



Managing Yellow fever epidemics





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Introduction

The 21st century has already been marked by major epidemics. Old diseases – Cholera, Plague and Yellow fever – have returned, and new ones have emerged - SARS, Pandemic Influenza, MERS, Ebola and Zika. These epidemics and their impact on global public health have convinced the world's governments of the need for a collective and coordinated defense against emerging public health threats and accelerated the revision of the International Health Regulations (2005), entered into force in 2007.

Another Ebola epidemic, another Plague epidemic or a new Influenza pandemic are not mere probabilities, the threat is real. Whether transmitted by contaminated water, mosquitoes, other insects, via contact with animals or person-to-person, the only major uncertainty is when and where they, or a new, but equally lethal epidemic, will emerge. These diseases all have the potential to spread internationally highlighting the importance of immediate and coordinated response.

This manual is an excerpt from the *Managing epidemics: Key facts about major deadly diseases* handbook. Although originally developed as guidance for WHO officials, this publication is available to a wide readership including all frontline responders - communities, government officials, non-State actors and public health professionals – who need to respond rapidly and effectively when an outbreak is detected.



is essential; for other diseases, vaccination is vital.

Response tips and checklists



Note: Although Communicating risk (C) is part of Health Interventions (HI); it is seen here as a separate component in order to underscore the importance of risk communications.

Coordinating responders

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).

Coordinating responders checklist

- What are characteristics of the event that describe it as a crisis?
- Who are the people, groups and organizations who should work for the response?
- / What should they do? (terms of reference, functions)
- / Where can responders meet? (emergency operation centre)
- How do they share information? (sharepoint, telephone numbers, generic email)



For more information about coordinating responders:

- Public Health Emergency Operations Centre Network (EOC-NET) http://www.who.int/ihr/eoc_net/en/
- WHO Emergency Response Framework (ERF) http://www.who.int/hac/about/erf/en/

Health Information

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 shows 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.

Health Information checklist

Surveillance

- Is there a case definition shared by all stakeholders?
 - Which laboratories are involved in the testing / confirmation of cases and deaths, and where are they situated?
- Is there an updated epidemiological curve and mapping of cases and deaths?
- Which are risk groups, by gender and age?

Interventions

- / What is the target population?
- What material and human resources are needed and how much?
- What are the indicators of success? (e.g. vaccine coverage, households targeted, number of people treated)

Communicating risk

During the evolution of any major outbreak, cases and deaths will inevitably increase. An epidemic is the rapid spread of infectious disease to a large number of people in a given population within a short period of time. Similarly, there may well be another kind of epidemic – the rapid spread of information of all kinds, including rumours, gossip and unreliable information. We describe this phenomenon as an "**infodemic**".

Infodemics, like epidemics, can be managed. Field epidemiology is an important part of outbreak response. It encompasses three main areas: (1) monitoring and identifying health threats, (2) outbreaks investigation, and (3) actions for mitigation and control. Similarly, successful management of infodemics will be based on (1) monitoring and identifying them, (2) analysis of them, and (3) control and mitigation measures¹.

Risk communication is an essential intervention in any response to disease outbreaks, and is equally necessary to manage infodemics. Communicating risk in epidemics involves two-way communication that is dynamic and evolving as the outbreak develops.

Outbreak risk communication involves three main strands that must work together.

- 1. Talk. Authorities, experts and response teams must quickly relay information on the nature of the event and the protective measures that people can take. We can use mass media including television, radio, newspapers and internet; social media and text-messaging; community radio; and leaflets and posters. We can use social mobilizers and frontline responders; encourage community engagement; as well as face-to-face communication via trusted interlocutors such as community leaders, religious figures and community health workers. We must use translational communication approaches to develop messages that are appropriate for the target populations in terms of language, educational level and cultural contexts.
- **2. Listen.** Responders, experts and authorities must quickly assess and understand the fears, concerns, perceptions and views of those affected; and tailor their interventions and messages to address such concerns. This requires the use of social science and community engagement expertise and methods.
- **3. Manage rumours.** Disease outbreaks are often accompanied by the presence of false rumours and misinformation. Responders need to have ways to listen to such misinformation and correct examples of it in appropriate ways without delay.



