspecific and difficult to distinguish from symptoms of other acute febrile diseases

- People infected with plague begin to develop nonspecific symptoms after an incubation period of 1–7 days.
- Typical symptoms in the initial stages of all types of plague include sudden onset of fever, chills, head and body aches and weakness, vomiting and nausea. These symptoms are difficult to differentiate from symptoms of other common endemic pathogens.
- Painful and inflamed lymph node secondarily appears during bubonic plague. It is a distinguishing feature of bubonic plague in endemic regions.
- Symptoms of pneumonic plague appear quickly after infection (sometimes less than 24 hours). They include severe respiratory symptoms, such as shortness of breath and coughing, often with blood-tainted sputum. Pneumonic plague does not differ from other severe pneumonias, but rapid deterioration and death are classic clinical features of pneumonic plague.

7

Plague is treatable and early treatment is essential for survival

- Human plague is a severe disease. For bubonic plague the case-fatality ratio is between 10–30% and this rises to a 100% case-fatality ratio for untreated pneumonic plague.
- However, plague is treatable. When rapidly diagnosed and promptly treated, plague can be successfully managed with antibiotics, reducing mortality to less than 15%.
- Treatment with common antibiotics and supportive care are very efficient in curing human plague but their efficacy depends on early administration, which presumes early detection.

- Early detection and rapid treatment are especially important for the pneumonic form of plague, which is highly contagious, can kill in less than 24 hours and is invariably fatal in the absence of treatment.
- If people are treated in time, all forms of plague have good recovery rates.
- Recommended antibiotics to treat plague are:
 - For bubonic plague: tetracycline, doxycycline, fluoroquinolones.
 - For pneumonic and septicaemic plague: aminoglycosides, fluoroquinolones.
 - For postexposure chemoprophylaxis: tetracycline, doxycycline, sulfamethoxazole/ trimethoprim.



8

Rapid diagnosis is essential and easy-to-use point of care tests are available

- Confirmation of plague requires laboratory testing. The best practice is to identify the plague-causing bacteria, *Y. pestis*, in a sample of pus from a bubo, blood or sputum. It can be detected by different techniques:
 - Microscopy: staining and direct examination.
 - Isolation: colony morphology, biochemical reactions, phage lysis.
 - Detection of antigen/antibody: ELISA, fluorescent antibody test.
 - PCR
- An RDT is available and is helpful both for rapid diagnosis and as an alert tool.
- This easy-to-use, robust, reliable, and sensitive rapid diagnostic test for bubonic plague (dipstick test) detects a specific antigen and produces reliable results in 15 minutes, greatly facilitating containment efforts.
- This rapid diagnostic test is recommended for use in all endemic regions

9

Health education, IPC, safe and dignified burial and vector and rodent control are critical to prevent and manage epidemics

- Plague can be a very stigmatized disease. It was previously known as the Black Death due to the millions of deaths caused by plague in the past. Health education is particularly essential to prevent panic during outbreaks.
- In plague-endemic areas, it is critical to educate people on the disease, its symptoms and modes of transmission. People should be informed when zoonotic plague is active in their environment.
- People in plague affected areas should be advised to take precautions including:
 - Wearing insect repellent to prevent flea bites.



- Avoiding handling animal carcasses or touching dead animals and wearing insect repellent will help prevent bubonic plague in endemic areas.
- Avoiding close contact (less than 2 metres) with suspected pneumonic plague patients who are coughing.
- Health workers should specifically be informed and trained in IPC. They should be provided with appropriate PPE and trained in how to use it.
- Safe and dignified burials can help prevent further infection
- The bacteria present in the bodily fluids of deceased plague patients can be a source of infection for people in contact with them during burial ceremonies.
- Safe burials, respecting local cultures and beliefs, must be implemented.
- In plague-endemic areas and during bubonic plague outbreaks, flea and reservoir (usually rodents) controls must be implemented before outbreaks including rat-proofing dwellings, insecticide dusting and the use of rodenticides.

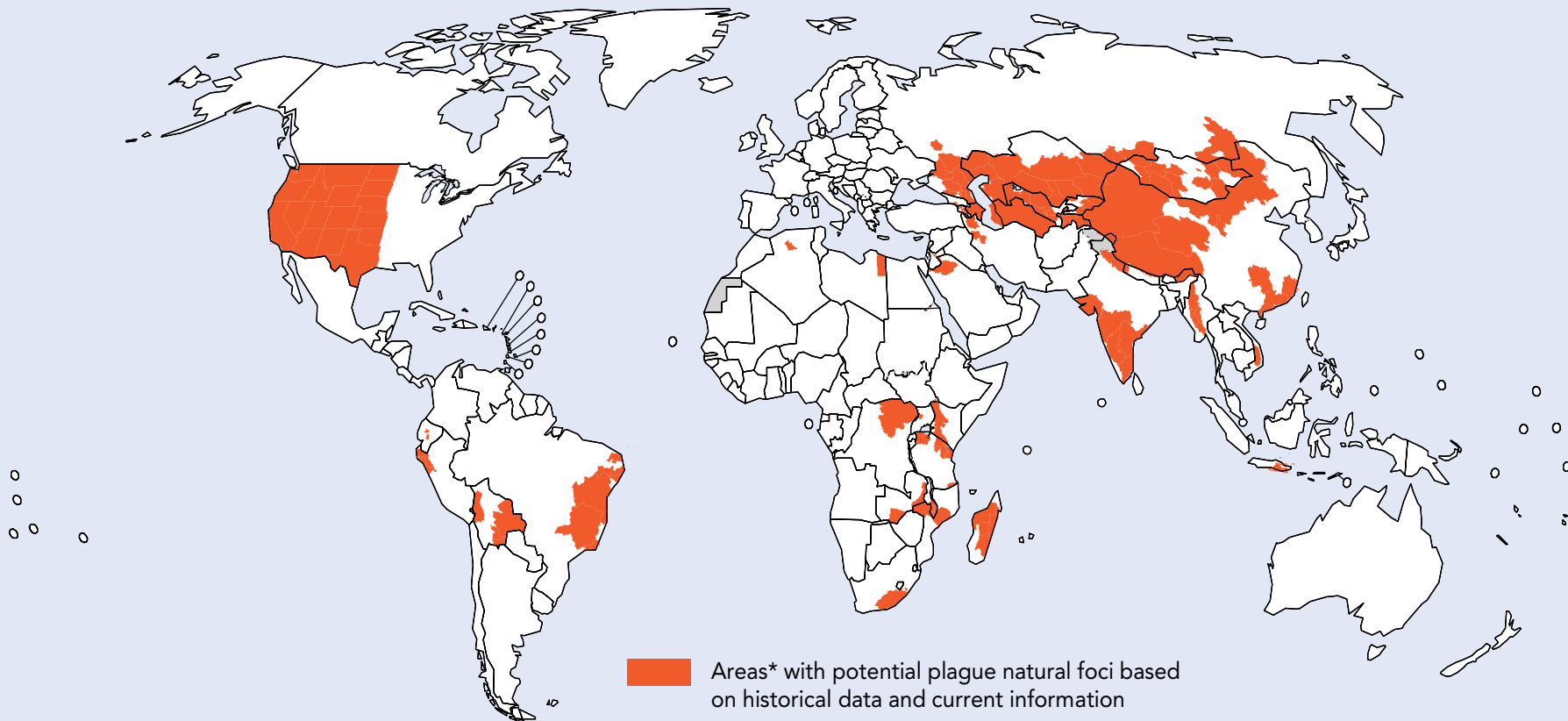
10

Plague usually disproportionately affects vulnerable populations

- Plague disproportionately affects vulnerable populations because it thrives in overcrowded places with poor sanitary conditions and inadequate health services.
- Outbreaks of plague can be linked to civil disturbances, war and breakdowns in health infrastructure and facilities.
- Strengthening health systems thus reduces the risk of plague epidemics.



Global distribution of natural plague foci, as of March 2016



* First administrative level representation

Source: WHO / IHM, as of March 2016

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
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More information about plague:

- Plague WHO fact sheet
<http://www.who.int/mediacentre/factsheets/fs267/en/>
- Plague WHO webpage
<http://www.who.int/csr/disease/Plague/en/>
- OpenWHO course on Plague
<https://openwho.org/courses/knowledge-resources-Plague>
- Plague manual: epidemiology, distribution, surveillance and control
<https://www.who.int/publications/i/item/WHO-CDS-CSR-EDC-99.2>

Leptospirosis

10 THINGS YOU SHOULD KNOW



1. Leptospirosis is an infectious disease caused by *Leptospira* bacteria and can be transmitted to humans from mammals (primarily rodents)
2. Leptospirosis epidemics are closely linked to the environment, rapid urbanization and climate change
3. Humans are infected through direct or indirect exposure to the urine of infected animals
4. The risk of infection is increased in poor socioeconomic situations and during some outdoor activities
5. Leptospirosis is under-recognized and often mistaken for other diseases
6. Common antibiotics, if given early, are effective against leptospirosis
7. Laboratory diagnosis is challenging but critical to confirm leptospirosis
8. Prevention and control measures should target the infection source, the route of transmission and the disease in humans
9. During leptospirosis outbreaks, strategic control measures include early detection and treatment
10. A One Health approach that is multisectoral and holistic is critical for leptospirosis prevention and control

Leptospirosis response tips

Collaborative surveillance

- Ensure laboratory confirmation of suspected cases.
- Detect cases as soon as possible in order to start appropriate antibiotic treatment and prevent an evolution to severe forms of leptospirosis.

Community protection

- Engage communities to avoid contact with rodents and their urine (including by rat-proofing in farming facilities) and to vaccinate their pets when and where possible.
- Provide the population with treated water during and following natural disasters.
- Encourage health authorities to:
 - Identify and target population at-risk for leptospirosis with tailored information delivered through trusted sources on how to protect themselves from infection and prevention transmission from animal reservoirs to humans.
- Key messages are:
 - Humans are infected through direct or indirect (through contaminated water) exposure to the urine of infected animals.
 - Avoid direct contact with rodents.
 - Immediately disinfect all skin injuries.
 - Seek treatment early if showing symptoms.
 - Risk of leptospirosis outbreaks may be greater after floods or other natural disasters.

Clinical care

- Provide empirical treatment (antibiotics) for all probable cases.
- Provide targeted chemoprophylaxis and protective equipment to very high-risk populations (for example rescue, sewage and sanitation workers).

Access to countermeasures

- Immunization in humans is recommended for occupational exposure. However, few human vaccines are available, and they are serogroup specific. Indication is consequently limited and must be evaluated case by case.

Emergency coordination

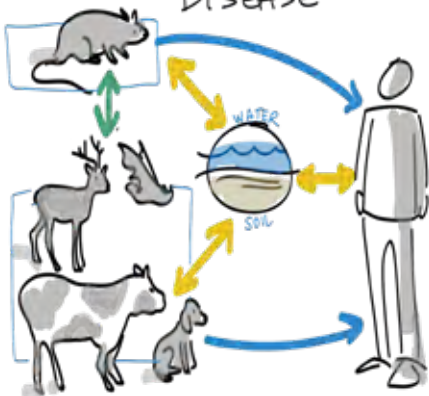
- Ensure coordination between the animal and human health sectors for effective prevention and control, as well as outbreak investigation and management.
- Ensure training of health workers for early detection and treatment.
- In case of an outbreak, prepare hospitals to receive a significant number of severe cases requiring intensive care.

1

Leptospirosis is an infectious disease caused by *Leptospira* bacteria and can be transmitted to humans from mammals (primarily rodents)

- Leptospirosis is an infectious disease caused by bacteria belonging to the genus *Leptospira*.
- Rodents are considered the primary source of infection in humans.
- Virtually all wild and domestic mammals can harbour *Leptospira* in their kidneys and urogenital tracts and can act as a source of infection to humans and other animals.
- Cattle, buffaloes, horses, sheep, goats, pigs and dogs are also common reservoirs of the bacteria that cause leptospirosis.
- The natural history of the disease is complex and specific to the local ecological conditions.

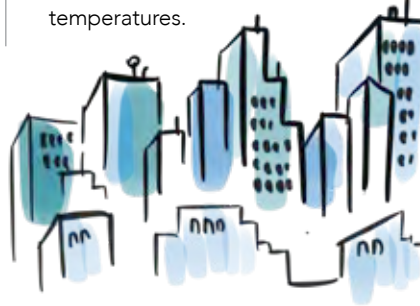
ZOOONOTIC + ENVIRONMENTAL DISEASE



2

Leptospirosis epidemics are closely linked to the environment, rapid urbanization and climate change

- Leptospirosis occurs worldwide but is most prevalent in tropical and subtropical regions.
- It often has a seasonal distribution, increasing with heavy rainfall or higher temperatures.
- Outbreaks classically occur in association with natural disasters, especially flooding.
- Past severe outbreaks have occurred after natural catastrophes with flooding such as in Nicaragua in 1995 (2,000 cases) and Manila, Philippines in 2009 (more than 500 cases).
- Leptospirosis infections are closely linked to the environment and climate change will lead to an escalation of the global burden of leptospirosis.
- Climate change is expected to increase the occurrence of heavy rainfall and flooding and the intensity of tropical cyclones and storms due to the rise of sea levels and the rise of sea and land-surface temperatures.



- Natural disasters also increase the risk of infectious disease by disrupting health services and infrastructures and damaging water and sanitation networks.

• Rapid and widespread urbanization increases the incidence and intensity of leptospirosis.

- Rapid urbanization is usually accompanied by development of urban slums, where overcrowding, poor sanitation, poor health care, poverty and abundance of rats and other animal reservoirs are risk factors for leptospirosis infection.



3

Humans are infected through direct or indirect exposure to the urine of infected animals

- Leptospirosis is a zoonosis, transmitted directly or indirectly from animals to humans.
- Humans become infected through direct contact with the urine of infected animals or with a urine-contaminated environment.
- The *Leptospira* bacteria enter the body through cuts or abrasions on the skin, or through the mucous membranes of the mouth, nose or eyes.
- Skin exposure through water contaminated by urine from infected animals is the most common route of infection.
- Leptospirosis can occasionally also be transmitted through the drinking of water or ingestion of food contaminated with urine of infected animals or by handling infected animal tissues

4

The risk of leptospirosis infection is increased in poor socioeconomic situations and during some outdoor activities

- The risk of infection depends on exposure to infection sources. Some people have more contact with water contaminated by rodents or other domestic animals.
- People can be exposed to leptospirosis through their occupations, for example outdoor and agricultural workers (such as rice-paddy and sugarcane workers), abattoir workers, veterinarians, meat handlers, pet-shop workers and sewer workers.
- People can also be exposed to leptospirosis through recreational activities such as water sports (for example swimming or canoeing).
- Survivors of natural disasters such as flooding are also at higher risk of infection.



5

Leptospirosis is under-recognized and often mistaken for other diseases

- Misdiagnosis is common because leptospirosis can have a nonspecific presentation that can mimic many other infectious diseases.
- The usual presentation is an acute illness with sudden onset of fever, headache, muscle ache (particularly the calf muscle) and prostration associated with any of the following symptoms/signs: conjunctival suffusion (red eyes), reduced or no urine output, jaundice, pneumonic symptoms (cough, sometimes with blood, and breathlessness), haemorrhages, meningitis, cardiac arrhythmia or failure and skin rash. Other common symptoms include nausea, vomiting, abdominal pain and diarrhoea.
- The incubation period of leptospirosis is usually 5–14 days, with a range of 2–30 days. Although the disease is self-limiting and often clinically unapparent in the majority of cases, 5–15% of untreated cases can progress to a more severe and potentially fatal stage.
- When symptomatic, leptospirosis may be mistaken for other diseases.

- The main broad clinical categories of leptospirosis are as follows:
 - Mild influenza-like illness (which can be confused with malaria, dengue, influenza and many other infectious syndromes).
 - Weil's syndrome (jaundice, renal failure, haemorrhage, myocarditis), which can be confused with hepatitis or yellow fever.
 - Pulmonary haemorrhage and respiratory failure, which can mimic viral haemorrhagic fevers or severe bacterial diseases such as plague, especially when there are clusters of cases.
- Suspicion of leptospirosis is increased for patients presenting with the above symptoms if there is a history of occupational or recreational exposure to infected animals or to an environment potentially contaminated with animal urine. Clinicians should consider leptospirosis in the differential diagnosis of febrile illnesses after flooding.
- Misdiagnosis or delayed diagnosis has significant clinical implications because early treatment is crucial to minimize morbidity and mortality and implement timely control measures.

Leptospirosis presentations	Diseases it could be confused with
Mild forms	Malaria, dengue, influenza
Febrile hemorrhagic forms	Viral haemorrhagic fevers
With severe pneumonia	Plague
When icteric fever	Yellow fever or hepatitis

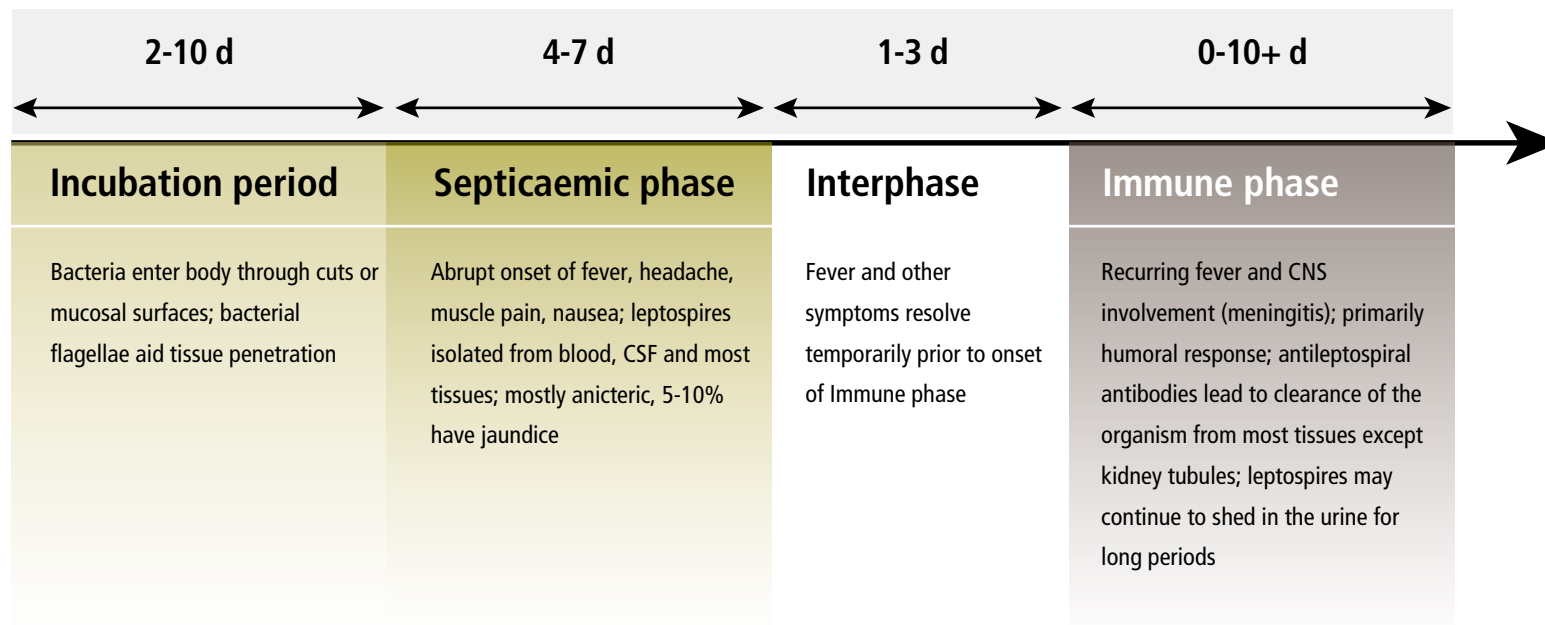
6

Common antibiotics, if given early, are effective against leptospirosis

- Leptospirosis can be treated with antibiotics that should be given as early in the course of illness as possible, preferably before the fifth day after onset.
- Clinicians should never wait for the results of laboratory tests for leptospirosis before starting treatment with antibiotics.
- Treatment options include antibiotics such as amoxicillin, tetracycline, ampicillin and doxycycline.
- The severe form of leptospirosis includes renal and cardiac failure, as well as haemorrhagic pneumonia and requires intensive care. In an epidemic situation, a significant number of people may have the severe form of leptospirosis, which can make case management logistically complex.



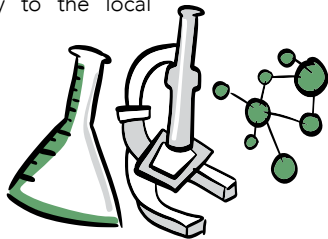
Typical course of Leptospirosis



7

Laboratory diagnosis is challenging but critical to confirm leptospirosis

- Laboratory diagnosis of leptospirosis is not easy because of the complexity of the pathogen.
- There are a wide variety of leptospire (some are not pathogenic in humans), leptospire have high genome plasticity and a wide variety of serogroups (250).
- Laboratory support is needed to:
 - Confirm the diagnosis and distinguish leptospirosis from other diseases.
 - Determine the serovar responsible for infection, which will help guide control strategies.
- Current recommendations for laboratory testing are the combination of:
 - Serology – The microscopic agglutination test (MAT) is the gold standard serologic test due to its high specificity, but it requires a bank of strains; and
 - PCR.
- IgM ELISA may be used but requires a lag period after infection before antibodies become detectable. Commercial RDTs need to be validated on site before being used routinely due to their varying sensitivity and specificity to the local circulating serogroups.



8

Prevention and control measures should target the infection source, the route of transmission and the disease in humans

- Control measures at the infection source (usually local reservoir species of animals):
 - Work with communities to reduce certain animal reservoir populations, particularly rodents, when they live close to human habitations.
 - Separate animal reservoirs from human habitations (for example with fences and screens).
 - Immunize dogs and livestock against leptospirosis.
 - Remove waste and keep areas around human habitations clean.
 - Dispose of excreta from domestic animals through regular cleaning, particularly in farming facilities, to avoid contamination.
 - Encourage people not to leave food around, especially in recreational areas where rats may be present.
 - Improve living conditions (for both humans and domesticated animals) and sanitation systems.
- Measures to prevent transmission by avoiding contact with animal urine, infected animals or an infected environment include:
 - Wear protective clothing such as rubber boots and gloves when working conditions allow.
 - Cover skin lesions with waterproof dressings.
- Prevent access to or give adequate warning about water bodies known or suspected to be contaminated.
- Wash or shower as soon as possible after exposure to urine splashes or potentially contaminated water.
- Wash and clean wounds.
- Strictly maintain the above hygienic measures during care and handling of animals.
- Where feasible, disinfect contaminated areas (for example scrub floors in stables, butcheries and abattoirs).
- Consume clean drinking water.
- Measures at the level of the human host:
 - Raise awareness in and provide education to both the general population and at-risk groups including information on the disease, how to avoid risks, and the importance of timely diagnosis and medication.
 - Ensure that doctors and veterinarians consider leptospirosis as part of the differential diagnosis in appropriate cases.
 - Use antibiotic prophylaxis for known exposures (for example laboratory accident or other high-risk exposure such as professionals involved in rescue operations after flooding in endemic areas).
 - Immunization in humans is recommended for occupational exposure. However, few human vaccines are available, and they are serogroup specific. Indication is consequently limited and must be evaluated case by case.

9

During leptospirosis outbreaks, strategic control measures include early detection and treatment

- Leptospirosis outbreaks may occur after natural disasters resulting in a high number of severe cases.
- Control measures in outbreak situations include:
 - Emphasize and prioritize early case detection.
 - Provide empirical treatment for all probable cases.
 - Provide the population with treated water.
 - Provide targeted chemoprophylaxis and protective equipment to very high-risk populations (for example rescue, sewage and sanitation workers); mass prophylaxis to the general population is not recommended.
 - During outbreaks, rodent control and animal immunization are not effective control strategies.



10

A One Health approach that is multisectoral and holistic is critical for leptospirosis prevention and control

- The global incidence of leptospirosis is estimated to be 1 million cases including 60 000 deaths, yet it remains an understudied and under-reported disease.
 - Leptospirosis transmission dynamics are complex and poorly understood, symptoms are not specific and laboratory diagnosis is complex.
 - A One Health approach is critical to prevent and control this environmental disease that affects both humans and animals.
- Relationships among animals, humans and ecosystems need to be considered to better understand and manage the disease.
- Research and control efforts require a truly integrated, multidisciplinary and coordinated approach to improve prediction, detection, prevention and response to outbreaks of leptospirosis.



More information about leptospirosis:

- Human leptospirosis: guidance for diagnosis, surveillance and control
<https://www.who.int/publications/i/item/human-leptospirosis-guidance-for-diagnosis-surveillance-and-control>
- Leptospirosis Fact Sheet
<https://www.who.int/publications/i/item/B4221>
- Leptospirosis Outbreak Toolkit
<https://www.who.int/emergencies/outbreak-toolkit/disease-outbreak-toolboxes/leptospirosis-outbreak-toolbox>
- OpenWHO course on Leptospirosis
<https://openwho.org/courses/pandemic-epidemic-diseases>
- Global Leptospirosis Environmental Action Network (GLEAN) website
<https://sites.google.com/site/gleanlepto/>



Meningococcal meningitis

10 THINGS YOU SHOULD KNOW



1. Meningococcal meningitis is an acute bacterial form of meningitis caused by *Neisseria meningitidis*
2. Meningococcal meningitis occurs worldwide, but the highest burden is in the African meningitis belt
3. Several types of *N. meningitidis* can cause epidemics
4. Meningococcal meningitis can have a fatality rate of up to 50% when untreated
5. Specific vaccines are used for prevention and outbreak response
6. Laboratory diagnosis is essential
7. Surveillance is critical to detect outbreaks and inform the epidemic response
8. Early antibiotic treatment is key to saving lives and reducing complications
9. Antibiotics reduce transmission risk for close contacts when given promptly
10. WHO and partners are developing a global Defeating Meningitis by 2030 strategy

Meningococcal meningitis response tips

Collaborative surveillance

- Identify the pathogen; if it is *meningococcus*, identify the serogroup through laboratory testing.
- Monitor whether incidence thresholds defined for alerts or outbreaks are being crossed (thresholds are defined according to specific regional or country epidemiology). This may trigger emergency vaccination.

Community protection

- Encourage health authorities to ensure populations receive the appropriate vaccine during outbreak response.
- Key messages are:
 - Human-to-human transmission occurs through droplets of respiratory or throat secretions.
 - Asymptomatic carriers can transmit the disease.
 - It is important to practice hand hygiene and respiratory hygiene.
 - Early antibiotic treatment is crucial to reduce mortality and complications.
 - Early recognition of symptoms is essential for seeking rapid medical treatment.

Clinical care

- Early antibiotic treatment.
- Prophylaxis for close contacts (according to local epidemiology, prophylaxis is not recommended in epidemic situations in the African meningitis belt).

Access to countermeasures

- Prompt vaccination campaigns (according to local epidemiology).

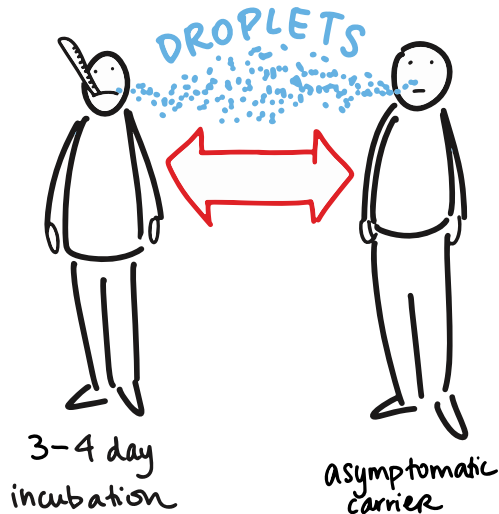
Emergency coordination

- Establish an epidemic preparedness and response committee before the epidemic season.
- Ensure strong collaboration among surveillance officers, clinicians and national reference laboratory officers.
- Contact the ICG for emergency vaccines and antibiotics.

1

Meningococcal meningitis is an acute bacterial form of meningitis due to *Neisseria meningitidis*

- *N. meningitidis* can affect diverse areas of the body, including the brain.
- Invasive meningococcal disease (IMD) encompasses the various diseases caused by *N. meningitidis* including meningitis and septicemia (most commonly), but also arthritis, myocarditis, pericarditis, invasive pneumonia, necrotizing fasciitis and endophthalmitis.
- *N. meningitidis* only infects humans. There is no animal reservoir.

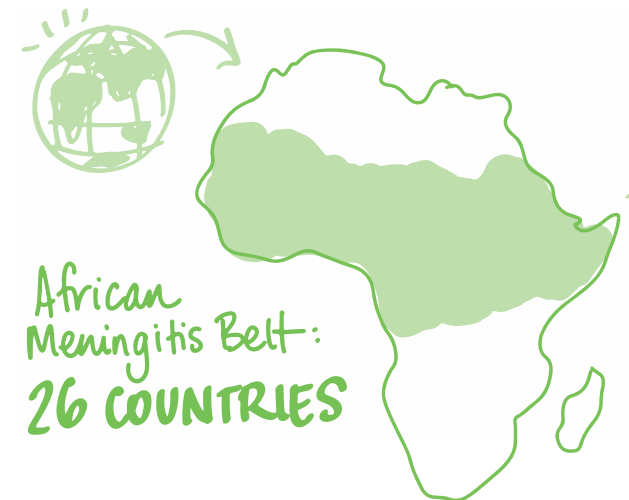


- The bacteria can be carried in the throat (asymptomatic carrier).
- Sometimes, it can overwhelm the body's defenses and spread through the bloodstream to the brain, causing meningitis.
- The bacteria are transmitted from person to person through droplets of respiratory or throat secretions from carriers.
- Smoking, close and prolonged contact – such as kissing, sneezing or coughing on someone, or living in close quarters with an infected person (a carrier) – facilitate the spread of the disease.
- Asymptomatic carriers can transmit the disease. It is believed that 1–10% of the population carries *N. meningitidis* in the throat in endemic situations. In epidemics, the carriage rate is higher (up to 10–25%).
- Transmission of *N. meningitidis* can occur during mass gatherings (for example the Hajj pilgrimage, jamborees).
- Infants and young adults are most at risk of infection.
- The incubation period is 2–10 days, usually 3–4 days.

