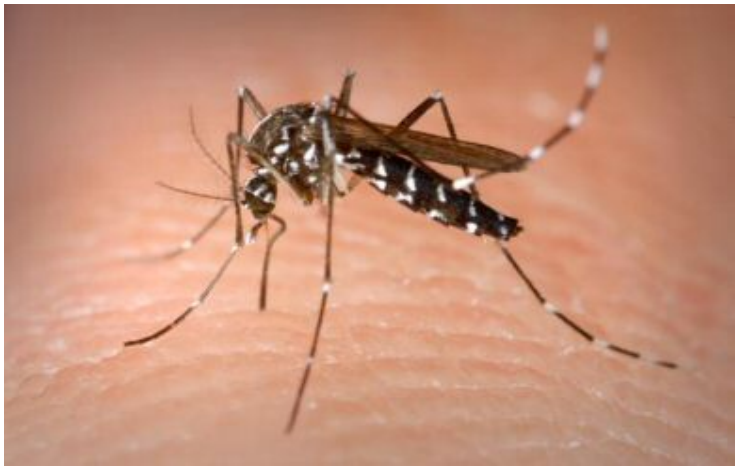
Informal Expert Consultation on Yellow Fever Threat to India and other SEA Region Countries

Report of the Consultation
Goa, India, 23 – 25 March 2011



World Health Organization
Regional Office for South-East Asia

SEA-CD-235
Distribution: General

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Printed in India

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Acronyms

APHO	Assistant Public Health Officer
BI	Breteau Index
CI	Container Index
CRI	Central Research Institute
DGHS	Director General of Health Services
DHF	Dengue haemorrhagic fever
DIC	Disseminated intravascular coagulation
EHO	Environmental Health Officer
EPHO	Environmental Public Health officer
EPI	Expanded Programme on Immunization
FNV	French neurotropic vaccine
GoI	Government of India
HI	House Index
IHR (2005)	International Health Regulations (2005)
HQ	Headquarters (WHO)
JE	Japanese encephalitis
MoHFW	Ministry of Health and Family Welfare
PHO	Public Health Officer
PoE	points of entry
QC	Quality control
SARS	Severe acute respiratory syndrome
SEA	South-East Asia
VHF	viral haemorrhagic fever
WHA	World Health Assembly
WHO	World Health Organization
YF	yellow fever

1. Background

Yellow fever (YF) is a viral disease, endemic to tropical regions of Africa and the Americas, which principally affects humans and non-human primates and is transmitted by *Aedes aegypti*. It can cause devastating epidemics of potentially fatal, haemorrhagic disease. Despite vaccination campaigns to prevent and control these outbreaks, the risk of major YF epidemics has greatly increased. Consequently, YF is considered an emerging and re-emerging disease of considerable importance. The density and habitats of *A.aegypti* have expanded both in urban and rural areas. It is currently spreading beyond endemic zones in South America.

The risk of the international spread of YF is greater than before due to new fast air routes connecting South America and Africa into Asia. In the past, devastating outbreaks occurred mainly in seaports. Today, most cities are connected to most of the world by more rapid means of transport. So far, circulation of the virus has remained within the borders of historically endemic countries, but the virus could spread quickly and cause epidemics in areas with a high density of vectors and a non-immune population such as India and other countries in the South-East Asia (SEA) Region.

An Informal Expert Consultation on Yellow Fever Threat to India and other SEA Region countries was held from 23 to 25 March 2011, in Goa, India to discuss the various issues related to the threat of the introduction of YF in India, and SEA Region countries and also to arrive at practical methods of addressing the risks. The meeting was attended by 28 participants from five Member States of the Region. The agenda and the list of participants are placed at Annexure 1 and 2, respectively.

2. Objective

The objectives of the consultation were:

- to review the current situation of YF and its threat to South-East Asia Region countries;

- to review current prevention and control methods, including quarantine systems at Points of Entry (PoE); and
- to discuss appropriate preventive measures and existing capacity in Member countries of the SEA Region.

3. Opening session

Dr A.P. Dash, Regional Adviser, Vector-Borne and Neglected Tropical Diseases Control, welcomed the participants and highlighted the importance for Member States to strengthen measures at ports for prevention of YF entry into their territories.

The meeting was chaired by Dr R.K. Srivastava, Director-General, Health Services (DGHS), Ministry of Health and Family Welfare (MoHFW), Government of India (GoI), and co-chaired by Dr W.A.S. Settinayake, Deputy Director-General (PHS), Ministry of Health, Sri Lanka. Dr A. Gunasekar, National Professional Officer, WHO Country Office for India and Dr Ashwani Kumar, Deputy Director and Scientist F, Officer-in-Charge, National Institute of Malaria Research, Field Station, Goa, India, were the rapporteurs.

Dr R.K. Srivastava, DGHS, MoHFW, GoI, in his opening address welcomed the participants and stressed the importance of scientific debate on the subject of prevention of YF entry into countries in the region. He encouraged the members of the consultation to arrive at broad recommendations for implementation by all Member States and WHO.

4. Proceedings of the meeting

4.1 Global review of yellow fever and the threat of its introduction to Asia

Dr John P. (Jack) Woodall, the external expert, gave an overview of the global situation of YF. He gave a historical perspective on the entry of YF cases into various countries in the recent past, such as into the Netherlands from Suriname (2000), Belgium from Gambia (2001), and the USA from

Brazil (2002). In Europe, the urban YF vector mosquito *Aedes aegypti* occurs only in Spain, Portugal and southernmost parts of Italy and Greece. Therefore, imported cases of YF into northern parts of Europe did not cause any epidemics.

The question that arises is that if YF can be imported to cause outbreaks in USA and Europe, why this cannot happen in Asia, as all of tropical Asia is infested with the urban YF mosquito, i.e. *Aedes aegypti*. There is also a history of recent escapes of mosquito-borne viral diseases into the Asia-Pacific, such as chikungunya from Africa to Indian Ocean islands such as Madagascar, Maldives, Mauritius and Reunion in 2005, and zika from Africa or Asia to Pacific islands Yap and Guam in 2007. The emergence of a new YF subtype-1E responsible for breakout of YF into areas from which it has been absent for about 100 years, e.g. Paraguay, was discussed.

Outbreaks of YF have recently occurred in six African countries—Cameroon, Congo Democratic Republic, Cote d'Ivoire, Gambia, Guinea and Uganda—and two countries in the Americas—Peru and (in monkeys) in Venezuela. Capital cities with international airports which have YF cases are Abidjan in Cote d'Ivoire and Asuncion in Paraguay. The threat of YF spread through various airline routes was discussed.

The various theories on why YF has so far not broken out in Asia were discussed. The Asian population may have cross-immunity due to infections with flaviviruses such as dengue and Japanese encephalitis (JE) but it has been seen that dengue immunity does not protect urban Nigerians. The vector competence theory is that Asian *A. aegypti* mosquitoes may not be efficient vectors of YF like African and South American strains, but it has been seen that low competence *A. aegypti* strains in Nigeria have spread urban epidemics. The Houston strain of *A. albopictus* has also been found to be a competent vector serving as a bridging vector between the jungle YF cycle and the urban cycle.

The current situation in Asia is that no one is expecting to see a case of YF and therefore a case of fever with jaundice and haemorrhagic symptoms will be diagnosed as dengue haemorrhagic fever (DHF), hepatitis or some other disease and no laboratory investigation for YF will be done.

Facilities for testing for YF may also be not available in most non-endemic countries, except possibly in national reference laboratories.

Stocks of YF vaccine are insufficient for a major epidemic occurring in Asia. The worldwide production of YF vaccine also cannot be geared up fast enough to provide it to all the population at risk in Asia. Even though cold chain facilities exist in Asian countries, these may only be adequate to handle the load of Expanded Programme on Immunization (EPI) vaccines. A crash mass training programme of vaccinators will also be beyond the budgetary capacity of many Asian countries. Adverse effects, with one or two deaths, inevitable during such mass vaccination campaigns, might also create enough alarm to shut down the campaign.