¹ This is called "infodemiology".



Communicating about the risks during outbreaks leads to specific outcomes.

First, early, transparent and understandable communication on the event establishes lines of dialogue with affected populations and stakeholders, and builds trust in the response. This type of communication must have facts and information (that cater to the head); and include messages that acknowledge and respond to people's concerns and fears (catering to the heart).

Second, frequent but evolving communication will help create a trusted and dynamic relationship that can deliver advice on protective behaviors that populations and individuals can adopt.

Third, communication must scope the risk in lay language, and also propose practical actions people can take. It must identify and help enable changes in people's behaviours or practice (a temporary change) that can reduce exposure to and protection from the infectious hazard.

Fourth, communication must display accountability by keeping people updated on the situation, on what is being done, and the impact of those actions in bringing the outbreak under control.

Communicating risk checklist

- Has the situation been well analyzed in terms of audience, sources and specificity of the context?
- Are tools in place in place to monitor an infodemic? Is monitoring reactive and adaptable enough?
- Has translational communication taken place (to transform scientific information into lay language and format)?
- Are the communication channels (and messengers) adequate, effective and acceptable to communities? (culturally, cost-effectively)?
- / 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, and consistent messaging?

Health Interventions

Each disease requires a different set of health interventions with the objectives of reducing (a) transmission, (b) severe morbidity and mortality (c) the impact on health systems and also on the political and other sectors.

Health Interventions checklist

- What are the key interventions needed to control the outbreak at this stage of the event?
- Who should implement them?
- How is the impact measured on morbidity, mortality, transmission, and whole of society?





The **Emergency Response Framework (ERF)** is an internal WHO tool that outlines a set of procedures to better respond to emergencies. Under this framework, for any emergency that requires a WHO operational response, the Organization activates the Incident Management System (IMS); recognized best practice for emergency management. WHO has adapted the IMS to consist of six critical functions. The four blocks and response tips are integrated into the Incident Management System. Although, all six functions of the IMS are critical for a successful response, the four blocks will highlight what is specific for each disease.

Six critical functions of the Incident Management System (IMS)



Yellow fever 10 THINGS YOU SHOULD KNOW



- 2. Outbreaks of YF in urban areas can be devastating
- **3.** Emergency mass vaccination and vector control are the two main pillars of YF outbreak response
- 4. YF vaccine is safe and provides lifelong immunity
- 5. Vaccine production is limited but there is a global emergency stockpile
- 6. Routine immunization in children is the key to preventing outbreaks
- **7.** The risk of YF international spread exists but can be prevented by applying the International Health Regulations (IHR) recommendations
- 8. YF is hard to distinguish from some other diseases with similar symptoms
- 9. Early clinical management improves survival
- 10. African Ministers of Health (MOH) are committed to eliminating YF epidemics



Yellow fever response tips

Coordinating responders

- Contact WHO/ICG for emergency vaccines
- Engage partners and communities for vector control around cases
- Organize emergency mass vaccination campaigns including cold chain and waste management

Health Information

- Laboratory diagnosis 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)

Communicating risk

- 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 Vaccine is safe and provides lifelong immunity
- Seek medical care early as this increases chances of survival

Health Interventions

- Community engagement
- **Emergency mass vaccination**
- Vector control
- Control at borders (airports)
- Patient supportive care, with bed nets (also during the day)



Urban Yellow fever (YF), the most threatening form of YF epidemics, is transmitted through *Aedes aegypti* mosquito bites

- The yellow fever virus is transmitted to humans by infected mosquitoes, most commonly from the Aedes species (Aedes aegypti, which can transmit the disease from human to human in urban settings) – it is the same mosquito that spreads Zika, Chikungunya and Dengue viruses.
- Outbreaks usually occur in areas where mosquitoes breed.
- The current distribution of Aedes aegypti is the widest ever recorded and Aedes mosquitoes are present in all continents. Urbanization with resulting increased population densities, further enhanced by man-made larval habitats, amplifies mosquito-transmitted diseases.
- Aedes mosquitoes usually bite during the day, peaking during early morning and late afternoon/evening.