2

Meningococcal meningitis occurs worldwide, but its highest burden is in the African meningitis belt

- The highest burden is observed in the meningitis belt that stretches across Africa from Senegal to Ethiopia and impacts 26 countries.
- The meningitis belt is affected by seasonal endemicity and cyclical large-scale epidemics during the dry season (December to June).



3

Several types of *N. meningitidis* can cause epidemics

- *N. meningitidis* serogroups are named by a letter (A, B, C, etc.).
- Six (of 12) serogroups (A, B, C, W, X, Y) can cause large epidemics. Geographic distribution differs according to serogroup.
- Before 2010 in the meningitis belt, serogroup A *meningococcus* accounted for an estimated 80-85% of all cases.
- Since the introduction of a new and very effective meningococcal A conjugate vaccine through mass preventive immunization campaigns, the proportion of serogroup A has declined dramatically.
- Since 2013, a new hyperinvasive strain of serogroup C has been circulating in the region causing outbreaks in West Africa.
- In Europe, introduction of routine vaccination for serogroup C led to the decline of serogroup C outbreaks.
- Independent of vaccination strategies, the epidemiology of serogroups fluctuates over time and space for reasons that are not fully understood.



4

Meningococcal meningitis can have a fatality rate of up to 50% when untreated

- The most common symptoms are high fever, headache, stiff neck, vomiting, confusion, sensitivity to light and bulging of the fontanelle in infants.
- Sometimes, a rash, ranging from a few petechiae (pinprick like red or purple spots on the skin) to widespread ecchymoses (bruise-like purpuric or red rash), occurs because of septicemia.
- Even when the disease is diagnosed early and adequate treatment is started, 8–15% of patients die, often within 24–48 hours after the onset of symptoms.
- If untreated, the disease is fatal in 50% of cases.
- After recovery, 10–20% of patients experience impairments (sequelae) such as seizures, hearing loss, vision loss, cognitive impairment, neuromotor disability, memory and behavior changes and limb loss.



5

Specific vaccines are used for prevention and outbreak response

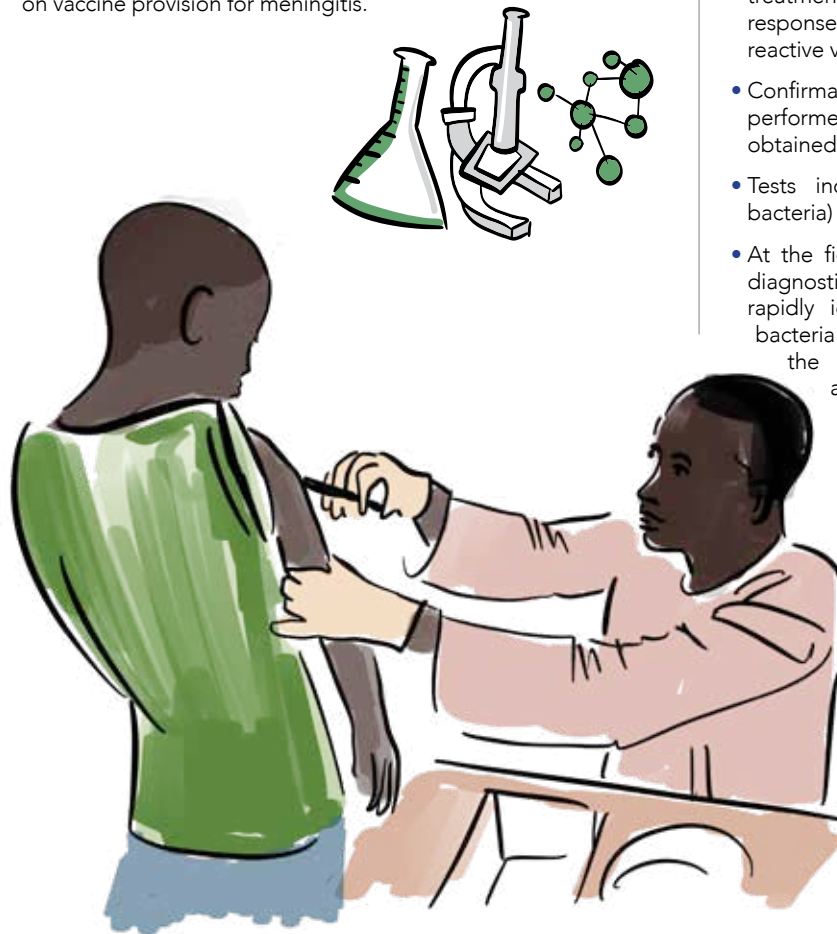
- Vaccines are serogroup specific and confer varying degrees of duration of protection.
- Three types of vaccines are available:
 - Polysaccharide vaccines are used for outbreak response mainly in Africa but are being progressively replaced by conjugate vaccines.
 - They offer 3-year protection but do not induce herd immunity.
 - They are trivalent (A, C and W).
 - Polysaccharide vaccines are not effective before 2 years of age.
 - Conjugate vaccines are used in prevention (in routine immunization schedules) and outbreak response. They confer longer-lasting immunity, prevent carriage and induce herd immunity. Available vaccines include:
 - Monovalent C and tetravalent (serogroups A, C, Y and W): Cost prevents the use of these vaccines on a large scale in low-income countries.
 - Monovalent A: This vaccine is used for mass preventive campaigns and routine infant immunization in African meningitis belt countries.
 - Protein-based vaccine against serogroup B protect against meningitis in all ages but are not thought to prevent carriage and transmission so do not lead to herd protection.

- Reactive vaccination in affected and at-risk populations should be conducted promptly to prevent the spread of disease during outbreaks.
- An international vaccine stockpile can be accessed by any country facing an outbreak, through a request to the ICG on vaccine provision for meningitis.

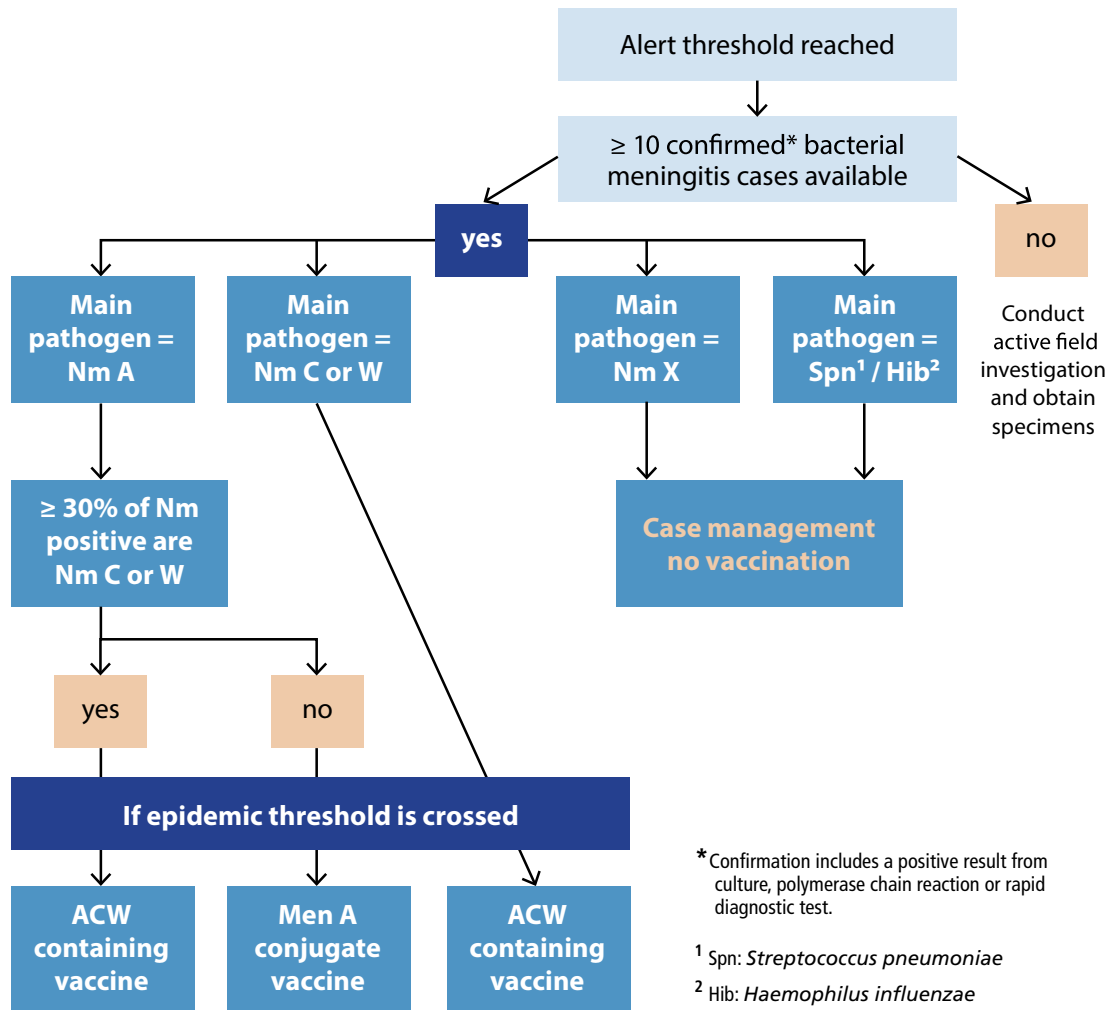
6

Laboratory diagnosis is essential

- A variety of other organisms, including bacteria, fungi and viruses can cause meningitis.
- Rapid confirmation of the pathogen is critical to determine the appropriate treatment, and to guide the epidemic response including determining if reactive vaccination is appropriate.
- Confirmation requires a laboratory test performed on cerebrospinal fluid (CSF) obtained through lumbar puncture.
- Tests include culture (growing the bacteria) and PCR.
- At the field level, rapid point-of-care diagnostic tests should be used to rapidly identify the *N. meningitidis* bacteria and the serogroups. However, the performance of currently available rapid tests does not allow for definitive case confirmation.



Indicative decision tree for meningitis vaccine choice in a reactive vaccination campaign



REMEMBER

If there are NmA cases in the population already vaccinated with MenA conjugate, conduct field investigation.

Source: WHO, *Managing meningitis epidemics in Africa*, Revised 2015

7

Surveillance is critical to detect outbreaks and inform the epidemic response

- Surveillance systems should be tailored to detect cases and outbreaks and to monitor disease trends and vaccine impact. Epidemiological and laboratory data should be linked.
- It is recommended to conduct IMD surveillance in all countries. However, meningitis surveillance (focusing on three main vaccine preventable bacterial causes of meningitis) should still be implemented in countries with a significant burden of bacterial meningitis or limited laboratory confirmation capacity (such as countries of the African meningitis belt).
- The definition of a meningococcal meningitis outbreak varies from country to country, based on local epidemiology and a comprehensive analysis of surveillance data.
- In the African meningitis belt, standard case definitions are:
 - Suspected case (based on clinical presentation): any person with sudden onset of fever ($>38.5^{\circ}\text{C}$ rectal or 38.0°C axillary) and neck stiffness or another meningeal sign including bulging fontanelle in infants and toddlers.
 - Probable case (based on non-specific laboratory test): any suspected case with macroscopic aspect of CSF turbid, cloudy or purulent, or with a CSF leukocyte count >10 cells/mm³, or with bacteria identified by Gram stain in

CSF, or positive antigen detection (for example by latex agglutination test) in CSF.

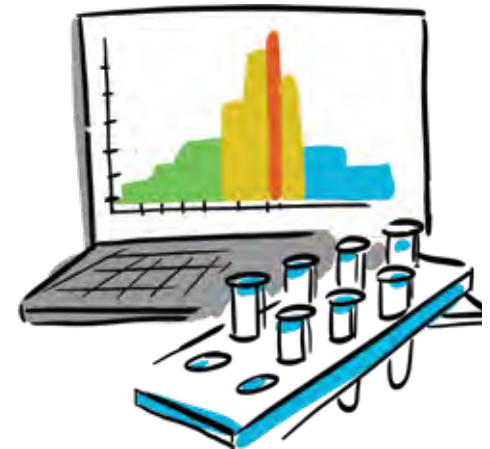
- In infants: CSF leucocyte count >100 cells/mm³; or CSF leucocyte count 10-100 cells/mm³ AND either an elevated protein (>100 mg/dl) or decreased glucose (<40 mg/dl) level.
- Confirmed (based on laboratory test): any suspected or probable case that is laboratory confirmed by culturing or identifying *N. meningitidis* in the CSF or blood.
- In the African belt, incidence thresholds that will trigger prevention and control interventions are shown in the table below.



8

Early antibiotic treatment is key to saving lives and reducing complications

- Prompt treatment (within one hour of diagnosis) is crucial to prevent death and complications.
- Five days of ceftriaxone IV (seven days in infants 0–2 months old) is recommended as a standard treatment during meningococcal epidemics in the African meningitis belt.
- Admission to a hospital or health centre is recommended, although patients do not require isolation.
- If there is no improvement in patients' condition within 48 hours of treatment or if exhibiting convulsions or comatose, they should be transferred to higher-level health facility.



Incidence thresholds for detection and control of epidemic Meningococcal meningitis (2014)

Intervention	POPULATION	
	30,000 – 100,000	Under 30,000
Alert threshold — Inform authorities — Strengthen surveillance — Investigate — Confirm (including laboratory) — Prepare for eventual response	<ul style="list-style-type: none"> 3 suspected cases / 100,000 inhabitants / week (Minimum of 2 cases in one week) 	<ul style="list-style-type: none"> 2 suspected cases in one week Or <ul style="list-style-type: none"> An increased incidence compared to previous non-epidemic years
Epidemic threshold — Mass vaccination within four weeks of crossing the epidemic threshold — Distribute treatment to health centres — Treat according to epidemic protocol — Inform the public	<ul style="list-style-type: none"> 10 suspected cases / 100,000 inhabitants / week 	<ul style="list-style-type: none"> 5 suspected cases in one week Or <ul style="list-style-type: none"> Doubling of the number of cases in a three-week period (e.g. <i>Week 1</i>: 1 case, <i>Week 2</i>: 2 cases, <i>Week 3</i>: 4 cases)
	If a neighbouring area to a population targeted for vaccination is considered to be at risk (e.g. cases early in the dry season, no recent relevant vaccination campaign, high population density), it should be included in a vaccination programme.	
	In special situations such as mass gatherings, refugees, displaced persons or closed institutions, two confirmed cases in a week should prompt mass vaccination.	

Source: WHO, *Managing meningitis epidemics in Africa*, Revised 2015

9

Antibiotics reduce transmission risk for close contacts when given promptly

- Chemoprophylaxis is recommended for close contacts within the household.
- However, in the meningitis belt, chemoprophylaxis for close contacts is recommended only in non-epidemic situations.
- Ciprofloxacin is the antibiotic of choice, with ceftriaxone an alternative.

10

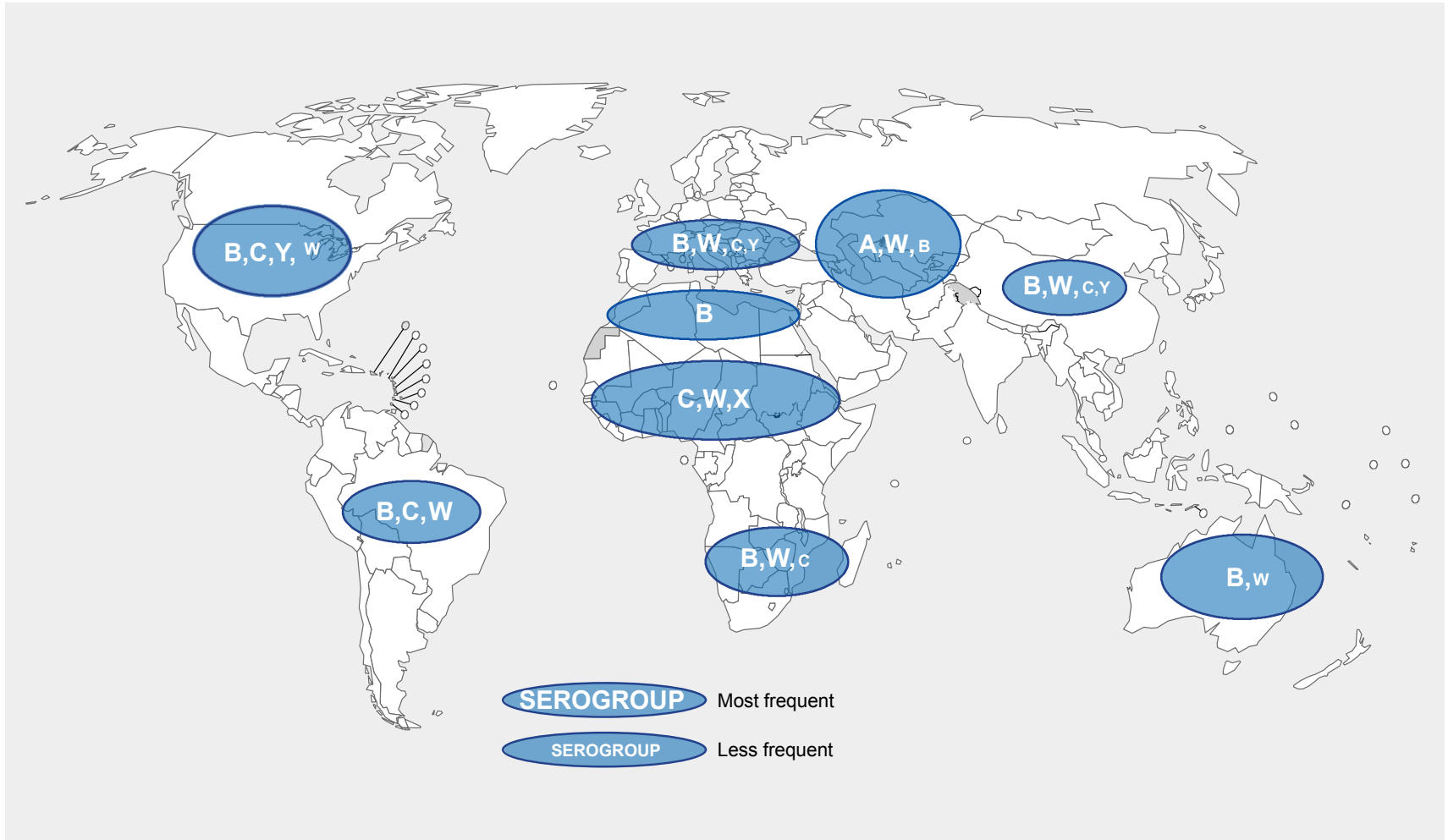
WHO and partners have developed a global Defeating Meningitis by 2030 strategy

- The strategy was introduced in answer to a call for action by countries and partners. In November 2020, the 73rd World Health Assembly endorsed a resolution to implement prevention and control actions through the global strategy.
- It is structured around five pillars:
 - Prevention and epidemic control: Development and enhanced access to affordable vaccines, effective prophylactic measures and targeted interventions.
 - Diagnosis and treatment: Access to appropriate diagnostic tests at all levels of care, health worker training and prompt and effective treatment.
 - Disease surveillance: Covering all main causes of bacterial meningitis and their sequelae to guide meningitis control policies and accurately monitor progress toward goals.
 - Support and care for patients and their families after meningitis: Effective systems for timely identification and management of sequelae; people and families affected by meningitis can access appropriate support and care services that meet their needs.
 - Advocacy and information: Raise public and political awareness of meningitis as a health priority, improve health-seeking behavior and access to control measures.

EFFECTIVE ANTIBIOTICS



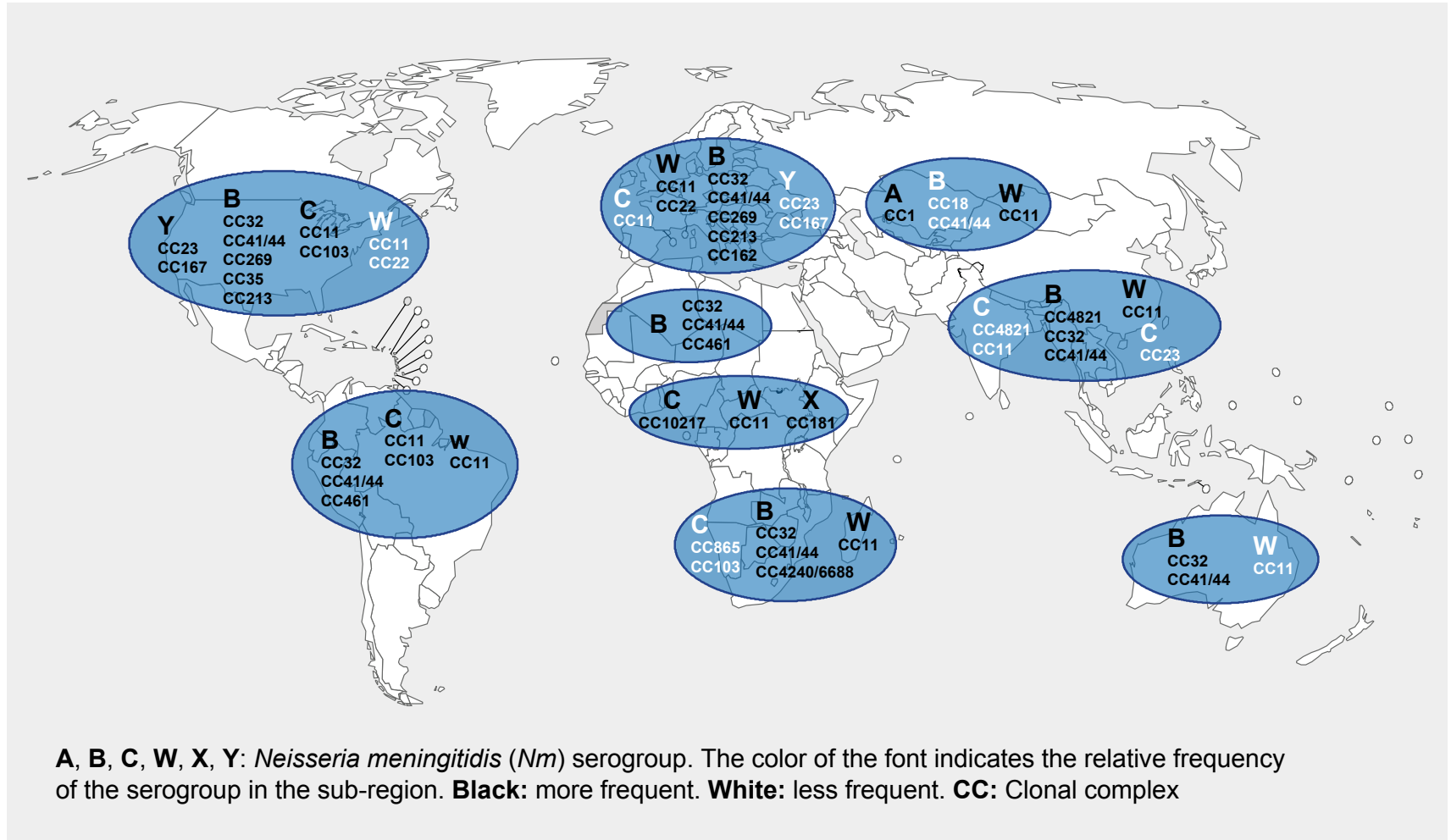
Invasive Meningococcal Disease – Serogroup distribution, 2018



Source: WHO Collaborating Centers for Meningitis

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
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Invasive Meningococcal Disease – Nm serogroup and clonal complex distribution, 2019



Source: WHO Collaborating Centers for Meningitis

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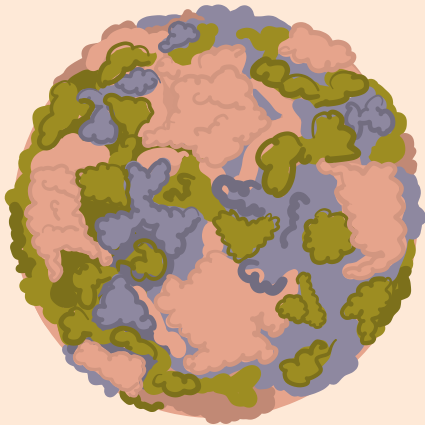
More information about meningococcal meningitis:

- Meningococcal meningitis WHO webpage
<http://www.who.int/csr/disease/meningococcal/en/>
- OpenWHO course on Pandemic and epidemic diseases
<https://openwho.org/courses/pandemic-epidemic-diseases>
- Meningococcal meningitis WHO fact sheet:
<http://www.who.int/mediacentre/factsheets/fs141/en/>
- Managing meningitis epidemics in Africa
<https://apps.who.int/iris/handle/10665/154595>
- Defeating meningitis by 2030: a global road map
<https://www.who.int/publications/i/item/9789240026407>
- International Coordinating Group (ICG) on vaccine provision for meningitis
<https://www.who.int/csr/disease/meningococcal/icg/en/>
- Vaccine preventable diseases surveillance standards for meningococcus
https://www.who.int/immunization/monitoring_surveillance/burden/vpd/WHO_SurveillanceVaccinePreventable_12_Meningococcus_R2.pdf?ua=1
- Standard operating procedures for surveillance of meningitis preparedness and response to epidemics in Africa
<https://apps.who.int/iris/bitstream/handle/10665/312141/9789290234241-eng.pdf>



Poliomyelitis

10 THINGS YOU SHOULD KNOW



TYPE 1

TYPE 2

TYPE 3

1. Poliomyelitis is a paralytic disease that mainly affects young children
2. Humans are the only natural reservoir for poliovirus
3. The faecal-oral route is the main route of poliovirus transmission
4. Diagnosis of poliomyelitis is critical for outbreak response and eradication of the disease
5. With no specific treatment for polio, vaccination is the cornerstone of polio eradication
6. Vaccine-derived polioviruses can emerge in rare instances in areas of low population immunity and can be the cause of outbreaks
7. Surveillance is key to identifying polio cases and ensuring eradication
8. The world is standing at the last mile of polio eradication
9. If a single child remains infected, children in all countries are at risk of contracting polio
10. All countries must plan for the eventuality of a poliovirus importation or emergence

Poliomyelitis response tips

Collaborative surveillance

- Ensure early confirmation of poliovirus infection.
- Detect, investigate and notify poliovirus detection to WHO, under the IHR (2005).
- Conduct detailed investigations and risk assessments.
- Implement surveillance response, including acute flaccid paralysis (AFP) surveillance intensification supplemented by environmental surveillance if appropriate.
- Conduct behavioural surveillance and engage communities.

Community protection

- Ensure proper sanitation and hygiene practices.
- Encourage health authorities to:
 - Rapidly detect, notify, investigate and monitor behavioural risks for polio.
 - Set up advocacy, communication and social mobilization structures.
 - Ensure high-quality and enhanced surveillance for timely detection of outbreaks.
 - Engage communities to participation in outbreak investigation, surveillance strengthening and vaccination services utilization.
- Key messages are:
 - Polio is transmitted through the faecal-oral route.
 - Oral polio vaccination used alone or sequentially with injected polio vaccination stops the transmission of the virus.
 - Practice good sanitation and hygiene (safe disposal of waste and regular handwashing) to reduce transmission risk.

Clinical care

- Treatment of polio is primarily to relieve symptoms.

Access to countermeasures

- Implement a vaccination response:
 - Intensify routine Expanded Programme on Immunization (EPI) immediately.
 - Plan to start supplemental immunization activities within 14 days of poliovirus notification.
 - Define routine immunization strengthening priorities for EPI recovery planning.

Emergency coordination

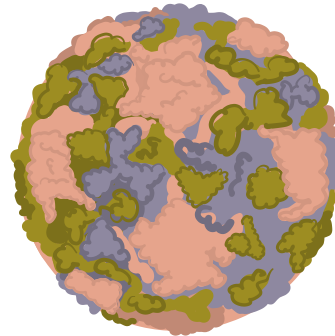
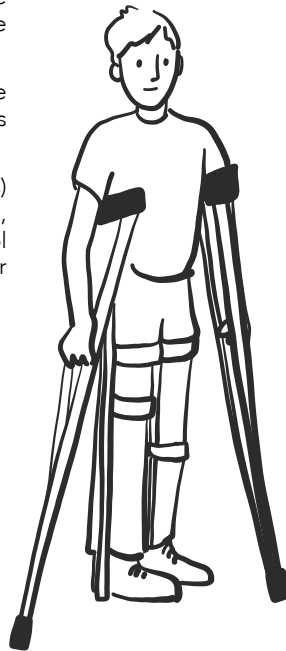
- Establish a national Emergency Operations Centre (EOC) supported by representatives from all Global Polio Eradication Initiative (GPEI) partners.¹
- International spread of poliovirus is a PHEIC, ensure adherence to temporary recommendations issued by the Emergency Committee under the IHR (2005).
- Establish outbreak response planning task teams within the country including rapid response team for coordination of detailed investigations, as well as teams for surveillance, laboratory, communications, and vaccination response.
- Engage with civic, political, religious and community leaders and influencers.
- Ensure coordination with Headquarters (WHO, UNICEF, CDC) and Regional Offices (WHO and UNICEF).

¹ WHO, Rotary International, the US Centers for Disease Control and Prevention, UNICEF and the Bill & Melinda Gates Foundation

1

Poliomyelitis is a paralytic disease that mainly affects young children

- Polio is one of the well-known causes of AFP, which is the sudden onset of paralysis/weakness in any part of the body. However, it is difficult to clinically distinguish AFP caused by poliovirus infection from that caused by other viruses/diseases.
- One in 200 polio infections leads to paralysis, usually in the legs.
- Asymptomatic polio virus infections do occur and can be responsible for transmission of the polio virus to others.
- Among those paralyzed, 5–10 % die when their breathing muscles become immobilized.
- Children under 5 years of age are the most at-risk population for polio virus infection.
- All children (usually under 15 years) who get AFP must be investigated, including collection of two stool specimen samples, to confirm or exclude polio as a cause.



