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Manual for the monitoring of yellow fever virus infection

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Glossary

ABTS (2,2'-azino-bis [3-ethyl-benzthiazoline 6 sulfonic acid]):	Substrate used with a peroxidase-based ELISA assay. Colour changes to green in presence of enzyme (see HRP).
Antibody capture technique:	Laboratory process for detecting virus-specific antibodies in patient's blood by first capturing patient's antibodies in wells of microtitration plate and then testing with virus-specific antigen.
CFT (complement fixation test):	Traditional immunoassay used to detect humoral antibody in serum.
CPE (cytopathic effect):	Visible changes to a virus-infected cell line.
E gene:	Part of the YF virus genome which codes for the envelope or E protein.
ELISA (enzyme-linked immunosorbent assay):	A highly specific and sensitive immunoassay that can be used to detect antibody or antigen.
Endemic disease:	A disease (or infectious agent) that is constantly present in a given geographical area or population group.
Enzootic disease:	A disease that is constantly present in a given animal population.
Epidemic:	An outbreak of disease in a human population.
Epizootic:	An outbreak of disease in an animal population.
Genotype:	Distinct familial cluster of viruses with genetic similarities, suggesting evolution from a common ancestor virus.
HI (haemagglutination inhibition):	Immunoassay used to detect antibody to viruses that spontaneously agglutinate red blood cells.
Horizontal transmission:	Spread of infection between vertebrates by passage of virus from one vertebrate host to another through a vector in which the virus replicates.
HRP (horseradish peroxidase):	Enzyme commonly used in ELISA.

IgG (immunoglobulin G):	The major class of circulating antibody that is produced several days to weeks after infection and remains to provide protection for months to years.
IgM (immunoglobulin M):	The first class of antibody to be produced in response to infection and the first to disappear from the blood.
MAb (monoclonal antibody):	Highly specific antibody directed against a single antigenic determinant; commonly used in immunoassays.
NT (neutralization test):	Immunoassay used to detect serum antibody capable of inhibiting virus replication.
OD (optical density):	Absorbence indicated by ELISA reader, measuring amount of colour change in substrate (see ABTS).
PBS (phosphate-buffered saline):	Physiological buffer commonly used in biological processes.
Quality assessment:	A system for testing the quality of a laboratory.
Quality assurance:	The process that guarantees the quality of laboratory results and encompasses both quality control and quality assessment.
Quality control:	The process of continually monitoring working practices, equipment and reagents.
Reservoir:	Any person, animal, arthropod, plant, soil or substance, or a combination of these, where an infectious agent lives and multiplies in such a manner that it can be transmitted to a susceptible host.
Room temperature:	Ambient laboratory temperature, usually considered to be approximately 20°C.
SD (standard deviation):	A measure of variability around the mean of a series of measurements.
Trophic preference:	The species on which an insect prefers to feed.
Tween 20:	Detergent used to minimize non-specific binding in ELISA.
Vector:	An insect that transports an infectious agent from an infected individual to a susceptible individual.
Vertical transmission:	Spread of infection to offspring directly from the mother.
Viraemia:	Spread of virus throughout the body via the bloodstream.

1. Introduction

1.1 Yellow fever control and prevention

Yellow fever (YF) is a viral haemorrhagic fever. It is transmitted by mosquitos infected with the YF virus. The disease is untreatable and case-fatality rates can exceed 50% among severe cases. YF can be prevented through immunization with the 17D YF vaccine, which is safe, inexpensive and reliable. A single dose provides protection against the disease for at least 10 years and possibly throughout life.

A high risk exists of an explosive outbreak in an unimmunized population even if there is only one laboratory-confirmed case in the population. Children are especially vulnerable. Effective disease surveillance activities remain the best tool for prompt detection of and response to outbreaks, particularly in populations where coverage rates for YF vaccine are not high enough to provide protection.

Each country at risk should include YF surveillance in its national priorities for disease surveillance. Current capacity for YF surveillance should be assessed and a plan of action for establishing or strengthening it should be implemented. The minimum requirements for a YF surveillance system are detection, investigation, specimen collection and a reporting system for suspected cases, linked to confirmatory testing of samples.