The existing vector control programmes in most countries in Asia are failing to control the spread of dengue. A crash programme of training and deployment of spray workers during an outbreak will also take time. During outbreaks the stocks of drugs, intravenous fluids and disposable items such as syringes, needles, gloves, etc. may also be exhausted. Populations in affected areas may flee to safer areas as occurred when a plague outbreak took place in Surat, India, in 1994.

It was concluded that even though YF has not yet been reported in Asian countries, the risk of introduction of YF into Asia is now greater than at any time in history. The countries in Asia need to develop and keep contingency plans ready for the possibility of YF outbreaks occurring in their countries.

4.2 Global strategies for prevention and control of yellow fever: the role of the International Health regulations (IHR)

Dr Gilles Poumerol, Communicable Disease Surveillance and Response, HSE/IHR/RPI/WHO-HQ, gave a presentation on the global strategies for prevention and control of YF and the role of the International Health Regulations (IHR). The 2005 revised version of IHR came into effect in June 2007. They provide an agreed framework for the collective international management of epidemics and other public health emergencies. They also aim at minimizing disruption to travel, trade and economies. With these regulations, both Member States and WHO have rights and obligations.

One of WHO's obligation is in Annex 7, which stipulates that WHO must determine areas where a risk of YF transmission is present.

The new foci of IHR are containment at source, a broad range of threats and adapted response. The new process for development puts Member States in the driving seat. The new implementation approach includes national focal points, WHO contact points in regional offices, IHR Department, annual reporting to the World Health Assembly, capacity-building, an event information system, major global events and the review process.

There are 44 YF endemic countries in the world, 33 of them in Africa and 11 in South America. Globally, 897 million people are at risk of YF, 20% of whom live in urban areas. There is increasing YF risk due to weak vaccination coverage in high-risk zones (less than 60%-80%), weak programmes in complex emergency countries, urbanization resulting in virus circulation from jungle to towns, migrations, internal displacements and increased vector density.

The risk of epidemics should be addressed by risk assessment and surveillance of the human population, animal reservoirs and vector mosquitoes. At present the four diseases that must be notified under IHR are polio (wild-type polio virus), smallpox, human influenza new subtype and severe acute respiratory syndrome (SARS). Diseases that must always lead to utilization of an algorithm are cholera, pneumonic plague, YF, viral haemorrhagic fever (Ebola, Lassa, Marburg), and West Nile fever. The algorithm includes four questions: (1) Is the public health impact serious? (2) Is the occurrence unusual or unexpected? (3) Is there risk of international spread? and (4) Is there any risk of travel/trade restrictions?

The YF vaccine initiative includes vaccination and outbreak response, securing vaccine supply, and monitoring reach, quality and safety. Preparations are made by global emergency vaccine stockpiling and preventive/routine vaccination. Securing the vaccine supply is achieved through supply and demand forecasting and supporting emerging manufacturers. Monitoring the reach, quality and safety of vaccination is done through immunization coverage monitoring and adverse events surveillance.

The revision of the YF risk maps was done by a task force based on human and non-human primate cases, clusters and outbreaks, results of serosurveys in human beings prior to YF vaccination, vector distribution and YF vaccination coverage. The second task of the group work was to apply on a country-by-country basis—and for 48 countries—the new categories of YF risk as defined by the consultation in 2008: endemic, transitional, low risk and no risk.

Endemic areas are areas with persistence of enzootic YF transmission over long periods of time and where YF vectors and non-human primate hosts are present; and human and/or non-human primate YF cases are reported repeatedly or human YF cases were reported regularly prior to the achievement of high YF immunization coverage, or human serosurveys completed before vaccination show evidence of high levels of YF infection. The risk of infection in these areas is high; Nigeria is an example of such a country.

Transitional areas are the ones bordering YF-endemic zones with periodic evidence of transmission during YF epizootic/epidemic expansions, and where: YF vectors and non-human primates are present; and human YF cases are reported at long intervals and during YF epizootic epidemic expansions from bordering endemic areas, and/or human serosurveys performed before vaccination show evidence of YF infection in persons born before the previous YF expansion. The risk of transmission in these areas is moderate to high; Paraguay is an example.

Low-risk areas are areas bordering YF-endemic or transitional areas, and where: YF vectors and non-human primate YF hosts are present; and no human or non-human primate YF cases have been reported; and there may be serological or other evidence of low levels of YF viral transmission in the past. The risk of infection in these areas is low; an example of such a country is Tanzania.

The recommendations of the group affect the IHR (2005), and in particular, the requirements at entry into countries. Low-risk countries are removed from the list of countries at risk of YF and travellers arriving from these countries will not require a YF certificate of vaccination. The changes will be posted on the WHO International Travel and Health website.

4.3 Early warning disease surveillance for yellow fever in South-East Asia

Dr Duane J. Gubler, Director, Signature Research Program in Emerging Infectious Diseases, Duke-NUS Graduate Medical School, Singapore, provided a description of the worldwide distribution of *A. aegypti* and YF. The reasons for the re-emergence of YF in Africa and South America can be attributed to increased global travel, low coverage with vaccination, human migration and urbanization, encroachment of humans into the sylvatic cycle and reinfestation of urban areas by the *A. aegypti* mosquito vector.

The surveillance of YF includes both disease surveillance and entomological surveillance. Entomological surveillance includes surveillance for the species, its geographic distribution, larval habitats, adult behaviour and seasonal distribution. Entomological data from dengue surveillance can be used for entomological surveillance of YF, chikungunya, epidemic polyarthritis and zika.

Disease surveillance should include both active surveillance and passive surveillance. Only a few countries have active surveillance, but most have passive surveillance systems for dengue. There is no passive surveillance for YF and there is also a low index of suspicion for the disease in Asia. The disease may often manifest as a mild illness which may undergo self-treatment. YF, if introduced to Asia, will most likely be misdiagnosed by the physician as dengue.

Early warning disease surveillance must be active and laboratory-based. The proactive early warning surveillance for YF in Asia will involve active detection and monitoring of transmission of YF-like disease and rapidly and accurately differentiating YF from dengue and other common infectious diseases. Active dengue surveillance can also be used for YF. This will involve actively monitoring infectious disease transmission in the catchment area with regard to time, location, pathogen and disease severity. Active surveillance requires a good virology/microbiology laboratory.

It is difficult to differentiate YF in the individual patient from many other diseases. YF closely resembles the other haemorrhagic fevers including DHF, leptospirosis and louse-borne relapsing fever. Overlapping

features of YF are also seen in viral hepatitis (especially hepatitis E in pregnancy), Q fever, typhoid, malaria, hepatic injury due to drugs and toxins and extrahepatic biliary duct obstruction.

The diagnostic assays for YF that should be used in surveillance are both serological assays and virus detection assays. Serological assays are conducted with acute/convalescent sera and include IgM ELISA, IgG ELISA, plaque reduction neutralization test, immunofluorescence assay, haemagglutination inhibition test and complement fixation test. Virus detection assays are conducted on acute serum, cerebrospinal fluid, tissues, blood, and mosquitoes and include Real Time RT-PCR, NASBA, virus isolation, antigen detection (ELISA) and immunohistochemistry.

It was concluded that only a few dengue-endemic countries have effective surveillance and emergency response programmes for dengue. However, those countries that have effective surveillance systems generally do not have effective response programmes. The standardized WHO case definitions are not widely used. International information exchange is poor and countries do not use available international surveillance information effectively. With proper and timely response, surveillance data can be used to abort incipient dengue/DHF epidemics, and if YF is included in the surveillance system, YF epidemics can also be aborted.