2

TYPE 1
TYPE 2
TYPE 3

Humans are the only natural reservoir for poliovirus

- Poliomyelitis is a viral disease caused by the poliovirus, which belongs to the genus Enterovirus in the family Picornaviridae.
- Three serotypes exist: 1, 2 and 3. None can survive for long outside the human body. If the virus cannot find an unvaccinated person to infect, it will die out.
- Type 1 wild poliovirus (WPV) is the most virulent and common.
- The last type 2 WPV was detected in 1999 and was declared globally eradicated in September 2015. In turn, oral polio vaccination against type 2 was stopped in 2016 in a globally synchronized trivalent OPV (tOPV) to bivalent OPV (bOPV) switch. However, type 2 vaccine-derived polio outbreaks continue to occur.
- The last type 3 WPV case was reported in November 2012 and was declared globally eradicated in October 2019.
- Type-specific immunity of lifelong duration follows both clinically recognizable and inapparent infections or vaccination with polio vaccines (OPV only or sequential OPV plus IPV schedules). Second attacks of poliovirus infection are rare and result from infection with a poliovirus of a different serotype.

3

The faecal-oral route is the main route of poliovirus transmission

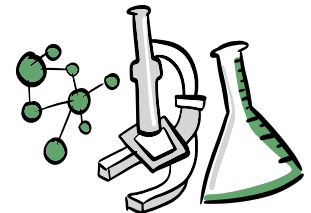
- In most developing countries, the virus is commonly transmitted from person to person through the faecal-oral route by a common vehicle (contaminated water or food).
- The virus enters the mouth, infecting the first cells with which it comes into contact in the pharynx or intestines. The virus begins to replicate soon after, before spreading to the tonsils, the intestinal lymphoid tissues, and the cervical and mesenteric lymph nodes, where it multiplies abundantly. Since the virus also replicates in the upper respiratory tract, polioviruses can spread through upper respiratory tract secretions.
- Once the intestinal mucosa and lymph node replications are established, the virus is absorbed into the bloodstream (viremia), which allows the poliovirus to spread throughout the body and invade the nervous system to cause paralysis.
- The incubation period ranges from 4–35 days, with a common range of 7–14 days for paralytic cases.
- Provision of clean water and improved hygiene practices and sanitation are important for reducing the risk of transmission.
- In areas with good sanitary conditions and uncontaminated drinking water, other routes of transmission (for example exposure to polioviruses in vaccine manufacturing and antiviral facilities or gene science and research laboratories) are more important.

4

Diagnosis of poliomyelitis is critical for outbreak response and eradication of the disease

- Since agents other than polioviruses can cause AFP (for example other enteroviruses, echoviruses, West Nile virus, adenoviruses), all cases of AFP among children under 15 years of age should be reported and tested for wild poliovirus or vaccine-derived polioviruses.
- All AFP cases should be identified and subjected to systematic investigation as suspected cases of polio infection, including collection of two stool specimens for isolation of poliovirus. Missing the virus in one case means that a thousand asymptomatic infections have been missed.
- Poliovirus can be detected in different specimens but faeces (stool) is the recommended specimen of choice.
- Global Polio Laboratory Network (GPLN) member laboratories follow standardized protocols for virologic testing of stool and environmental samples:
 - Isolation of poliovirus.
 - Typing of isolated virus to determine its serotype and to identify it as wild, VDPV or Sabin.
 - Genetic sequencing to determine its linkage and origin.
- A suspected AFP case whose specimen tests positive for WPV or VDPV is considered a confirmed case and should be reported by the GPLN to the GPEI for immediate response in line with standard operating procedures for polio outbreak response.

- Specimens from an identified AFP case, adequately collected and analysed per certification-standard guidelines, that test negative for poliovirus should be immediately discarded as non-polio AFP. These results are used only to calculate the non-polio AFP rate that determines the sensitivity of the surveillance system.
- A suspected case with no adequate specimens, no isolation of WPV or VDPV from the case or close contacts, and residual paralysis after 60 days, and that is deemed by the national expert review committee to be clinically and epidemiologically compatible with the disease, may be classified as compatible poliomyelitis. National programmes should conduct a detailed investigation, surveillance and vaccination response for all polio-compatible cases.
- During investigation of polio-compatible cases or positive environmental samples, isolation of polioviruses from contacts or healthy community contacts can also be used to confirm community infection and determine poliovirus transmission. Isolation of poliovirus from close contacts should be used to confirm infection in a primary AFP case whose specimens were collected late. Isolation of poliovirus from sampling of healthy children in the community is used to confirm local transmission.



5

With no specific treatment for polio, vaccination is the cornerstone of polio eradication

- Treatment of polio is primarily to relieve symptoms.
- Heat and physical therapy are used to stimulate the muscles and antispasmodic drugs are given to relax the muscles.
- Although these interventions can improve mobility, they cannot reverse permanent polio paralysis.
- Polio vaccine, given at least four times, almost always protects a child for life. Two different vaccines are used in polio vaccination:
 - Oral polio vaccine (OPV): Made in varied virus combinations, this vaccine initially contained all three poliovirus serotypes and was popularly known as trivalent OPV (tOPV) made of attenuated (weakened) virus. As of April 2016, tOPV is no longer produced or in use because of the eradication of wild type 2 virus in 1999. It has since been replaced with bivalent OPV (bOPV) containing only serotypes 1 and 3 or monovalent formulations containing one poliovirus serotype (mOPV1, mOPV2 and mOPV3 containing poliovirus serotypes 1, 2 and 3, respectively). This also limits the risk of new cases of circulating vaccine-derived type 2 polioviruses (cVDPV2).

- Inactivated polio vaccine (IPV): Administered by injection, this protects against poliovirus types 1, 2 and 3.
- Because OPV is an oral vaccine, it does not require administration by a health professional. It is therefore easy to administer in mass vaccination campaigns. OPV is also inexpensive.
- OPV and IPV each has advantages, and both vaccines are necessary to end polio.
- OPV is needed to interrupt person-to-person spread of the virus, thanks to its unique ability to induce mucosal immunity. Used in combination with IPV, it is most effective.
- IPV is used to maintain population immunity levels but on its own is unable to interrupt person-to-person circulation of the virus and hence is not recommended as a standalone tool in outbreak response. High routine immunization levels with IPV do, however, reduce the risk for and consequences of any poliovirus importation or emergence.
- Current eradication strategies recommended by WHO have proven successful and include:
 - High routine infant immunization coverage with at least three doses of OPV plus a dose at birth in polio-endemic countries.
 - National immunization days targeting all children under 5 years, providing an additional opportunity to children who missed their routine dose or had immunization failures.
 - AFP surveillance and laboratory investigations for timely detection of poliovirus infections and immediate response vaccinations.
 - Outbreak response vaccination campaigns to interrupt final chains of transmission.



6

Vaccine-derived polioviruses can emerge in rare instances in areas of low population immunity and can be the cause of outbreaks

- OPV contains an attenuated vaccine virus (Sabin strain), which is a weakened virus that activates an immune response in the body. When a child is vaccinated with OPV, the weakened vaccine virus replicates in the intestine and the virus is excreted in stools for a limited period.
- Sabin virus shedding should be monitored by all programmes. Detection of Sabin-like viruses type 1 and 3 should be monitored at the country level but requires no international notifications. However, detection of Sabin-like viruses type 2 (SL2) in countries/territories that have not used type 2-containing OPV should cause detailed investigation of the source and international notification.
- Circulating vaccine-derived polioviruses (cVDPVs) are extremely rare strains, genetically changed from the original strains contained in OPV. These genetic mutations occur because of prolonged replication in a population where routine or supplementary immunization activities are poorly conducted and large populations susceptible to poliovirus are left unvaccinated. Therefore, low OPV coverage is the most important risk to VDPV/cVDPV emergence.

- Use of type-specific OPV to raise population immunity remains the response of choice for control of cVDPV outbreaks. When type 2 oral polio vaccine (now available as mOPV2 or nOPV2) is used to respond to cVDPV2 outbreaks, countries are expected to follow rigorous protocols to ensure effective stock control and accountability of all vaccines received (unused and used/empty vials).
- The small risk of VDPV/cVDPV emergence is less significant compared to the tremendous public health benefits associated with OPV use in vaccination and polio eradication. Therefore, OPV should be used for all outbreaks with the aim of vaccinating every child to interrupt transmission, regardless of the origin of the poliovirus.



7

Surveillance is key to identifying polio cases and ensuring eradication

- To ensure certification-standard surveillance for polio in all countries, the following indicators should be attained and sustained pending global certification:
 - Identification and investigation of at least 1 AFP case per 100 000 population aged <15 years (including at subnational level).
 - Adequate stool collection and subsequent virologic analysis, including collection of two stool samples at least 24 hours apart and within 14 days of onset of paralysis.
 - All samples processed in a WHO-accredited laboratory of the GPLN.
- Environmental surveillance (for example testing sewage samples for poliovirus) is increasingly used as a supplemental surveillance system to identify poliovirus transmission that might occur in the absence of detected AFP cases.
- Detection of a positive isolate of poliovirus from any environmental sample must result in a detailed investigation, surveillance and vaccination response in accordance with international outbreak response protocols.

8

The world is standing at the last mile of polio eradication

- In 1988, the GPEI was created following a World Health Assembly resolution (WHA 41.28). Prior to this global resolution, polio paralyzed more than 350 000 people a year. Since that time, the number of polio cases has decreased by more than 99%.
- The GPEI launched the Polio Endgame Strategy 2022-2026 to guide the programme and its partners in overcoming the final hurdles to eradication and moving toward sustaining a polio-free future through strategic goals and objectives.
- The two Endgame strategic goals are:
 1. Permanent interruption of all poliovirus transmission in endemic countries.
 2. Stop transmission and outbreaks of vaccine derived polio viruses in non-endemic countries.
- The five Endgame strategic objectives to deliver the goals are:
 1. Create urgency and accountability through advocacy to generate greater political will.
 2. Generate vaccine acceptance through context-adapted community engagement.
 3. Improve frontline success through changes to campaign operations.
 4. Expedite progress through expanded integration and unified partnerships.
 5. Improve detection and response through sensitive surveillance.

- The Emergency Committee under the IHR (2005) considers detection of a polio virus in any part of the world a PHEIC.
- To mitigate risk for international spread of poliovirus, affected Member States must, with support of WHO and all polio eradication partners:
 - Officially declare that interruption of poliovirus transmission is a national health emergency.
 - Ensure that all residents and long-term visitors receive at least three doses of OPV in a well-coordinated outbreak response vaccination campaign.
 - Maintain the above conditions until 1) at least 6 months have passed without detection of poliovirus transmission in the country from any source, and 2) there is documentation of full application of high-quality eradication activities in all affected and high-risk areas.

POLIO GLOBAL ERADICATION INITIATIVE

9

As long as a single child remains infected, children in all countries are at risk of contracting polio

- Two countries have never stopped transmission of wild poliovirus: Afghanistan and Pakistan.
- Polio can spread from these endemic countries to infect children in other countries in which immunization levels are less than adequate.

EVERY
LAST
CHILD



- Every at-risk child living anywhere in the world should therefore be immunized until there is no one left to be infected. This includes those living in the most remote and/or underserved places on the planet.

- Days of Tranquility are negotiated so that vaccination teams can reach

children living in conflict zones. Varied modes of transportation are used – from donkeys to motorbikes to helicopters – to reach children in remote areas or areas with difficult terrain.

- Failure to vaccinate all children with OPV not only leaves the risk of wild polio virus infections but is also increasingly posing risks to emergence of outbreaks of vaccine-derived poliovirus. Therefore, coverage with OPV must be maintained at very high levels (above 90%) in all countries, provinces, districts and communities if a polio-free world is to be attained and sustained.

10

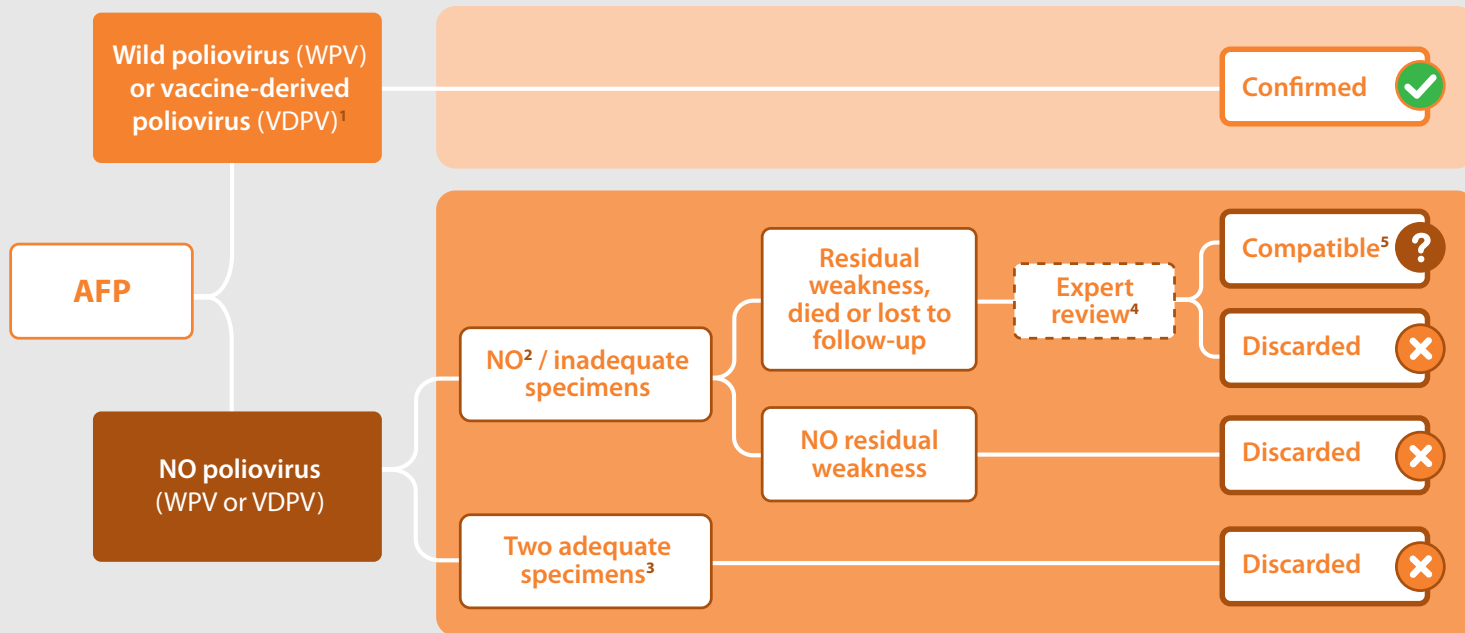
All countries must plan for the eventuality of a poliovirus emergence or importation

- All countries are required to have polio preparedness and response plans as part of their complete country documentation. These plans should be updated and tested routinely BUT not less than annually.
- Polio preparedness and response plans should have actionable interventions aimed at having the highest attainable core capacities for:
 - Timely poliovirus detections: Ensuring that country capabilities for case-based, laboratory-backed surveillance for AFP meet all performance indicators.
 - National adaptation of polio outbreak response standard operating procedures.
 - Trained national capacities in investigation, confirmation, and management of polio outbreaks, and
 - Effective coordination of polio outbreak response interventions using the incident management system.
- Planning and conducting polio preparedness simulation exercises is one strategic action to develop and maintain core capacities for polio outbreak responses.
- As soon as poliovirus is identified, the GPLN will inform the health authorities of the affected country.
 - Because international spread of poliovirus is a PHEIC, ensure adherence to temporary recommendations issued by the Emergency Committee under the IHR (2005), including:
 - Declare an outbreak a national public health emergency,
 - Ensure head-of-government oversight of outbreak response and
 - Explore vaccination of international travellers.
 - The national health authority, through the established IHR (2005) focal point, notifies the GPEI partners of a new poliovirus infection, or the spread of poliovirus to a new geographic area or population, to rapidly initiate the following response actions:
 - Detailed investigation and risk assessment.
 - Enhanced surveillance to increase sensitivity and confidence that any ongoing person-to-person transmission of poliovirus will be rapidly detected.
 - Planning of a vaccination response: All outbreaks (VDPV or WPV) require a vaccination response with an appropriate type-specific OPV within 14 days of laboratory notification.
 - To carry out these activities, establish outbreak response planning task teams within the country including:
 - Rapid response team for coordination of detailed investigations.

- Surveillance team to define surveillance intensification interventions.
- Laboratory team to define the scope and needs for an expected surge in AFP case/contact samples and/or increased environmental surveillance sampling.
- Vaccination response team to analyse the country's immunity profile and define the vaccination scope, target and strategies.
- Communications team to define the key behavioural factors of the epidemic and the programme and public communication strategies/interventions to address these factors.



Algorithm for classification of AFP cases, used by National Polio Expert Committees



¹ Isolation of poliovirus (WPV or VDPV) from a contact of an AFP case is also used to confirm poliovirus infection of the AFP case.

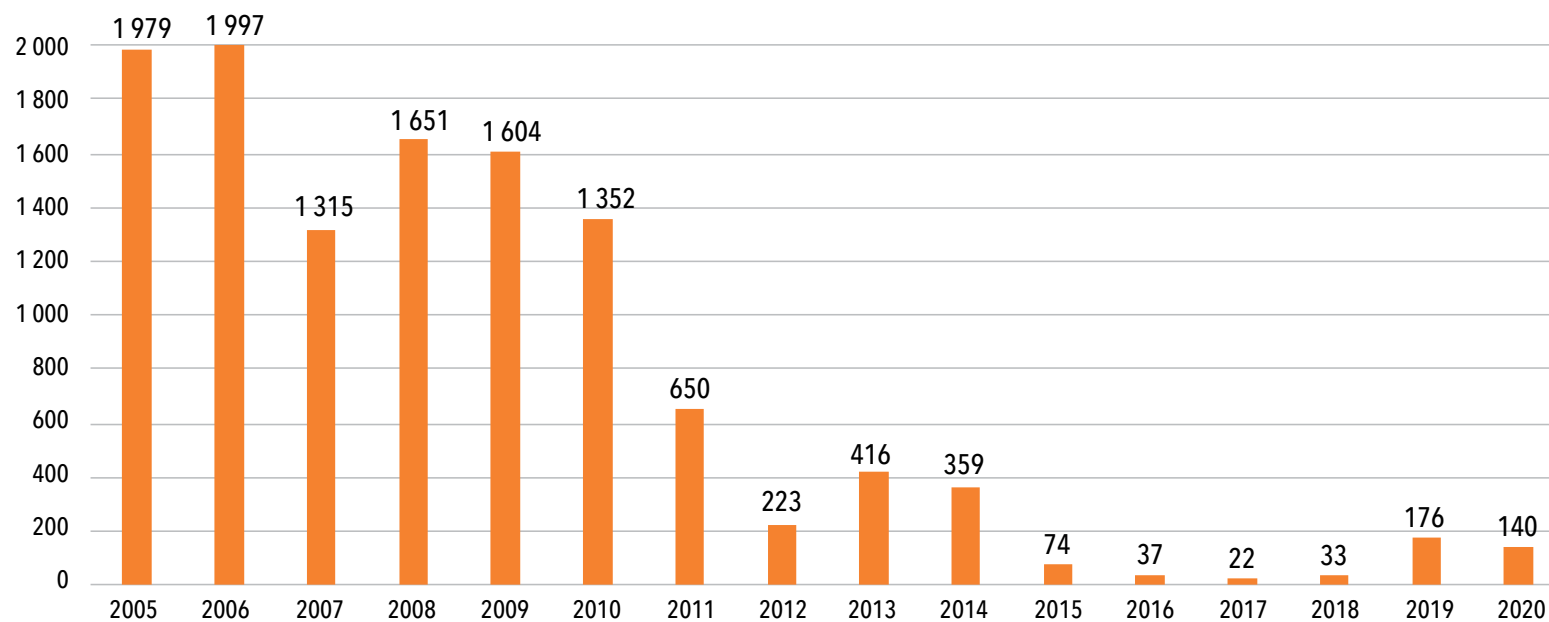
² All cases reported between 2 to 6 months after date of onset must be investigated even though a stool specimen is not collected on them. They follow the follow up needed for those with inadequate stools

³ Adequate specimens are two specimens (at least 8 grams) collected within 14 days of paralysis onset, at least 24 hours apart, and arriving at a WHO-accredited laboratory in good condition (no evidence of desiccation or leakage, and evidence that reverse cold chain was maintained).

⁴ Cases undergoing expert review and subsequently classified as 'discarded' or 'compatible' should be line listed.

⁵ Compatible cases represent a surveillance failure and should be scrutinised for clustering in space and time.

Globally reported wild poliovirus cases: 2005-2018



Source: WHO

Polio-affected countries in 1988 and 2021



Source: WHO

More information about poliomyelitis:

- Polio WHO webpage
<https://www.who.int/topics/poliomyelitis/en/>
- Poliomyelitis WHO fact sheet
<https://www.who.int/en/news-room/fact-sheets/detail/poliomyelitis>
- Polio Global Eradication Initiative webpage
<https://www.polioeradication.org>
- Polio Endgame Strategy 2022-2026
<https://polioeradication.org/gpei-strategy-2022-2026/>



PART III

Tool boxes

TOOL BOX 1

The role of WHO

WHO mandate, in light of infectious diseases

WHO is the directing and coordinating authority on international health within the United Nations' system, by its six main functions:

1. Providing leadership on matters critical to health and engaging in partnerships where joint action is needed

Example

- WHO is:
 - Working with countries to increase and sustain access to prevention, treatment and care.
 - Identifying priorities and setting strategies.
 - Leading and coordinating the health response during emergencies
<https://healthcluster.who.int>
- Through the IHR (2005), WHO helps the countries to strengthen their national core capacities for emergency risk management to prevent, prepare for, respond to and recover from health emergencies.



2. Shaping the research agenda and stimulating the generation, translation and dissemination of valuable knowledge

Example

- WHO Research & Development Blueprint is a global strategy and preparedness plan that allows the rapid activation of R&D activities during epidemics. Its aim is to fast-track the availability of effective tests, vaccines and medicines that can be used to save lives and avert large scale crisis. <http://www.who.int/blueprint/en/>
- The WHO public health research agenda for influenza provides a framework reflecting public health research priorities for pandemic, zoonotic and seasonal epidemic influenza to reduce the risk of emergence of pandemic influenza, limit the spread of pandemic, zoonotic and seasonal epidemic influenza, minimize the impact of epidemics, optimize the treatment of patients and promote the development of modern public health tools. <https://apps.who.int/iris/handle/10665/259892>
- The MERS-CoV research agenda has been developed by WHO to address key unknowns for this virus focusing on five major areas of research: i) virus origin and characteristics, ii) epidemiology and transmission, iii) clinical management and IPC measures, iv) product development and implementation, and v) impact of interventions and operational research. <http://www.who.int/emergencies/mers-cov/en/>



TOOL BOX 1



3. Setting norms and standards and promoting and monitoring their implementation

Example

- WHO developed a pocketbook to provide guidance on best management practices for Viral Haemorrhagic Fevers across health care facilities. <https://apps.who.int/iris/handle/10665/205570>
- WHO developed a rapid advance guideline on recommendations for the use of Personal Protective Equipment for use in a filovirus disease outbreak. <https://apps.who.int/iris/handle/10665/251426>
- Adhering to evidence-based approaches with critical appraisal. <https://www.who.int/groups/guidelines-review-committee>

4. Articulating ethical and evidence-based policy options

Example

- WHO publishes vaccine position papers, providing global vaccine and immunization recommendations that have an international public health impact. WHO position papers follow the recommendations of the WHO Strategic Advisory Group (SAGE) on immunization. The update of vaccine position paper depends on the availability of new scientific evidence and public health priorities. <https://www.who.int/teams/immunization-vaccines-and-biologicals/policies/position-papers>
- The WHO Research Ethics Review Committee (ERC) ensures that WHO only supports research of the highest ethical standards. The ERC reviews all research projects involving human participants supported either financially or technically by WHO. <https://www.who.int/groups/research-ethics-review-committee/guidance-for-submissions-of-documents>

5. Providing technical support, catalyzing change and building sustainable institutional capacity

Example

- WHO has developed a web-based platform offering online courses to transfer knowledge on infectious diseases and improve preparedness and response to epidemics. Courses include global knowledge on managing epidemics and public health interventions, as well as disease-specific knowledge.

OpenWHO Massive Open Online Courses (MOOCs):
<https://openwho.org/>

6. Monitoring the health situation and assessing health trends

Example

- WHO conducts regular global risk assessments regarding infectious diseases and assesses the risk for any event which could have public health impact.
- WHO publishes a summary of epidemiological situation and risk assessments of events that are being monitored through the disease outbreak news.
<https://www.who.int/emergencies/disease-outbreak-news>
- WHO also disseminates epidemiological information on outbreaks and on communicable diseases of public health importance through the Weekly Epidemiological Record.
<https://www.who.int/publications/journals/weekly-epidemiological-record>



TOOL BOX 1

WHO and the International Health Regulations (IHR) creation: A need for global cooperation in public health

The cholera epidemics that overran Europe between 1830 and 1847 were catalysts for intensive infectious disease diplomacy and multilateral cooperation in public health. They showed that collaboration between countries was needed to control the spread of dangerous diseases across the world. This led to the first International Sanitary Conference in Paris in 1851. In 1948, the WHO Constitution entered into force and in 1951



WHO Member States adopted the International Sanitary Regulations, which were replaced by and renamed the International Health Regulations in 1969. The 1969 Regulations were subject to minor modifications in 1973 and 1981.

The IHR were primarily intended to monitor and control six serious infectious diseases: cholera, plague, yellow fever, smallpox, relapsing fever and typhus. Under the IHR (1969), only cholera, plague and yellow fever remain notifiable, meaning that States Parties are required to notify WHO if and when these diseases occur on their territory.

Increase in cross-border travel and trade, the development of information and communication technologies, the resurgence of some well-known epidemic diseases, such as cholera and plague and the emergence of new infectious agents such as Ebola virus disease, as well as the limitations of IHR (1969) (narrow scope of three diseases and dependence on official country notifications), led to their revision.

The World Health Assembly adopted the IHR (2005) on 23 May 2005 and they entered into force on 15 June 2007. The IHR (2005) represent a binding international legal agreement involving 196 countries across the globe. They aim to prevent, protect against, control and respond to the international spread of disease while avoiding unnecessary interference with international traffic and trade.



Questions & Answers

1. What are the major changes between IHR (1969) and IHR (2005)?

- The scope of the IHR (2005) is purposely broader and more inclusive in respect of the public health event to which they have application in order to maximize the probability that all such events that could have serious international consequences are identified early and promptly reported by States Parties to WHO for assessment.
- The IHR (2005) explicitly allow WHO to take into account information from sources other than official notifications and consultations, and, after assessment, to seek verification of specific events from the concerned States Parties.

2. What are the general obligations of States under the IHR (2005)?

Under the IHR (2005), States Parties are required to:

- Designate a National IHR Focal Point (it may be a team). Focal points are required to be available on a 24-hour basis, seven days a week.
- Assess events occurring in their territory and to notify WHO of all events that may constitute a Public Health Event of International Concern (PHEIC) using the decision instrument.

- Respond to requests for verification of information regarding events that may constitute a public health emergency of international concern, to respond to public health risks which may spread internationally.
- Develop, strengthen and maintain the capacity to detect, report and respond to public health events. To provide routine facilities, services, inspections and control activities at designated international airports, ports and ground crossings to prevent the international spread of disease.
- Report to WHO evidence of a public health risk identified outside their territory which may cause international disease spread, manifested by exported/imported human cases, vectors carrying infection or contamination, contaminated goods.
- Respond appropriately to WHO-recommended measures.
- Collaborate with other States Parties and with WHO on IHR (2005) implementation.

3. What events should States Parties notify to WHO?

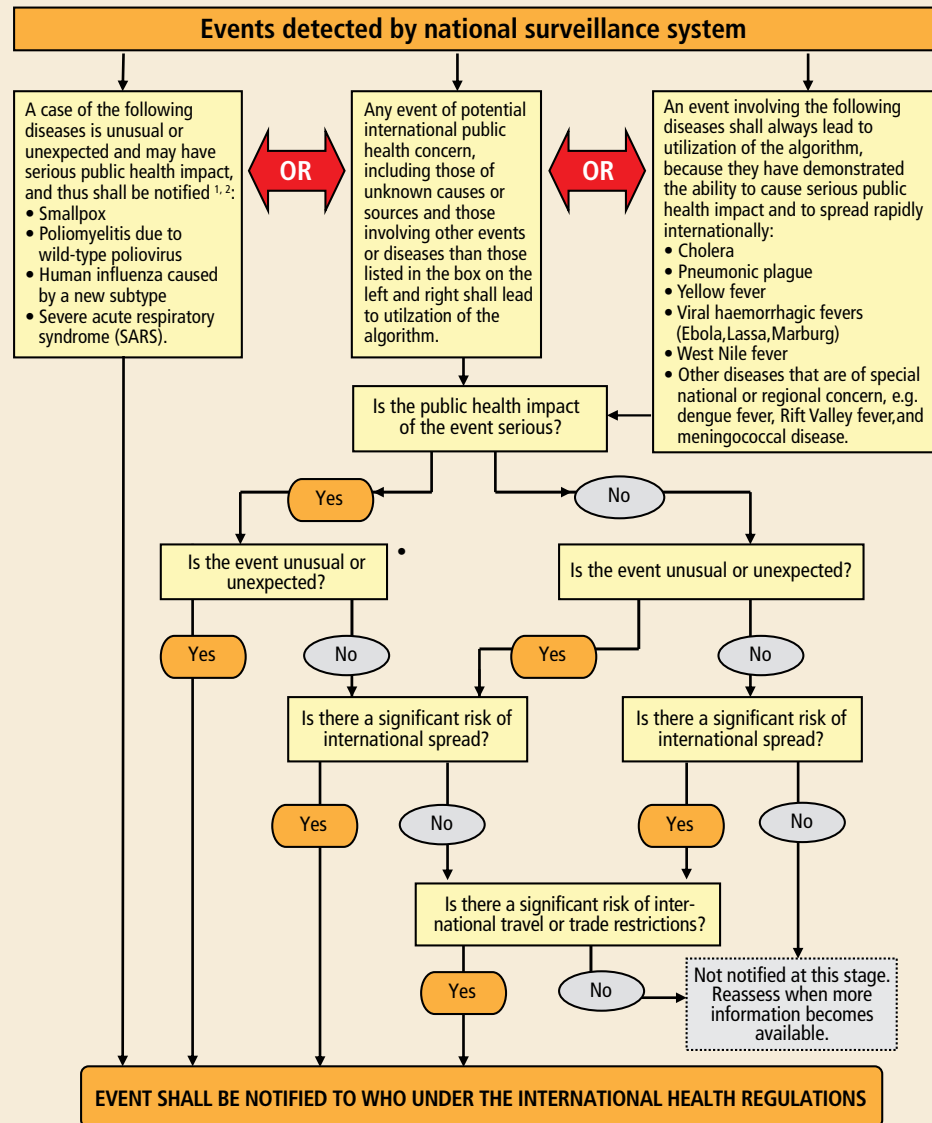
Under the IHR, States Parties are required to notify WHO of all events that are assessed as possibly constituting a PHEIC, taking into account the context in which an event occurs.