Outbreaks of YF in urban areas can be devastating

- YF outbreaks in urban settings can be very 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 mosquito vector of urban YF epidemics that breeds in man-made containers of water, feeds predominantly on human blood and 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, 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.

- There are three types of transmission cycles. However, with climate and demographic change in endemic settings, this classification may be reviewed.
- Sylvatic (or jungle) Yellow fever: In tropical rainforests, monkeys, which are the primary reservoir of yellow fever, are bitten by wild mosquitoes which pass the virus on to other monkeys. Occasionally, humans working or travelling in the forest are bitten by infected mosquitoes and develop yellow fever. This is the most common type of outbreak in the Americas;
- Intermediate Yellow fever: In this type of transmission, semi-domestic mosquitoes (those that breed both in the wild and around households) infect both monkeys and people. Increased contact between people and infected mosquitoes leads to increased transmission and many separate villages in an area can develop outbreaks at the same time;
- Urban Yellow fever: Large epidemics occur when infected people introduce the virus into heavily populated areas with high mosquito density and where most people have little or no immunity, due to lack of vaccination. In these conditions, infected Aedes Aegypti mosquitoes transmit the virus from person to person. This is the most serious outbreak because it amplifies quickly.





Emergency mass vaccination and vector control are the two main pillars of YF outbreak response

Vector control:

- 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 and eggs/larvae/pupae in standing water (e.g. cleaning roof gutters, clean-up campaigns, etc.);
- Targeted residual spraying of adult mosquitoes (in areas known to be resting sites for Aedes mosquitoes) and space spraying when there is an outbreak;
- Mosquito control programmes targeting wild mosquitoes in forested areas are not practical and not recommended for preventing jungle (or sylvatic) yellow fever transmission.



- Additionally, personal preventive measures such as clothing minimizing skin exposure, use of repellents, as well as windows screens and air conditioning are recommended to avoid mosquito bites. The use of insecticide-treated bed nets is limited by the fact that Aedes mosquitos bite during daytime.
- Mosquito surveillance is part of vector control and helps improve timeliness of decisions to control mosquito populations and prevention disease. Both larval and adult vector populations should be targeted for surveillance.
- Eventually, economic development will reduce mosquito-borne diseases by improving standards of living (e.g. people living in houses with solid floors and roofs, window screens, and air conditioning).

Emergency mass vaccination:

 Reactive mass vaccination campaigns, by increasing immunity in the population, reduce the possibility of transmission of the virus. Vaccine coverages greater than 80%, with a 60-80% security threshold, are necessary to interrupt autochthonous transmission (humanmosquito-human) of YF virus within a community and ensure that sporadic unvaccinated cases do not generate secondary cases.



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YF vaccine is 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 yellow fever within 10 days for more than 90% of people vaccinated and within 30 days for 99% of people vaccinated. A single dose provides lifelong protection. A booster dose of yellow fever vaccine is not needed.
- Adverse effects of the Yellow fever vaccine are generally mild and may include headaches, muscle aches, and low-grade fevers. Serious adverse effects are rare.
- In Yellow fever 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 effect of the vaccine);
- People with severe allergies to egg protein; and
- People with severe immunodeficiency.





Vaccine production is limited but there is a global emergency stockpile

- They are four prequalified vaccine manufacturers and global supply production is limited. There is a global emergency stockpile of six million vaccine doses, which can be accessed by any country facing an outbreak, through a request to the International Coordinating Group (ICG).
- For outbreak response, in case of shortage of vaccine, it is possible to use a fraction of the vaccine doses (1/5), in order to rapidly increase the population immunity and stop human-to-human transmission.
- Children under two years of age should be offered a full dose, as they may have a weaker immune response to the vaccine than older people;
- There is no evidence of increased serious adverse effects when using a fractional dose.