It was recommended that a passive surveillance system should exist for dengue, YF and haemorrhagic fevers in general. Clear-cut case definitions should be available for dengue and YF. Active/proactive surveillance should include laboratory-based sentinel systems, an algorithm on testing priorities and sequence, and establishment of national and regional reference laboratories for quality control (QC). There should be standardized reporting requirements at the national and regional level, and regional coordination of surveillance data.

4.4 Laboratory diagnosis of yellow fever

Professor R.C. Mahajan, Emeritus Scientist, Postgraduate Institute of Medical Education and Research, Chandigarh, India, gave a presentation on laboratory diagnosis of YF. The YF virus is an arthropod-borne virus which is a prototype member of the flavivirus genus. The virus is 40-50 nanometers in diameter with an enveloped genome of positive-sense RNA. The virus is

inactivated by heat and antiseptics. It may be preserved in 50% glycerol saline at 00 °C for 3 months or preferably at -800 °C or by dry freezing.

Diagnosis of YF may be done by any one of the following tests:

- Isolation of YF virus.
- Isolation of YF virus-specific Ig M.
- Fourfold or greater rise in serum IgG.
- Positive findings on post-mortem liver histopathology.
- Detection of YF antigen in tissues by immunohistochemistry (the only commercially available test).
- Detection of YF viral genomic sequences by PCR.

The histopathology of liver in YF shows midzonal necrosis, presence of Councilman bodies (evidence of coagulative hyaline necrosis) and inclusion bodies (Torres bodies) which are acidophilic, pleomorphic, intranuclear bodies surrounding nucleoli with granular appearance.

Virus isolation can be made in the acute stage (the first three to seven days of illness) by inoculation into mosquitoes (most sensitive method), suckling mice (intracerebral inoculation with serum and confirmed by neutralization test), mosquito cell cultures (*Ae. pseudoscutellaris* – AP61) or mammalian cell lines (Vero, SW13, BHK-21).

The Reverse Transcriptase PCR for detection of YF genome is a test which can be done rapidly in samples negative for virus isolation with primers taken from NS5 region. The test is highly sensitive and specific. The basic features of various laboratory tests were discussed including the period for conducting the test, sensitivity and specificity.

4.5 Clinical diagnosis and management

Dr A. Gunasekar, National Professional Officer (Malaria and Vector Borne Diseases), WHO Country Office for India, gave a presentation on the clinical diagnosis and management of YF. After the introduction of YF virus into a human being, infection may be fought off by the host's immune system, or symptoms may be so mild that the disease is not identified. The

chance of symptoms developing is about 5%-20%. Symptoms manifest in about 5% of partially immune persons and 20% of immunologically naive persons. The disease may range in severity from a self-limited infection to life-threatening haemorrhagic fever. Among those who develop symptoms, 15%-25% progress to severe disease due to liver and kidney failure. Mortality depends on the susceptibility of human beings and virulence of the virus strain. Mortality in severe disease ranges from 20%-50%.

The incubation period is usually from three to six days after bite by the infected mosquito. Viremia occurs even before symptoms appear. The three stages in the clinical course of YF are invasion, remission and intoxication. The invasion stage starts with an abrupt onset of symptoms. Common symptoms are fever and chills. The fever is high in grade and associated with a slow heart rate (Faget's sign). Other symptoms include severe headache and low backache, muscle and joint pain, loss of appetite, nausea and vomiting. The tongue may have a white, furry coating at the centre with red, swollen margins. There may be extreme exhaustion. Fever and other symptoms decrease in severity and go away, usually within three to four days. Most patients recover completely at this stage. In some patients, remission lasts for up to 48 hours. This is the calm before the storm of the third stage of intoxication. Some patients may move onto the third stage within 24 hours without remission.

Intoxication is the most severe and potentially fatal phase of the illness. It may last three to nine days. Fatty degeneration of internal organs occurs in this stage, particularly in the liver, kidneys and heart. Multiorgan dysfunction occurs in which the liver is the most important organ affected. The hepatocellular damage causes accumulation of bilirubin pigment in blood giving yellow discoloration of sclera (whites) of eyes, skin and urine. There is hepatomegaly and abdominal pain. Liver dysfunction leads to consumption of platelets and clotting factors and causes disseminated intravascular coagulation (DIC) and bleeding diathesis. Fibrin deposition in microcirculation leads to ischemia of organs, mainly the kidneys, and the central nervous system.

Bleeding occurs due to reduced production of clotting factors by liver, thrombocytopenia and platelet dysfunction. Bleeding manifests as petechiae and purpura in the skin and bleeding from mucosa, gastrointestinal tract, gum and nose. Deposits of fibrin in blood vessels to kidneys cause acute tubular necrosis with albuminuria and oliguria. Volume

overload in circulation is manifested with jugular vein distension, crepitations in lungs, S-3 gallop in heartbeat and oedema. There is reduced blood supply to brain with cerebral oedema and brain haemorrhages. Brain dysfunction may lead to altered mental status with somnolence, delirium, seizures and coma. Erosion of the gastric mucosa leads to bleeding seen as haematemesis (black vomit) and melena (black stools). Fatty infiltration of heart muscle and the electrical conduction system of the heart leads to myocarditis and arrhythmias, respectively.

In the late stages of YF, septicaemia and shock occur, manifested by tachycardia, hypotension, hypothermia/hyperthermia, severe hypoperfusion with cyanosis, tachypnea, acute respiratory distress syndrome, respiratory failure with hypoxia and multi-organ dysfunction syndrome. Patients who survive the period of intoxication enter into a stage of convalescence. Recovery may occur with no long-term effects. Infection results in lifelong immunity against repeated infection with the virus. The disease varies in severity. Severe infections with hemorrhagic fever may cause death in up to half of cases. Early appearance of jaundice indicates a poor prognosis. Death may occur due to massive bleeding, often following a coma.

Clinical diagnosis of YF is based on clinical features, place of residence, place and date of travel to endemic area, exposure in high-risk areas and history of immunizations. The differential diagnosis of YF includes Lassa fever, Marburg, Ebola virus infection, Crimean-Congo hemorrhagic fever, Rift Valley fever, West Nile virus fever, malaria, dengue, JE, typhoid fever, typhus, leptospirosis, hepatitis, DIC, sepsis from any cause and multi-organ system dysfunction.

During the initial invasion phase, the white blood cell count is reduced (leukopenia) and direct bilirubin and liver transaminases are elevated. In the toxic phase, prothrombin time and clotting time are prolonged. In DIC, the clotting factors and platelets are diminished and there is presence of fibrin split products. In kidney failure, there is presence of albumin in urine, increase in blood urea and serum creatinine. The ELISA for IgM is about 95% sensitive 7-10 days after onset of symptoms. The other tests include testing paired sera for elevation of IgG and PCR for viral RNA in acute infection. Electrocardiogram changes may also be noticed.

There is no specific antiviral treatment available for treatment of YF. Fever and pain may be treated with acetaminophen (paracetamol). Treatment with aspirin and Ibuprofen should be avoided as they may increase the risk of bleeding. Fever may also be treated with cooling blankets and cold sponging. Hypothermia will require gradual rewarming. Dehydration should be avoided with increase intake of oral/intravenous fluids.

Hypoglycaemia may require infusion of 10%-20% glucose solution. Bleeding in stomach is treated with antacids. Blood transfusion may be required for haemorrhages, and dialysis for kidney failure. Sepsis requires specific antibiotics. For respiratory failure, endotracheal intubation and mechanical ventilation may be required. Nasogastric suction is required in some cases to prevent stomach distension and aspiration of gastric contents.

While travelling to an area where YF is common, preventive measures include vaccination, sleeping in screened housing, using mosquito repellents and wearing clothing that covers the body well.