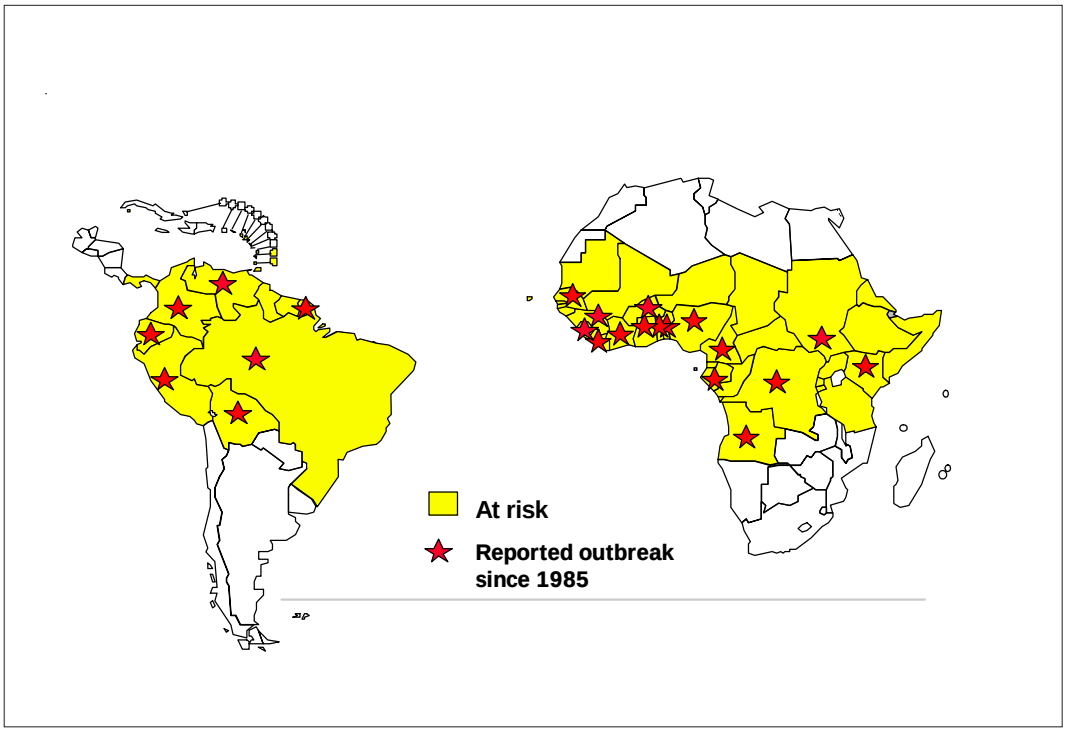
All countries at risk should have access to a qualified laboratory capable of confirming YF by an IgM test. All countries should be aware of the regional reference laboratories that can aid them in confirmatory testing. Procedures for transporting specimens between laboratories and for testing the specimens should be formally established.

This manual provides guidelines on the establishment and maintenance of an effective laboratory network capable of reliably providing confirmation of YF infection.

1.2 Yellow fever epidemiology

YF occurs most often in Africa and South America (Fig. 1). The epidemiology of the disease differs between the continents, even though the disease is caused by the same virus. In South America it mainly affects forest workers, whereas in Africa there have been serious epidemics in unimmunized populations in both rural and urban areas. The potential exists in African and South American cities for epidemics if *Aedes aegypti*, the mosquito that carries the YF virus, occurs in densely populated areas.

Fig. 1. Countries at risk from yellow fever which have reported at least one outbreak, 1985–2004



There has been an increase in the number of reported YF cases in Africa during the last five to 10 years. WHO estimates that there are 200 000 cases annually and that 30 000 deaths occur each year in 44 countries at risk, almost all of them occur in sub-Saharan Africa. The increase is probably attributable to reduced coverage rates for YF immunization and to the abandonment of mosquito control programmes. Movement from rural to urban areas has resulted in large numbers of people living in conditions of poverty, crowded housing and poor sanitation. These circumstances amplify the risk of YF transmission.

The precise extent of illness and death attributable to YF is unknown. Estimates by WHO and other international agencies suggest that only 1–2% of cases are reported. An outbreak of YF may not be detected because the signs and symptoms of the disease are similar to those of viral hepatitis, malaria, leptospirosis, typhoid fever, Ebola haemorrhagic fever and other viral haemorrhagic fevers. It is difficult for