Routine immunization in children is the key to preventing outbreaks

- Vaccination is the single most important measure for preventing yellow fever. The prevention of outbreaks can only be achieved if the majority of the population is immunized.
- YF routine immunization in the Expanded Programme on Immunization (EPI) can provide sufficient population immunity. However, it takes about 30 years to build the population immunity to adequate levels to stop potentially large scale outbreaks. Mass preventive vaccination campaigns to 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





The risk of YF international spread exists but can be prevented by applying the *International Health Regulations (IHR)* recommendations

- With the increasing occurrence of urban YF outbreaks comes an increased risk of international spread of diseases, 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 lead to local transmission.
- For Yellow fever, exportation of cases to Asia is especially worrisome as all favorable conditions for local transmission (vector such as *Aedes aegypti*, non-immune populations) are present in this continent, as demonstrated by dengue activity.

- It is recommended that major sectors recruiting international workers, with potential sylvatic exposure (extractive, mining, construction and forestry industries), take measures to ensure their staff and families are vaccinated.
- To prevent international spread, it is essential that the International Health Regulations (2005) are applied and that travelers present yellow fever vaccination certificates. Under the 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 the IHR (2005).





YF is hard to distinguish from some other diseases with similar symptoms

 Yellow fever 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 arbovirus diseases, Ebola virus disease (when haemorrhagic) as well as with poisoning.

- Once contracted, the Yellow fever virus incubates in the body for three to six days;

- Most people (about 88% of those infected) do not experience symptoms;
- Symptoms usually develop in two phases:
- o First to occur are common, unspecific symptoms, including fever, muscle pain with prominent backache, headache, loss of appetite, and nausea or vomiting. In most cases, symptoms disappear after three to four days.
- o A small percentage of patients (about 2-3% of infected people) will then 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 kidney, hence the characteristic jaundice – which gives yellow fever its name - dark urine and abdominal pain with vomiting. Bleeding can occur from the mouth, nose, eyes or stomach. Half of the patients who enter the toxic phase die within seven to ten days. The rest recover without significant organ damage.

- Laboratory tests are necessary to confirm yellow fever and access the global stockpile:
- In the first phase, blood is collected for RT-PCR – Reverse Transcription Polymerase Chain Reaction, to confirm the presence of the virus (viremia);
- In later stages of the disease, serology testing to identify antibodies is needed (ELISA, Enzyme-Linked Immunosorbent Assay and PRNT, Plaque Reduction Neutralization Test, for neutralizing antibodies). The detection of antibodies indicates that the person has either been infected or vaccinated, but it cannot

distinguish between the two. The level of antibodies' 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, Rift Valley Fever) and viral haemorrhagic fever (VHF, such as Ebola, Lassa, Crimean-Congo haemorrhagic fever);
- YF tests should be realized in laboratories with appropriate capacity to test for both YF and the differential diagnosis.





Early clinical management improves survival

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





African Ministers of Health (MOH) are committed to eliminating YF epidemics

- Yellowfever is an acute viral haemorrhagic disease. The virus is endemic in tropical areas of Africa and the Americas. Susceptible non-human primates are the animal reservoir, they are necessary to maintain the endemicity.
- Forty of the 47 YF-affected countries have been identified as priority nations 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 the 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



More information about Yellow fever

- Yellow fever WHO webpage http://www.who.int/csr/disease/yellowfev/en/
- Yellow fever WHO fact sheet: http://www.who.int/mediacentre/factsheets/fs100/en/
- EYE Strategy http://apps.who.int/iris/bitstream/10665/255040/1/WER9216.pdf?ua=1
- Yellow fever WHO MOOC https://openwho.org/courses/pandemic-epidemic-diseases
- WHO standard case definitions http://www.who.int/csr/disease/yellowfev/case-definition/en/



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