4.6 The risk of a yellow fever epidemic in Asia and barriers to its spread

Dr Gubler gave a comprehensive presentation on the risk of YF epidemics in Asia and barriers to the spread of the disease to Asia. Epidemic YF was effectively controlled in the American tropics for over 50 years by the hemispheric *A. aegypti* eradication programme. That programme was disbanded in the early 1970s, and *A. aegypti* immediately began to reinfest those countries from which it had been eliminated. Coincident with that period was unprecedented urban growth in Central and South America. As of 2011, over 70% of the population in those countries live in urban areas, all of which have become reinfested with *A. aegypti*.

The American tropics today are at the highest risk in 60 years for urban epidemics of YF. Another trend that has occurred during this time is globalization with unprecedented movement of people, commodities and pathogens via modern transportation. In 2010, more than two billion people boarded an airplane. It has been shown that if an urban epidemic of YF began in the American tropics today, the virus could move around the world in one to two days. Asia is especially vulnerable because there are

two billion people living in areas of risk, with no effective mosquito control and no early warning surveillance for epidemic YF. Introduced YF would likely be misdiagnosed as dengue, and thus become widespread before it was detected. This scenario would create a global public health emergency that makes the SARS epidemic pale by comparison. In summary, Asia is also at highest risk for the introduction of YF in its history.

Dr Gubler gave some background on incidents of YF being spread among the continents in recent times via travellers from endemic countries to nonendemic countries. The various hypotheses to explain the absence of YF in Asia were discussed in detail, including cross-protective flavivirus immunity, low vector competence of Asian *A. aegypti*, geographic and demographic obstacles to the spread of YF virus, and evolutionary exclusion.

4.7 Yellow fever threat to India and other Asian countries

Dr P. Jambulingam, Director, Vector Control Research Centre, Pondicherry, India, gave a presentation on the YF threat to India and other Asian countries. He presented a comparative situation of the reintroduction of the chikungunya fever in Asian countries in the recent past. The factors affecting introduction of YF are vulnerability of the virus, receptivity in the area with favourable environment, susceptible host and contact and infectivity in the competent mosquito.

In the 1930s it was recognized that India was receptive to YF during the *Aedes* survey conducted by Barraud. It was seen that the common Indian monkey, *Macacus rhesus*, was very susceptible to YF.

In 1940, it was considered that the YF virus might be used as a biological warfare agent and therefore appropriate steps should be taken. Dr Pandit from India was deputed to go to the USA in 1941 to study techniques of YF vaccine manufacture at the laboratories of the Rockefeller Foundation in New York. Even though the threat did not materialize, the expertise to produce YF vaccine was developed and vaccine was produced as an insurance against possible introduction of the virus. Effective implementation of the International Health Regulations (IHR) 2005 was done by ensuring that vaccination certificates are produced before entry. Risk assessment was made in terms of conditions existing, facilities available

for dealing with the infection if introduced and the probability of its establishing itself as a permanent focus of infection among forest animals, especially monkeys and small mammals. Lapses that can occur in enforcing the quarantine regulations were also considered, especially when a region had been free of YF for many decades.

One of the important issues is that the chances of appearance and disappearance of YF may be similar to those of at least some other arbovirus infections. However, after the initial episodes of dengue and chikungunya in the 1960s, contrary to expectations, large-scale DHF and chikungunya epidemics did not occur. Dengue fever viruses continued off and on, but the chikungunya virus had almost disappeared before its re-emergence during the last decade.

The most commonly-held view is that the YF virus was never introduced into India even though the biological environment for its propagation and maintenance is favourable. The various views for absence of YF in Asia include cross-protection given by dengue and other arboviruses, low competence of the local vector *A. aegypti*, and that fewer people from remote areas with risk travel by air. However, it may be concluded that the threat is real, as *A. aegypti* is extensively present in Asian countries and can be considered to be a competent vector of YF, while *A. albopictus* is also an efficient epidemic viral vector.

4.8 *Aedes aegypti* behaviour

Dr B.N. Nagpal, Scientist E, National Institute of Malaria Research, New Delhi, India gave a presentation on the behaviour of the *A. aegypti* mosquito. The mosquito originated in Africa but is now found in tropical and subtropical regions throughout the world.

A. aegypti is an urban vector in India and populations typically fluctuate with rainfall and water storage habits. In other countries of South-East Asia, where the annual rainfall is greater than 200 cm, *A. aegypti* populations are more stable and established in urban, semi-urban and rural areas. Because of traditional water storage practices in Indonesia, Myanmar and Thailand, densities of *Aedes* are higher in semi-urban areas than in urban areas. In Singapore the house index (HI) (the percentage of houses or

premises positive for *Aedes* larvae) was highest in slum houses, shop houses and multistorey apartments.

The life cycle of *A. aegypti* can be completed within one-and-a-half to three weeks. The capacity of eggs to withstand desiccation facilitates the survival of the species during adverse climatic conditions.

Throughout most of South-East Asia, *A. aegypti* oviposits almost entirely in domestic, man-made water receptacles. These include a multitude of receptacles found in and around urban environments (households, construction sites and factories), such as water storage jars, plates on which flower pots stand, flower vases, cement baths, foot baths, wooden and metal barrels, metal cisterns, tyres, bottles, tin cans, polystyrene containers, plastic cups, discarded wet-cell batteries, glass containers associated with "spirit houses" (shrines), drain pipes and ant-traps in which the legs of cupboards and tables often stand. Natural larval habitats are more rare, but include tree-holes, leaf axils and coconut shells. In hot and dry regions, overhead tanks, groundwater storage tanks and septic tanks may be primary habitats. In areas where water supplies are irregular, inhabitants store water for household use, thereby increasing the number of available larval habitats.

A. aegypti prefers to rest in dark, humid, secluded places inside houses or buildings, including bedrooms, closets, bathrooms and kitchens. Less often it can be found outdoors in vegetation or other protected sites. The preferred indoor resting surfaces are the undersides of furniture, hanging objects such as clothes and curtains, and on walls. The adult species are usually found near the breeding sites in the close proximity to dwellings.

A. aegypti is highly anthropophilic, although it may feed on other available warm-blooded animals. *A. aegypti* generally does not bite at night, but it will feed at night in lighted rooms. Being a diurnal species, females have two periods of biting activity, one in the morning for several hours after daybreak and the other in the afternoon for several hours before dark. The actual peaks of biting activity may vary with location and season. *A. aegypti* may feed with interrupted feeding on more than one person. This behaviour greatly increases the epidemic transmission efficiency. Thus, it is not uncommon to see several members of the same household with an onset of illness occurring within 24 hours, suggesting that they were

infected by the same infective mosquito. The dispersal of *A. aegypti* is very restricted with a maximum of 300 m–400 m. They therefore maintain a high degree of contact with humans.

A vector mosquito may become infected when it feeds on a viraemic human host. After an incubation period of 10-12 days, the virus grows through the midgut to infect other tissues in the mosquito, including the salivary glands. If it bites other susceptible persons after the salivary glands become infected, it transmits the disease virus to those persons by injecting the salivary fluid.

The HI (the percentage of houses or premises positive for Aedes larvae) has been widely used to calculate the presence and distribution of *Aedes* populations in a given locality. However, HI does not take into consideration the number of positive containers per house. The container index (CI) is the percentage of water-holding containers positive for *Aedes* larvae. The pupae index (PI) is the number of pupae per 100 houses. The Breteau Index (BI) is the number of positive containers per 100 houses in a specific location.

The BI establishes a relationship between positive containers and houses and is considered the most useful single index for estimating *Aedes* density in a location. The BI and HI are commonly used for the determination of priority (risk) areas for control measures. Generally, a HI greater than 5% and/or a BI greater than 20 for any locality are an indication that the locality is dengue-sensitive. For epidemiological purposes, the HI is extremely important and indicates potential spread of virus through an area once an infected case becomes established.

