



Yellow Fever Epidemiology, South America 1st April 2008

1. YELLOW FEVER BACKGROUND

- Yellow fever (YF) Y is a viral haemorrhagic fever. The disease burden is estimated to about 200 000 cases per year (30 000 deaths) worldwide among which only a small proportion is notified to WHO.
- Agent : Flavivirirus.
- Vectors: in Africa Mosquitoes mainly from Aedes genus. In South-America, different genus *Haemagogus* & *Sabethes* (sylvatic mosquitoes) and *Aedes* spp. (urban mosquitoes).
- **Reservoir:** Monkeys and mosquitoes (due to transovarian transmission of the virus).
- Geographic distribution: Sub-tropical Africa & South America.
- **Transmission**: Only through the daytime bite of an infected mosquito. There are three types of transmission cycle: sylvatic, intermediate and urban. All three cycles occur in Africa, but only two in South America (sylvatic and urban).
 - ✓ Sylvatic (jungle) cycle: It is a mosquitoes-monkeys cycle. Humans get contaminated sporadically in the rain forest through the bite of "wild" infected mosquitoes. This cycle is the main source of human cases in South America.
 - ✓ Intermediate cycle: Semi-domestic mosquitoes infect both monkey and human in African savannahs. This can result in small-scale epidemics in rural villages. In Africa, this type of transmission is responsible for most documented human cases. Without adequate control, these outbreaks can yield more severe epidemics in urban areas.
 - ✓ Urban Cycle: Following the introduction of a viremic human case in an urban area (high population density), the virus is transmitted to the urban vector Aedes aegypti. It is then carried from person to person by these "domestic" mosquitoes. These outbreaks have the potential tend to spread rapidly and to cover wide areas.
- Incubation period: From 3 to 6 days
- Clinical features :
 - Asymptomatic forms: frequent (50 to 85%).
 - Symptomatic forms: Characterised by fever, muscle pains, nausea and headache. Symptoms generally recede after 3 to 4 days.
 - ✓ Severe forms (15 to 25% of symptomatic forms): after a short remission period, fever reappears and several systems are affected; liver failure including jaundice, kidney failure (albuminuria, anuria), and in some cases, haemorrhagic syndrome (epistaxis, melaena, haematemesis...)
- Case fatality rate: 20-50% of severe forms

• Treatment : only symptomatic

Network for Communicable Disease Control in Southern Europe and Mediterranean Countries

 Vaccin: <u>WHO</u> highly recommends vaccination for travellers to high-risk areas. A vaccination certificate is required for entry to many countries, particularly for travellers arriving in Asia from Africa or South America.

2. YELLOW FEVER IN SOUTH AMERICA

The last large urban outbreak In South America dates back to 1954. However, sylvatic (jungle) fever human cases and/or epizootic are regularly documented in the countries of the Amazonian region: Brazil, Bolivia, Colombia, Ecuador, Paraguay, Peru, Venezuela, extreme North of Argentina (cf. Figure 1). These human cases are often linked to population migrating from YF free zones to forested area where the disease is enzootic. These forested zones host many species of monkeys and mosquitoes from the genus *Haemagogus*, *Sabethes* and *Aedes*.

Figure 1: Yellow fever endemic zones in the Americas, 2007 (Source <u>CDC</u>).



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Argentina

Pop. 40 M inhabitants (2006)

- In Argentina (cf. Figure 2), the last YF human cases were reported to WHO in 1967.
- YF virus sporadically circulates in the countryside and forest in the North-East province of Misiones (including in the famous Iguazú Falls areas)
- In January 2008, health authorities reported the suspect death of monkeys in the Piñalito wildlife reserve located in the San Pedro Department, Misiones province (Bordering Brazil).
- On March 3rd, 2008, the 1st case of human jungle yellow fever was reported since 1967.
- As of March 31st, 2008, 5 human cases (1 death) of sylvatic YF have been reported in the Misiones province.
- None of the reported cases had been immunized against yellow fever during the last 10 years. All cases had stayed in the forest before onset of the infection.
- In 2006, the immunisation coverage of the target population living in at risk areas was estimated to 70%.
- YF immunisation is not compulsory to visit Argentina but is strongly recommended for travellers to the area.
- To date, almost 1 million people have been vaccinated in the Misiones and the Formosa provinces (Northern Argentina near the Paraguayan border).

Figure 2: Argentina map and Misiones Province.





Bolivia

Pop. 9 M inhabitants (2007)

- Sylvatic yellow fever suspect cases are notified every year through the syndromic surveillance system implemented in 1960 (Figure 4)
- From 1977 to 2007: 1,026 case were notified to WHO (mean = 86/year; median = 18/year).
- In 2007, 57 suspect cases (7 confirmed cases including 6 deaths) were notified to WHO.
- Affected regions are mainly rural areas in the Departments of La Paz, Santa Cruz and Cochabamba.
- Following the implementation of specific programmes, immunisation coverage reported to WHO for the target-population living in these areas rose from 12% in 2001 to 76% in 2006.