A decision instrument, provided in Annex 2 of the Regulations, identifies four criteria that States Parties must follow in their assessment of



TOOL BOX 1

Decision instrument for the assessment & notification of events that may constitute a Public Health Emergency of International Concern (PHEIC)



¹ As per WHO case definitions.

² The disease list shall be used only for the purposes of these Regulations.

TOOL BOX 1

events within their territories and their decision as to whether an event is notifiable to WHO:

- Is the public health impact of the event serious?
- Is the event unusual or unexpected?
- Is there a significant risk of international spread?
- Is there a significant risk of international restriction(s) to travel and trade?

4. What if States Parties have difficulties to assess an event?

State Parties have an option of initiating confidential consultations with WHO and seeking advice on evaluation, assessment and appropriate health measures to be taken, in case they are unable to complete a definitive assessment.

5. How and when to report these events?

- These notifications must occur within 24 hours of assessment by the country.
- Notifications must be followed by ongoing communication of detailed public health information on the event, including, where possible, case definition, laboratory results, source and type of the risk, number of cases and deaths, conditions affecting the spread of the disease and the health measures employed.

6. What States Parties should do if they identify a public health risk outside their territory?

States Parties must inform WHO through the National IHR Focal Point within 24 hours of receipt of evidence of a public health risk identified outside their territory that may cause international disease spread, as manifested by imported or exported human cases, vectors which carry infection or contamination, or by contaminated goods.

7. Can WHO require more information to States Parties about events unofficially reported?

States Parties are required under the IHR (2005) to respond to WHO Requests for Verification. WHO has an express mandate to obtain verification from States Parties concerning unofficial reports or communications, received from various sources, about events arising within their territories which may constitute a PHEIC. States Parties must acknowledge verification requests by WHO within 24 hours and provide public health information on the status of the event, followed, in a timely manner.

8. What are the diseases that should be mandatorily notified to WHO?

Under the IHR (2005), all cases of four diseases must be automatically notified to WHO: smallpox, poliomyelitis due to wild-type poliovirus, SARS and cases of human influenza caused by a new subtype.

9. What are the core capacities?

- Under the IHR (2005), each State Party is required to develop, strengthen and maintain core public health capacities for surveillance and response.
- Public health capacity under the IHR (2005) is defined as the indispensable, fundamental actions that are the primary responsibility of each State Party for achieving the goal of national health security, i.e., to prevent the spread of diseases and to detect and investigate health risks in the community by efficient multisectoral action (e.g., integrated disease surveillance systems, laboratory services and national, regional and global networks).



TOOL BOX 1

- Core capacities at the local (community), intermediate and national levels, as well as key sanitary and health services needed at designated international airports, ports and ground crossings are described in Annex 1 of the IHR (2005).

10. What are the specific requirements for yellow fever?

- A proof of vaccination or prophylaxis against yellow fever may be required for travellers as a condition of entry to a State.
- States Parties must designate at least one yellow fever vaccination centre.

11. Why developing the necessary public health capacities at points of entry will limit the spread of public health hazards?

Today's high traffic at points of entry (airports, ports and ground crossings), can play a key role in the international spread of diseases through persons, conveyances and goods. This is why countries should be prepared to detect and respond to any health event that may be of international concern and contain risks at source, limiting unnecessary health-based restrictions on international traffic and trade and protecting the health of travellers and populations.

12. What are the guiding principles for preparedness at points of entry?

- Simplicity
- Proportionality and practicality: one size does not fit all
- Minimal disruption
- Collaboration: multisectoral approach
- (Risk) Communication

More information on the role of WHO:

- International Health Regulations (2005)
<http://www.who.int/ihr/publications/9789241580496/en/>
- More information about IHR
<http://www.who.int/ihr/about/en/>
- More information about implementing IHR
<https://www.who.int/activities/supporting-national-implementation-of-international-health-regulations>
- More about public health at points of entry:
http://www.who.int/ihr/ports_airports/en/
- Joint External Evaluation Tool and Process Overview
<http://apps.who.int/iris/bitstream/10665/252755/1/WHO-HSE-GCR-2016.18-eng.pdf?ua=1>



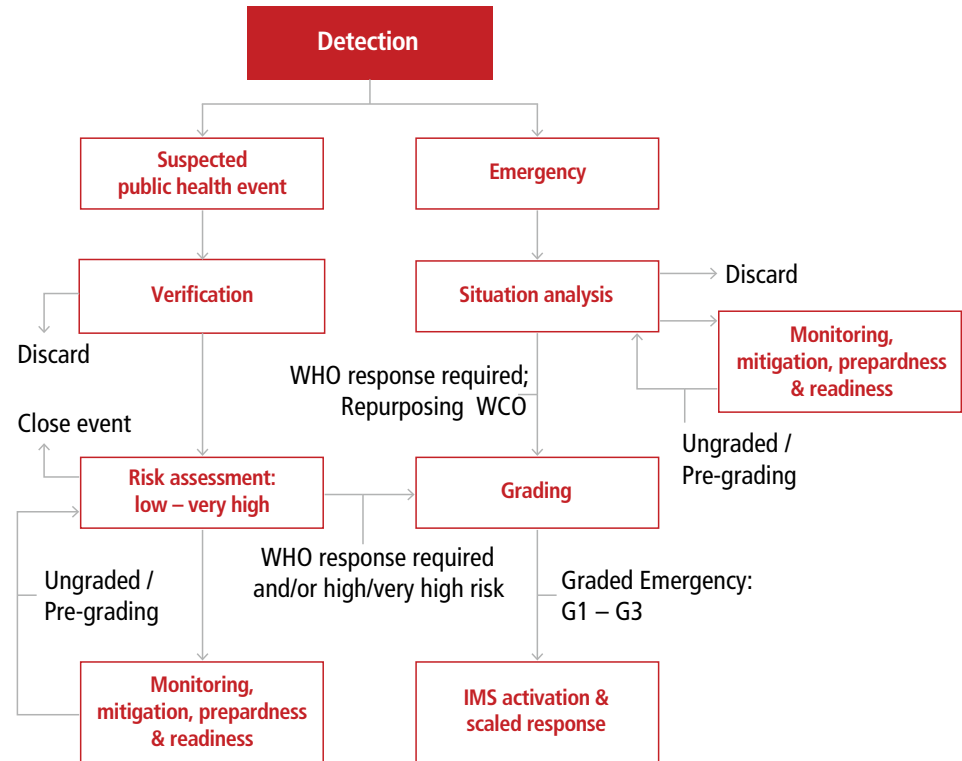
TOOL BOX 1

WHO management of events under the Emergency Response Framework (ERF)

The ERF is an internal WHO tool that outlines a set of procedures to better respond to emergencies. The ERF provides WHO staff with essential guidance on how the Organization manages the assessment, grading and response to public health events and emergencies with health consequences, in support of Member States and affected communities.



Linking risk assessment and situation analysis to WHO grading and operational response



For acute events and emergencies, grading occurs within 24 hours of risk assessment/situation analysis

Source: Emergency Response Framework, second edition, WHO

TOOL BOX 1

WHO internal grading of events

- Once an event is detected or notified to WHO, it will be verified and analysed. Risk assessment would be conducted if the event is confirmed. Risk assessment by WHO team may result in:
 - Monitoring, mitigation, preparedness and readiness if the risk is low or very low.
 - Grading the event and activating the Incident Management System and scaled response if the risk is high or very high.
- Grading an event is a WHO internal process which purpose is to define the level of operational response required by WHO. Grading takes into consideration five criteria: scale, complexity, urgency of the event, capacity to respond at local and national levels and reputational risk for WHO.
- There are four levels for graded emergencies:
 - Ungraded
 - Grade 1
 - Grade 2
 - Grade 3

Levels for graded emergencies

Ungraded	A public health event or emergency that is being monitored by WHO but that does not require a WHO operational response.
Grade 1	A single country emergency requiring a limited response by WHO, but that still exceeds the usual country-level cooperation that the WHO Country Office (WCO) has with the Member State. Most of the WHO response can be managed with in-country assets. Organizational and/or external support required by the WCO is limited. The provision of support to the WCO is coordinated by an Emergency Coordinator in the Regional Office.
Grade 2	A single country or multiple country emergency, requiring a moderate response by WHO. The level of response required by WHO always exceeds the capacity of the WCO. Organizational and/or external support required by the WCO is moderate. The provision of support to the WCO is coordinated by an Emergency Coordinator in the Regional Office. An Emergency Officer is also appointed at headquarters to assist with the coordination of Organization-wide support.
Grade 3	A single country or multiple country emergency, requiring a major/maximal WHO response. Organizational and/or external support required by the WCO is major and requires the mobilization of Organization-wide assets. The provision of support to the WCO is coordinated by an Emergency Coordinator in the Regional Office(s). An Emergency Officer is also appointed at headquarters, to assist with the coordination of Organization wide inputs. On occasion, the WHE Executive Director and the Regional Director may agree to have the Emergency Coordinator based in headquarters. For events or emergencies involving multiple regions, an Incident Management Support Team at headquarters will coordinate the response across the regions.

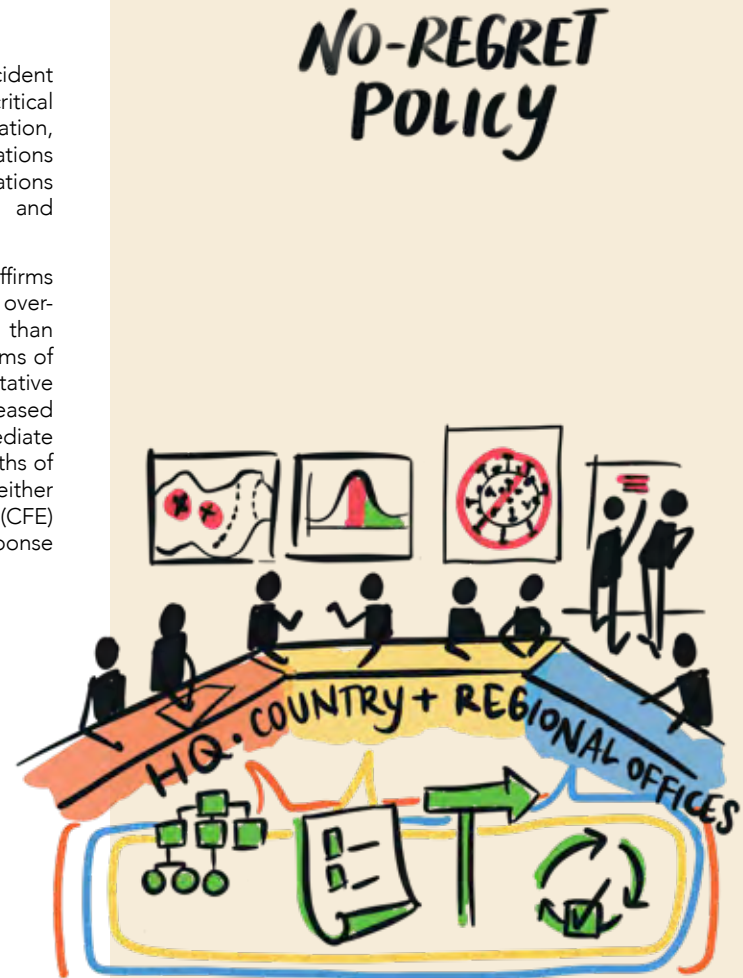
Source: *Emergency Response Framework, second edition, WHO*

TOOL BOX 1

WHO operational response through the ERF

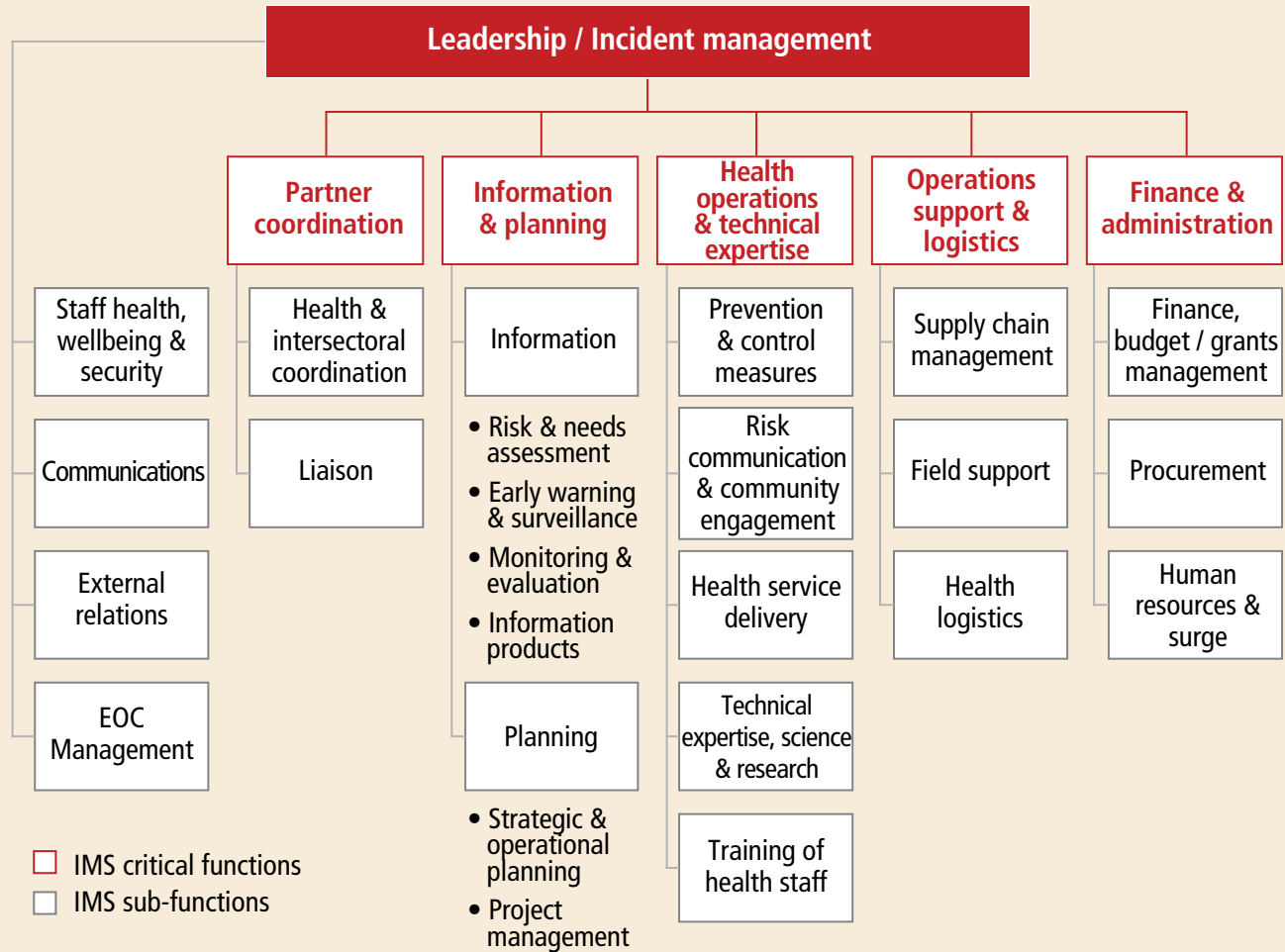
- Grading will trigger WHO emergency procedures and activities for the management of the response. It will activate the Incident Management System (IMS). The IMS is recognized best practice for emergency management. It is simple, flexible and adaptable to any scenario: it may be applied in small, simple, or large, complex incidents. Scaling up or down the response can be quickly done to suit the changing needs.
- The IMS is the combination of facilities, equipment, personnel, procedures and communications operating within a common organizational structure. It enables:
 - Common terminology and structure that enhance interoperability.
 - Clarification of roles and responsibilities.
 - Flow of information and resources.
 - Rapid mobilization, deployment and tracking of resources.
- The IMS implies:
 - Determining the overarching objectives (for example stop transmission of an infectious agent).
 - Establishing specific and measurable objectives for various functional activities.
 - Developing strategies and issuing plans, directions, procedures and protocols.

- Assigning tasks.
- Establishing an evaluation process.
- WHO has adapted the Incident Management System to consist of six critical functions: Leadership, Partner Coordination, Information and Planning, Health Operations and Technical Expertise, Operations Support and Logistics, and Finance and Administration.
- WHO applies a no regret policy which affirms that "it is better to err on the side of over-resourcing the critical functions rather than risk failure by under-resourcing." In terms of financial resources, the WHO representative and/or the Incident Manager has increased authority to approve expenditure. Immediate access to funds, for the first three months of an acute emergency, is provided from either the Contingency Fund for Emergency (CFE) or the Regional Office's rapid response accounts.



TOOL BOX 1

WHO's Incident Management System organizational structure: critical functions and sub-functions



Source: Emergency Response Framework, second edition, WHO

TOOL BOX 1

WHO monitoring of the response: a criteria for success

- It is critical to evaluate the response to an event and learn the lessons from past responses, improving things that could have gone better and enforcing best practices.
- During grade 2 and 3 emergencies, WHO performance standards and key performance indicators are monitored.
 - Performance standards should be monitored with the ERF Monitoring Tool. The responsibility for completing the ERF Monitoring Tool is with the Country Office, with oversight from the Regional Office.
 - Key performance indicators (not more than eight) are agreed upon on a case-by-case basis for each response (for example case fatality ratio, vaccination coverage, etc.).



For more information:

- Emergency Response Framework: <https://www.who.int/publications/i/item/9789241512299>

TOOL BOX 2

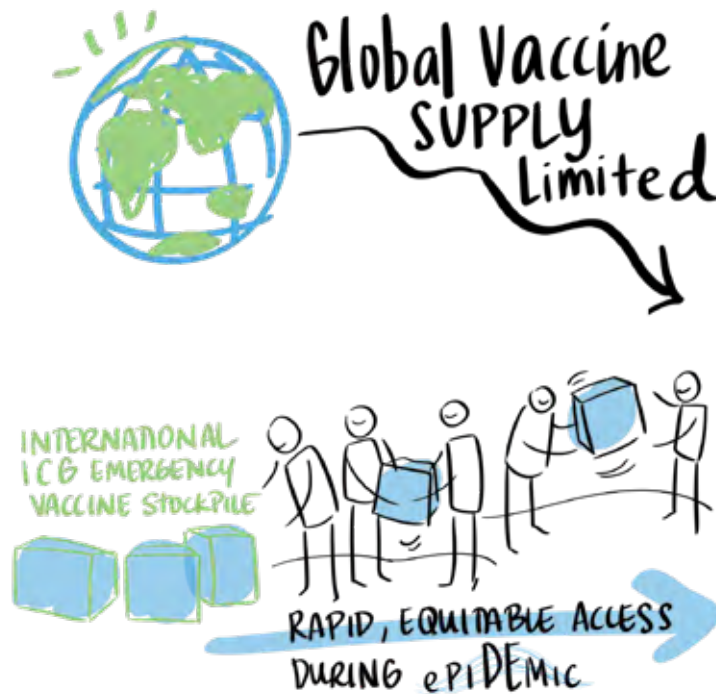


The International Coordinating Group (ICG) on vaccine provision

What is the ICG?

- The ICG was established in 1997 following major outbreaks of meningitis in Africa as a mechanism to manage and coordinate the provision of emergency vaccine supplies and antibiotics to countries during major outbreaks.
- The ICG monitors global licensed vaccine stock levels for cholera, meningitis, yellow fever and Ebola virus disease (EVD) to ensure availability of sufficient supplies to respond to disease outbreaks.
- The ICG brings partners together to improve coordination of epidemic preparedness and response.
- The ICG works on forecasting licensed vaccine stocks, negotiating vaccine prices through its networks and partners, and evaluating interventions and standard protocols for managing diseases.

TOOL BOX 2



Why is such mechanism needed?

Though outbreaks of meningitis, yellow fever, EVD and cholera are unpredictable events, they can each be controlled by the timely use of vaccine. Vaccine-preventable diseases typically affect people in vulnerable settings who have limited access to vaccines. But vaccines can take months to manufacture, and they are not always readily available in the amounts needed during emergencies. The resulting shortages have raised difficult issues about how limited supplies should be allocated during periods of high demand. That is why, after public health organizations found themselves unprepared to respond in a timely manner to a large-scale outbreak of meningitis in Nigeria, the ICG mechanism was created in 1997.

What is the ICG mandate?

- The core mandate of the ICG is to make available and ensure equitable access to licensed vaccines for cholera, meningitis, yellow fever and EVD during outbreaks.
- The ICG mechanism seeks to ensure timely and targeted deployment so that vaccines can be used as effective medical tools to control outbreaks where they are most needed.
- The ICG also manages the global emergency vaccine stockpiles and, working with manufacturers, determines their size and composition with the goal of ensuring that adequate stocks of emergency supplies are accessible for emergency response.

What are the guiding principles of the mechanism?

Three principles guide the mechanism:

- **Equity:** Distribution of vaccine based on public health priorities.
- **Rapid and timely access:** Delivery of vaccine within a defined timeframe to control outbreaks.
- **Independence:** Decisions made independent of any political or economic influences with the sole goal of improving public health.



TOOL BOX 2

Who are the ICG's partners?

The ICG is made up of four member agencies:

- International Federation of the Red Cross and Red Crescent Societies (IFRC): Has strong country presence for community health promotion, local social and resource mobilization and support to States during disasters and epidemics.
- Médecins sans Frontières (MSF): An independent, field-based NGO providing health care to vulnerable populations in emergency settings.
- United Nations Children's Fund (UNICEF): Conducts wide-scale vaccine procurement and shipment and provides in-country technical support on campaign planning and implementation, focusing mainly on social mobilization and cold chain.
- WHO: Provides global public health advice and technical support to countries. During outbreaks, WHO focuses on vaccine stockpile management, surveillance, and preparedness and response to disease outbreaks.

Additional expertise and technical advice are provided on a case-by-case basis from partners including: Agence de Médecine Préventive, Epicentre, WHO Collaborating Centres, the US Centers for Disease Control and Prevention (CDC) and the European Community Humanitarian Office (ECHO). Vaccine manufacturers, vaccine equipment providers, and financial donor institutions are also engaged in the ICG operations.

Which vaccine stockpiles are available through the ICG?

ICGs have been established to provide access to licensed vaccines for cholera, meningitis, yellow fever and EVD.

Cholera

Meningitis

Yellow Fever

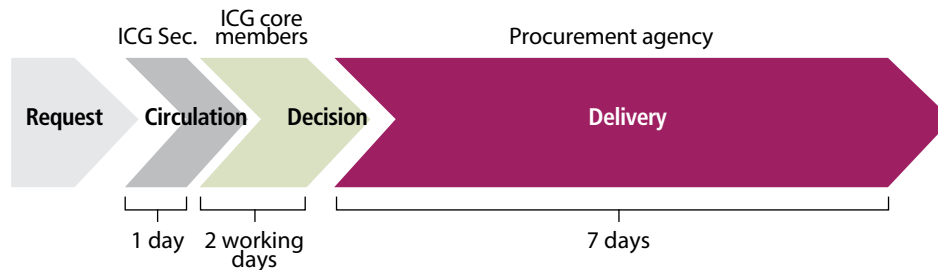
Ebola Virus Disease

TOOL BOX 2

How can a country access emergency vaccine stockpiles?

- Vaccine security stocks can be accessed by any country facing an epidemic anywhere in the world, as long as the country's request fulfills ICG's criteria for release of vaccine stocks.
- As a first step, a country must complete and submit a request to the ICG Secretariat at WHO using the standard application form.
- The ICG Secretariat circulates the request to the four ICG's core members for review and assessment. Requests for additional information are sent back to the country, if needed. Following a rapid consultation and evaluation process, the decision to release vaccines and other supplies is communicated to the requesting country within 48 hours, once all necessary information has been provided.
- If approved, UNICEF procures vaccines and injection materials and organizes delivery of vaccines to the country, ideally within seven days.
- Requests are evaluated based on the epidemiological situation, vaccination strategy, pre-existing stocks in the country and operational aspects of the epidemic response.

Lead time for request reception to vaccine delivery



For more information on the International Coordinating Group (ICG) on vaccine provision:

- **General information on the ICG**
<https://www.who.int/groups/icg>
- **Application forms and guidelines for cholera**
<https://www.who.int/groups/icg/cholera>
- **Application forms and guidelines for meningitis**
<https://www.who.int/groups/icg/meningitis>
- **Application forms and guidelines for yellow fever**
<https://www.who.int/groups/icg/yellow-fever>
- **Application forms and guidelines for EVD**
<https://www.who.int/groups/icg/ebola-virus-disease>

TOOL BOX 3

Tables for disease diagnosis

Clinical syndromes;
differential diagnoses;
sample collection,
storage and shipment

TOOL BOX 3

Table 1: Clinical syndromes

Following syndromes (syndrome: a group of symptoms) are used to alert front-line health care workers and for syndromic surveillance.

(Note) 'Acute' refers to a condition that any disease having a recent onset, and following a short course in persons without predisposing factors or illness (1).

SYNDROME	DESCRIPTION
Acute diarrhoeal Syndrome	<p>Diarrhoea: passage of three or more loose or watery stools per day (or more frequent passage than is normal for the individual).</p> <p>Acute watery diarrhoea: lasts several hours or days; and an alert for cholera.</p> <p>Acute bloody diarrhoea: acute diarrhoea with visible blood in the stool, also called dysentery, an alert for shigellosis.</p> <p>Reference: (2)</p>
Acute haemorrhagic fever syndrome	<p>Acute onset of fever of less than 3 weeks duration in a severely ill patient* and any two of the following:</p> <ul style="list-style-type: none"> • haemorrhagic or purpuric rash • epistaxis (nose bleed) • haematemesis (blood in vomit) • haemoptysis (blood in sputum) • blood in stool • other haemorrhagic symptom** <p>* Loss of consciousness / coma, delirium, convulsion, severe dehydration, and signs of multi-organ failure such as low blood pressure.</p> <p>** Bleeding in the gums, haematuria (blood in urine), red eyes, bleeding or oozing at the point of puncture, an alert for Ebola virus disease (EVD), Margburg virus disease (MVD), Rift Valley fever (RVF), dengue, yellow fever (YF), Lassa fever, Crimean-congo haemorrhagic fever (CCHF) and other viral haemorrhagic fevers (VHF) depending on the location.</p> <p><i>Note: During epidemics use disease-specific case definitions. For example, include diarrhoea for EVD case definition if appropriate. Early notification is required by the IHR (2005), without awaiting causal agent to be identified.</i></p>
Acute Jaundice syndrome	<p>Acute onset of fever, with jaundice* appearing within 14 days of onset of the first symptoms.**</p> <p>An alert for yellow fever or hepatitis A, E.</p> <p>(Hepatitis B, C, D viruses are unlikely to manifest acute jaundice, unless exacerbated. It may take several years to detect outbreak after common exposure).</p> <p>* Yellowing of skin and/or conjunctiva.</p> <p>** Symptoms include but not limited to: nausea, vomiting, abdominal pain, loss of appetite, itching, joint pain, dark urine, malaise and headache.</p>

TOOL BOX 3

Table 1: Clinical syndromes, continued

SYNDROME	DESCRIPTION
Acute neurological syndrome	<p>Acute onset of fever and neurological manifestations* is an alert for encephalitis, encephalopathy, and meningitis.</p> <p>* Including but not limited to: headache, altered mental status (derillium, confusion, loss of consciousness), cognitive disorders, seizures, movemet disorder, sensitivity to light and/or sound.</p> <p><i>Note: Acute Flaccid Syndrome (acute onset of weakness or paralysis with reduced muscle tone, alert for poliomyelitis) and Guillian-Barré Syndrome (progressive muscle weakness or paralysis, not specific to particular pathogens) are other conditions potentially caused by infectious etiology.</i></p>
(Severe) Acute respiratory syndrome (Severe) Acute Respiratory Infection	<p>Acute onset of fever and progressive respiratory symptoms.*</p> <p>Severe acute respiratory syndrome (SARS) often refers to atypical pneumonia while SARI (Severe acute respiratory infection) includes typical community-acquired pneumonia of bacterial origin (pneumococcal, haemophilus influenzae) affecting lower respiratory tract (bronchitis and pneumonia). Alert for zoonotic influenza, novel influenza, coronavirus SARS including Middle East Respiratory Syndrome (MERS) and SARS-CoV-2, adult measles, anthrax, pneumonic plague, and Legionnaires Disease.</p> <p>* Including but not limited to: cough, sore throat, rhinorrhoea, shortness of breath / breathing difficulty, sputum, chest pain. Severe cases often require hospitalization for treatment such as oxygen therapy.</p>
Acute fever and rash syndrome	<p>Acute febrile illness and rash or other skin manifestations.</p> <p>An alert for measles, rubella, particularly when clustered in children</p>
Sepsis	<p>Life-threatening organ disorder caused by a dysregulated host immune function to infection. Common cause of maternal and neonatal deaths in LMICs.</p> <ul style="list-style-type: none"> • Fever or hypothermia (history of febrile illness) • Shock (lethargy, fast breathing, cold skin, prolonged capillary refill, fast weak pulse and sometimes low blood pressure) • Seriously ill with no apparent cause <p>Sepsis can follow any infection, such as respiratory, urinary tract, gut and skin infection. Reference: (3)</p>

TOOL BOX 3

Table 2: Outbreak differential diagnoses and sample collection for common syndromes

Differential diagnoses for outbreaks vary depending on region and potential known risk factors. This list is not exhaustive and requires adaptation to the local context and specific situation.