Surveys of adult *Aedes* mosquitoes are more time-consuming (labour-intensive), and the results less satisfying, than larval surveys. There are several ways of surveying adult vectors. In landing rates, human bare-leg catches of *Aedes* adults (both males and females) are normally used to assess adult populations. Adult mosquitoes can be collected resting inside houses. Human bare-leg catches are presently being discouraged because of risk of further spread of the disease. Oviposition traps provide a sensitive and economical method for detecting the presence of *A. aegypti* in situations where the *Aedes* density is low and general larval surveys produce unsatisfactory results (e.g. when the BI is 5 or less).

A case study of *Aedes* breeding and various breeding sites of the vector mosquito were discussed.

4.9 Yellow fever vaccination as an emergency response tool

Dr Gubler gave a presentation on YF vaccination as an emergency response tool. Eradication of *A. aegypti* in the Americas controlled urban epidemics of YF in that region for over 50 years. The advent of live attenuated YF vaccines, such as. 17D vaccine and French Neurotropic Vaccine (FNV) also helped control the disease. The FNV, which effectively controlled YF in French West Africa for over 40 years, was subsequently discontinued. The countries where recent YF activity has been reported were discussed. The current policy in many countries— emergency vaccination in response to epidemic transmission—has many problems because of poor surveillance, slow response time, delay in vaccine protection and inadequate stockpiles.

The 17D vaccine is derived through serial mouse brain and chick embryo passage and the virus subsequently has reduced viscerotropism and neurotropism. It is immunogenic and safe and its efficacy has been proven by historical observations. Immunity is long-lasting and possibly lifelong.

The serious adverse effects associated with the 17D vaccine are vaccine-associated neurotropic disease (YEL-AND), known since the 1930s, and vaccine-associated viscerotropic disease (YEL-AVD), known since the 1990s. Encephalitis is a very rare complication, observed chiefly in children.

The production issues with 17D vaccine are that there are at present only six manufacturers in the world who can produce only 200 million doses per year. The vaccine is still produced in embryonated chicken eggs with a technology which has not changed since the 1940s. In spite of the availability of a safe, economical and effective vaccine, however, there are still about 200 000 YF cases worldwide annually.

4.10 Vaccine strategy and supply chain

Professor R.C. Mahajan gave a presentation on the YF vaccine strategy and supply chain. French neurotropic vaccine was discontinued in 1980 because of the high risk of encephalitis. The 17D vaccine is a live

attenuated vaccine developed by empirical passage principally in chicken embryo tissue, resulting in multiple mutations in viral S and NS gene. It is produced from embryonated eggs. It has been used for over 60 years.

Although recipients of the vaccination develop low-level viremia, mosquitoes biting such patients do not get infected. Two different substrains derived from the YF-17D strain, YF-17DD and YF-17D-204, are used for the production of YF vaccines today. In India, it is produced at Central Research Institute (CRI) Kasauli. The government approved vaccine is available at 22 centres in the country. It is available as Inj. Stamaril and Sanofi Aventis (a single dose of 0.5 ml having 500 LD50). The vaccine is stored at 0-4 °C and should be used within two to three hours of reconstitution.

The adverse effects are fever, headache and backache, occurring from three to seven days after vaccination in 5%-15% of those vaccinated. There may be inflammation at the injection site one to five days after vaccination in 1%-30% of cases. Mild neutropenia has been reported in one study and liver AST elevation in another study. The overall reported rate for serious adverse events is 4.7 per 100 000 doses. The three primary serious adverse events are anaphylaxis (0.8-1.4 per 100 000 doses), neurologic disease (0.4-0.8 per 100 000 doses) and viscerotropic disease (0.3-0.4 per 100 000 doses).

The onset of neurologic disease takes place about 11 days following vaccination (2-28 days) and the most common presentation is meningoencephalitis with others are Guilleain-Barré Syndrome, bulbar palsy and Bell's palsy. Fatalities are rare with one death reported in a HIV-positive patient with CD4 count $< 200/mm^3$ in Thailand, one death in a healthy three-year-old child in the USA and three deaths in Kenya in the mass vaccination campaign in the 1990s.

Viscerotropic disease is a severe illness similar to wild-type disease with vaccine virus proliferating in multiple organs. Over 40 cases have been reported since the first case was recognized in 2001. The onset takes place three days following vaccination (one to eight days). Mortality has been seen in 53% cases with this complication.

The indications for YF vaccine are persons ≥9 months of age planning travel to or reside in an endemic area or planning travel to a country with

an entry requirement. The vaccine needs to be given ≥10 days prior to arrival in the endemic area. It offers full protection for six years and 70% protection for up to nine years. Revaccination is required at 10-year intervals.

Contraindications to YF vaccination are infants under six months of age, a history of hypersensitivity to eggs, chicken protein or gelatin, immunosuppression from illness or drugs, history of thymus disorder, current radiation therapy and pregnancy. In a prospective trial early in pregnancy, there were no increases in major malformations but higher rate of abortions were reported. Precautions should be taken in YF vaccination in adults ≥60 years of age, infants six to eight months old and people with asymptomatic HIV infection.

The IHR 2005 required proof of YF vaccination during travel to endemic countries. The goal is to prevent importation and indigenous transmission of YF virus. The proof of vaccination must be documented in an International Certificate of Vaccination or Prophylaxis. Yellow fever vaccine is the only vaccine currently required under the IHR. Those lacking proof of vaccination can be quarantined.

The medical waivers for YF vaccination include a complete Medical Contraindication to Vaccination, which should be given to the traveller in the form of a signed, dated, and stamped exemption letter on physician's letterhead; the traveller should be informed about the increased risk of YF without vaccination and about mosquito bite prevention measures. Issuance of the waiver does not guarantee its acceptance by the destination country. The traveller should consider contacting the destination country's embassy for further guidance.

4.11 Routes for disinsection

Dr Gilles Poumerol gave a presentation on the routes of spread of vectors in the past and disinsection principles in aircrafts. Aerosol DDT spray was used in the 1960s, and pyrethroid aerosol sprays are now used for disinsection of aircrafts.

Issues with disinsection of airports and planes are as follows:

- It prevents breeding and resting sites of mosquitoes inside airports.
- It prevents mosquitoes from entering planes.
- It kills mosquitoes inside planes.
- It prevents the escape of mosquitoes at stops and the final destination.
- It prevents establishment of mosquitoes and disease transmission from/to airport (stop and final destination)

The following articles of IHR (2005) were discussed:

- Article 19 – PoE provide information on request
- Article 20 – Designated PoE: vector control capacities
- Article 24 – Conveyance operators "permanently keep conveyances for which they are responsible free of sources of infection or contamination, including vectors and reservoirs".
- Article 34 – Containers and loading areas "free from sources of infection or contamination, including vectors and reservoirs".
- Article 39 – Ship sanitation certificates.

The challenges include conducting vector control activities based on risk assessment done from updated information about the epidemiological situation, vector surveillance in containers and cargo terminals areas, monitoring of reservoirs and updating and harmonizing with IHR at PoEs.

There is a need for an integrated vector control plan with appropriate methods and its application at different locations at PoEs. There is also a need for cooperation among PoEs between competent authorities and the local level to apply vector control in a minimum range of 400 m from terminals and operational areas. Training should be imparted for conveyance operators in international traffic to apply measures on board, in harmonization with WHO recommendations and international practices. National legislation, technical guidance and standard operating procedures should be updated.

