Are booster doses of yellow fever vaccine needed?

Yellow fever is a major public health problem. A live attenuated vaccine, developed by Max Theiler and colleagues in the 1930s, has helped to control yellow fever, but the duration of protective immunity has been questioned.

In The Lancet Infectious Diseases, Cristina Domingo and colleagues report on the duration of immunity in infants vaccinated at 9 months of age. This study has practical importance, because 9 months is the recommended age at which to administer the vaccine as part of the Expanded Program of Immunization in endemic countries. Domingo and colleagues studied two cohorts, one in Ghana and the other in Mali, and showed waning immunity less than 6 years after vaccination in both, which is quicker than reported in some adult studies.

Despite high concentrations of seroprotective neutralising antibodies within 3 months of vaccination in around 98% of vaccinees, serum neutralisation titres decline over time, so booster doses were given every 10 years. In 2013, WHO recommended that the 10-year boosters be abandoned, except for special populations. This recommendation was endorsed by the WHO Strategic Advisory Group of Experts on Immunization, and a WHO position paper was published. This position paper recognised that few data on the immunisation of infants existed. Domingo and colleagues’ study provides some information to fill this gap in knowledge and suggests that booster doses of vaccine are needed in this population.

Similar indications have come from studies in adults, especially in Brazil, with strong evidence that a booster dose is needed at 10 years to obtain long-term protection against yellow fever. These studies showed that yellow fever antibody concentrations decline considerably in both Brazilian children and adults after primary 17D vaccination and that boosters of vaccine should be used to protect travellers and inhabitants of endemic areas. Thus, Domingo and colleagues’ study reinforces the need for additional research to determine whether different yellow fever vaccines stimulate the immune system differently. Equivalent studies will also be needed in some of the other 40 countries where yellow fever is endemic, assessing all four WHO prequalified vaccines, to provide more information on whether booster doses are needed for children and, consequently, whether modifications to the current immunisation regimen are necessary.

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The chameleonic genetics of Lassa virus

In The Lancet Infectious Diseases, Michael R Wiley and colleagues\(^1\) report 23 near-complete genome sequences of Lassa virus from Liberia.\(^1\) Lassa virus is a member of the Mammarenavirus genus and is the causative agent of Lassa fever, a febrile disease that can be associated with high morbidity and mortality. Lassa virus is maintained in nature as a chronic infection of its natural reservoir *Mastomys natalensis*, a rodent widely distributed in sub-Saharan Africa. Lassa virus infection in humans can occur by inhalation of contaminated dust, contact of abraded skin with contaminated material, or ingestion of contaminated food. Lassa virus endemic areas cover large parts of the Mano River Union region (Guinea, Liberia, and Sierra Leone), as well as Nigeria, Togo, Benin, and some regions in Ghana. The alarming increase in Lassa fever cases in recent years, together with the lack of licensed vaccines and specific therapies to treat Lassa fever led WHO to include Lassa virus in the list of top priority pathogens for which vaccines and therapeutics are urgently needed.

The genetic diversity of Lassa virus poses challenges for the development of vaccines and therapeutics that are effective against all circulating Lassa virus lineages, as well as for the implementation of diagnostic tests. Despite a long history of Lassa fever in Liberia, information about the genetic diversity of Lassa virus strains circulating in this country is scarce—a knowledge gap that has been greatly narrowed by the work of Wiley and colleagues.\(^1\)

The newly determined Liberian Lassa virus sequences were genetically very diverse, but most of them belonged to Lassa virus lineage IV, the prevalent lineage causing Lassa fever in the neighbouring Sierra Leone and, possibly, Guinea.\(^1\) Liberian Lassa virus lineage IV genomes grouped into two clades: clade IV.A was mainly detected in Lassa fever cases in the central part of Liberia, whereas clade IV.B was associated with Lassa fever cases in the western part of Liberia, closer to Sierra Leone, where this clade is also dominant.\(^1\) Phylogenetic analyses estimated that Lassa virus was introduced in the Mano River Union region 300–350 years ago, and that from Liberia the virus spread to Sierra Leone and Guinea.\(^1\)

The findings by Wiley and colleagues\(^1\) are consistent with previous observations on Lassa virus sampled in other countries, including studies done during the 2018 spike in Lassa fever cases in Nigeria,\(^4,5\) indicating that Lassa virus sequences cluster more closely by geography than by isolation date, and that most cases result from spillovers from the natural reservoir. As with the geographical clustering of Lassa virus strains in Nigeria,\(^4\) rivers might have contributed to the spatial structuring of rodent populations, and consequently of Lassa virus, in Liberia. Nonetheless, human movements exacerbated by armed conflicts in Liberia might also have played an important role in the spatial distribution of Lassa virus diversity, by facilitating incidental transport of rodents over geographical barriers. Lassa virus is thought to originate from Nigeria,\(^2\) and the results by Wiley and colleagues\(^1\) suggest Liberia as the Lassa virus entry point to the Mano River Union region. Therefore, a better understanding of the westward spread pattern of Lassa virus would be facilitated by examining Lassa virus diversity in countries between Nigeria and Liberia (ie, Benin, Togo, Ghana, and Côte d’Ivoire).

A limitation of the study by Wiley and colleagues\(^1\) is that the majority of Lassa virus sequences examined were obtained from Lassa fever cases, whereas no Lassa virus genome sequences were obtained from the natural rodent reservoir in Liberia. An indication that more is to be uncovered on Lassa virus diversity in these regions is the identification of viruses with either small or large segments belonging to previously unrecognised Lassa virus lineages.\(^6\)

The results reported by Wiley and colleagues\(^1\) have important implications for Lassa virus diagnostic tests.

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