This list is not suitable for individual patient care as it only covers potential outbreak pathogens with acute disease manifestations.

Samples should be sent to diagnostic laboratories that meet the quality requirements to perform reliable diagnosis and that comply with regulatory, biosafety and biosecurity requirements (4-8).

CLINICAL SYNDROME	MAIN DISEASE (PATHOGEN) (NOT EXHAUSTIVE LIST)	SAMPLES TO COLLECT
<p>Acute diarrhoeal syndrome</p> <p><u>Most common causes of bloody diarrhoea are underlined.</u></p>	<p>Rotavirus and <i>Escherichia coli</i>, are the two most common etiological agents of moderate-to severe diarrhoea in low-income countries as well as pathogens such as <i>cryptosporidium</i> and <i>shigella</i> species.</p> <p>Viral: Norovirus infection, rotavirus infection, initial presentation of <u>Ebola and other viral haemorrhagic fevers</u> see acute haemorrhagic fever algorithm, MERS, SARS coronavirus infections (for additional diagnostics see also acute respiratory syndrome).</p> <p>Bacterial: Cholera (<i>Vibrio cholerae</i>), shigellosis (<i>Shigella dysenteriae</i>, <i>S. flexneri</i>, <i>S. boydii</i>, <i>S. sonnei</i>), diarrheagenic <i>Escherichia coli</i> (e.g. shigatoxigenic / or verocytotoxigenic enterohaemorrhagic <i>E.coli</i> (STEC or VTEC) and enterotoxigenic <i>E.coli</i> (ETEC)), <u>salmonellosis</u> (<i>Salmonella</i> species), <u>campylobacteriosis</u> (<i>Campylobacter jejuni</i> and other species), <u>yersiniosis</u> (<i>Yersinia enterocolitica</i>), Listeriosis (<i>Listeria monocytogenes</i>), <u>clostridium infection</u> (<i>Clostridium difficile</i>), toxin produced by bacteria (<i>Staphylococcus aureus</i>, <i>Clostridium perfringens</i>, <i>Bacillus cereus</i>), typhus (<i>Rickettsia prowazekii</i>), <i>Bacillus cereus</i> infection.</p> <p>Parasitic: <u>Amoebic dysentery</u> (<i>Entamoeba histolytica</i>), giardiasis (<i>Giardia lamblia</i>/<i>G. intestinalis</i>/<i>G. duodenalis</i>), cryptosporidiosis (<i>Cryptosporidium</i> species), cyclosporiasis (<i>Cyclospora cayetanensis</i>), <u>schistosomiasis/bilharzia</u> (<i>Schistosoma</i> species), Isosporiasis (<i>Isospora</i>), microsporidiosis (<i>microsporidia</i>).</p>	<p>Faeces;</p> <p>If deceased: Consider rectal swab.</p>
<p>Acute haemorrhagic fever syndrome</p>	<p>Viral: Ebola Disease (Ebola, Sudan, Reston, Thai Forest, and Bundibugyo viruses), Marburgvirus infection, Lassa fever (Lassa virus), Crimean-Congo haemorrhagic fever (CCHF virus), Rift Valley fever (RVF virus), dengue (dengue virus), hantavirus infection, yellow fever (yellow fever virus), New world arenaviruses.</p> <p>Bacterial: Meningococcal disease (<i>Neisseria meningitidis</i>), rickettsial disease and severe sepsis.</p> <p>Parasitic: Malaria (<i>Plasmodium</i> species).</p> <p>Noninfectious: Intoxication, for example anticoagulant rodenticides (list is non-exhaustive).*</p>	<p>Blood cultures, whole blood, plasma, serum (include second convalescent sample if cause has not been identified), blood smear (thick and thin);</p> <p>If deceased: Oral swab and consider post-mortem tissues.</p>

* The environmental history is very important in addressing an event of possible chemical etiology (9).

TOOL BOX 3

Table 2: Outbreak differential diagnoses and sample collection for common syndromes, continued

CLINICAL SYNDROME	MAIN DISEASE (PATHOGEN) (NOT EXHAUSTIVE LIST)	SAMPLES TO COLLECT
<p>Acute Jaundice syndrome</p>	<p>Viral: Yellow fever (yellow fever virus), hepatitis A, E (hepatitis B, C, D viruses are unlikely to manifest acute jaundice, unless exacerbated. It may take several years to detect outbreak after common exposure).</p> <p>Bacterial: Leptospirosis (<i>Leptospira</i> species), Brucellosis (<i>Brucella</i> species)</p> <p>Parasitic: Malaria (<i>Plasmodium</i> species).</p>	<p>Blood culture, plasma, serum (include second convalescent sample if cause has not been identified), urine, stool;</p> <p>If deceased: Postmortem tissues (for example liver biopsy).</p>
<p>Acute neurological syndrome</p>	<p>Viral: Arbovirus infection (e.g., Japanese encephalitis, dengue virus, West Nile virus, yellow fever virus, tick-borne encephalitis, Rift valley fever virus), Nipah virus infection, rabies, and enteroviral meningitis (for example polio virus, enterovirus D68, A71).</p> <p>Bacterial: Meningococcal disease (<i>Neisseria meningitidis</i>), pneumococcal meningitis (<i>Streptococcus pneumoniae</i>), haemophilus meningitis (<i>Haemophilus influenzae</i>), group B streptococcal meningitis, tuberculosis (<i>Mycobacterium tuberculosis</i>), leptospirosis (<i>Leptospira</i> species), listeriosis (<i>Listeria monocytogenes</i>), meningial plague (<i>Yersinia pestis</i>), Lyme disease.</p> <p>Fungi: Cryptococcosis (e.g., <i>Cryptococcus neoformans</i> var. <i>gatii</i>), <i>Histoplasma</i>, <i>Coccidioidomycosis</i>, <i>Blastomycosis</i>.</p> <p>Parasitic: Malaria (<i>Plasmodium</i> species), African trypanosomiasis (<i>Trypanosoma brucei</i>).</p>	<p>Cerebrospinal fluid (CSF), blood culture, blood smear, faeces, plasma, serum (include second convalescent sample if cause has not been identified), throat swab;</p> <p>If rabies is suspected: Saliva, CSF and skin biopsy from hairline in the neck;</p> <p>If deceased: Consider postmortem materials including brain tissue.</p>
<p>(Severe) Acute respiratory syndrome (Severe) Acute respiratory infection</p>	<p>Viral: Influenzavirus, respiratory syncytial virus, MERS/SARS coronavirus infections, other coronavirus and respiratory virus infections, hantavirus pulmonary syndrome (hantavirus).</p> <p>Bacterial: Pneumococcal pneumonia (<i>Streptococcus pneumoniae</i>), haemophilus influenzae pneumonia, <i>Staphylococcus aureus</i>, anthrax (<i>Bacillus anthracis</i>), diphtheria (<i>Corynebacterium diphtheriae</i>), pertussis /whooping cough (<i>Bordetella pertussis</i>), pneumonic plague (<i>Yersinia pestis</i>), scarlet fever (<i>Streptococcus pyogenes</i>), Legionnaires' disease/Pontiac fever, <i>Mycoplasma pneumoniae</i> and <i>Chlamydia psittaci</i> pneumonia, leptospirosis (<i>Leptospira</i> species), Q-fever (<i>Coxiella burnetii</i>), scrub typhus (Scrub: <i>Orientia tsutsugamushi</i>).</p> <p>Parasitic: Malaria (<i>Plasmodium</i> species), acute pulmonary schistosomiasis.</p>	<p>Respiratory material (throat swab, nasopharyngeal swab, sputum, broncho alveolar lavage (BAL)), serum (include second convalescent sample if cause has not been identified), plasma, blood culture, urine (legionella and pneumococcal antigen detection).</p>

TOOL BOX 3

Table 2: Outbreak differential diagnoses and sample collection for common syndromes, continued

CLINICAL SYNDROME	MAIN DISEASE (PATHOGEN) (NOT EXHAUSTIVE LIST)	SAMPLES TO COLLECT
Acute fever and rash syndrome	<p>Viral: Measles (measles virus), rubella (rubella virus), chickenpox (varicella zoster virus), arboviral (for example Zika, chikungunya, dengue virus), mpox (monkeypox virus), smallpox (variola virus)*, erythema infectiosum/slapped cheek syndrome/fifth disease (parvovirus B19), other viruses that can cause dermatological presentations include enteroviruses, human herpes virus 6, 7.</p> <p>Bacterial: Anthrax (<i>Bacillus anthracis</i>), leptospirosis (<i>Leptospira</i> species), invasive meningococcal disease (<i>Neisseria meningitidis</i>), bubonic plague (<i>Yersinia pestis</i>), other bacterial infections (for example <i>Streptococcus pyogenes</i>, <i>Staphylococcus aureus</i>).</p> <p>Rickettsial disease: including rickettsialpox, flea-borne (murine) typhus (<i>Rickettsia typhi</i>).</p> <p>Parasitic: Schistosomiasis (<i>Schistosoma</i> species), scabies (<i>Sarcoptes scabiei</i> var. <i>hominis</i>), malaria (<i>Plasmodium</i> species), cutaneous leishmaniasis (<i>Leishmania</i> species).</p>	<p>Vesicular fluid / crusts / exudate / roof of lesion, serum (include second convalescent sample if cause has not been identified), plasma or blood if systemic symptoms, blood smear (thick and thin);</p> <p>In some cases, biopsies after consulting dermatologist / laboratory;</p> <p>If suspicious for bubonic plague: Bubonic aspirate;</p> <p>Abscesses: Pus aspirate.</p>
Sepsis	<p>Although fungal and viral infections can cause sepsis, bacterial pathogens are the most frequent causative agents, with <i>Staphylococcus aureus</i> and <i>Streptococcus pneumoniae</i> representing the most relevant Gram-positive bacteria, and <i>Escherichia coli</i>, <i>Klebsiella</i> species, and <i>Pseudomonas aeruginosa</i> dominating the Gram-negative bacteria. The relative contribution by each of these different organism types is heavily influenced by local population characteristics.</p> <p>Viral: See acute haemorrhagic fever syndrome.</p> <p>Bacterial: Meningococcal disease (<i>Neisseria meningitidis</i>), leptospirosis (<i>Leptospira</i> species), typhoid fever (<i>Salmonella</i> serotype typhi), paratyphoid fever (<i>Salmonella</i> serotype paratyphi), anthrax (<i>Bacillus anthracis</i>), brucellosis (<i>Brucella</i> species: <i>B. melitensis</i>, <i>B. suis</i>, <i>B. abortus</i>, <i>B. canis</i>), Group A streptococcal infection (<i>Streptococcus pyogenes</i>), Group B streptococcal infection, <i>Haemophilus influenzae</i> septicaemia, plague (<i>Yersinia pestis</i>), relapsing fever (<i>Borellia recurrentis</i> and other species), trench fever (<i>Bartonella quintana</i>).</p> <p>Rickettsial: Typhus (Epidemic: <i>Rickettsia prowazekii</i>), flea-borne/murine: <i>Rickettsia typhi</i>), scrub typhus (Scrub: <i>Orientia tsutsugamushi</i>), spotted fever (e.g., <i>Rickettsia africae</i>, <i>R. conorii</i>) and other rickettsial diseases (<i>Ehrlichia</i>, <i>Anaplasma</i>, <i>Wolbachia</i>, <i>Neorickettsia</i> species).</p> <p>Parasitic: Malaria (<i>Plasmodium</i> species), visceral leishmaniasis/kala-azar (<i>Leishmania</i> species), African trypanosomiasis (<i>Trypanosoma brucei</i>).</p>	<p>Blood cultures, urine, serum (take second convalescent sample if cause has not been identified), plasma, blood smear (thick and thin);</p> <p>If suspicious for bubonic plague: Bubonic aspirate;</p> <p>If also neurological signs include CSF;</p> <p>If respiratory signs include respiratory materials (see section acute respiratory syndrome);</p> <p>If deceased: Consider post-mortem specimens.</p>

TOOL BOX 3

Table 3: Sample storage/shipment* by sample type

Differential diagnoses for outbreaks vary depending on region and potential known risk factors. This list is not exhaustive and requires adaptation to the local context and specific situation. This list is not suitable for individual patient care as it only covers potential outbreak pathogens with acute disease manifestations.

Samples should be sent to diagnostic laboratories that meet the quality requirements to perform reliable diagnosis and that comply with regulatory, biosafety and biosecurity requirements (4-8).

SAMPLE TYPE	TEST	SPECIMEN COLLECTION MATERIALS	MINIMAL AMOUNT NEEDED (might vary per test, sometimes test must be repeated and confirmed, thus if available collect more)	RECOMMENDED TEMPERATURE STORAGE	TRANSPORTATION
Plasma/Whole blood	PCR	<ul style="list-style-type: none"> • EDTA tubes • Citrate plasma can also be used for RT-PCR but not heparin as this may cause interference with PCR reagents and testing 	<ul style="list-style-type: none"> • Minimum 1mL 	<ul style="list-style-type: none"> • If samples are being transported to the laboratory within a few hours, refrigerate but do not freeze them (Storage at 0–4 °C /2–8 °C) • If the samples must be stored for more than 24 hours, freeze them at -20 °C or -70 °C (preferable). If this is not possible, store them in the refrigerator 	<ul style="list-style-type: none"> • Use a cooler or ordinary domestic vacuum flask to transport the samples • Make sure to pack the samples with cotton wool against the walls of the cooler to avoid breakage especially if glass tubes or bottles are used • If no flask is available, make a cooler from a cardboard box lined with two to three inches of polystyrene or foam rubber and with cotton wool • Place tubes or bottles in a plastic bag, if one is available, and surround it with packing material or alternatively, with fabric or something absorbent to avoid breakage
Serum	Serology	<ul style="list-style-type: none"> • Serum separator tubes 	<ul style="list-style-type: none"> • 3–5 mL blood of adults • 1–2 mL for infants and young children 	<ul style="list-style-type: none"> • Sera can be stored at 0–4 °C /2–8 °C for 1 week but should be frozen at -20 °C for periods longer than this • >48 hours, serum should be separated 	<ul style="list-style-type: none"> • Ship frozen specimen on dry ice

* These standards are general and can differ per required diagnostic test. For specific cases follow the instructions on sample storage for the specific diagnostics and requirements requested by the laboratory that the sample is sent to.

TOOL BOX 3

Table 3: Sample storage/shipment* by sample type, continued

SAMPLE TYPE	TEST	SPECIMEN COLLECTION MATERIALS	MINIMAL AMOUNT NEEDED (might vary per test, sometimes test must be repeated and confirmed, thus if available collect more)	RECOMMENDED TEMPERATURE STORAGE	TRANSPORTATION
Nasopharyngeal/ nasal/ pharyngeal swab	Culture	<ul style="list-style-type: none"> Dacron or polyester flocked swabs with universal transport medium 	Not applicable.	<ul style="list-style-type: none"> Specimens for virus isolation should be placed at 4 °C immediately after collection and promptly transported to the laboratory 	
	PCR	<ul style="list-style-type: none"> Dacron or polyester flocked swabs with universal transport medium For PCR sometimes a dry swab is preferred 	Not applicable.	<ul style="list-style-type: none"> Specimens received cold should be stored refrigerated (0–4 °C /2–8 °C) for up to 72 hours before processing If testing of a fresh specimen is not possible within 72 hours the specimen may be frozen at ≤ -70 °C and tested at a later time Store any sample received frozen and residual specimens at ≤ -70 °C Avoid repetitive thawing and freezing 	<ul style="list-style-type: none"> Ship frozen specimen on dry ice

* These standards are general and can differ per required diagnostic test. For specific cases follow the instructions on sample storage for the specific diagnostics and requirements requested by the laboratory that the sample is sent to.

TOOL BOX 3

Table 3: Sample storage/shipment* by sample type, continued

SAMPLE TYPE	TEST	SPECIMEN COLLECTION MATERIALS	MINIMAL AMOUNT NEEDED (might vary per test, sometimes test must be repeated and confirmed, thus if available collect more)	RECOMMENDED TEMPERATURE STORAGE	TRANSPORTATION
CSF	Microscopy, chemistry and culture	<ul style="list-style-type: none"> • Sterile screw-cap collection tubes 	<ul style="list-style-type: none"> • 3 mL, more if available** distributed in 4 separate tubes: <ul style="list-style-type: none"> - 1 mL microbiology (Gram, Crag or indian ink, Lowenstein/GeneXpert-TB and cultures for bacterial/fungal/TB) - 1 mL biochemistry (glucose and protein) - 1 mL cell count with differential (tube 1 and 4) 	<ul style="list-style-type: none"> • Ambient for leptospirosis meningococcal disease • Virus culture: Specimens for virus isolation should be placed at 4 °C immediately after collection and promptly transported to the laboratory 	
	PCR	<ul style="list-style-type: none"> • Cryotube • If not available sterile screw-cap collection tube 	<ul style="list-style-type: none"> • 0.5–1 mL 	<ul style="list-style-type: none"> • CSF in Cryotube: stored at refrigerator temperature and transported in cold chain • CSF isolates: stored frozen at -20 °C to allow further testing 	<ul style="list-style-type: none"> • Ship frozen specimen on dry ice

* These standards are general and can differ per required diagnostic test. For specific cases follow the instructions on sample storage for the specific diagnostics and requirements requested by the laboratory that the sample is sent to.

** Alert for low-CSF pressure syndrome to not overdraw CNF and not draw too frequently. This is an invasive technique which requires trained staff with attention to sterile method.

TOOL BOX 3

Table 3: Sample storage/shipment* by sample type, continued

SAMPLE TYPE	TEST	SPECIMEN COLLECTION MATERIALS	MINIMAL AMOUNT NEEDED (might vary per test, sometimes test must be repeated and confirmed, thus if available collect more)	RECOMMENDED TEMPERATURE STORAGE	TRANSPORTATION
Stool Rectal swab	Culture	<ul style="list-style-type: none"> Leak proof container for stool sample Longer than 2 hours before processing: Cary-Blair transport medium 	<ul style="list-style-type: none"> Scoop Swab: Not applicable 	<ul style="list-style-type: none"> Stored refrigerated (0–4 °C / 2–8 °C) Should arrive at accredited laboratory within 72 hours after collection 	<ul style="list-style-type: none"> 24–72 hours cold box 2–8 °C (0–4 °C), between frozen ice packs, should arrive at accredited laboratory within 72 hours after collection If not, specimen should be frozen with dry ice or cold packs that have been frozen to -20 °C
	PCR	<ul style="list-style-type: none"> Leak proof container for stool sample 	<ul style="list-style-type: none"> Scoop Swab: Not applicable 	<ul style="list-style-type: none"> If samples are being transported to the laboratory within a few hours, refrigerate but do not freeze them (Storage at 0–8 °C) If the samples must be stored for more than 24 hours, freeze them at -20 °C or -70 °C (preferable). If this is not possible, store them in the refrigerator 	<ul style="list-style-type: none"> Ship frozen specimen on dry ice
Blood smear (thick and thin)	Microscopy	<ul style="list-style-type: none"> Microscopy slides and preferably with storage box if transport is needed 	<ul style="list-style-type: none"> Consider making multiple slides 	<ul style="list-style-type: none"> Ambient temperature 	

* These standards are general and can differ per required diagnostic test. For specific cases follow the instructions on sample storage for the specific diagnostics and requirements requested by the laboratory that the sample is sent to.

TOOL BOX 3

Table 3: Sample storage/shipment* by sample type, continued

SAMPLE TYPE	TEST	SPECIMEN COLLECTION MATERIALS	MINIMAL AMOUNT NEEDED (might vary per test, sometimes test must be repeated and confirmed, thus if available collect more)	RECOMMENDED TEMPERATURE STORAGE	TRANSPORTATION
Blood culture	Culture	<ul style="list-style-type: none"> Commercial or home brewed blood culture bottles Collected blood should be diluted in blood culture broth in order to obtain blood cultures Specimens should be immediately inoculated (within one minute) into a blood culture bottle (anaerobic, aerobic bottles, and AFB if available, if concerned about fungal infection that is not cryptococcus or Candida then if available should order fungal culture) 	<ul style="list-style-type: none"> Adult: 5–10 mL Child: 1–3 mL 	<ul style="list-style-type: none"> Inoculated blood culture media should be protected from temperature extremes (<18 °C or >37 °C) Do not place in the refrigerator Incubate as soon as possible in ideal circumstances as instructed by manufacturer/ laboratory 	<ul style="list-style-type: none"> Inoculated blood culture media should be protected from temperature extremes (<18 °C or >37 °C) with a transport carrier and thermal insulator (such as extruded polystyrene foam)

* These standards are general and can differ per required diagnostic test. For specific cases follow the instructions on sample storage for the specific diagnostics and requirements requested by the laboratory that the sample is sent to.

TOOL BOX 3

Table 3: Sample storage/shipment* by sample type, continued

SAMPLE TYPE	TEST	SPECIMEN COLLECTION MATERIALS	MINIMAL AMOUNT NEEDED (might vary per test, sometimes test must be repeated and confirmed, thus if available collect more)	RECOMMENDED TEMPERATURE STORAGE	TRANSPORTATION
Urine	Microscopy Culture PCR	<ul style="list-style-type: none"> • Sterile urine collection container/tube 	<ul style="list-style-type: none"> • 10 mL 	<ul style="list-style-type: none"> • If samples are being transported to the laboratory within a few hours, refrigerate but do not freeze them (for microbiological examination) • If the samples must be stored for more than 24 hours, freeze them at -20 °C or colder. If this is not possible, store them in the refrigerator (for PCR only) 	<ul style="list-style-type: none"> • Use a cooler or ordinary domestic vacuum flask to transport the samples • Make sure to pack the samples with cotton wool against the walls of the cooler to avoid breakage especially if glass tubes or bottles are used • If no flask is available, make a cooler from a cardboard box lined with 2–3 inches of polystyrene or foam rubber and with cotton wool • Place tubes or bottles in a plastic bag, if one is available, and surround it with packing material to avoid breakage

* These standards are general and can differ per required diagnostic test. For specific cases follow the instructions on sample storage for the specific diagnostics and requirements requested by the laboratory that the sample is sent to.

TOOL BOX 3

Table 3: Sample storage/shipment* by sample type, continued

SAMPLE TYPE	TEST	SPECIMEN COLLECTION MATERIALS	MINIMAL AMOUNT NEEDED (might vary per test, sometimes test must be repeated and confirmed, thus if available collect more)	RECOMMENDED TEMPERATURE STORAGE	TRANSPORTATION
Pus	Microscopy Culture PCR	<ul style="list-style-type: none"> • Sterile container for specimen • Bacterial transport medium for culture if not processed within few hours • Sterile container for specimen 	<ul style="list-style-type: none"> • What is available or 3 mL • What is available min 0.2 mL 	<ul style="list-style-type: none"> • Fresh materials storage at 2–8 °C/room temperature depending • Bacterial transport medium for culture if not processed within few hours • If samples are being transported to the laboratory within a few hours, refrigerate but do not freeze them • If the samples must be stored for more than 24 hours, freeze them at -20 °C or colder. If this is not possible, store them in the refrigerator 	<ul style="list-style-type: none"> • Ship frozen specimen on dry ice
Skin	Microscopy Culture PCR	<ul style="list-style-type: none"> • Vesicular fluid/ crust/ exudate • Skin biopsy (only be taken by dermatologist or other trained health worker) 	<ul style="list-style-type: none"> • Sterile swab • Sterile container • For skin biopsy consult local expert 	<ul style="list-style-type: none"> • Depends on suspected disease consult dermatologist and disease specific diagnostics in Table 4 	<ul style="list-style-type: none"> • Depends on suspected disease consult dermatologist and disease specific diagnostics in Table 4

* These standards are general and can differ per required diagnostic test. For specific cases follow the instructions on sample storage for the specific diagnostics and requirements requested by the laboratory that the sample is sent to.

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

Information to be recorded:

Patient information (name, date of birth, sex and residence address, unique identification number).

Other useful information may include: patient hospital number, surveillance identification number (such as EPID number), patients hospital, hospital address, room number, physicians' name and contact information, name and address for report recipient), clinical symptoms and relevant patient history (including vaccination and antimicrobial therapies received, epidemiological information), date and time of sample collection, anatomical site and location of specimen collection (for example CSF, blood, skin), tests requested.

For detection, specimens should be collected during the acute phase of illness. Test results are highly dependent on timing of specimen collection in relation to disease onset; therefore, often, especially with serological tests multiple specimens over time are required to confirm/exclude diagnosis.

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
PARASITIC INFECTIONS				
<i>Malaria</i> (10-13)				
<ul style="list-style-type: none"> • Microscopy; • RDT; • PCR (at present, no role in clinical management of malaria or routine surveillance systems). 	<ul style="list-style-type: none"> • Finger prick blood (50-75µL) to prepare: thick and thin blood film and/or RDT; • EDTA blood. 	<ul style="list-style-type: none"> • Lancet; • RDT blood transfer device; • Microscopy slides; • If transporting samples - blood collection kit including EDTA tubes or filter paper. 	<ul style="list-style-type: none"> • Microscopy and RDT can be performed onsite with fresh finger prick blood samples; • If molecular analysis is required (e.g., markers for drug resistance, pfhrp2 deletions) blood spots on filter paper can be prepared from finger prick or venous blood samples • Store in cool and dry prior to transport • Refrigerate fresh blood samples • See references (10-12, 14) 	<ul style="list-style-type: none"> • UN3373 - Biological Substance B • Category B • Packing Instruction 650 • Follow national regulations for transport of dried blood spots on filter paper

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
<p>BACTERIAL INFECTIONS</p> <p><i>Specimens should be collected during the acute phase of illness and ideally before commencement of antibiotic treatment (for serologic test additionally a convalescent sample needs to be collected).</i></p> <p><i>Treatment should be started as soon as possible, according to protocol, not awaiting diagnostic confirmation. As most of these diseases can be rapidly fatal, specimen collection should never delay administration of antibiotics.</i></p>				
<p>Plague (<i>Yersinia pestis</i>) (15)</p>				
<ul style="list-style-type: none"> • Culture, determination and susceptibility testing • PCR • Serology • Rapid dipstick test (F1 antigen detection) • ELISA anti-F1 anti-body titer IgM (requires two serum samples taken in the acute phase and 4 weeks later) • Direct fluorescent antibody testing (anti-F1 antibody) 	<ul style="list-style-type: none"> • Bubonic: bubo aspirate plus, swabs in bacterial transport media (e.g., Cary-Blair) • Pneumonic: sputum plus swabs in bacterial transport media (e.g., Cary-Blair) • Septicaemic plague: three blood cultures taken over a 45-minute period • Pharyngeal: tracheal washes • Meningeal: CSF • All forms: blood for serology • Postmortem materials include: lymph nodes, liver, spleen, bone marrow, lung, tissues <p>For serological confirmation a second sample is needed at least 4 weeks later</p>	<ul style="list-style-type: none"> • Standard testing kits for RDT and reference sample sending exist for bubonic/pulmonary plague • For bubonic aspirate 18–22 gauge needle and syringe and sterile saline 1–2 mL • Sterile container for specimen • Transport medium for specimen or swab (e.g., Cary-Blair, swabs should be made of nylon, polyester, or Dacron material): • Blood cultures • Serum separator tubes • Touch/smear preparation slides 	<ul style="list-style-type: none"> • Fresh materials storage at 2–8 °C • Frozen on dry ice • Blood cultures according to manufacturer’s/laboratory instructions 	<p>Diagnostic specimens:</p> <ul style="list-style-type: none"> • UN3373 - Biological Substance • Category B • Packing Instruction 650 <p>Cultures/bacterial isolate:</p> <ul style="list-style-type: none"> • UN2814 - Infectious substance affecting humans • Category A • Packaging instruction 620

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
<i>Leptospirosis (16,17)</i>				
<ul style="list-style-type: none"> Serology: microscopic agglutination test (MAT), latex agglutination, lateral flow, dipstick test, etc PCR Culture 	<ul style="list-style-type: none"> Whole blood (250 uL) Serum (250 uL) CSF (250 uL) Urine (10 mL) <p>Serology: paired samples obtained at least 2 weeks apart.</p>	<ul style="list-style-type: none"> Blood specimens should be collected in EDTA or Sodium Citrate tubes, blood specimens collected in heparin are not acceptable due to interference with PCR Media to inoculate clinical specimens (blood, tissue and urine) 	<ul style="list-style-type: none"> Clinical specimens to be kept frozen at -20 °C Serum to be stored at 4 °C Cultures should be stored at room temperature 	<ul style="list-style-type: none"> UN3373 - Biological Substance Category B Packing Instruction 650
<i>Anthrax For case definition and details on testing algorithms see reference (18)</i>				
<ul style="list-style-type: none"> Microscopy (M'Fadyean polychrome methylene blue) stained smears, evidence of <i>Bacillus anthracis</i> in a clinical specimen by immunohistochemical staining) Culture, determination and susceptibility testing PCR Toxin detection 	<ul style="list-style-type: none"> In all cases: blood culture and whole blood Cutaneous: skin lesion fluid (3 sterile swabs) Inhalation/Pulmonary: blood (10 mL), CSF (0.5 mL), nasal swab (2 sterile swabs), sputum, vomitus, pleural fluid Gastrointestinal: blood culture, Ascitic fluid (2 mL), Peritoneal fluid (2 mL) faeces, rectal swab, ascites Meningitis: CSF (0.5 mL), blood cultures (10 mL) Where appropriate: other fluids or tissues. E.g., pharyngeal: throat swab, tissues from biopsy or autopsy 	<ul style="list-style-type: none"> Blood culture bottles Blood collection tubes Sterile screw-capped container Sterile swabs Blood specimens should be collected in EDTA or Sodium Citrate tubes (not heparin) Tissues for Immunohistochemistry (IHC) should be formalin-fixed 	<ul style="list-style-type: none"> Most samples can be stored and sent at 2–8 °C Fresh tissue should be processed or stored/sent frozen and fixed tissue can be stored/sent at room temperature 	<ul style="list-style-type: none"> Clinical specimens: <ul style="list-style-type: none"> UN3373 - Biological Substance Category B Packing Instruction 650 Cultures only: <ul style="list-style-type: none"> UN2814- Infectious substance affecting humans Category A Packaging instruction 620