The recommendations of a WHO consultation of experts held in 2009 are as follows:

- Areas/countries of origin of conveyances should be classified on three levels for disinsection recommendations, i.e. (a) no disinsection measures needed (exclusion); (b) measures recommended for part of the year or uncertain and need for more data (transitional); (c) disinsection measures required (inclusion).
- The level of classification should mainly be based on evidence of presence of malaria, dengue, chikungunya or YF and the presence of vectors.
- Diseases should be taken into consideration independent of the number of cases (e.g. YF could still be a risk even without cases diagnosed) or number of years of transmission (e.g. dengue risk could be present for four years in a row with the four subtypes; chikungunya might not be a risk for a number of years following an outbreak).
- Exclusion of airports located in areas classified as levels 1 or 2 should be based on evidence of effective vector control and/or favourable environmental conditions in the area of the airport.
- Disinsection needs to be applied not only to cabins, but also baggage holds and their container, and cargo planes.
- Whenever feasible, disinsection around airports should extend to at least 1 km when *Anopheles* vectors are present.
- WHO is mandated to produce maps and list of areas (preferably a list of countries or airports requiring disinsection).
- When generating these maps and lists, one should be aware of economic, political and travel implications.
- Countries will have to decide if airports are at risk.
- Countries wanting to exclude an airport will need to submit relevant data.
- Classification is a dynamic process to be periodically reassessed and updated.
- Attention needs to be paid to mobilizing political support.

4.12 Border control measures including disinfection of conveyances during travel for *Aedes* and other vectors

Dr D.T. Mourya, Scientist F, National Institute of Virology, Pune, India, gave a presentation on border control measures including disinfection of conveyances during travel for *Aedes* and other vectors. India has a land frontier of 15 200 km and a coastline of 7 517 km. There is extensive population movement across the porous borders with Nepal, Bhutan and Myanmar.

Border control measures include recognition of any reports of suspected cases of YF and immediate epidemiological investigation to determine whether the virus is active in human beings, mosquitoes or monkey populations. Investigation in human populations is based on clinical diagnosis of suspected cases and laboratory confirmation. Since IgM appears after seven days following infection, mosquito control is necessary to limit the transmission of the virus during this acute phase period. Isolation of the patient in a mosquito-proof environment is most important. Disinsection of the premises of those infected should be done with aerosol sprays/fogging/source reduction. Entomological investigation should be conducted to determine the vector species, its biological characteristics, breeding sites, and sensitivity to insecticides.

Strategies for newer areas include advance preparation to assess the current availability of vaccines, cold chain supplies, immunization equipment and trained personnel. Funds should be made available for emergency immunization activities for additional amounts of vaccine and other supplies.

Coordination should be done between international, national and local resources to support the emergency immunization activity. Clinical and serological monitoring should be conducted for the human population and surveys for mosquitoes and monkeys. Case definition of YF should be broad, i.e. febrile illness with jaundice with haemorrhagic manifestations. Control measures should be instituted when indicated by the higher mosquito density as revealed by HI/CI/BI. It may be required to regularly conduct susceptibility tests of *A. aegypti* to the principal insecticides, for necessary action.

All persons coming to India from YF-endemic countries should be vaccinated; the certificate of YF vaccination is valid for a period of 10 years. As *A. aegypti* are present in India, the quarantine period should be of six days for non-immunized persons arriving from endemic countries. Disinfection of cruisers, vessels, steamers, ships, aircrafts, etc. must be accomplished in a strict fashion. Disinfection should be performed before departure from the seaport/airport and also prior to reaching the destination seaport/airport.

There have been multiple opportunities for the introduction and spread of YF in Asia. After the opening of the Panama Canal in 1914, Asiatic ports came into more direct contact with the old endemic homes of the disease. A marked increase in air travel also increases the risk as many travellers to Asian countries have not been checked for a valid YF vaccination certificate.

There is no convincing evidence of innate differences in susceptibility to YF, and the Indian population may have cross-protection from other flaviviruses. Serologic cross-reactions between flaviviruses lead to difficulties in laboratory diagnosis, and cross-immunity of other flaviviruses has been seen to influence susceptibility to other flavivirus infections. The Indian *A. aegypti* strain was thought to be a less effective vector than the African strains, but recent studies show Asian populations of *A. aegypti* to be better vectors than West African populations. Even 17D strain of YF virus is seen to multiply well in Indian strains.

4.13 Current preventive methods at points of entry

Dr Ashwani Kumar, Scientist, National Institute of Malaria Research, gave a presentation on the current methods at PoEs. The various articles in IHR (2005) in relation to preventive methods at PoEs were discussed. As per the recommendations, surveillance for vectors and vector-borne diseases in and around international airports and ports should be implemented or improved. The requirement of disinsection should be discretionary based on international surveillance information so that these procedures are limited only to those arrivals that pose risk. The use of chloroflurocarbons as propellants for disinsection of aircraft should be eliminated.

The recommended methods of disinfection are block-away, pre-flight and top-of-descent spraying and residual treatment. Block-away takes place prior to take-off, after passengers have boarded and the doors have been closed. The cabin crew members walk through and discharge approved single-shot aerosols containing quick-acting knockdown insecticides in the prescribed dosage. Prior to disinsection, passengers should be advised to close their eyes and/or cover their faces for a few seconds while the procedure is carried out.

For effective disinsection, the aircraft air-conditioning system should be tuned off while spraying is carried out and the crew must treat all possible insect harbourages including toilets, galleys, wardrobes, etc. Empty cans used must be retained for inspection by the Port Health Authority on arrival. The holds and the flight deck are sprayed prior to departure. The flight deck is sprayed prior to boarding by the crew.

Pre-flight and top-of-descent spraying are methods similar to the block-away method, except that the aircraft cabin is sprayed on the ground with an aerosol containing a residual insecticide before passengers board the aircraft. This allows proper treatment of overhead lockers, wardrobes and toilets with minimum inconvenience to passengers. Pre-flight spraying is followed by a further in-flight spraying of quick-acting knockdown insecticide carried out at "top-of-descent" as the aircraft starts its descent to the airport of arrival. Empty cans must be retained for inspection and an entry made in the register.

In residual treatment, internal surfaces of the aircraft (except food preparation areas) are regularly sprayed with a residual insecticide at intervals based on the duration of effectiveness. Any treated surfaces which are subsequently deep-cleaned or refurbished must be retreated.

2% permethrin is the insecticide formulation used in aerosol sprays with the can discharge rate of 1 g/second. The median droplet diameter should be 8 μ and range within 3-10 μ. The can size is 100 g and the formulation should be clearly shown on the label. The propellant must be registered with the appropriate authority and all cans must conform to the appropriate standards.

The development of core capacities at POEs is comparatively lacking due to lack of awareness and advocacy, limited manpower and

infrastructure at POEs and lack of adequate training and regular updating of standard procedures.

A case study of integrated vector control at Mormugao Port at Goa was also presented along with findings of the *Aedes* survey and corrective action taken.

4.14 Contingency plans for yellow fever epidemics

Dr Woodall gave a presentation on contingency plans for YF epidemics. The five key areas of contingency planning are public information, diagnosis and surveillance, mosquito vector control, vaccination and hospitalization. There is a need to be prepared for YF epidemics because this will shorten the reaction time when a YF emergency arises, allow for immediate implementation of prevention and control measures and ultimately save lives.

It must be remembered that rumours are dangerous, causing fear and confusion. However, YF outbreaks should never be covered up. The situation should never be played down by saying that it is only an outbreak and not an epidemic and it is already under control. It should instead be stated that all necessary steps are being taken for protection of the community and what are the actions that the community should do to help the health services.

Information should be provided to the media right from the start. The draft press release should be made in all key languages and the messages should include the following questions and answers:

- What is YF? A fever like dengue haemorrhagic fever.
- How is it transmitted? By mosquito bites.
- How to prevent it? By mosquito control; the community must help.
- Is there a vaccine? Yes.

Eyecatching, printer-ready leaflets containing the above information should be designed. A website should be created with the above questions and answers along with daily updates on the number of cases occurring,

their locations, priority vaccination groups and routes, and dates and time of anti-mosquito spraying. Emergency telephone lines must be established for public information.