Figure 3: Map of Bolivia.

Figure 4: YF cases and estimated immunisation coverage* Bolivia 1977-2007 (source: WHO).



^{*}Immunisation coverage in area where YF vaccination is included in the immunisation schedule.



Brazil

Pop. 190 M inhabitants (2006)

- Jungle YF (sylvatic cycle) is endemic or sporadic in the Amazonian zone of the country (cf. Figure 5).
- Between 1980 and 2008, Brazil reported 998 cases of sylvatic YF (median: 30/year; mean: 47/year) (cf. Figure 6)
- In Brazil, vaccination against YF is included in the immunisation schedule from the age of 9 months.
- Vaccination is recommended after the age of 6 months when viral circulation becomes more intense.
- According to data provided to WHO, immunisation coverage was about 99% in 2006. (cf. Figure 6).

Figure 5: YF Modes of transmission by zones, Brazil (source: MoH, Brazil).



Figure 6: Sylvatic YF cases and estimated immunisation coverage*, Brazil 1980-2008 (source: MoH &WHO).





Colombia

Pop. 45 M inhabitants (2005)

- Between 1977 and 2007, Colombia has notified 472 case of sylvatic YF to WHO (mean: 15 cases/year; median: 6 cases/year). (cf. Figure 8).
- Of the 32 cases notified in 2004, 28 cases (including 11 deaths) were reported in the touristic area of Sierra Nevada de Santa Marta following an epizootic that took place in Las Besotes national park (Cesar Province).
- Areas affected between 1990 and 2003 were the South-Eastern half of the country and the province of Norte de Santander bordering Venezuela (cf. Figure 9).
- In 2006 immunisation coverage of the target-population was estimated at 88%.



Figure 8: Sylvatic YF cases notified to WHO, Colombia, 1977-2007 (source: WHO).



Figure 9: Sylvatic YF cases, by Department, Colombia 1990-2003 (source: MoH).



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Ecuador

Pop. 13,3 M inhabitants (2005)

- Between 1977 and 2006, 125 sylvatic YF cases were reported (source MoH) (cf. Figure 11). The last human sylvatic YF case was notified to WHO in 2000.
- Cases reported since 1997 occurred in the provinces of Napo, Pastaza and Sucumbíos.
- According to data reported to WHO, immunisation coverage of the target-population remains around 99% since 2002 (cf. Figure 11).



Figure 11: Sylvatic YF cases and estimated immunisation coverage*, Ecuador 1977-2007 (source: MoH & WHO).



*Immunisation coverage in area where YF vaccination is included in the immunisation schedule.



Guyana

Pop. 765 000 inhabitants (2003)

- The last human YF case in Guyana (cf. Figure 12) was notified to WHO in 1968.
- Estimated immunisation coverage of the target population reported by Guyana rose from 7% in 1998 to about 90% in 2006.





French Guyana

Pop. 209 000 inhabitants (2006)

- The last human case in French Guyana (deceased) was identified in 1998; it occurred in a person living on the border with Surinam.
- YF vaccination is compulsory in French Guyana (since 1967.
- In 2000, immunization coverage was high in the coastal areas and on the main waterways. However, it remained suboptimal in children aged less than 2 in some health districts of the interior.

Figure 13: Map of French Guyana.





Panama

Pop. 3,3 M inhabitants (2006)

- The last human cases in Panama were notified to WHO in 1974 when 5 sylvatic cases (including 1 death) were identified in Darien jungle, Bayano area.
- Since 2004, the estimated immunisation coverage of the target population is about 99% in the Panamá Este, Darién et Kuna Yala regions.





Paraguay

Pop. 6,3 M inhabitants (2005)

NORTH PACIFIC OCEAN

- On February 6th, 2008, the Paraguayan health authorities reported a confirmed human case (deceased) of jungle yellow fever; the 1st in 35 years and the 1st death in a century.
- As of March 31st, 2008, 26 human cases (8 deaths, CFR 31%) were reported in 3 departments: San Pedro (15 cases), Central (10 cases) and Caaguazú (one case).
- The cases reported in the Central department were probably infected in an urban area.
- As of March 31st, 2008, 1.6 million people had been vaccinated in the priority districts and vector control activities are ongoing in areas with a risk of transmission
- Since 2000 in Paraguay, vaccination is recommended for children (from the age 1 year) living in areas bordering Brazil or Bolivia.
- Immunisation coverage in the target population was estimated to 24% in 2005 and 31% in 2006.