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
<p><i>Invasive meningococcal disease</i> (Meningitis and/or sepsis, and rarely arthritis, myocarditis, pericarditis, invasive pneumonia, necrotizing fasciitis, endophthalmitis) Specimen collection should never delay administration of antibiotics. (19,20)</p>				
<ul style="list-style-type: none"> • Microscopy: Gram-stain • Culture, determination and susceptibility testing, serogrouping • PCR • Serology, antigen detection (e.g., agglutination test, rapid diagnostic test) 	<ul style="list-style-type: none"> • Blood culture (Adult: 5–10 mL / Child: 1–3 mL) • Cerebrospinal fluid (CSF – 3mL), if possible, 3 tubes with each 1 mL, one for chemical analysis, protein and glucose test, one for microbiological test and one for overall appearance and leucocyte count: • Aspirate or biopsy of any normally sterile site if clinically safe and appropriate to collect (e.g., synovial fluid, cardiac fluid) and/or purpuric skin lesion) 	<ul style="list-style-type: none"> • CSF • 1 dry tube and 1 cryotube (for PCR); • If dry tube cannot be processed in <2 hours, inoculate into trans-isolate (T-I) medium • Blood: Collected blood should be diluted in blood culture broth in order to obtain blood cultures. Specimens should be immediately inoculated (within one minute) into a blood culture bottle 	<ul style="list-style-type: none"> • CSF in dry tube: room temperature • CSF in cryotube: stored at refrigerator temperature and transported in cold chain • CSF isolates: stored frozen at -20 °C to allow further testing • Trans-isolate (T-I) media vials should never be frozen. Before inoculation T-I vials should be kept in the refrigerator. Once inoculated, T-I vials should be kept at room temperature. Inoculated T-I vials must be ventilated if not transported the same day • If specimen cannot be processed in 1-2 hrs inoculate 0,5-1 mL into transisolate (T-I medium) and incubate vented at 35-37 °C with 5% CO2 overnight or until transport is possible up to 4 days). If transport is delayed beyond 4 days store at room temperature (unvented) until referral • Inoculated blood culture media should be protected from temperature extremes (<18 °C or >37 °C) with a transport carrier and thermal insulator (such as extruded polystyrene foam) • Inoculated blood culture bottles should not be placed in the refrigerator 	<ul style="list-style-type: none"> • UN3373 - Biological Substance • Category B • Packing Instruction 650

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
Cholera				
<i>Specimens should be collected as soon as possible, preferably before antibiotic therapy if required. Specimen collection should never delay administration of antibiotics. (12,19,21)</i>				
<ul style="list-style-type: none"> • Culture, identification, antibiotic susceptibility testing, subtyping; • RT-PCR • Serology (incl. Hemagglutination Inhibition Test (HAI), neutralization assay) • RDT (for surveillance, early outbreak detection, and monitoring, not for individual diagnosis of patients, needs confirmation) 	<ul style="list-style-type: none"> • Liquid stool specimen • Rectal swab 	<ul style="list-style-type: none"> • Leak proof container for stool sample if processed in 2 hours • Longer than 2 hours before processing: Cary-Blair transport medium for the swab, or if not available dip filter paper in liquid stool sample and add this to a screw cap microtube with two or three drops of normal saline solution to stop sample from drying out 	<p>Stools:</p> <ul style="list-style-type: none"> • Sample in Cary-Blair can be stored at room temperature • Sample on dry or moistened filter paper can be stored at room temperature. <p>Isolated strain from culture:</p> <ul style="list-style-type: none"> • Solid non-selective culture medium in test tubes stored at room temperature for a few days • In stock culture agar at room temperature 	<ul style="list-style-type: none"> • UN3373 - Biological Substance • Category B • Packing Instruction 650
VIRAL INFECTIONS: Respiratory viral infections				
Influenza (12, 19, 22, 23)				
<ul style="list-style-type: none"> • PCR • Culture*: virus isolation, followed by confirmatory test • Serology (incl. Hemagglutination Inhibition Test (HAI)) 	<ul style="list-style-type: none"> • Respiratory clinical specimens (i.e., nasopharyngeal swabs, nasal swabs, throat swabs, nasal aspirates, nasal washes, lower respiratory tract specimens, broncho lavage) • Serum (two-time points acute not later than 7 days of symptom onset and 2–4 weeks later) 	<ul style="list-style-type: none"> • Dacron or polyester flocced swabs with universal transport medium • For respiratory samples with large volume add remaining material in sterile container with universal transport media • Serum separator tubes (collect 3–5 mL whole blood) 	<ul style="list-style-type: none"> • Specimens received cold should be stored refrigerated (2–8 °C) for up to 72 hours before processing • If testing of a fresh specimen is not possible within 72 hours the specimen may be frozen at ≤ -70 °C and tested at a later time • Store any sample received frozen and residual specimens at ≤ -70 °C • Avoid repetitive thawing and freezing. Ship extracted RNA and frozen specimen on dry ice 	<p>Diagnostic clinical samples:</p> <ul style="list-style-type: none"> • UN3373 - Biological Substance • Category B • Packing Instruction 650 <p>Cultures of avian influenza and suspected avian/pandemic influenza:</p>

* Pathogen propagation/culture should only be performed for specific situation where routine diagnostics is insufficient, and only in laboratories that have the required permits and can comply with the required biosafety and biosecurity measure. See also reference (44).

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
Influenza, continued (12, 19, 22, 23)				
	For suspected avian influenza samples and lower respiratory tract infections: collect lower respiratory tract specimens in addition to upper respiratory tract specimens		<ul style="list-style-type: none"> Specimens for virus isolation should be placed at 4 °C immediately after collection and promptly transported to the laboratory; Sera can be stored at 4 °C for 1 week but should be frozen at -20 °C for periods longer than this. 	<ul style="list-style-type: none"> UN2814- infectious substance affecting humans; Category A; Packaging instruction 620.
COVID-19 (SARS-CoV2 infection) (24)				
<ul style="list-style-type: none"> RT-PCR (2 targets, or 1 target and sequencing) Antigen test Serology (incl. ELISA, IFA, PRNT) - Virus isolation by cell culture followed by confirmatory test* (not routine diagnostics) 	<ul style="list-style-type: none"> Respiratory clinical specimens (i.e., nasopharyngeal swabs, nasal swabs, throat swabs, nasal aspirates, nasal washes, lower respiratory tract specimens, broncho lavage) Faecal sample Serum (two-time points acute not later than 7 days of symptom onset and 2–4 weeks later) 	<ul style="list-style-type: none"> Dacron or polyester flocked swabs with universal transport medium For respiratory samples with large volume add remaining material in sterile container with universal transport media - Serum separator tubes (collect 3–5 mL whole blood) 	<ul style="list-style-type: none"> Specimens received cold should be stored refrigerated (2°–8 °C) for up to 72 hours before processing If testing of a fresh specimen is not possible within 72 hours the specimen may be frozen at ≤ -70 °C and tested at a later time Store any sample received frozen and residual specimens at ≤ -70 °C; Avoid repetitive thawing and freezing. Ship extracted RNA and frozen specimen on dry ice Specimens for virus isolation should be placed at 4 °C immediately after collection and promptly transported to the laboratory Sera can be stored at 4 °C for 1 week but should be frozen at -20 °C for periods longer than this 	<p>Diagnostic clinical samples:</p> <ul style="list-style-type: none"> UN3373 - Biological Substance Category B Packing Instruction 650 <p>Viral isolate:</p> <ul style="list-style-type: none"> UN2814- infectious substance affecting humans Category A Packaging instruction 620

* Pathogen propagation/culture should only be performed for specific situation where routine diagnostics is insufficient, and only in laboratories that have the required permits and can comply with the required biosafety and biosecurity measure. See also reference (44).

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
MERS (25,26)				
<ul style="list-style-type: none"> • RT-PCR (2 targets, or 1 target and sequencing) • Serology (incl. ELISA, IFA, PRNT) • Virus isolation by cell culture followed by confirmatory test* (not routine diagnostics) 	<ul style="list-style-type: none"> • Lower respiratory tract (preferred if possible): Sputum, endotracheal aspirate for patient on mechanical ventilation, bronchial alveolar lavage for those in whom it is indicated for patient management • Upper respiratory tract: naso-pharyngeal and oro-pharyngeal swabs or wash; • Serum (repeat after 3 weeks) (1 mL) <p>A case confirmed by serology requires demonstration of sero-conversion in two samples ideally taken at least 14 days apart</p> <p>Collection of both upper and lower respiratory tract specimens is recommended</p>	<ul style="list-style-type: none"> • Dacron, polyester swabs with universal transport medium • For samples with large volume add remaining material in sterile container (e.g., sputum/BAL) • Blood: EDTA 	<ul style="list-style-type: none"> • < 24 hours: room temperature • 24–72 hours: 0–4 °C • Long term storage: -20 °C or -70 °C (preferable) 	<p>Diagnostic clinical samples:</p> <ul style="list-style-type: none"> • UN3373 - Biological Substance • Category B • Packing Instruction 650 <p>Viral isolate:</p> <ul style="list-style-type: none"> • UN2814- infectious substance affecting humans • Category A • Packaging instruction 620

* Pathogen propagation/culture should only be performed for specific situation where routine diagnostics is insufficient, and only in laboratories that have the required permits and can comply with the required biosafety and biosecurity measure. See also reference (44).

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
<p>VIRAL INFECTIONS: Flavivirus infections (arboviral infection)</p> <p>Note: serological cross-reactivity with vaccination against and infections with other flaviviruses, makes serological diagnosis challenging. Other flaviviruses not covered here include St. Louis encephalitis, Powassan and tick-borne encephalitis, Kyasanur Forest disease virus, Omsk haemorrhagic fever (27)</p>				
<p>Dengue (12, 28, 29)</p>				
<ul style="list-style-type: none"> • RT-PCR • Serology (incl. antigen detection, IgM, IgG (ELISAs, RDTs)) • Virus isolation on cell culture followed by confirmatory test (not recommended as routine diagnostics) 	<ul style="list-style-type: none"> • Whole blood collected in EDTA • Whole blood, serum (4–5 mL venous blood) • Urine 	<ul style="list-style-type: none"> • EDTA tubes • Serum separator tubes • Sterile urine collection container/tube 	<ul style="list-style-type: none"> • Keep it refrigerated at 2–8 °C if it is to be processed or sent to a reference laboratory within 48 hours • Keep it frozen at -10 to -20 °C if it is to be processed after 48 hours but not after 7 days • Keep it frozen at -70 °C if it is to be processed after a week. At this temperature the sample will be adequately preserved for a long time • If possible, pack with dry ice, or at least ensure a cold chain by using cooling gels • Dispatch within 48 hours 	<p>Clinical specimen:</p> <ul style="list-style-type: none"> • UN3373 - Biological Substance • Category B • Packing Instruction 650 <p>Virus isolate:</p> <ul style="list-style-type: none"> • UN2814-infectious substance affecting humans • Category A • Packaging instructions 620

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
<p>Yellow fever For case definition and details on testing algorithms see references (19, 30, 31)</p>				
<ul style="list-style-type: none"> • RT-PCR • Serology (incl. ELISA, neutralization assay*) • Post-mortem: liver histopathology, detection of antigen in tissue by immunohistochemistry • Virus isolation on cell culture followed by confirmatory test * (not recommended as routine diagnostics) 	<ul style="list-style-type: none"> • Whole blood, 5 mL (in EDTA) for PCR; 5 mL whole blood (in serum separator tubes) yields ~2 mL serum collected in acute phase and repeat collection after 7-10 days or at discharge from the hospital, or post-mortem • Other: urine (10 mL) has been recommended but is not a validated specimen type • Fatal case: liver biopsy/sample 	<ul style="list-style-type: none"> • EDTA tubes • Serum separator tubes • Sterile urine collection tube • Use a liver biopsy needle or biopsy punch to take a sample of liver tissue. This is especially important if a blood sample was not collected. Place the liver sample in a vial containing 10% formalin in normal saline or Ringer's lactate solution 	<ul style="list-style-type: none"> • If samples are being transported to the laboratory within a few hours, refrigerate but do not freeze them • If the samples must be stored for more than 24 hours, freeze them at -20 °C or colder. If this is not possible, store them in the refrigerator • Use a cooler or ordinary domestic vacuum flask to transport the samples. Make sure to pack the samples with cotton wool against the walls of the cooler to avoid breakage especially if glass tubes or bottles are used. If no flask is available, make a cooler from a cardboard box lined with two to three inches of polystyrene or foam rubber and with cotton wool. Place tubes or bottles in a plastic bag, if one is available, and surround it with packing material to avoid breakage 	<p>Clinical specimen:</p> <ul style="list-style-type: none"> • UN3373 - Biological Substance • Category B • Packing Instruction 650 <p>Virus isolate:</p> <ul style="list-style-type: none"> • UN2814-infectious substance affecting humans • Category A • Packaging instructions 620

* Pathogen propagation/culture should only be performed for specific situation where routine diagnostics is insufficient, and only in laboratories that have the required permits and can comply with the required biosafety and biosecurity measure. See also reference (44).

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
Zika virus infection				
For case definition and details on testing algorithms see references (12, 32)				
<ul style="list-style-type: none"> • RT-PCR • Serology (incl. EIA, IFA, PRNT) • Virus isolation on cell culture followed by confirmatory test* (not recommended as routine diagnostics) 	<ul style="list-style-type: none"> • Whole blood plasma (4–5 mL venous blood) • Urine • Cerebrospinal fluid (CSF – 0.25 mL) • Other: semen, amniotic fluid, saliva • Serum (4–5 mL venous blood) 	<ul style="list-style-type: none"> • EDTA tubes • Serum separator tubes • Sterile urine collection tube • CSF: sterile screw-cap collection tubes 	<ul style="list-style-type: none"> • Keep it refrigerated at 2 to 8 °C if it is to be processed or sent to a reference laboratory within 48 hours • Keep it frozen at -10 to -20 °C if it is to be processed after 48 hours but not after 7 days • Keep it frozen at -70 °C if it is to be processed after a week. At this temperature the sample will be adequately preserved for a long time • If possible, pack with dry ice, or at least ensure a cold chain by using cooling gels. - Dispatch within 48 hours • Serum storage at 4 °C; >48hrs, serum should be separated 	<p>Clinical specimen:</p> <ul style="list-style-type: none"> • UN3373 - Biological Substance • Category B • Packing Instruction 650 <p>Virus isolate:</p> <ul style="list-style-type: none"> • UN2814-infectious substance affecting humans • Category A • Packaging instructions 620
Japanese encephalitis				
Confirmation of Japanese encephalitis virus infection is important as it would trigger a vaccination campaign (19)				
<ul style="list-style-type: none"> • RT-PCR, LAMP • Serology on CSF and serum (IgM capture ELISA in blood or CSF, IgG), JE virus antigens in brain tissue by IHC or IFA • Virus isolation on cell culture followed by confirmatory test* (not recommended as routine diagnostics) 	<ul style="list-style-type: none"> • CSF • Blood/Serum/Plasma (acute and on day 10 of illness) 3–5 mL blood of adults, 1–2 mL for infants and young children • Post-mortem: brain tissue <p>For serology specimens should be collected at least 14 days apart</p>	<ul style="list-style-type: none"> • CSF: sterile screw-cap collection tubes preferable three times chemistry and leucocyte count and virology. JE laboratory confirmation requires 0.5–1 mL • EDTA tubes • Serum separator tubes • Sterile container for tissue 	<ul style="list-style-type: none"> • CSF: CSF must be received in the lab within one hour of collection or stored at 2–8 °C before transport (-20 °C for long-term storage) • Blood: Storage at 0–4 °C. Long term storage: -20 °C or -70 °C (preferable) 	<p>Clinical specimen:</p> <ul style="list-style-type: none"> • UN3373 - Biological Substance • Category B • Packing Instruction 650 <p>Virus isolate:</p> <ul style="list-style-type: none"> • UN2814-infectious substance affecting humans • Category A • Packaging instructions 620

* Pathogen propagation/culture should only be performed for specific situation where routine diagnostics is insufficient, and only in laboratories that have the required permits and can comply with the required biosafety and biosecurity measure. See also reference (44).

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
West Nile virus infection (33,34)				
<ul style="list-style-type: none"> • RT-PCR • Serology serum and CSF (IgM, IgG ELISA, IFA neutralization assay*) • Virus isolation on cell culture followed by confirmatory test* (not recommended as routine diagnostics) 	<ul style="list-style-type: none"> • Whole blood, serum, plasma (4–5 mL venous blood) • CSF • Urine (persistent detection has been described, negative result does not exclude infection) <p>Serology: two sera collected with an interval of at least 1 week</p>	<ul style="list-style-type: none"> • EDTA tubes • Serum separator tubes • Sterile container for tissue • CSF: sterile screw-cap collection tubes 	<ul style="list-style-type: none"> • CSF: CSF must be received in the lab within one hour of collection or stored at 2–8 °C before transport (-20 °C for long-term storage); • Bloo/urine: Storage at 0–4 °C. Long term storage: -20 °C or -70 °C (preferable) 	<p>Clinical specimen:</p> <ul style="list-style-type: none"> • UN3373 - Biological Substance • Category B • Packing Instruction 650 <p>Virus isolate:</p> <ul style="list-style-type: none"> • UN2814-infectious substance affecting humans • Category A • Packaging instructions 620
<p>VIRAL INFECTIONS: Alphavirus infection (arboviral infection)</p> <p>Note: serological cross-reactivity, makes serological diagnosis challenging if other alphaviruses cocirculate. Other alphaviruses include Eastern, western and Venezuelan equine encephalomyelitis virus, Mayaro virus, Ross River virus, Sindbis virus (27)</p>				
Chikungunya (33)				
<ul style="list-style-type: none"> • RT-PCR • Serology (incl. IgM, IgG, ELISA, IFA neutralization assay*) • Virus isolation on cell culture followed by confirmatory test * (not recommended as routine diagnostics) 	<ul style="list-style-type: none"> • Whole blood, serum (4–5 mL venous blood) • Other: urine has been recommended but is not a validated specimen type • CSF in meningoencephalitis cases • Synovial fluid in arthritis with effusion • Autopsy material – serum or available tissues • For serology, 2 time points: Acute and convalescent 	<ul style="list-style-type: none"> • EDTA tubes • Serum separator tubes • Sterile urine collection tube 	<ul style="list-style-type: none"> • Storage at 0–4 °C • Long term storage: -20 °C or -70 °C (preferable) 	<p>Clinical specimen:</p> <ul style="list-style-type: none"> • UN3373 - Biological Substance • Category B • Packing Instruction 650 <p>Virus isolate:</p> <ul style="list-style-type: none"> • UN2814-infectious substance affecting humans • Category A packaging instructions 620

* Pathogen propagation/culture should only be performed for specific situation where routine diagnostics is insufficient, and only in laboratories that have the required permits and can comply with the required biosafety and biosecurity measure. See also reference (44).

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
<p>VIRAL INFECTIONS: Orthopox virus infections</p> <p>Orthopox viruses have been detected and isolated from various body fluids such as: oropharynx, conjunctiva, urine, blood. Materials can be collected accordingly, however, a negative test result does not exclude disease</p>				
<p><i>Mpox (35,36)</i></p>				
<ul style="list-style-type: none"> • PCR, sequencing 	<ul style="list-style-type: none"> • Lesion fluid, vesicle/pustule crust/biopsy 	<ul style="list-style-type: none"> • Swabs without individual holders may be stored in a sterile container; • Dry swabs without viral transport media 	<ul style="list-style-type: none"> • Storage at 4 °C, shipment within 72 hours 	<ul style="list-style-type: none"> • UN2814- Infectious Substance affecting humans • Category A • Packing Instruction 620
<p><i>Smallpox</i></p> <p>Smallpox has been eradicated. Synthesis and deliberate release of variola virus, accidental exposure, or natural emergence of a similar virus are still possible and would constitute low probability/high impact events. If smallpox is suspected do NOT culture, this is only allowed in designated laboratories and contact WHO immediately (35)</p>				
<ul style="list-style-type: none"> • PCR, sequencing 	<ul style="list-style-type: none"> • Lesion fluid, vesicle/pustule crust/biopsy. 	<ul style="list-style-type: none"> • Swabs without individual holders may be stored in a sterile container • Dry swabs are preferred but a minimal amount of viral transport media may be added 	<ul style="list-style-type: none"> • Storage at 4 °C, shipments within 72 hours 	<ul style="list-style-type: none"> • UN2814- Infectious Substance affecting humans • Category A • Packing Instruction 620

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
VIRAL INFECTIONS: Enterovirus infections				
<i>Poliovirus (19,37)</i>				
<ul style="list-style-type: none"> • Virus isolation by cell culture* • RT-PCR • Sequencing 	<ul style="list-style-type: none"> • Faeces, two samples 24–48 hours apart ideally within 14 days of paralysis onset (maximum 60 days); • Volume of stools 8–10 gram 	<ul style="list-style-type: none"> • Container for stool specimen 	<ul style="list-style-type: none"> • >24–72 hours cold box 2–8 °C, between frozen ice packs, should arrive at accredited laboratory within 72 hours after collection. If not, specimen should be frozen with dry ice or cold packs that have been frozen to -20 °C • Long term storage: -20 °C or -70 °C (preferable) 	<p>Clinical specimen:</p> <ul style="list-style-type: none"> • UN3373 - Biological Substance • Category B • Packing Instruction 650 <p>Virus isolate:</p> <ul style="list-style-type: none"> • UN2814-infectious substance affecting humans • Category A • Packaging instructions 620
<i>Meningitis/encephalitis or AFP caused by non-polio enterovirus infection (19,37,38)</i>				
<ul style="list-style-type: none"> • RT-PCR, followed by typing with sequencing; • Virus isolation by cell culture* 	<ul style="list-style-type: none"> • Faeces • Whole blood (minimum 1mL) collected on EDTA • CSF (0.5 –1 mL) • Respiratory clinical specimens (i.e., nasopharyngeal swabs, nasal swabs, throat swabs, nasal aspirates, nasal washes) 	<ul style="list-style-type: none"> • Container for stool specimen • EDTA tubes • Sterile CSF collection tube • Dacron or polyester flocced swabs with universal transport medium 	<ul style="list-style-type: none"> • Stools: > 24–72 hours cold box 2–8 °C, between frozen ice packs, should arrive at accredited laboratory within 72 hours after collection. If not, specimen should be frozen with dry ice or cold packs that have been frozen to -20 °C. Long term storage: -20 °C or -70 °C (preferable); • Blood, CSF, respiratory: 24–72 hours: 0–4 °C; • Long term storage: -20 °C or -70 °C (preferable) 	<p>Clinical specimen:</p> <ul style="list-style-type: none"> • UN3373 - Biological Substance • Category B • Packing Instruction 650 <p>Virus isolate:</p> <ul style="list-style-type: none"> • UN2814-infectious substance affecting humans • Category A • Packaging instructions 620

* Pathogen propagation/culture should only be performed for specific situation where routine diagnostics is insufficient, and only in laboratories that have the required permits and can comply with the required biosafety and biosecurity measure. See also reference (44).

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
VIRAL INFECTIONS: Henipavirus infection				
<i>Nipah virus infection</i> (35)				
<ul style="list-style-type: none"> • RT-PCR • Serology (incl. ELISA, neutralization assay*) • Tissue immunohistochemistry 	<ul style="list-style-type: none"> • Whole blood (minimum 1mL) collected on EDTA; • Whole blood, serum (4–5 mL venous blood); • Fatal cases isolate virus from brain, lung, kidney, spleen. <p>For serology, testing of acute and convalescent specimens is strongly recommended</p>	<ul style="list-style-type: none"> • EDTA tubes • Serum separator tubes 	<ul style="list-style-type: none"> • 24–72 hours: 0–4 °C; • Long term storage: -20 °C or -70 °C (preferable) 	<ul style="list-style-type: none"> • UN2814 - Infectious Substance affecting humans • Category A • Packing Instruction 620
VIRAL INFECTIONS: Filoviridae				
<i>Ebola virus disease</i> (35, 39, 40)				
<ul style="list-style-type: none"> • RT-PCR • Serology (incl. ELISA) • Ag-RDT (only on oral swabs for Ebola virus disease suspected deaths)** 	<ul style="list-style-type: none"> • Whole blood (minimum 1mL) collected on EDTA (alternative serum); • Oral fluid collected from deceased patients; • Frozen tissue specimens; • Other: formalin-fixed tissue or paraffin-embedded tissues. <p>For serology, testing of acute and convalescent specimens is strongly recommended.</p>	<ul style="list-style-type: none"> • EDTA tubes; do not use heparin as this can cause interfere with PCR tests • Dacron/polyester swab with flocced tip stored in universal transport medium • Serum separator tubes • Heparin can cause interference with PCR reagents and tests 	<ul style="list-style-type: none"> • < 24 hours: room temperature; • > 24–72 hours: 0–4 °C • Long term storage: -20 °C or -70 °C (preferable) 	<ul style="list-style-type: none"> • UN2814 - Infectious Substance affecting humans • Category A • Packing Instruction 620

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** Ebolavirus antigen detection, including antigen detection rapid diagnostic tests (Ag-RDTs) shows lower performance compared with NAAT. For this reason, they are not currently recommended to confirm ebolavirus infections, but may be used in some situations to test deceased individuals if NAAT cannot be accessed within 48 hours. In addition, Ag-RDTs are currently only available for Zaire ebolavirus. More information on use of Ag-RDTs can be found in the interim guidance on the use of rapid Ebola antigen tests (44).

TOOL BOX 3

Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
Marburg virus disease (35, 39, 41)				
<ul style="list-style-type: none"> • RT-PCR • Serology (incl. ELISA) 	<ul style="list-style-type: none"> • Whole blood (minimum 1mL) collected on EDTA (alternative serum); • Oral fluid collected from deceased patients; • Frozen tissue specimens. <p>For serology, testing of acute and convalescent specimens is strongly recommended</p>	<ul style="list-style-type: none"> • EDTA tubes • Serum separator tubes • Heparin can cause interference with PCR reagents and tests 	<ul style="list-style-type: none"> • < 24 hours: room temperature • > 24–72 hours: 0–4 °C • Long term storage: -20 °C or -70 °C (preferable) 	<ul style="list-style-type: none"> • UN2814 - Infectious Substance affecting humans • Category A • Packing Instruction 620
VIRAL INFECTIONS: Arenaviridae				
Other arenaviruses that can cause disease in human include lymphocytic choriomeningitis, Junin, Machupo, Guanarito, Sabia, Whitewater Arroyo virus.				
Lassa fever (35)				
<ul style="list-style-type: none"> • RT-PCR • Serology (incl. ELISA, IFA) 	<ul style="list-style-type: none"> • Whole blood (minimum 1mL) collected on EDTA (alternative serum) • Frozen tissue specimens <p>For serology, testing of acute and convalescent specimens is strongly recommended.</p> <p>Virus isolation during the febrile phase up to 14 days.</p>	<ul style="list-style-type: none"> • EDTA tubes • Serum separator tubes • Heparin can cause interference with PCR reagents and tests 	<ul style="list-style-type: none"> • <24 hours: room temperature • > 24–72 hours: 0–4 °C; • Long term storage: -20 °C or -70 °C (preferable) 	<ul style="list-style-type: none"> • UN2814 - Infectious Substance affecting humans • Category A • Packing Instruction 620

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Table 4: Diagnostic tests, specimen collection, storage, shipment by disease, continued

DISEASE DIAGNOSTIC TESTS	PREFERRED SPECIMEN TYPES AND MINIMUM VOLUMES	SPECIMEN COLLECTION MATERIALS	IN-LABORATORY STORAGE OF SPECIMENS AND TRANSPORTATION CONDITIONS	SHIPMENT CLASSIFICATION FOR DIAGNOSTIC CLINICAL SPECIMENS
VIRAL INFECTIONS: Bunyaviridae				
Rift Valley fever (<i>Phlebovirus Genus</i>) (35)				
<ul style="list-style-type: none"> • RT-PCR • Serology (incl. ELISA) 	<ul style="list-style-type: none"> • Whole blood (minimum 1mL) collected on EDTA (alternative serum) • Frozen tissue specimens; • Other: formalin-fixed tissue or paraffin-embedded tissues <p>For serology, testing of acute and convalescent specimens is strongly recommended</p>	<ul style="list-style-type: none"> • EDTA tubes • Serum separator tubes • Heparin can cause interference with PCR reagents and tests 	<ul style="list-style-type: none"> • <24 hours: room temperature; • > 24–72 hours: 0–4 °C; • Long term storage: -20 °C or -70 °C (preferable) 	<ul style="list-style-type: none"> • UN3373 - Biological Substance • Category B • Packing Instruction 650
Crimean-Congo haemorrhagic fever (<i>Nairovirus Genus</i>) (35, 42, 43)				
<ul style="list-style-type: none"> • RT-PCR • Serology (incl. ELISA, neutralization assay*) 	<ul style="list-style-type: none"> • Whole blood (minimum 1mL) collected on EDTA (alternative serum) • Tissue specimens <p>The virus and antigen are usually detectable up to 1–2 weeks after onset of illness. Fatal cases rarely show significant antibody response, however those who survive, IgM and IgG antibodies are frequently detectable after about a week of illness.</p> <p>For serology, testing of acute and convalescent specimens is strongly recommended</p>	<ul style="list-style-type: none"> • EDTA tubes • Serum separator tubes • Heparin can cause interference with PCR reagents and tests 	<ul style="list-style-type: none"> • <24 hours: room temperature; • > 24–72 hours: 0–4 °C; • Long term storage: -20 °C or -70 °C (preferable). 	<ul style="list-style-type: none"> • UN2814 - Infectious Substance affecting humans • Category A • Packing Instruction 620

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TOOL BOX 3

Box 1

Turnaround time depends on various steps

- ✓ Have materials for sample collection and packaging available at the national laboratory and other strategic levels to quickly respond during outbreaks.
- ✓ Collect, store and ship samples according to guidelines.
- ✓ Collect clinical information and correctly complete all case investigation and laboratory forms.
- ✓ Transport samples to the relevant testing facility either at national level (if diagnostic capacity exists) or at a regional, or if these are not available, at an international reference laboratory.
- ✓ Establish pre-agreed arrangements with shipment companies and laboratories for rapid transportation.
- ✓ Provide clinical information to the receiving laboratory, including already performed tests, known results, and specify which diseases need to be investigated and (if applicable) which test(s) to be performed on which material.
- ✓ Communication with receiving laboratory to inform them on incoming shipment including clear communication about urgency and assurance that sample taking is done according to their guidelines/instructions.
- ✓ Frequency of testing (in case of emergency, discuss if test can be performed on receipt of sample).
- ✓ Duration of the test varies per assay: Some nucleic acid amplification assays can be run in less than 90 minutes, but it can also take up to a day. Serology depends on the technique and might require overnight incubation sometimes requiring two days. Cultures can take days to sometimes several weeks. Ask laboratory for specific duration from specific test to result.
- ✓ Communication of the results: Assure that the laboratory that receives the sample knows to whom and how to report the result back in a timely manner.

