

TAG RECOMMENDATIONS FOR YELLOW FEVER

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PAHO



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Organization



World Health
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1999 Recommendations

- Yellow fever endemic countries must achieve 100% vaccination coverage in enzootic yellow fever zones, as well as in contiguous areas infested with *A. aegypti*. These steps will provide protection to those persons exposed to the sylvatic cycle and will help prevent the introduction of the disease to urban settings.
- Given that it is difficult to predict demographic movements, countries with high migrant movements from non-enzootic to enzootic areas should consider national mass vaccination campaigns to immunize the entire population. Brazil is planning to conduct such a campaign.
- Yellow fever vaccination is also recommended for all travelers entering enzootic areas.
- In order to maintain high levels of population immunity to yellow fever, countries at risk should incorporate yellow fever vaccine into routine childhood vaccination schedules. Yellow fever vaccine should be given, as a separate injection, when measles vaccine is administered.
- Yellow fever surveillance must be strengthened. Timely yellow fever surveillance will allow the rapid implementation of control activities when an outbreak is detected. All suspected cases meeting the WHO surveillance case definition and those with icteric syndrome, in whom other infectious etiologies have been ruled out, should be investigated.
- Countries should prepare emergency rapid response guidelines to be used in the event of a yellow fever outbreak.
- Adequate planning of vaccine supply for routine vaccination and outbreak control is critical. A stockpile of vaccine should be available at all times.
- The implementation of a comprehensive vector control and surveillance program will keep the density of *A. aegypti* low in urban environments. This approach will also help to prevent dengue outbreaks.

2000 Recommendations

- Yellow fever endemic countries must achieve 100% vaccination coverage in enzootic yellow fever zones. Yellow fever vaccination is necessary for all travelers entering enzootic areas.
- Yellow fever surveillance must be strengthened. Timely yellow fever surveillance will allow the rapid implementation of control activities when an outbreak is detected.
- Countries should prepare emergency rapid response guidelines to be used in the event of a yellow fever outbreak.
- Adequate planning of vaccine supply for routine vaccination and outbreak control is critical. Vaccine should be available at all times to deal with emergencies.
- The implementation of a comprehensive vector control and surveillance program will keep the density of *A. aegypti* low in urban environments. This approach will also help to prevent dengue outbreaks.

2002 Recommendations

- Countries should continue strengthening surveillance of clinical cases compatible with yellow fever, to ensure the expeditious implementation of control measures. Icteric syndrome and epizootic surveillance should be carried out in a systematic way in sentinel areas to enhance the capacity of countries to detect yellow fever virus circulation.
- Enzootic countries should consider the implementation of the following recommendations in municipalities within enzootic areas, or in areas with a level of house infestation index by *A. aegypti* greater than 5%:
 - Immunize the entire population.
 - Incorporate yellow fever vaccine in the routine schedule for children.
- Provision should be made by the Americas to stockpile sufficient vaccine for use in emergency outbreak control efforts.

2004 Recommendations

- Countries with enzootic areas should view yellow fever as a public health priority, providing political, technical, and financial support for the implementation of national plans for yellow fever prevention and control.
- Epidemiological surveillance of yellow fever virus circulation should be strengthened both in enzootic and non-enzootic areas to allow rapid implementation of outbreak control measures when a human case or an epizootic is detected.
- To enhance the early detection of yellow fever virus circulation, the implementation of epizootic and febrile icteric syndrome surveillance in both enzootic and non-enzootic areas is advised.
- The yellow fever vaccination plan should target 100% of the population residing in enzootic areas and areas that are the source of migration into enzootic areas. Yellow fever coverage in these areas should be maintained at >95% among children aged 1 year, as should measles coverage.
- The maintenance of low infestation rates of *Aedes aegypti* is important, not only to prevent the reurbanization of yellow fever, but also to avoid extensive outbreaks caused by the dengue virus.
- An adequate yellow fever vaccine stock should be maintained both for the regular program and campaigns, with reserves for control of possible outbreaks.
- Epidemiological monitoring of adverse events attributable to the yellow fever vaccine should be strengthened.

