Journal of Clinical Virology 64 (2015) 160–173

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Yellow fever

Thomas P. Monath[a,b,*], Pedro F.C. Vasconcelos[c,d,e,f,1]

[a] Hookipa Biotech AG, Vienna, Austria
[b] PaxVax Inc., Menlo Park Redwood City, CA, USA
[c] Department of Arbovirology and Hemorrhagic Fevers, National Reference Laboratory of Arboviruses, Instituto Evandro Chagas, Ministry of Health, Rodovia BR 316 Km 07, S/N, CEP 67030-000 Ananindeua, Brazil
[d] National Institute of Science and Technology for Viral Hemorrhagic Fevers, Instituto Evandro Chagas, Ministry of Health, Rodovia BR 316 Km 07, S/N, CEP 67030-000 Ananindeua, Brazil
[e] PAHO/WHO Collaborating Center for Arbovirus Research and Diagnostic Reference, Instituto Evandro Chagas, Ministry of Health, Rodovia BR 316 Km 07, S/N, CEP 67030-000 Ananindeua, Brazil
[f] Pará State University, Belém, Pará, Brazil

ARTICLE INFO

Article history:
Received 27 July 2014
Accepted 25 August 2014

Keywords:
Yellow fever
Pathogenesis
Epidemiology

ABSTRACT

Yellow fever, a mosquito-borne flavivirus disease occurs in tropical areas of South America and Africa. It is a disease of major historical importance, but remains a threat to travelers to and residents of endemic areas despite the availability of an effective vaccine for nearly 70 years. An important aspect is the receptivity of many non-endemic areas to introduction and spread of yellow fever. This paper reviews the clinical aspects, pathogenesis, and epidemiology of yellow fever, with an emphasis on recent changes in the distribution and incidence of the disease. Recent knowledge about yellow fever 17D vaccine mechanism of action and safety are discussed.

© 2014 Elsevier B.V. All rights reserved.

1. Introduction

Yellow fever (YF) is caused by the prototype member of the genus *Flavivirus* (family *Flaviviridae*), which contains approximately 70 positive-strand, single-strand RNA viruses, the majority of which are transmitted by arthropods (mosquitoes and ticks). Yellow fever is endemic in tropical regions of Africa and South America, and many review articles describe its epidemiology in the two continents [1–3]. A recent analysis of country-by-country geographic risk re-defined the borders of the YF endemic zone, but emphasized the fluid nature of virus activity and the occurrence of periodic expansions and retractions [4]. The virus has a relatively narrow host range for productive infection, and is maintained in nature by transmission between non-human primates and blood-feeding mosquitoes mainly belonging to the genera *Haemagogus* and *Aedes* (*Stegomyia*) in South America and Africa, respectively, and by transovarial transmission in these vectors. Humans are infected sporadically when bitten by sylvatic mosquitoes that previously fed on a viremic monkey (so-called **jungle yellow fever**), but may also serve as the viremic host for inter-human transmission, mainly by *Aedes aegypti*, a species that breeds in water-containing vessels inside dwellings or in close proximity to them (so-called **urban yellow fever**). The epidemiology of YF in Africa is often mixed, involving both sylvatic and domestic vector species in inter-human transmission. Consequently, the force of infection in Africa is higher (generally 20–30×) than in South America, the consequence being large epidemics. In recent years, new efforts have been made to vaccinate the populations of high-risk countries in West Africa; the long-term consequences of this effort will be a reduction in major epidemics.

Yellow fever was a major threat to human health from the 18th Century to the early 20th Century, with repeated epidemics following introductions to coastal towns and cities distant from endemic areas in North America, the Caribbean and Europe. The identification in 1900 of *A. aegypti* mosquitoes as the agency whereby YFV was transmitted, and subsequent efforts to control the vector, resulted in a decline in yellow fever outside the tropical, endemic zone. The development of two live, attenuated YF vaccines in the 1930s, and their wide deployment in the 1940s, led to a further decline of the disease. Subsequently, there have been periodic upsurges of YF activity in endemic regions without routine immunization programs.

* Corresponding author at: 295 Townsend Hill Rd., Townsend, MA 01469, USA. Tel.: +1 978 549 0708; fax: +1 978 456 3705.
E-mail addresses: tpmonath@gmail.com (T.P. Monath), pedrovasconcelos@iec.pa.gov.br (P.F.C. Vasconcelos).
[1] Tel.: +55 91 3214 2271; fax: +55 91 3214 2299.

http://dx.doi.org/10.1016/j.jcv.2014.08.030
1386-6532/© 2014 Elsevier B.V. All rights reserved.

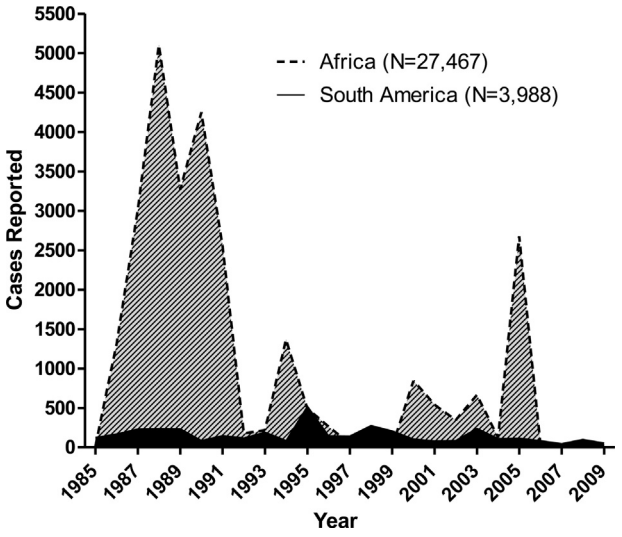

Fig. 1. Cases of yellow fever in Africa and South America, 1985–2009, officially notified to the World Health Organization.