TOOL BOX 3

References and further reading

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TOOL BOX 4



Transport of infectious substances

This tool box highlights some important features of the *WHO Guidance on regulations for the transport of infectious substances 2021—2022*. The transport of infectious substances is regulated by recommendations or regulations developed by international groups. The objective of these is to control and reduce the risk and exposure for people and the environment while transporting materials containing biological agents.

One of the most widely known and referenced set of recommendations are the *Recommendations on the Transport of Dangerous Goods—Model Regulations (21st revised edition)* (hereafter referred to as the UN Model Regulations). These recommendations are made by the Committee of Experts on the Transport of Dangerous Goods (UNCETDG), a committee of the United Nations Economic and Social Council, comprising expert advisors from various countries, non-governmental organizations and specialized agencies including WHO representatives.

The UN Model Regulations aim to provide a minimum set of provisions to follow to safely transport any dangerous goods, which includes infectious substances. The use of this same set of provisions as a basis across various national and international regulations aims to introduce provide conformity and harmonization across them all.

TOOL BOX 4

Infectious substances: definition

For the purposes of transport, infectious substances are defined as substances which are known or are reasonably expected to contain pathogens. Pathogens are defined as micro-organisms (including bacteria, viruses, parasites, fungi) and other agents (such as prions), which can cause disease in humans or animals. In this context, the terms infectious substances, infectious materials and infectious products are considered synonymous.

The definition is applied to all specimens (apart from those explicitly exempted) including:

- cultures
- patient specimens
- biological products
- medical or clinical wastes
- medical devices and equipment.

Infectious substances: exceptions

There are some circumstances where, although the material or product being shipped falls under one of the definitions above, it will not meet the definition for an infectious substance.

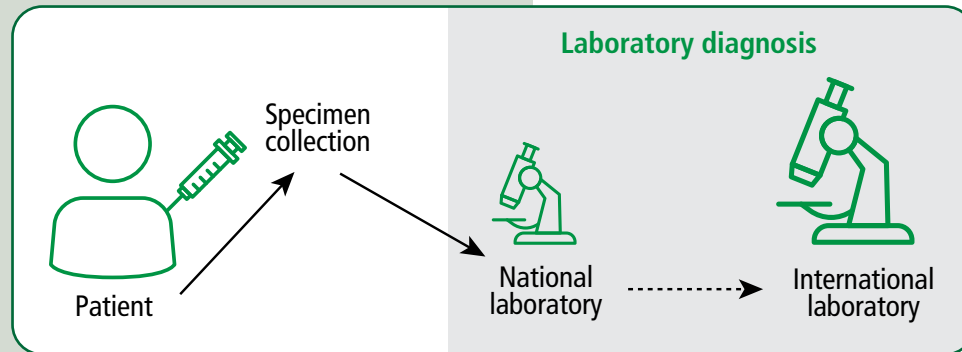
This is due to the following circumstances:

1. The confirmed absence of biological agents; or
2. That any biological agents present are known to be incapable of causing disease in humans or animals (in other words non-pathogenic OR inactivated or neutralized through a decontamination process).

In such cases, the materials or products are not considered to pose a health risk and are therefore not subject to transport regulations providing certain provisions are followed. That is unless it meets the criteria for a dangerous goods in another class. Specific examples of these complete exceptions include:

- Cultures where the biological agent is non-pathogenic to humans or animals.
- Patient specimens for faecal occult blood screening samples, or testing using a dried blood spot.
- Biological products such as blood/blood products for transfusion or body parts for transplant.
- Medical or clinical waste which has been appropriately decontaminated using inactivation methods such as autoclaving or incineration.

- Medical equipment which has been drained and confirmed to be free of any contaminated liquid. Note that certain packaging requirements apply.
- Environmental samples (for example food, soil, water) shipped for investigational purposes, but which are not thought to pose a risk of infection to humans or animals, also fall under this definition.



TOOL BOX 4

Classification

Should professional judgement find that the material to be shipped is reasonably expected to contain biological agents capable of causing disease in humans or animals, and cannot be defined as an exemption, it is an infectious substance. Classification of an infectious substance must therefore be made according to the materials composition and the level of risk it poses to human or animal health.

It is this classification that will be used to assign the substance a proper shipping name and a UN number that will be used in all aspects of the package preparation including its packaging composition, marking, labelling and for documentation purposes.

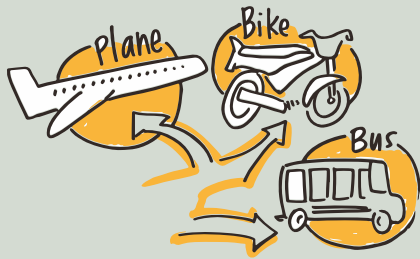
All infectious substances are assigned to Dangerous Goods Division 6.2. Once classified as a dangerous good under Division 6.2, the material must then be further subclassified based upon the material composition, the type of biological agent present, and the severity or harm that may be caused by that biological agent.

Infectious substances are subclassified into the following categories:

- **Category A:** An infectious substance which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease in otherwise healthy humans or animals.
- There are two different UN numbers and proper shipping names associated with Category A infectious substances:
 - Infectious substances capable of causing disease in humans, or both humans and animals, are assigned to **UN 2814**, and a proper shipping name of **INFECTIOUS SUBSTANCE, AFFECTING HUMANS**.
 - Infectious substances capable of causing disease only in animals are assigned to **UN 2900**, with the proper shipping name of **INFECTIOUS SUBSTANCE, AFFECTING ANIMALS**.
- **Category B:** Contain biological agents, capable of causing infection in humans or animals, but **NOT** meeting the criteria for Category A (in other words, the consequences of an infection are not considered severely disabling or life-threatening).
- Except for substances containing high risk biological agents, most shipments of infectious substances can be transported under Category B.
- The UN number and proper shipping name for most shipments of Category B infectious substances is **UN 3373, BIOLOGICAL SUBSTANCE, CATEGORY B**.



TOOL BOX 4



Transporting medical or clinical waste

- Category A infectious substances must be assigned to UN 2814, UN 2900 or UN 3549, as appropriate.
- Medical waste, Category A, AFFECTING HUMANS solid or MEDICAL WASTE, CATEGORY A, AFFECTING ANIMALS only, solid.
- Infectious substances generated from the medical treatment of humans or veterinary treatment of animals may be assigned to UN 3549.

The UN 3549 entry must not be used for waste from bioresearch or liquid waste. This UN number is forbidden as cargo in air transport, unless prior approval is obtained from the appropriate authority of the State of origin and the State of the operator under the written conditions established by those authorities.

- Category B infectious substances must be assigned to UN 3291.

Exemptions:

- The material/substance is not subject to any transport regulation.

General preparation of shipments for transport

Because of the differences in the hazards posed by Category A infectious substances (UN 2814 and UN 2900) and Category B infectious substances (UN 3373), there are variations in the packaging, labelling and documentation requirements for the two categories.

The UN Model regulations, as well as other modal agreements, produce information sheets that outline the detailed packaging requirements for various classifications and sub-classifications of dangerous goods. These instruction sheets are generally referred to as packing instructions, of which four may be applicable to the shipment of infectious substances. These include:

- P620 for Category A Infectious Substances;
- P650 for Category B infectious substances assigned to UN3373;
- P621 for Medical or Clinical Wastes containing a Category B infectious substance (assigned to UN3291); and
- P622 for Medical waste, Category A, affecting humans or Medical waste, Category A, affecting animals (assigned to UN3549)

A packing instruction, PI954, is also provided in the ICAO Technical Instructions for the use of dry ice as a coolant, which may be applicable to infectious substances being transported by air.

Note 1: Hand carriage of Category A and Category B infectious substances and transport of these materials in diplomatic pouches are strictly prohibited by international air carriers.

Note 2: Inner packaging containing infectious substances shall not be consolidated with inner packaging containing unrelated types of goods.

Quantity limits for Category A transports – Packing instruction P620

- For shipments being carried in the cargo hold of passenger aircraft, no more than 50 mL or 50 g of Category A infectious substance per package is allowed.
- For shipments being carried on a cargo only aircraft, no more than 4 L or 4 kg of Category A infectious substance per package is allowed.
- For shipments being carried via surface transport (road, rail or maritime), there are no quantity limits per package

Quantity limits for Category B transports – Packing Instruction P650

- For shipments being carried by air (passenger or cargo aircraft), the primary inner receptacle must not contain more than 1 L and the outer packaging must not contain more than 4 L of material. This excludes any quantity of coolants used, such as dry ice or liquid nitrogen.
- For shipments being carried via surface transport (road, rail or maritime), there are no quantity limits per package.

The carriage of infectious substances as hand carriage on passenger aircraft – even in diplomatic pouches – is strictly prohibited.

Shippers of infectious substances shall ensure that packages are prepared in such a manner that they arrive at their destination in good condition and present no hazard to persons or animals during transport.

TOOL BOX 4

Basic triple packaging system

This system of packaging shall be used for all infectious substances. It consists of three layers as follows:

- **Primary receptacle.** A primary watertight, leakproof (for liquid), or sift-proof (for solids) receptacle containing the specimen. The receptacle is packaged with enough absorbent material to absorb all fluid in case of breakage or leakage.
- **Secondary packaging.** A second durable, watertight, leakproof or sift-proof packaging to enclose and protect the primary receptacle(s). Several cushioned primary receptacles may be placed in one secondary packaging, but sufficient additional absorbent material shall be used to absorb all fluid in case of breakage or leakage.
- **Outer packaging.** Secondary packagings are placed in outer shipping packagings with suitable cushioning material. Outer packagings protect their contents from outside influences, such as physical damage, while in transit. The smallest outer packaging must have a minimum dimension of 100 mm × 100 mm.

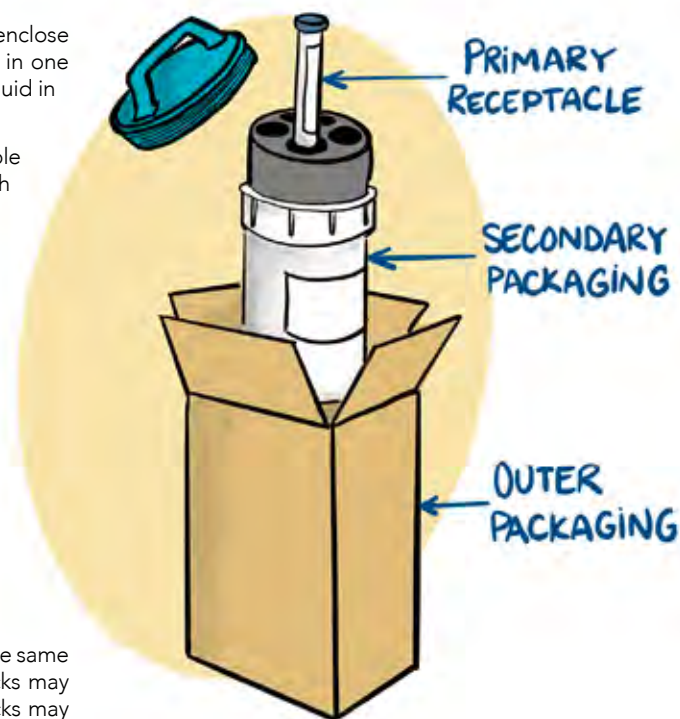
Specimen data forms, letters, supplementary documentation and other types of information that identify or describe the infectious substance should be placed between the secondary container and outer layers of packaging. If necessary, these documents may be taped to the secondary container.

Each completed package is normally required to be correctly marked, labelled and accompanied with appropriate shipping documents (as applicable).

There are specific packaging, labelling and documentation requirements for infectious substances in **Category A** and requirements with lesser constraints for substances in **Category B** (see above the references to packing instructions per category).

Overpacks

- For both categories it is possible to use overpacks.
- Overpack is the term used when several packages are combined to form one unit and sent to the same destination by a single shipper. When refrigerants are used to protect contents, the overpacks may comprise insulated vessels or flasks. If dry ice is being used to protect contents, the overpacks may be comprised of insulated vessels or flasks to allow dissipation of carbon dioxide gas. Whenever an overpack is used, the required marks and labels shown on the outer packaging must be repeated on the outermost layer of the overpack. This requirement applies to infectious substances in Categories A and B. Overpacks are also required to be marked with the word overpack.
- It is very important to not reproduce by hand or other means any UN specifications markings on the overpack.



TOOL BOX 4

Reusing and re-cycling packaging materials

Shipping packages and packaging materials can be reused or returned. Before an empty packaging is returned to the consignor, or sent elsewhere, it must be disinfected or sterilized to nullify any hazard and any label or mark indicating that it contained an infectious substance must be removed or obliterated. If the packaging is being re-used, the shipper must ensure that all marks and labels reflect the substances actually being shipped and not the substance it was used for previously.

Re-used packaging must maintain its ability to comply with relevant quality testing procedures outlined in later sections on Category A and Category B packaging requirements. If packaging material becomes damaged or reduced in strength, it should no longer be used.

Coolants/refrigerants

A coolant (also known as a refrigerant) is a substance which is used to maintain a cool temperature around the dangerous goods to preserve its integrity until it reaches its final destination. Many commonly used coolants are themselves dangerous goods of other classes. Therefore, in addition to following the requirements of the relevant packing instructions for infectious substances (P620, P621 and P650), other packing requirements specific to these substances may need to be observed.

Special provisions applicable to the use of dangerous goods as coolants may be found in Chapter 5.5.3 of the UN Model regulations.

Some of the general requirements for packaging used to contain infectious substances together with a coolant material include:

- Packaging used must be capable of maintaining integrity at the temperature afforded by the coolant.
- The coolant must be placed between the secondary container and outer packaging, or in an overpack used to transport multiple packages together.
- Persons handling the packages should be appropriately trained on the coolants in use.
- Coordination between the shipper and carrier should ensure that the cargo transport unit being used to carry the packages is well ventilated for the coolants in use. This is especially important in the case of air transport, to ensure ventilation safety procedures are followed. The carrier may also need to ensure cargo transport units are appropriately marked with warning and hazard labels.

Coolants may be used to stabilize infectious substances in Categories A and B during transit. Further information on how to pack infectious substances requiring the use of coolants as well as their description and characteristics can be found in the Guidance on regulations for the Transport of Infectious Substances 2021-2022.



TOOL BOX 4

Trainings

- The Dangerous Goods Regulations require all personnel involved in transport to undergo appropriate training. According to the UN Model Regulations, all individuals involved in the transport of dangerous goods shall be trained in the contents of dangerous goods requirements commensurate with their responsibilities.
- It should be noted that most modal agreements include provisions that require the testing and verification of an individual's knowledge and competency in the aforementioned areas for any person involved in dangerous goods transportation
- For the transport of Category A infectious substances, personnel must undergo training in accordance with the modal requirements.
- For the transport of Category B infectious substances, there is a requirement that clear instructions on the use of the packaging are supplied to the user; this is regarded as sufficient training for the shipping of these substances. However, if such specimens are consigned with other dangerous goods (for example flammable liquids, radioactive materials, liquefied gases, etc.), then personnel must be trained in the proper procedures for their transport.



TOOL BOX 4

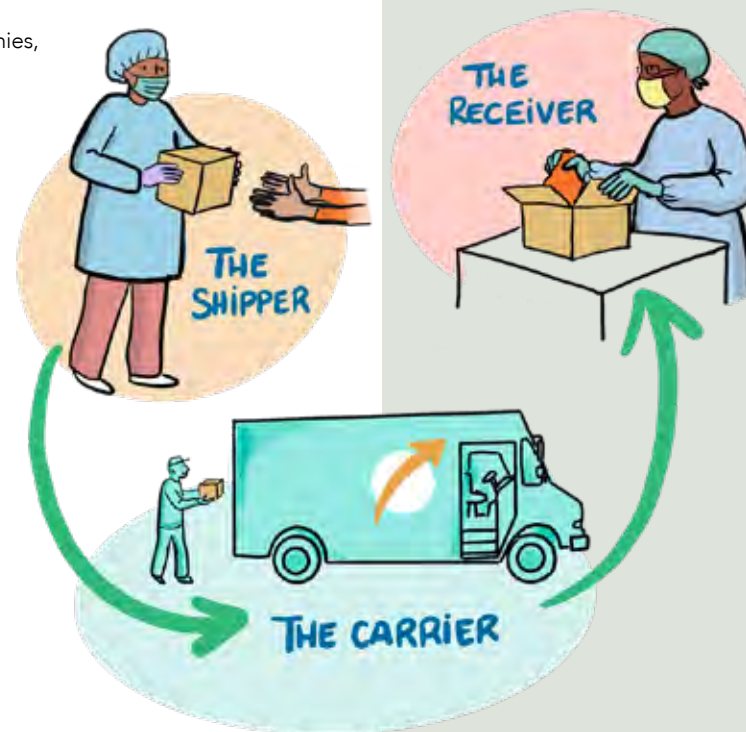
Transport

- It is the responsibility of the shipper to ensure the correct classification, packaging, labelling, and documentation of all infectious substances destined for transport.
- The efficient transport and transfer of infectious substances requires good coordination between the sender, the carrier and the receiver to ensure that the material is transported safely and arrives on time and in good condition. Such coordination depends upon well-established communications and a good working relationship between the three parties.

Main actors in the infectious substance transport chain are:

- **The shipper:** may also be known as the consignor or the sender.
- **The packing supplier:** manufactures and tests lines of packaging materials according to applicable regulations.
- **The carrier or operator:** may include logisticians, courier companies, airline freight forwarders or other transport operators.
- **The receiver:** may also be known as the consignee, importer or buyer.

Descriptions of their respective responsibilities and duties can be found in the Guidance on regulations for the Transport of Infectious Substances 2021-2022.

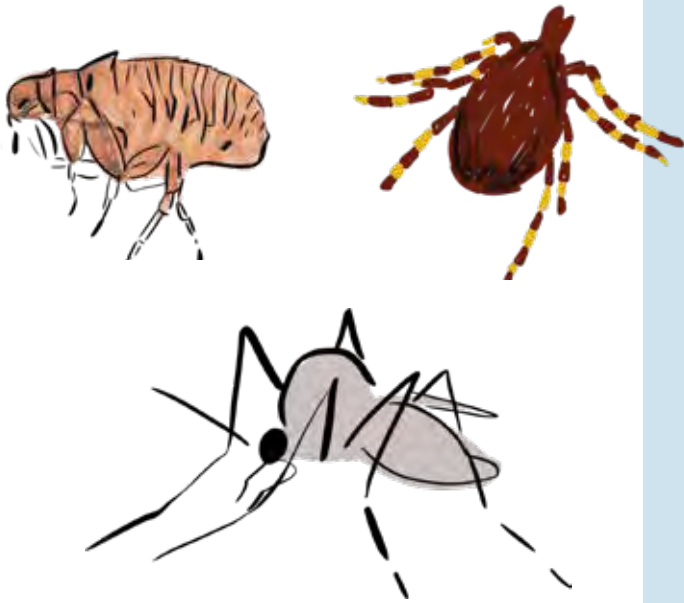


For more information on the transport of infectious substances:

- Guidance on regulations for the Transport of Infectious Substances 2021-2022
<https://apps.who.int/iris/handle/10665/339825>

TOOL BOX 5

Prevention of vector-borne diseases and control through measures against vectors before and during epidemic situations



Some epidemic diseases are transmitted by arthropod vectors, such as, mosquitoes, ticks and other insects. To prevent the transmission of these infectious diseases, called Vector-borne diseases (VBDs), actions can be taken to protect human beings from contact with the vectors and/or to eliminate or reduce vector populations. These actions include vector control operations, community engagement and participation, and personal protection.

TOOL BOX 5

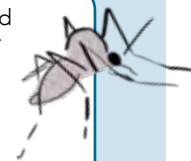
Below is a list of epidemic-prone VBDs included in this handbook. These are transmitted by different vectors but share a common transmission mode, via **the bite** of a vector. While bites are a common mode of pathogen transmission, it is important to know that there may be other modes of transmission, such as passing through the skin in the case of Chagas disease.

Epidemic-prone VBDs transmitted by the bite of a vector include:

- **Crimean-Congo haemorrhagic fever virus** (CCHFV) is transmitted by *ticks* of the family *Ixodidae*, mainly by *Hyalomma* genus. In the Mediterranean, central Asia and Africa, the most prominent vector is *Hyalomma marginatum*.



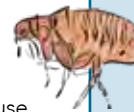
- **Yellow fever** (YFV), **dengue** (DENV1, DENV2, DENV3, DENV4), **Zika** (ZIKV) and **chikungunya** (CHIKV) viruses are transmitted by *mosquitoes*. Epidemics may occur in rural and urban environments, with the primary vector being *Aedes aegypti*, and secondary vector being *Aedes albopictus*. Some of these arboviruses (YFV and ZIKV) circulate through different cycles from sylvatic (wild) to rural, peri-urban and urban cycles, with different vector species according to the cycle. In monkeys and other non-human primates, zoonoses of YFV occurs in sylvatic transmission involving various vector species. For this reason, vaccination of all people living in high-risk environments for YFV is recommended as a primary intervention for prevention and control, which can be complemented by targeted vector control measures to help interrupt transmission.



Note that the mosquito vector control guidance here does not include guidance for anopheline mosquitoes.

Please refer to the latest *WHO Guidelines for malaria* available at: <https://app.magicapp.org/#/guideline/6832>

- **Plague** is a bacterial disease transmitted by *fleas* into zoonotic cycles in which fleas on rodents play a major role in transmission. Zoonotic cycles are transmission cycles between vector-host and pathogen that are found in the wild environment, as opposed to domestic environments. For epidemics in domestic environments, fleas from rodents are major vectors. The most well-known flea species being *Xenopsylla cheopis*. However, many flea species can act as plague vectors because the association between the disease caused by the *Yersinia pestis* bacteria, and the flea species is not very specific.



These different vectors have different ecologies, behaviors, biting times and transmission cycles. Understanding the vector in relation to its environment (its **bionomics**), as well as the pathogen life and transmission cycles, affects the type of actions taken to prevent and control VBDs. However, for all of these vectors and in all situations, there are four key types of action which must be integrated into an operational plan and regularly evaluated:

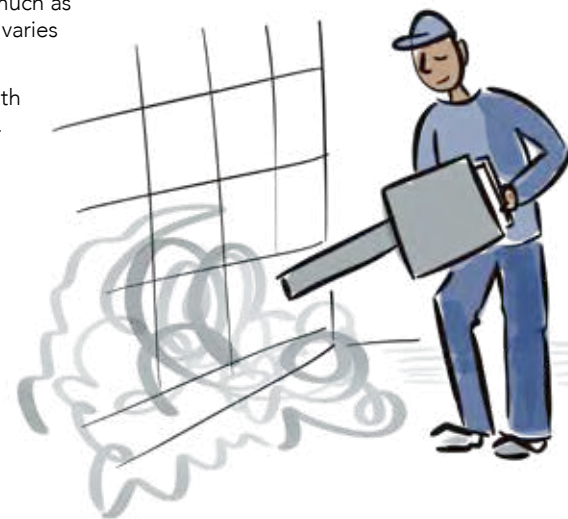
1. **Vector control operations** implemented by public and/or private agencies and deployed to reach individuals/households in all communities. **Table 1** summarizes vector control tools available for each vector type.
2. **Community engagement**, which is essential for outbreak response.
3. **Personal protection tools** to prevent bites. **Table 2** summarizes the biting behavior of the different vectors and the type of personal protection available.
4. **Communication** of the different actions, as an essential component for success. Public Health recommendations must take into account local social and cultural factors.

TOOL BOX 5

Vector control activities are deployed in order to prevent and/or control the transmission of VBDs. These activities include eliminating or reducing the adults and immatures of insects such as mosquitoes and tick vectors as much as possible, as well as reducing contact between the vectors and hosts. The operationalization of vector control varies according to the type of vector and transmission intensity (WHO, 2012).

- Vector control strategies should ideally address all life stages of the vectors from the egg to larva and adult, with prioritization of the interventions according to the vector species, the disease they transmit and the context.
- Among control measures, **insecticide applications** are the most frequently used in three ways, 1) either on the animal carrying the vectors, such as the ticks and the fleas, 2) in vector breeding sites to kill larvae, and 3) as adulticides to eliminate adult including application to bed nets and/or resting sites.
- Other vector control activities include:
 - **Environmental measures** including sanitation, habitat management and livestock management.
 - **Mechanical measures** including trapping vectors.
 - **Biological tools** using natural enemies and biological larvicides for mosquitoes.
 - **Other chemicals** such as the use of natural hormone mimics to stop insect development.
- A new generation of vector control products are also currently being tested that uses modified organisms. This includes 1) vector sterilization, such as in the Sterile Insect Technology (SIT), 2) harboring of bacteria which suppress transmission and/or reduce populations (e.g., bacteria *Wolbachia*) and 3) genetically modified mosquitoes through gene-drive technology.
- Vector control tools can be used alone, or can be recommended to be used in combination, through an Integrated vector management (IVM) approach (WHO, 2012).¹ The integrated nature of this approach means that interventions will be applied based on the vectors, disease, and context. The deployment, efficiency and results of vector control activities require Monitoring and Evaluation (M&E). However, the methods and infrastructure required to perform M&E, both at the vector population level, and in terms of disease transmission, are often weak or lacking.
- **Vector surveillance** is an essential part of a successful vector control programme and helps improve timeliness of decisions to control vector populations and minimize disease burden. Both larval and adult vector populations should be targeted for surveillance. Entomological surveillance and indicators should be collected and analysed in close collaboration with epidemiological data. This entomological surveillance will include:
 - Vectors densities and geographical distribution.
 - Bionomics such as biting behaviour and contacts with human hosts and resting sites.
 - Effectiveness of control tools (for example susceptibility or resistance to insecticides).

¹ WHO, Handbook for integrated vector Management, 2012 http://apps.who.int/iris/bitstream/10665/44768/1/9789241502801_eng.pdf



TOOL BOX 5

TABLE 1: Vector control tools for CCHF, YFV, DENV1-4 CHIKV, ZIKV, plague and leishmaniasis

Type of vector (VBDs)	Ticks (CCHF)	<i>Aedes</i> mosquitoes (YFV, DENV1-4, CHIKV, ZIKV)	Fleas (plague)	Sand Flies (Leishmaniasis)
Endemic situation				
Insecticide against larvae	+	+++	+++	-
Insecticide against adults	+	+	+++	+++
Animal sprayed with insecticide	Yes	No	Yes	No
Physical elimination of breeding sites/larval habitats (public and domestic)	+	+++	+++	+
Mechanical trapping	+	+	++	(+)
Environmental measures	+	+++	+++	++
Epidemic situation				
Insecticide against larvae	+++	+++	+++	-
Insecticide against adults	+++	+++	+++	+++
Animal sprayed with insecticides	Yes	No	Yes	No
Physical elimination of breeding sites (public and domestic)	++	+++	+++	++
Mechanical trapping	+	+++	+++	++
Environmental measures	++	+++	+++	++

Table 1 legend: The efficacy of the tool/intervention in reducing the vector population and/or the contact between the vectors and the humans, varies from very low efficacy ((+)), to low efficacy (+), medium efficacy (++) and great efficacy (+++). No information is available or no efficacy has been reported for -.

TOOL BOX 5

TABLE 2: Personal protection tools according to vector type

Type of vector (VBDs)	Ticks (CCHF)	Aedes mosquitoes (YFV, DENV1-4, CHIKV, ZIKV)	Fleas (plague)	Sand Flies (Leishmaniasis)
Vector bionomics				
Natural environment	Forest, wild	Wild, rural and ur-ban	Domestic, wild	Wild, rural, urban
Peak biting time	Day	Day	Day and night	Night
The pathogen needs to complete part of its life cycle within an animal	Yes	No	Yes/No	Yes/No
Personal and household protection tools				
Insecticide treated net (e.g., bed net, window nets, etc.)	-	+	-	++
Repellent	++	+++	++	++
House screening (e.g., window screens)	-	+++	-	++
Insecticide sprays	+	+++	++	+++
Electric devices (e.g., de-vices to release insecti-cides or electric racquets)	-	++	-	-
Elimination of domestic breeding sites	-	+++	+++	-

Table 2 legend: The efficacy of the tool/intervention in reducing the vector population and/or the contact between the vectors and the humans, varies from low efficacy (+), medium efficacy (++) and great efficacy (+++). No information is available or no efficacy has been reported for -.