It must be remembered that cases will be misdiagnosed as dengue, hepatitis or something else as nobody is expecting to see a YF case. Therefore, no laboratory test will be requested and in any case, the test will not be locally available and YF may not be a reportable disease. Therefore, ultimately YF may be neither suspected or reported.

The actions which should be taken now include making YF a reportable disease and preparing YF case definitions (suspected, probable, confirmed). Travel history should be obtained from all suspected cases of viral haemorrhagic fever, including whether patients travelled to Africa or South America travel in the previous two weeks. Rapid YF lab testing should be installed in key locations Region-wide and nationwide to begin random testing of all haemorrhagic fever cases. Active surveillance for dead monkeys should also begin.

It should be remembered that the YF vector mosquito is the same as dengue vector mosquito and therefore good dengue control is equal to good YF control. There is no evidence that Asian mosquitoes are less able to transmit YF, and even poorly transmitting mosquitoes can cause large urban epidemics, as seen in Nigeria in 1987. Regarding mosquito control, it may be required to switch to using DDT in some countries. Dengue hot spots should be identified for spray and larviciding. All health facilities should be sprayed. Larvicides and adulticides should be stockpiled.

Paperwork should start for priority importation of spray equipment and supplies, if required. Loudspeaker vans must be arranged to warn neighbourhoods ahead of spraying. Solid waste collection should be improved. Media should be used to motivate the community for action. It may be required to mobilize the police forces to help the spray teams enter vacant premises for adulticide spraying and larviciding. Community organizations like Lions, Rotary, etc., may be coopted for arranging solid waste removal transport vehicles, and even the military may be required for certain actions.

It must be remembered that immunity to dengue, West Nile fever or JE does not protect against YF. YF vaccine is one of the safest vaccines in

use, and the protection it offers lasts at least 10 years and probably even for the entire life. However, it takes 10 days to take effect and needs a cold chain for storage and transportation. Risk groups and priority groups should be identified and vaccinated. Priority groups include health, public safety and essential services personnel and their families.

Priority administration and economic centres should be designated. Public vaccination centres (schools, etc.) should be designated in advance. The cold chain should be verified and crash expansion undertaken. A source for YF vaccine procurement should be identified and the necessary paper work started for it. Case definitions should be established for adverse effects and for the reporting system, Explanations should be kept ready to allay public concern. The regional YF vaccine production should be rebuilt. In emergency, all EPI vaccination centres should be converted into YF vaccination centres.

It should be remembered that YF is not transmitted by contact and therefore there is no need for barrier nursing. As YF may spread by blood, routine blood precautions should be practised. It is essential to have mosquito meshing in doors and windows of hospitals and insecticide-treated bednets for use by patients. Mosquito control activities should be intensified around all health facilities. Contact information of all health facilities should be updated. Arrangements should be made for military hospitals to take possible overflow from civil hospitals.

4.15 Country presentations

Bangladesh

Dr Moazzem Hossain, Ex-Director, Disease Control, DGHS, gave a presentation on the country situation for YF control. Bangladesh has a land area of 147 570 km^2 and a total population of 146.6 million. The nation has three international airports (Dhaka, Chittagong and Sylhet) and two seaports (Chittagong and Mongla). Cox's Bazar has the longest sea beach, which is a tourist spot. There are three hill districts (Banderban, Khagrachari and Rangamati) which also attract tourists. Bangladesh has land borders with Myanmar and India with huge cross-border population movement due

to trade and commerce. The country has a YF threat and it is considered that the current measures of YF surveillance are inadequate.

Bangladesh has reported outbreaks of dengue, chikungunya and JE caused by mosquito vectors. The International Certificate of Yellow Fever vaccination is required for travellers above one year of age travelling from a country any part of which is endemic for YF. Any person arriving by air or sea without a certificate within six days of departure from, or transit through, an infected area will be isolated for up to six days. Forty-seven doses of YF vaccination were given during 2010, and 17 doses were given so far in 2011.

The major strengths are the availability of the diagnostic laboratory, i.e. Institute of Epidemiology, Disease Control and Research and sentinel laboratories at strategic locations. There are Rapid Response Teams at district levels and past experience with control of dengue, chikungunya, nipah and H1N1 outbreaks. Major constraints are inadequate infrastructure and lack of trained staff in all international airports and seaports. There is no contingency plan for YF prevention and control at the ports. There is also a lack of quarantine hospital facilities at the ports. The YF vaccine supply chain and management is also poor.

India

Dr Sujeet Singh, Airport Health Office, New Delhi gave a presentation on the country situation for prevention of entry of YF into India. India, with a population of 1.2 billion, is so far free from YF, but is potentially receptive due to favourable climatic conditions, presence of vector and susceptible population. There are 15 airports, five sea ports and one ABQP as designated PoEs. The DGHS is the overall controlling authority.

India implements the IHR 2005, Indian Aircraft (Public Health) Rules 1954 and Indian Port Health Rules 1955. The GoI reserves the right to consider the whole territory of the country as infected with YF if YF is notified under Article 6 and other relevant articles of IHR 2005. The GoI also reserves the right to continue to regard an area as infected with YF until there is definite evidence that YF infection has been completely eradicated from that area.

The broad initiatives taken by India are that the national rules have been revised in accordance with IHR 2005. Comments on the revision were invited and incorporated and are being submitted to the Ministry for legal approval. Points of entry where core capacities and public health measures will be undertaken will be designated. The core capacities will be reassessed and manual and contingency plans for POEs made. There will be development of trained manpower and vector surveillance and strengthening of control strategies at POEs. New hospitals are established at Delhi and Mumbai with mosquito-proofing of the entire building, air curtains at entry doors, international vaccination centre, negative pressure isolation rooms, training rooms with WHO assistance and satellite connectivity.

The current practices for YF at all times for surveillance and response are passenger surveillance, vector surveillance and control, vaccination, dead body clearance, quarantine and training activities.

Screening of arriving passengers is done by immigration staff and travel/transit from affected country in the last six days is looked for. Inspection of valid YF vaccination certificate is done for date and time of vaccination and particulars of person, i.e. name, passport number, signature, date of birth, vaccination centre stamp, name and designation of vaccinator, batch number of vaccine, etc., in accordance with IHR (2005). When necessary, the traveller is referred to the Airport Health Officer for verification of travel and vaccination documents.

All passengers who have travelled/transited from known YF-endemic countries six days prior to arrival at POE, and who do not possess a valid YF vaccination certificate, are quarantined for a maximum period of six days or until the YF vaccination certificate becomes valid. The ship is also quarantined. The payment for the period of stay is made by the traveller at the rate fixed by the GoI. The person has the choice to go back to his own country or country of embarkation. Approximately 260 passengers are quarantined every year. The core staff members are the Assistant Public Health Officer (APHO) and Public Health Officer (PHO), medical officers, staff nurses, health inspectors, insect collectors, fumigation/field workers, ward boys and female attendants. 17D vaccine supplied by CRI Kasauli is used for vaccination and the charge is Rs. 300 per dose. A certificate is

issued in accordance with the IHR 2005. On average 25 000 vaccinations are given annually.

The content of core staff training includes the IHR 2005, affected countries/areas, epidemiology of YF, travel itinerary review, YF vaccination certificate, do's and don'ts, and quarantine procedures.

Vector surveillance is carried out for 400 m around the periphery of the airport by the agency designated for vector control. The plan for New Delhi Airport was prepared in consultation with the National Vector-Borne Disease Control Programme. Source reduction and space spray activities are carried out to maintain the *A. aegypti* index at less than 1. The surveillance of vector breeding is done by the APHO/PHO. Independent surveillance is done periodically by National Centre for Disease Control entomologists. Conveyance (aircraft/ship) disinsection is also done. There are 22 vaccination centres in India recognized by MoHFW.