2006 Recommendations

- Countries with enzootic areas should consider yellow fever a public health priority, gathering all the political, technical, and financial support to continue with implementation of national plans for yellow fever prevention and control.
- It is essential to complete vaccination of all the population residing in enzootic areas and in communities where immigration to enzootic areas originates. The strengthening of the information system and analysis is crucial to evaluate and monitor the plans in order to focus vaccination in municipalities or areas with low vaccination coverage.
- The three remaining countries that did not do so, should include yellow fever vaccine in their national schedule so the vaccine is administered at the same time as MMR to children reaching one year of age.
- Countries should continue to improve the quality and sensitivity of the epidemiological surveillance for yellow fever. In non-enzootic areas, outbreak control measures should be strengthened and include increasing the sensitivity of the surveillance system, improving the capacity for adequate outbreak response, maintaining a vaccine supply at national level, and conducting vector control to avoid re-urbanization of the disease.

2009 Recommendations

- Countries with enzootic areas should consider completing their plans for yellow fever control vaccinating all residents in these areas aged >1 year. Travelers to these enzootic areas should also be vaccinated.
- Countries should assess vaccination coverage through rapid monitoring or other methodologies to ensure that the entire population living in risk areas is vaccinated.
- The four remaining countries with enzootic areas that have not yet introduced the yellow fever vaccine in their routine program should target children aged one year in order to have protected cohorts in the long term. Vaccination coverage should be maintained at over 95% in routine vaccination programs for the first year of life.
- Epidemiological information and careful yellow fever risk assessment, considering ecological, environmental, and cultural factors that favor disease transmission, should guide vaccination activities. Therefore it is important that countries maintain and improve their epidemiological surveillance systems.
- Countries should ensure the quality and sensitivity of the epidemiological surveillance system for yellow fever, including surveillance of icterohaemorrhagic febrile illnesses, epizootics, vaccination coverage, and adverse events associated with yellow fever vaccination. In non-enzootic areas of these countries, the sensitivity of the surveillance system should be increased and outbreak control measures strengthened. It is recommended that countries have a national stock of vaccines.
- In light of outbreaks in Brazil, Paraguay, and Argentina in 2008, Regional and Global Emergency vaccine supplies were consumed in their entirety in January and February 2008. Given the limited availability of yellow fever vaccines, priority should be given to primary vaccination and re-vaccination should be avoided.
- Given the current risk of the reurbanization of yellow fever in the Region, a comprehensive approach should be adopted that highlights vector control of *Aedes aegypti* in urban centers bordering enzootic areas. Elimination of breeding sites should be undertaken and, insofar as possible, environmental conditions should be improved so that they don't foster mosquito reproduction.
- Countries should have a risk communication plan in order to avoid crisis situations due to yellow fever outbreaks and ESAVIs related to the vaccine.
- Countries should consider adequate screening mechanisms to identify vaccine contraindications and precautions before vaccination.

2013 Recommendations

- TAG endorses the recommendations issued by SAGE:
 - One yellow fever vaccine dose is sufficient to provide sustained immunity and life-long protection against the disease, therefore no booster is required.
 - In regards to special populations, immunocompromising conditions including symptomatic HIV or CD4+ counts < 200 cells/mm³ are contraindications to vaccination while age ≥60 years, pregnancy, and breastfeeding are precautions to vaccination. A risk-benefit analysis is recommended for individuals with a precaution to vaccination.
 - The recommendation for the simultaneous administration of MMR and yellow fever is maintained, given that to date there is no sufficient evidence to change current recommendations.
- TAG calls for further studies to better understand the potential need for boosters in special groups, as well as the simultaneous administration of yellow fever and other live vaccines such as MMR in children. Also, additional studies are needed on the immunogenicity and safety of yellow fever vaccine in persons aged >60 years, HIV- infected adults and children, and pregnant and breastfeeding women.
- TAG reemphasizes the importance of yellow fever vaccination through the routine immunization program and of maintaining high coverage levels in order to prevent cases and outbreaks of the disease.
- PAHO should work towards addressing the long-standing issue of insufficient yellow fever vaccine supply in the Region through technology transfers and other mechanisms. Similarly, TAG strongly urges PAHO, WHO, partners, and vaccine manufacturers to develop a strategy to increase the global production capacity for yellow fever vaccine.