TOOL BOX 5

Disease-specific approaches based on the vectors' ecology and control options



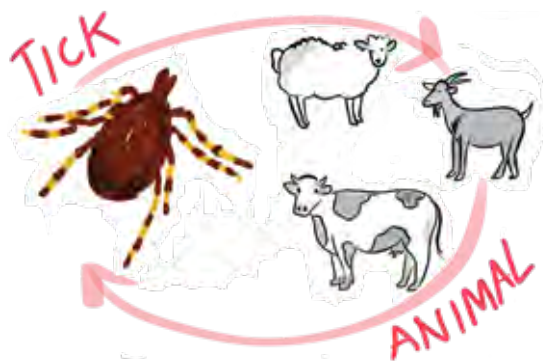
The **Crimean-Congo haemorrhagic fever virus** (CCHFV) is transmitted by *Hyalomma sp.* ticks.

- These ticks blood feed at all stages, from the six-legged larval stage to the eight-legged adult stage, to complete their development and mature their eggs. In addition to being transmission vectors, ticks are also **reservoir of CCHFV**.
- The larval stages of these ticks usually feed on small animals, and the adult stages feed on larger animals such as deer, sheep and cattle. The ticks do not have feeding preference and humans are considered accidental hosts. CCHFV circulates into animal populations without causing diseases (except in ostriches) and humans are considered dead-end hosts. This means that the virus cannot be amplified in humans and thus cannot be directly transmitted from human to human. CCHFV needs animals as amplifying hosts (domestic and wild animals).
- In regions with transmission risk (in other words where animals are infected by CCHFV) the main objective of vector control activities is to **inform the public** and local communities how to promote practices that decrease disease transmission. Such practices include preventing contact with the blood of virus-infected animals (e.g., slaughtering activities), preventing tick bites, and preventing transmission during home care for infected individuals or during funerals.

Key behavioral interventions	
Animal settings	<ul style="list-style-type: none"> • Reduce ticks in the environment and decrease tick infestations on animals or in stables/barns. <i>The tick vectors are numerous and widespread and tick control with acaricides (chemicals intended to kill ticks) is only a realistic option for well-managed livestock production facilities.</i> • Implement quarantine for animals before they enter slaughterhouses or routine treatment of ruminants with pesticides two weeks prior to slaughter. <i>This activity will decrease the risk for animal to be viraemic during its slaughtering.</i> • Wear PPE (masks, gloves and gowns) when slaughtering and butchering animals in slaughterhouses or at home. <i>This will prevent skin contact with infected animal tissue or blood.</i>
Home settings	<ul style="list-style-type: none"> • Wear protective clothing (long sleeves, long pants, etc.) and light-colored clothing (to allow easy detection of ticks on the clothes). • Avoid areas where tick vectors are abundant when they are most active (spring to fall). • Examine clothing and skin for ticks regularly. • Use repellents on the skin (e.g. DEET) and clothing (e.g. permethrin). • Remove ticks safely from the skin.
Health care settings	<ul style="list-style-type: none"> • Seek early treatment for fever after a history of tick bites or contacts with CCHF patients. • Avoid any direct unprotected contact with blood or body fluids when managing patients. • Wash hands with soap and clean water regularly. • Organize safe and dignified funerals.



TOOL BOX 5



- **Current vector control measures are not fully satisfactory:**

- Chemical methods of vector control (for example insecticides and other chemical products to eliminate vectors) produce resistant ticks, food contamination, and environmental pollution. Furthermore, chemical tick control is only realistic for well-managed and sufficiently resourced livestock production facilities that are rare in most affected countries.
- Physical methods of vector control (for example heavy grazing, burning of grasslands) have detrimental impacts on the natural environment.
- Biological methods of vector control (for example use of hormones and growth regulators, use of predators, bacteria, nematodes, and fungi) have not demonstrated full efficacy.
- Vaccination is a promising alternative to control tick infestations. An **animal vaccine effective against *Hyalomma* ticks** that prevents the tick-animal-tick cycle would decrease tick population, decrease CCHF prevalence in animals, and therefore decrease human exposure.

Yellow fever, dengue, Zika, and chikungunya viruses are transmitted at an epidemic level predominantly by **mosquitoes** belonging to the species *Ae. aegypti* and *Ae. albopictus*.

- The *Ae. aegypti* and *Ae. albopictus* species are responsible for epidemics of these viruses in human populations. Although some of these viruses can also be transmitted by other mosquito vectors species in sylvatic environments (wild environments), and potentially cause zoonoses.
- *Ae. aegypti* and *Ae. albopictus* mosquitos have adapted to urban settings and can lay eggs in any kind of water-containing recipient (for example roof gutters, containers, etc.) in and around houses and other human dwellings both in urban and scattered rural areas (human dwellings far away from urban or rural settings).
- The larval development stage can be very short, less than a week. This can lead to an exponential increase in the mosquito population if the conditions are favourable (in other words where there are favourable water temperatures and food availability) and in the absence of any habitat management and/or vector control.
- It is strongly recommended to maintain regular control of mosquito populations through the physical elimination of all breeding sites, both in private and public spaces, and by using larvicides in breeding places that cannot be eliminated. Biological larvicide using *Bacillus thuringiensis* var. *israelensis* toxins is recommended given that such larvicide has a lack of resistance and no environmental drawback.



TOOL BOX 5

- **During epidemic level transmission, all tools to protect humans from mosquito bites (Table 2), as well as all available tools to eliminate adult mosquitoes, are recommended with reinforcement of the elimination of breeding sites, use of larvicide and use of adulticide.²**
- **The efficacy of the products must be monitored in advance with tests for resistance and, if necessary, an integrated resistance management plan must be developed.**
- The spraying of adulticides must be done on a daily basis as much as possible until the mosquito populations are cut down under the necessary Breteau Index (BI) (that is the number of positive containers in 100 houses) which should be less than one.³
- **Community engagement** is also a very important component for controlling *Ae. aegypti* and *Ae. albopictus* populations. Communities can take action in several important ways including, following recommendations for personal protection in public and private spaces including homes, workplaces and schools, participating in activities to eliminate of breeding sites, installing window screens, and participating in overall surveillance of the environment to make it less favorable for mosquitoes.
- While there are many challenges to control *Ae. aegypti* and *Ae. albopictus*, (including unplanned urbanization and lack of resources), these tools are often the only available control measures against all arboviruses such as, dengue (DENV1-4), chikungunya and Zika viruses with the exception of yellow fever for which a safe and efficient vaccine is available. If integrated vector control measures are applied thoroughly, and consistently, they can help to control virus transmission.
- More information on yellow fever, dengue, Zika and chikungunya can be found in each disease-specific chapter.



² WHO, Pesticide and their application for the control of vectors and pests of public health importance, 2006. http://apps.who.int/iris/bitstream/10665/69223/1/WHO_CDS_NTD_WHOPES_GCDPP_2006.1_eng.pdf

³ Bowman LR, Runge-Ranzinger S and McCall PJ. *Assessing the Relationship between Vector Indices and Dengue Transmission: A Systematic Review of the Evidence*. PLoS Negl Trop Dis. 2014 May; 8(5): e2848. doi: 10.1371/journal.pntd.0002848

Plague circulates into mammals, especially rodents, in almost all regions of the world.

- Humans are affected by plague epidemics through two main transmission modes. At the beginning of an epidemic, rodents are affected by the disease with fleas as vectors, then the fleas leave the dying rodents and move on to humans. At this stage, the plague is called bubonic because bubonic abscesses are the main clinical symptoms. With the spread of the bacteria into the lungs, humans can then directly transmit the plague bacteria to other humans. At this stage the plague is called pneumonic.
- The fleas that cause plague are host-specific and these animal fleas bite humans by accident.
- **Sanitation and rat control are the best practices to prevent human plague. When plague cases are reported, control measures must first target fleas and secondarily rodents.** This is because the use of raticide may result in an adverse effect, where fleas leave the dead rats and move onto humans and transmit the bacteria. However, depending on environmental context, **large deployment of insecticide baited traps for rats can be recommended.**
- Vector control for the plague can be supported by environmental measures to repel the rat population, including house disinfection, use of rodent repellents, storage of grains or food sources. As well as ensuring that insect elimination measures, such as applying insecticide in all places where rodents inhabit or congregate, as well as applying insecticides where domestic animals such as dogs or cats, which may be carrying fleas, sleep or congregate.
- **Community engagement** is also very important for coordinated rat control activities, management of wastes and domestic environment.
- More information can be found in the plague chapter of this handbook.

TOOL BOX 5



For more information on prevention of vector-borne diseases and control through measures against vectors before and during epidemic situations:

- WHO Global vector control response 2017–2030
<https://www.who.int/publications/i/item/9789241512978>
- WHO Handbook for integrated vector management
<https://apps.who.int/iris/handle/10665/44768>
- WHO Pesticides and their application for the control of vectors and pests of public health importance
<https://apps.who.int/iris/handle/10665/69223>
- Bowman, L.R., Runge-Ranzinger, S. and McCall, P.J., 2014. Assessing the relationship between vector indices and dengue transmission: a systematic review of the evidence. *PLoS neglected tropical diseases*, 8(5), p.e2848
<https://doi.org/10.1371/journal.pntd.0002848>
- WHO Guidelines for malaria
<https://app.magicapp.org/#/guideline/6832>

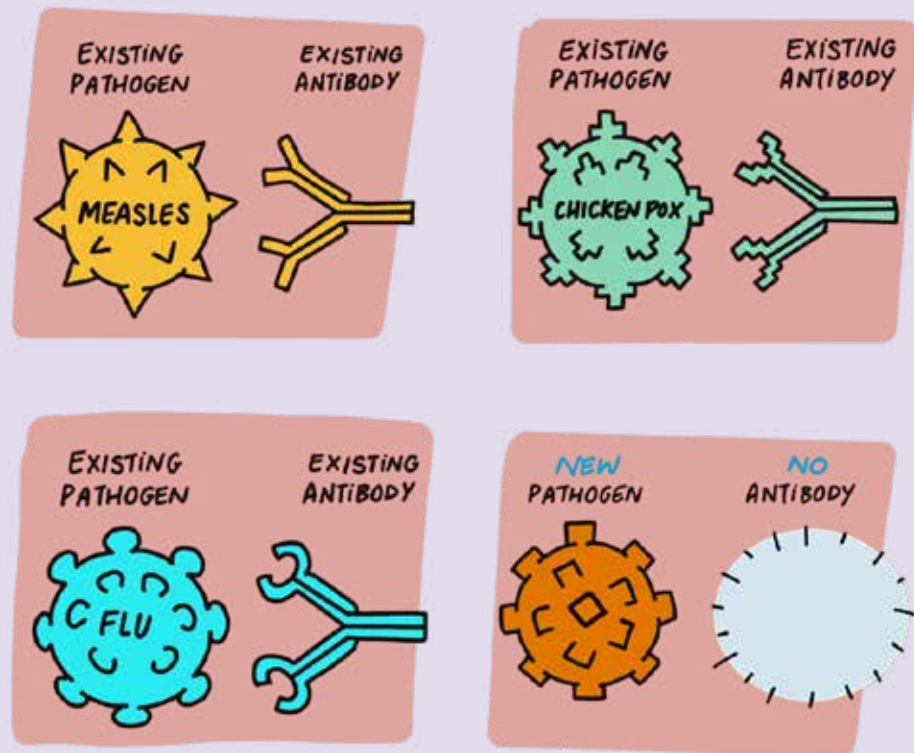
TOOL BOX 6

What do vaccines do?

Vaccines can prevent or lower the risk of a range of infectious diseases including measles, polio, and influenza amongst many others. When most people in a community are protected by vaccination, the ability of the pathogen to spread is limited. This is called herd or population or community immunity. When many people have immunity, this also indirectly protects people who cannot be vaccinated, such as those who have compromised immune systems.

Vaccines prevent or greatly reduce the risk of infection by training the immune system to recognize and fight pathogens such as viruses or bacteria. This is done by producing an immune response to a specific part of the pathogen called the antigen. If a vaccinated person is infected by the pathogen later on, the immune system uses these antibodies to recognize the pathogen. The body is prepared to attack the pathogen, which in turn protects the person from severe illness, or in the case of some pathogens, prevents them from experiencing any illness caused by the pathogen.

Vaccine development and types



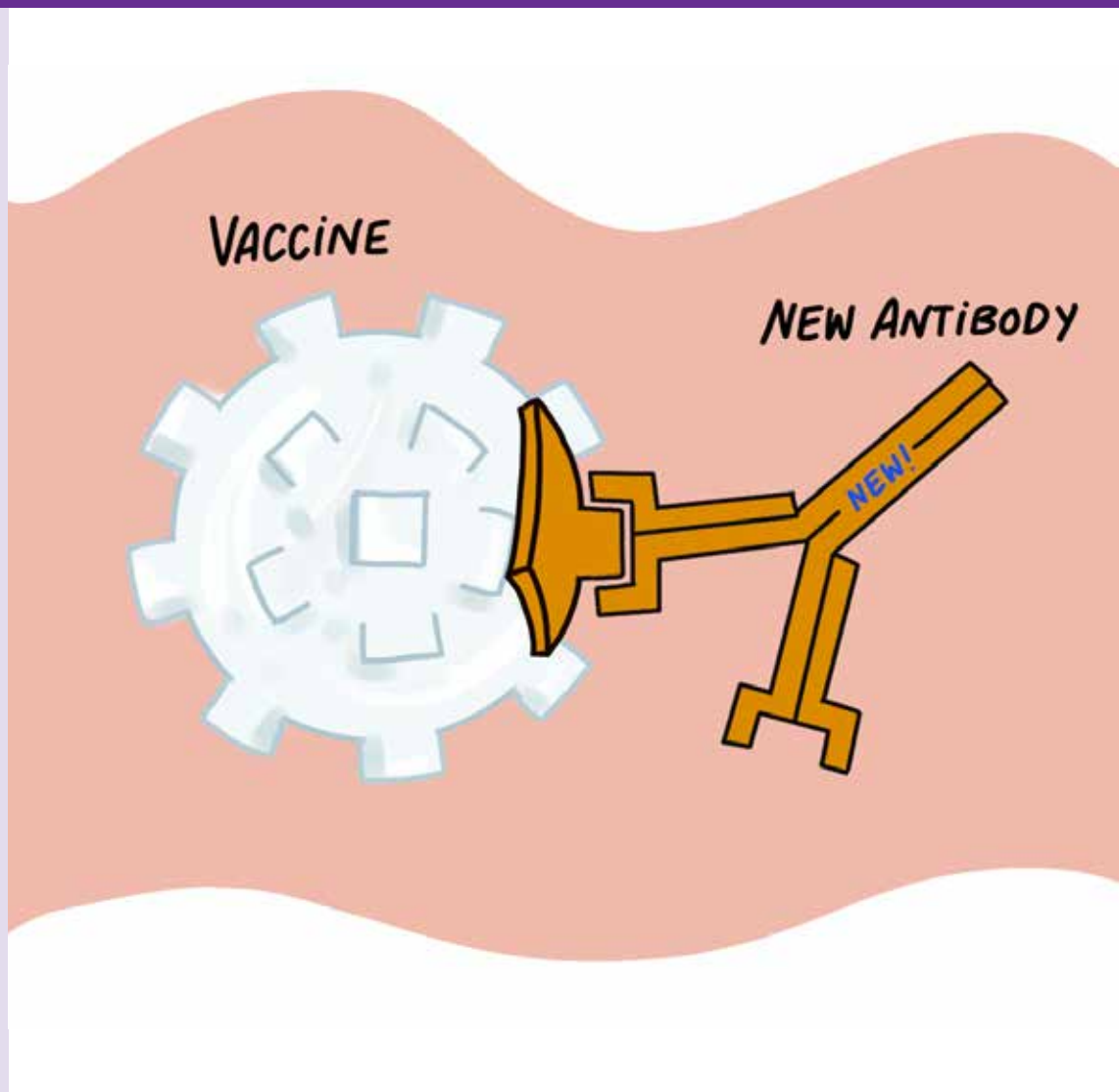
TOOL BOX 6

How do vaccines help?¹

Vaccines contain weakened or inactive parts of a particular organism (antigen) that triggers an immune response within the body. Newer vaccines contain the blueprint for producing antigens rather than the antigen itself. Regardless of whether the vaccine is made up of the antigen itself or the blueprint so that the body will produce the antigen, this weakened or inactivated version will not cause the disease in the person receiving the vaccine, but it will prompt their immune system to respond much as it would have on its first reaction to the actual pathogen. Some types of vaccines, for example the chickenpox vaccine, contain a weakened but live version of the organism that cause chickenpox. In this case the vaccine causes a mild case of the disease that is non-harmful and a sign that the vaccine is working.

Some vaccines require multiple doses, given weeks or months apart. This is sometimes needed to allow for the production of long-lived antibodies and development of memory cells. In this way, the body is trained to fight the specific pathogen, building up memory of the pathogen to rapidly fight it if and when exposed in the future.

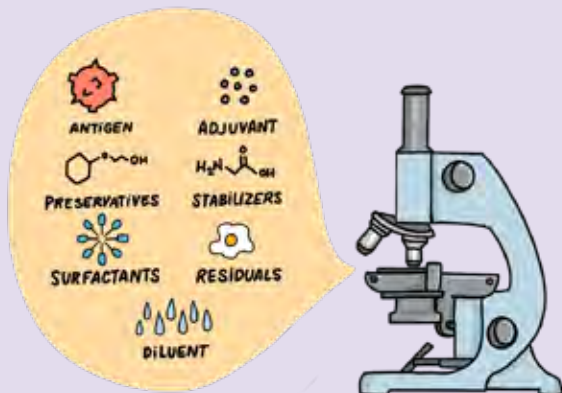
¹ <https://www.who.int/news-room/feature-stories/detail/how-do-vaccines-work>



TOOL BOX 6

What are the ingredients in a vaccine?²

Vaccines contain tiny fragments of the pathogen or the blueprints for making the tiny fragments. They also contain other ingredients to keep the vaccine safe and effective. Each vaccine component serves a specific purpose, and each ingredient is tested in the manufacturing process. All ingredients are tested for safety. These ingredients are included in most vaccines and have been used for decades in billions of doses of vaccine therefore they are known to be safe.



² <https://www.who.int/news-room/feature-stories/detail/how-are-vaccines-developed>

Vaccine ingredients		
<p>Antigen</p> <p>All vaccines contain an active component (the antigen) which generates an immune response, or the blueprint for making the active component. The antigen may be a small part of the disease-causing organism, like a protein or sugar, or it may be the whole organism in a weakened or inactive form.</p>	<p>Preservatives</p> <p>Preservatives prevent the vaccine from becoming contaminated once the vial has been opened, if the vial contains more than one dose and therefore will be used for vaccinating more than one person. Some vaccines don't have preservatives because they are stored in one-dose vials and are discarded after the single dose is administered.</p>	<p>Stabilizers</p> <p>Stabilizers prevent chemical reactions from occurring within the vaccine and keep the vaccine components from sticking to the vaccine vial.</p>
<p>Surfactants</p> <p>Surfactants keep all the ingredients in the vaccine blended together. They prevent settling and clumping of elements that are in the liquid form of the vaccine. They are also often used in foods like ice cream.</p>	<p>Residuals</p> <p>Residuals are tiny amounts of various substances used during manufacturing or production of vaccines that are not active ingredients in the completed vaccine. Substances will vary depending on the manufacturing process used and may include egg proteins, yeast or antibiotics. Residual traces of these substances which may be present in a vaccine are in such small quantities that they need to be measured as parts per million or parts per billion.</p>	<p>Diluent</p> <p>A diluent is a liquid used to dilute a vaccine to the correct concentration immediately prior to use. The most commonly used diluent is sterile water.</p>
<p>Adjuvant</p> <p>Some vaccines also contain adjuvants. An adjuvant improves the immune response to the vaccine, sometimes by keeping the vaccine at the injection site for a little longer or by stimulating local immune cells.</p> <p>The adjuvant may be a tiny amount of aluminium salts (like aluminium phosphate, aluminium hydroxide or potassium aluminium sulphate). Aluminium has been shown not to cause any long-term health problems, and humans ingest aluminium regularly through eating and drinking.</p>		

TOOL BOX 6

What are the different types of vaccines?

mRNA vaccines

- mRNA vaccines are a blueprint of messenger RNA (mRNA) delivered inside a lipid coat
- Once inside cells, the mRNA is translated into the protein antigen
- mRNA is recognized by cells as a 'pathogen' stimulating a strong immune response
- The antigen is recognized, inducing an immune reaction seen by the body as if a virus is inside a cell and an immune response is induced (T-helper, cytotoxic T-cells and antibodies)
- Examples include: COVID-19 (Pfizer-BioNTech and Moderna)

Inactivated vaccines

- Uses an inactive version of the pathogen being vaccinated against
- The pathogen is grown in culture under controlled conditions and then the genetic material of the pathogen is destroyed so it is not able to produce disease
- Inactivated pathogens cannot reproduce in the body, so higher doses are needed
- Sometimes an adjuvant is used to help strengthen the immune response
- These types of vaccines often require multiple injections over time to provide an effective immune response
- Examples include polio vaccine, influenza vaccine

Live-attenuated vaccines

- Use a weakened or attenuated form of the pathogen that causes the disease being vaccinated against
- These vaccines often elicit a long-lasting immune response since they are very similar to the natural infection that they prevent
- Examples include: Measles, mumps, and rubella (MMR) vaccine, varicella (chickenpox) vaccine

Viral vector vaccines

- Viral vector vaccines use a harmless virus to deliver genetic material that encodes a target antigen to allow the body to make the antigen to cause an immune reaction
- Can be replicating or non-replicating
 - Replicating: upon infection produces an antigen in that cell and new viruses that can infect other cells
 - Non-replicating: infects a cell and produces an antigen in that cell but does not produce new virus
- Examples include: The Ervebo® vaccine for use against Zaire Ebolavirus species, COVID-19 vaccine (AstraZeneca and Johnson & Johnson)

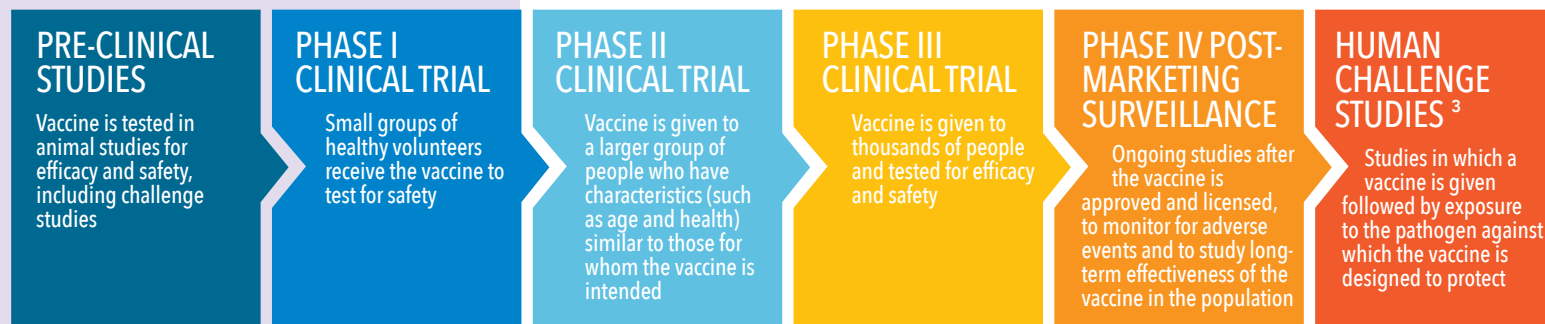
Subunit recombinant, polysaccharide & conjugate vaccines

- Subunit vaccines use parts of the pathogen without any genetic material, usually with an adjuvant to give a better immune response
- Usually made using a recombinant expression system (made in a cell without using the pathogen)
- With the help of antigen-presenting cells, the antigens are recognized by T helper cells as with a real infection
- Subunit vaccines generally induce antibody-mediated immunity
- Examples include: Haemophilus influenzae type B (Hib) vaccine (conjugate), pneumococcal vaccine (polysaccharide or conjugate), shingles vaccine (recombinant protein), hepatitis B (recombinant protein), acellular pertussis, MenACWY (conjugate)

Toxoid vaccines

- Use a toxin produced by the pathogen that cause the disease being vaccinated against
- Create immunity to the parts of the pathogen that cause diseases, with the immune response targeted to the toxin rather than the pathogen
- Examples include tetanus vaccine and diphtheria vaccine

TOOL BOX 6

**How are vaccines developed?**⁴

Most vaccines have been in use for decades, with millions of people receiving them safely every year. As with all medicines, every vaccine must go through extensive and rigorous testing to ensure it is safe before it can be introduced in a country's vaccine programme.

Each vaccine under development must first undergo screening and evaluation to determine which antigen should be used to invoke an immune response. This preclinical phase is done with testing on animals to evaluate its safety and potential to prevent disease.

³ Such trials are uncommon in people as they present ethical challenges.

⁴ <https://www.who.int/news-room/feature-stories/detail/manufacturing-safety-and-quality-control>

What is an emergency use listing?

The WHO Emergency Use Listing Procedure (EUL) is a risk-based procedure for assessing and listing unlicensed vaccines, therapeutics and in vitro diagnostics with the ultimate aim of expediting the availability of these products to people affected by a public health emergency. This will assist interested UN procurement agencies and Member States in determining the acceptability of using specific products, based on an essential set of available quality, safety, and efficacy and performance data.

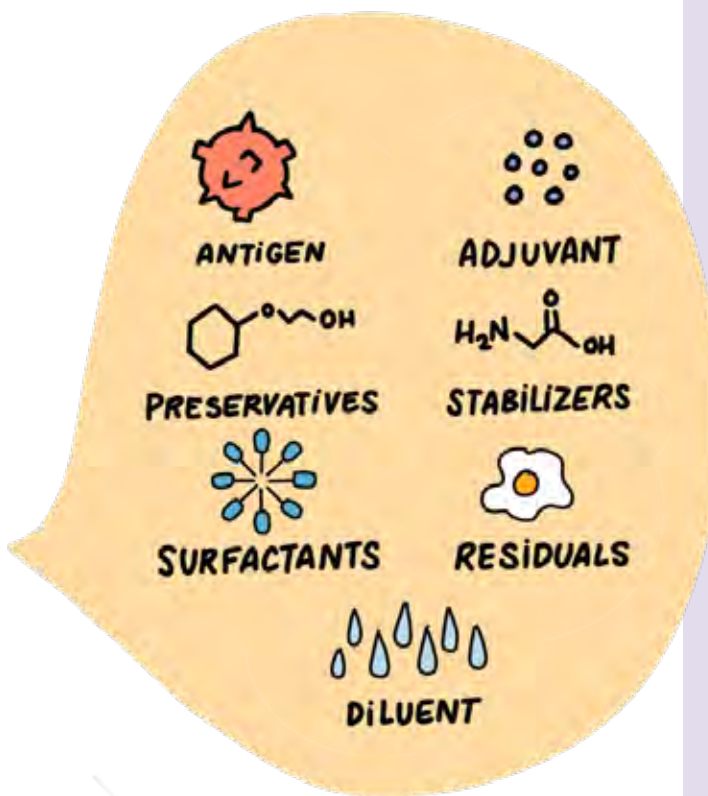
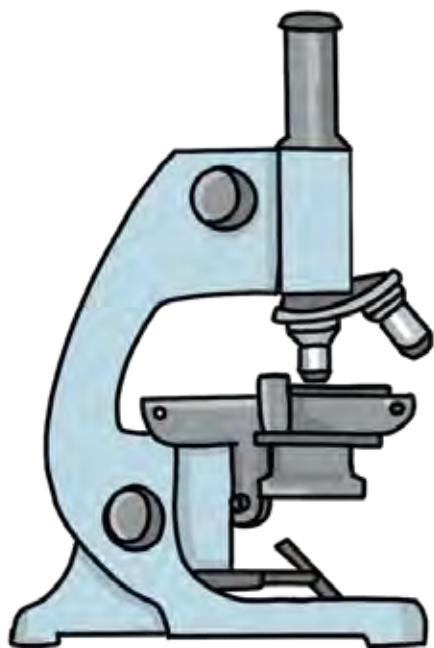
What is done to fast-track vaccine development during a health emergency?

The WHO R&D Blueprint is a global strategy and preparedness plan that allows the rapid activation of R&D activities during epidemics. Part of its aim is to fast-track the availability of efficacious vaccines that can be used to save lives and avert large scale crisis.

Continuous dialogue between developers and regulatory experts and early scientific advice also helps speed up vaccine development. Advising companies on regulatory requirements helps ensure that standards of safety and efficacy are embedded early in the development process and are not compromised by the need for speed. Resource mobilization for vaccines is done simultaneously which allows for accelerated development and manufacturing of vaccines.

Companies may use various approaches to reduce development timelines, such as:

- Mobilize more staff to analyse results from studies more quickly and map out next steps in terms of resources, funding and regulatory strategy.
- Combine clinical trial phases or conducting some studies in parallel where safe to do so.
- Companies may expand manufacturing capacity and large-scale production, to facilitate vaccine deployment without delay once approved.



More information on vaccine development and types:

- How do vaccines work?
<https://www.who.int/news-room/feature-stories/detail/how-do-vaccines-work>
- How are vaccines developed?
<https://www.who.int/news-room/feature-stories/detail/how-are-vaccines-developed>
- Manufacturing, safety and quality control of vaccines
<https://www.who.int/news-room/feature-stories/detail/manufacturing-safety-and-quality-control>
- WHO Emergency use listing for vaccines
<https://www.who.int/teams/regulation-prequalification/eul/eul-vaccines>
- WHO R&D Blueprint
<https://www.who.int/observatories/global-observatory-on-health-research-and-development/analyses-and-syntheses/who-r-d-blueprint/background>

thank
you



Managing epidemics

Key facts about major deadly diseases

World Health Organization
Avenue Appia 20
1211 Geneva
Switzerland