Indonesia

Dr Oenedo Gumarang, Port Health Officer of Indonesia gave a presentation on the surveillance system in seaports and airports in Indonesia. Indonesia has 48 Port Health Offices and 10 international airports. Prevention of YF is done by control of *A. aegypti*, especially in the perimeter areas in seaports and airports. YF vaccination is required for travellers arriving from or leaving for endemic areas. Those travellers who do not have a valid vaccination certificate are quarantined.

Sri Lanka

Dr A.D.S.R.T Siriwardhane, Airport Health Officer, Bandaranayake International Airport gave a presentation on current practices at the airport. Sri Lanka has one international airport at Katunayake and three main sea ports in Colombo, Galle and Trincomalle. Nearly 6500 passengers arrive daily in the airport.

YF vaccination is required for those arriving within six days of leaving or transiting through countries with infected areas. Persons without a valid YF certificate, if required, are subjected to quarantine. Presently there is no active screening of YF vaccination status at health counters or immigration

desks at the airport, and only voluntary checks are done. A display board is kept mentioning "All passengers arriving or transiting from Africa and South America are kindly requested to report to the health counter". Voluntary declarations were made by 96 persons in 2009, 14 persons in 2010 and 7 so far in 2011. There is no declaration on the present immigration card for countries visited in last six days. The immigration card is being revised to include a new segment (travel itinerary and destination), as this method would be more helpful for the surveillance of YF vaccination status of passengers.

Thailand

Dr Waraluk Tangkanakul, Head, Suvarnabhumi Port Health Control Office gave a presentation on current practices at the airport. Those passengers who have travelled from YF-affected areas or those travellers who hold a passport issued by government of countries declared YF-affected area must submit the passport, filled arrival card/TM6 (immigration form), filled T8 Forms (Health Questionnaires) and International Certificate of Yellow Fever Vaccination (YF book) to the health control officer at the Port Health Office.

The name on the certificate should be the same as given in the passport. The YF vaccination certificate should clearly indicate the lot number of the vaccine and date of vaccination. The date of the vaccination should be within 10 years but no fewer than 10 days before arrival. The certificate should bear the signature of the health provider and seal of the hospital or clinic. The certificate should not have any erasures or amendments and should be complete.

5. Group work

The participants were divided into two groups and worked on the following issues to arrive at conclusions which formed the basis of final recommendations of the regional meeting:

Group I: Existing infrastructure and development of core capacity in the Region and in countries.

Group II: Strategies to prevent YF entry and contingency plans including disease and vector surveillance.

Group I: Existing infrastructure and development of core capacity in the Region and in countries

The group made the following recommendations:

- IHR should be mandatorily followed by all the countries. WHO should help in convincing administrators of all the countries in Asia to implement IHR in toto.
- In all the countries, it should be made mandatory that when booking international travel tickets YF vaccination information should be provided and this information should be mandatorily passed on by airlines/airport authorities of the country of origin to the Environmental Public Health officer (EPHO) or Environmental Health Officer (EHO) of the port of entry and made readily available at the health desk.
- Immigration forms and procedures should be modified in such a way that passengers arriving from YF-endemic countries or routed through them first report to the health desk, before immigration checks.
- Every country should create adequate infrastructure in at least one of the main ports by 2012, which can then be replicated in other ports in the country.
- Medical officers with adequate numbers of paramedics and other disinsection staff should be available round the clock.
- Each international port should have at minimum a 10-bedded quarantine facility. WHO should provide guidelines for construction, maintaining uniformity and biosafety.
- At least one WHO reference laboratory is needed in the Asian region.

Group II: Strategies to prevent yellow fever entry and contingency plan including disease and vector surveillance

The group made the following recommendations:

- The most cost-effective way to prevent the spread of YF to Asia is to immunize the total population of all endemic countries. This goal should be part of the national immunization schedule of each country, and should be suggested by international health agencies. Individual countries can prioritize the areas according to disease status and the risk to the population in their country for implementing YF vaccination programme in collaboration with WHO.
- IHR implementation must be carried out effectively in all non-endemic countries. At the Regional level, a commission of experts from all countries should be formed by WHO to develop a detailed plan and monitor its implementation, core capacities at POEs and public health measures for YF surveillance and response.
- Yearly collaborative meetings should be conducted between member countries to review the implementation of IHR.
- Vector control measures must be strengthened in all endemic and non-endemic countries.
- Every non-endemic country should be proactive in incorporating YF into its national surveillance system. This surveillance should be active, and supported by a competent laboratory testing facility. Surveillance systems for YF could be merged with dengue surveillance systems through the use of sentinel sites and should be syndromic systems.
- Every country should establish at least one national-level public health laboratory which can function as national reference laboratory for undertaking training and quality control for regional and district-level labs.
- Information and awareness about YF should be communicated to the medical community, public health workers and staff working in POEs.

- Each country should develop a rapid assessment plan and emergency response for verification, containment and control if a case of YF occurs. These plans should have automatic triggers that facilitate rapid and effective implementation.
- Unusual mortality of monkeys also should be immediately investigated.
- The WHO's emergency vaccine stocks should be quickly mobilized if the introduction of YF occurs in any country.
- All countries should have a specific programme for *Aedes* control both in POEs and urban communities. In urban communities it can be incorporated in dengue and other vector transmitted disease control programmes.
- Regional YF vaccine manufacturing centres should be strengthened to enhance the capacity of regional vaccine production as well as to undertake research on new YF vaccines using the latest technology.
- All countries should have a contingency plan in accordance with the WHO framework on rapid assessment, emergency response and response by WHO.
- All countries should develop emergency hospitalization plans to accommodate patient overload in hospitals in the event of an introduction or outbreak of YF disease.

6. Recommendations

The recommendations of the groups were deliberated upon and the following final recommendations of the consultation were made:

6.1 Member States

(1) Member States should review their existing infrastructure for IHR implementation and strengthen organizations/agencies responsible for vector surveillance and control at their international airports/seaports for effective implementation of IHR round the clock.

(2) Member States should develop contingency plans for rapid assessment and emergency response in the event of the occurrence of YF, including case verification, containment, control and treatment of cases.

(3) Member States should establish at least one national-level Yellow Fever Reference Laboratory for diagnosis and quality control of provincial/state-level laboratories.

(4) Member States should modify their immigration procedures and forms so that all passengers arriving from YF-endemic countries are routed to a health desk for confirmation of their vaccination status before an immigration check is done.

6.2 WHO

(1) WHO should encourage Member States to give priority to capacity-building of organizations at airports/seaports for effective implementation of IHR.

(2) WHO should facilitate the creation of a Regional Reference Laboratory for YF in SEA Region and the strengthening of YF vaccine production capacity in the Region.

(3) WHO should promote action aimed at immunization of the entire population of all endemic countries at risk of YF transmission so as to reduce chances of its spread to populations living in non-endemic countries.

Annex 1

Agenda

Wednesday, 23 March 2011

- Registration
- Opening Session
- Status and Strategies
- Risk of spread to new areas
- Prevention and control

Thursday, 24th March 2011

- Prevention and control (Continued)
- Country Experiences and current practices
- Group work

Friday, 25th March 2011

- Group work (continued)
- Presentation of group work
- Way forward
- Conclusion and recommendations
- Closing

Annex 2

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Yellow fever (YF) is a viral disease endemic in the tropical Regions of Africa and the Americas transmitted by *Aedes aegypti*. The risk for international spread of yellow fever is now greater than before due to the regularly used air routes connecting endemic countries. An informal expert Consultation on the yellow fever threat to India and other Member States of the WHO South-East Asia Region was held on 23 - 25 March 2011 which discussed various issues concerning the yellow fever threat to the Region and made recommendations to Member States and WHO.

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SEA-CD-235