Peru

Pop. 28 M inhabitants (2005)

- The largest YF outbreak which occurred in Peru (Figure 16) since 1954 was documented in 1995 when 440 cases (CFR: 38%) were reported.
- The YF virus circulates in the foothills (between 400 and 2000 m) and in jungle areas in the North and the East of the country (cf. Figure 17 and Figure 18)
- The zones mainly affected are forested areas of Puno, Cusco, Cajamarca, Amazona and Iquitos provinces (cf. Figure 17 and Figure 18).
- YF is also present in some deep river valleys of mountainous areas (e.g. Rio Marañon & Rio Huallaga) (cf. Figure 19). River basins from San Martin, Junin, Huánuco, Pasco, Uyacali and Madre de Díos Regions are also affected.



Figure 17: YF circulation zones, 1972-2001, Peru Figure 18: Zones with notified YF cases in 200

ru notified YF cases in 2007



YF circulation

High

Moderate



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- Between 1977 and 2007, 2,588 cases were notified to WHO (mean: 83 cases/year; median: 63 cases/year) (cf. Figure 20). Cases are reported every year.
- Early 2007, an outbreak (10 confirmed cases, 1 probable) was documented in Echarate district, La Convencion province (forested area in northern Cusco Department). The city of Cusco was not affected.





*Immunisation coverage in area where YF vaccination is included in the immunisation schedule.

- During the immunisation campaign that followed the 2007 outbreak, an unexpected level of vaccination adverse events was observed, and 4 deaths were reported among the nearly 43,000 persons vaccinated with a specific YF vaccine lot (source: <u>PAHO</u>). Investigations on the 20-fold higher incidence of adverse events concluded to the absence of unwanted characteristics in the vaccine lot and the possible contribution of underlying disease.
- According to data reported to WHO, immunisation coverage of the target-population rose from 8% in 2000 to 91% in 2006.



Suriname

Pop. 434 000 inhabitants (2001)

- The last reported human YF cases were reported to WHO in 1972 (2 sylvatic cases)
- According to data reported to WHO, immunisation coverage of the target-population were 80% in 2001, 97% in 2005 but only 14% in 2006.





Venezuela

Pop. 26 M inhabitants (2005)

- Between 1996 and 2007, 79 sylvatic cases including 38 deaths (CFR 48%) were notified to WHO by Venezuelan authorities (cf. Figure 23).
- Yearly mean of death and cases were 11 and 5, respectively, while the yearly median was 5 cases and 3 deaths.

Figure 22: Map of Venezuela.



Figure 23: Sylvatic YF cases and estimated immunisation coverage*, Venezuela, 1996-2006 (source: WHO).



- In 2002: 3 cases including 2 deaths were reported in Zulia Province (Jesus Maria Semprum district).
- In 2003, the outbreak which affected Venezuela was contemporary to an outbreak in neighbouring Colombia:
 - ✓ 43 cases incl. 20 deaths (CFR: 46,5%).
 - Cases were reported in 9 districts from 3 provinces: Zulia, Tachira and Portuguesa.
- In 2004: 5 cases, including 3 deaths, were reported in Merida and Monagas provinces.
- The last cases were documented in 2005 (No cases in 2006, no data for 2007).

Figure 24: YF transmission zones Venezuela, 2004 (source MoH).



3. COMMENTS

- Yellow fever is enzootic in the Amazonian forest. Sporadic sylvatic (jungle) human cases are regularly reported by the different countries which are part of the Amazonian region.
- Occurrence of these cases is often related to population movement i.e. the migration of people originating from "YF free areas" to zones where the virus is circulating among the local fauna.
- The major threat posed by yellow fever is the establishment of an urban transmission cycle which could be triggered by the importation of cases from rural areas. The vectors potentially involved in an urban transmission cycle are present in most South American cities (notably *Aedes aegypti*)
- However, the importation of sporadic human cases in an urbanized area does not necessary trigger the onset of an urban cycle.
- Over the last decade, the WHO regional office (PAHO) has closely collaborated with countries on YF immunisation. The immunisation coverage of the population living endemic areas has noticeably increased in most countries.
- The observed increase in immunisation coverage has not been sufficient to fully prevent the occurrence of human YF jungle cases.

- Since December 2007, the circulation of YF has become more intense in monkeys in the South-East of the Amazonian region: Brazil, Paraguay and Argentina. Spill-over human cases have been diagnosed in these three countries.
- To date, the increase in viral circulation remains mainly a sylvaltic phenomenon. There is no evidence to support the establishment of an urban transmission cycle in any of these three affected countries
- However, because of the geographical spread of the epizootic, the situation in the area will be carefully monitored.
- Immunisation against yellow fever is strongly recommended to travellers visiting rural areas in Brazil, Paraguay and Argentina, including the Iguazú Falls (WHO)