2016 Recommendations

- The TAG reiterates its previous recommendations regarding the application of a single dose of YF in endemic areas:
 - One YF vaccine dose is sufficient to provide sustained immunity and life-long protection against the disease, therefore no booster dose is required.
 - Vaccination of at least 95% of the population residing in the area (urban, rural and jungle areas).
 - Countries should ensure that vaccination recommendations for travelers to YF endemic areas are enforced.
- The TAG reemphasizes the importance of YF vaccination through the routine immunization program and of maintaining high coverage levels to prevent cases and outbreaks of the disease. However, in the current outbreak situation of Brazil, YF endemic countries should consider postponing childhood vaccination in non-enzootic areas in order to re-allocate doses for priority areas until the vaccine is more readily available at the regional and global levels.
- The TAG endorses the current WHO recommendation regarding the use of fractional doses in response to outbreaks. PAHO should support countries in the roll out and implementation of fractional doses of YF vaccination as needed, including strengthening of AEFI surveillance following vaccination with fractional doses.
- Given the current outbreak in Brazil and the emergence of cases in areas where cases have not been detected in several years, the TAG urges countries to continue prevention and control efforts as part of a comprehensive plan to:
 - Strengthen epidemiological, virological, vector, epizootic and AEFI surveillance.
 - Reassess the YF risk in endemic countries taking into entomological makeup, account migration patterns, global warming and other human (eco-tourism) trends, among others.
 - Reassess the risk of YF re-urbanization.
 - Monitor and maintain high vaccination coverage among target groups.

2017 Recommendations

- TAG calls on endemic countries to optimize vaccination delivery, maintain high vaccination coverage among target groups, and strengthen the monitoring of vaccination coverage and of adverse events following immunization (AEFIs).
- TAG reiterates its endorsement of the use of subcutaneous (SC) fractional YF vaccine in response to outbreaks occurring in a context of limited vaccine availability. PAHO should support endemic countries in the rollout and implementation of SC fractional YF vaccination as needed.
- TAG also reminds endemic countries that have temporarily postponed routine childhood vaccination in areas that are not currently at high risk of YF as a dose-sparing strategy, that they should resume routine vaccination as soon as vaccine supply allows it.
- In the case of Brazil, TAG emphasizes the importance of continuing vaccination activities among residents of and travelers to all affected areas beyond the duration of the outbreak. Priority should be given to closing the vaccination gap with the aim to achieve 95% coverage of all residents eligible for vaccination. TAG also commends Brazil's MOH for adopting a single-dose YF vaccine schedule and supports the Ministry's decision to adopt universal vaccination of all children eligible for vaccination in the country in 2018.
- TAG urges endemic countries to strengthen YF epidemiological, virological, vector, and zoonotic surveillance and to reassess YF risk, taking into account ecological factors, migration, and other population movements, vaccination coverage levels, and entomological trends, among others. The assessment should also consider the specific risk of YF re-urbanization. Information from surveillance activities and the risk assessment should be used to prioritize vaccination and control measures.
- TAG endorses the Global EYE Strategy and credits its initiative in providing visibility to YF in the global public health agenda, and in including PAHO's RF as a member of its governing body.
- In the context of global YF vaccine shortage, TAG recognizes the efforts of the RF in ensuring the YF-endemic Member States' vaccine needs are met.