The annual reporting rate of officially reported cases in South America and Africa shown in Fig. 1, but these rely on passive surveillance and thus significantly underestimate the true incidence. The latter remains unknown, except in some discrete epidemics that have been actively investigated. In non-epidemic periods, estimates of 200,000 cases derived from serosurvey data and the rate of inapparent to apparent cases (7–12:1) have been cited from paper to paper for over 15 years, without supporting evidence. Since 2008, more active laboratory-based surveillance activities suggest that, of several thousand suspect clinical cases in Africa investigated, only 1–2% have laboratory evidence for YF. The World Health Organization (WHO) appropriately treats the detection of a case of YF as an emergency, since it reflects transmission of the virus and a risk of a further spread; if the affected region is an area of low vaccination coverage, a regional mass vaccination campaign is generally conducted in response. Between 2007 and 2010, 57 million people were vaccinated against YF in 10 countries at risk in Africa, and during the same period, 17 million people were protected through emergency vaccination [5]. In the 1990s, despite 50 years of use and over 500 million doses distributed, new safety concerns about the live attenuated YF 17D vaccine have come to light, revealing that in rare circumstances the vaccine can cause a disease similar to parental wild-type virus. This fact has modified vaccine policy and regulations in some circumstances, as will be discussed later on.

Despite the availability of vaccines since the 1940s, large epidemics occurred in areas without a background of naturally acquired or artificial immunity. Dramatic upsurges in YFV activity occurred in Africa in the 1960s and the late 1980s each involving >100,000 cases, and recent outbreaks affected southern Brazil, Paraguay and Argentina (2007–2009), Uganda (2010), and Sudan and Ethiopia (2012–2013). Although the absence of an immune barrier in the human population is a key factor, the underlying reasons for virus amplification remain unclear, and are multifactorial, involving deterministic (vector density and competence, viral virulence), and stochastic factors. Expansions of YFV activity have sometimes been associated with the emergence of a new virus lineage [6], but the lack of information about biological correlates of genetic change, make it difficult to assign causality. Perturbations of weather, particularly prolonged increases in rainfall and high temperatures have been associated with outbreaks of YF in Africa and South America.

In humans, YF is a severe acute illness with fever, nausea, vomiting, epigastric pain, hepatitis with jaundice, renal failure, hemorrhage, shock and death in 20–60% of cases. Yellow fever is the prototypical viral hemorrhagic fever, and shares many pathophysiological features with unrelated diseases associated with a similar syndrome, except that the severity of hepatic dysfunction is generally greater in YF patients. The lower case fatality in Africa (~20%) than in South America (40–60%) [7], suggests that genetic factors determine lethality of the infection, a subject that deserves further study. Interestingly, the neutralizing antibody response to YF 17D vaccine is statistically higher in Caucasians than in African-Americans [8] possibly indicating genetic resistance to YF in the latter. Some New World monkeys, notably *Alouatta* (howling monkeys), are also susceptible to lethal infections, and epizootics associated with monkey deaths may precede the occurrence of human cases, a useful surveillance tool [9]. In contrast, almost all African nonhuman primates have inapparent, viremic infections. This reflects the origin of yellow fever virus (YFV) in Africa several thousand years ago, and a balanced co-evolution of virus and hosts. Based on these factors and genetic analyses, YFV was introduced into the Americas from West Africa during the slave trade about 400 years ago [10], and rapidly invaded a new ecological niche involving local hosts and vectors, much like another flavivirus, West Nile, did after its more recent introduction into the Americas.

A serious concern for the future is whether YFV could be introduced by a viremic air traveler to *A. aegypti*-infected areas outside the endemic zone, and particularly India and Southeast Asia. The recent spread of another virus transmitted in a human-*Aedes* cycle—Chikungunya—in islands of the Indian Ocean, India, southern Europe, and the Caribbean illustrates the threat. Although the WHO maintains an emergency YF 17D vaccine stockpile, an extensive outbreak could create a significant shortfall in vaccine supply.

2. Advances in epidemiology

2.1. Geographic distribution

2.1.1. Yellow fever outbreaks in the Americas

Beginning in 1997 and extending throughout the years of the first decade of the present century, intense YFV circulation was observed in Brazil (Pará and Goiás states) which has extended to areas in contiguous states of Goiás and Mato Grosso do Sul (Central Brazil), and then outside endemic region, as well as to countries such as Paraguay and Argentina, which had not identified YFV circulation for the previous 34 and 41 years, respectively. Additionally, many outbreaks were reported in Colombia and Peru, both being endemic countries, the latter being responsible for almost 50% of all YF cases reported in the Americas [11].

In Paraguay, YF was recognized in 2008 when cases of jungle yellow fever were diagnosed in San Izidro and San Pedro Departments. A few weeks later, a cluster of cases was diagnosed in the district of Laurelty in the metropolitan area of Asunción, the Paraguayan capital. This was only the second instance of urban YF in South America since the early 1940s. Urban transmission was limited to 14 recognized cases (8 fatal), though undoubtedly there were many more people infected. After vector control measures and a mass vaccination campaign, no further cases were reported. Before the occurrence of cases, *A. aegypti* Breteau and house indices were approximately 30% in the affected area.

In Argentina, 5 jungle YF cases and a single death were reported in Misiones Province. An interesting finding in this country was the implication of a new vector, *Sabethes albiprivus* in yellow fever transmission [12].

In Brazil, the spread of YF in 2008–2009 was impressive. Initial cases were reported in State of Pará (municipalities of Afua and

Download English Version:

https://daneshyari.com/en/article/6120237

Download Persian Version:

https://daneshyari.com/article/6120237

Daneshyari.com