2018 Recommendations

- TAG urges countries facing large YF outbreaks such as the current YF outbreak in Brazil, to activate the mechanisms in place for the rapid mobilization and deployment of all resources needed to control YF outbreaks in a timely manner, in agreement with the Member States' legal frameworks. The highest political commitment is needed at all levels to achieve high vaccination coverage rates in such vaccination campaigns. The lessons learned from Brazil's implementation of the measles-rubella vaccination campaigns should be applied to this YF campaign, including the highest political commitment, resource mobilization, supervision and coordination, accurate microplanning, risk communication and accountability.
- TAG reiterates its endorsement of the use of a fractional YF vaccine dose in response to outbreaks occurring in a context of limited vaccine availability. Children aged less than two years, pregnant women and individuals known to be HIV-infected should be vaccinated using a standard 0.5 ml dose, given the lack of data on immunogenicity and reactogenicity in those population groups.
- TAG stresses the importance of achieving 95% fractional YF vaccine coverage levels in a short time period for the intervention to be effective at controlling an outbreak. Strategies should be developed to reach high risk groups such as young males in rural or urban areas. Countries should implement a nominal immunization information system to monitor the corresponding coverage levels and vaccine safety.
- Based on available data from an 8-year follow-up study in adult males vaccinated with 17DD vaccine, which demonstrated sustained immunity in individuals who seroconverted after vaccination, TAG considers that a fractional dose could provide protection for at least eight years. Based on current evidence, re-vaccination is not required in an area in which vaccination with a fractional dose has been conducted in response to an outbreak. This recommendation will be revisited when new evidence becomes available.
- Given that data on the immunogenicity and safety of fractional YF vaccine are currently only available for one product that is administered via the same route as the full dose product; countries should give preference to this product. Endemic and non-endemic countries that are vaccinating against yellow fever should consider the potency of the vaccine batch, the supply situation and availability of suitable injection devices when deciding on the use of a fractional dose (**table 2**).

Table 2. Potency of the Various Available YF Vaccine Products

Batch potency* International units (IU)	Product 1	Product 2	Product 3**	Product 4
Average	43651	25704	18977	12874
Maximum	114815	125896	177827	26284
Minimum	13490	3715	4169	7578
Average 1/5	8709	5129	4467	2569
Minimum 1/5	2692	741	832	1516

- TAG recommends that endemic and non-endemic countries that use fractional doses of the YF vaccine, conduct further follow-up, product-specific immunogenicity and safety studies to increase the body of evidence on the use of fractional vaccine doses.
- TAG re-emphasizes the need to administer YF vaccine to national and international travelers following a thorough individual risk assessment, which considers both clinical risk and opportunities for exposure to the YF virus. TAG also emphasizes that under the current International Health Regulations, the International Certificate of Vaccination or Prophylaxis, with proof of vaccination against YF, which might be requested as a condition for entering and/or exiting a country, is only valid if the administration of a full standard 0.5 ml YF vaccine dose is documented.
- TAG urges the continued utilization of information from surveillance activities and risk assessments to prioritize vaccination, control measures and the allocation of the limited vaccine supply to countries.
- In the context of the global YF vaccine shortage, TAG urges PAHO's RF to continue all efforts to ensure that the vaccine needs of YF-endemic Member States are met.

2019 Recommendations

- TAG stresses the importance of achieving yellow fever vaccination coverage levels of 95% in endemic areas through optimal routine immunization and campaigns where indicated.
- In view of the available evidence supporting coadministration of MR/MMR and YF vaccines and the experience of increased drop-outs when YF vaccination is scheduled beyond 12 months of age, TAG recommends that both vaccines be given during the same visit at 12 months. If administered separately, they should be at least four weeks apart and full coverage with both vaccines should be ensured.
- TAG recommends that further research be conducted in the Region to examine the effect of lower antibody titers against rubella, mumps and YF viruses observed after co-administration on long-term immunity and to rule out the possibility of secondary vaccine failure.