Antiviral Research 100 (2013) 38–43

Contents lists available at ScienceDirect

Antiviral Research

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

Commentary

The pandemic potential of Nipah virus

Stephen P. Luby *

Woods Institute of the Environment, Stanford University, Yang and Yamazaki Environment and Energy Building, Room 231, 473 Via Ortega, Stanford, CA 94305, United States

ARTICLE INFO

Article history:
Received 8 June 2013
Revised 9 July 2013
Accepted 19 July 2013
Available online 30 July 2013

Keywords:
Nipah virus
Henipavirus
Nosocomial transmission
Pandemics
Zoonosis
Chiroptera

ABSTRACT

Nipah virus, a paramyxovirus whose wildlife reservoir is *Pteropus* bats, was first discovered in a large outbreak of acute encephalitis in Malaysia in 1998 among persons who had contact with sick pigs. Apparently, one or more pigs was infected from bats, and the virus then spread efficiently from pig to pig, then from pigs to people. Nipah virus outbreaks have been recognized nearly every year in Bangladesh since 2001 and occasionally in neighboring India. Outbreaks in Bangladesh and India have been characterized by frequent person-to-person transmission and the death of over 70% of infected people. Characteristics of Nipah virus that increase its risk of becoming a global pandemic include: humans are already susceptible; many strains are capable of limited person-to-person transmission; as an RNA virus, it has an exceptionally high rate of mutation: and that if a human-adapted strain were to infect communities in South Asia, high population densities and global interconnectedness would rapidly spread the infection. Appropriate steps to estimate and manage this risk include studies to explore the molecular and genetic basis of respiratory transmission of henipaviruses, improved surveillance for human infections, support from high-income countries to reduce the risk of person-to-person transmission of infectious agents in low-income health care settings, and consideration of vaccination in communities at ongoing risk of exposure to the secretions and excretions of *Pteropus* bats.

1. Introduction

Nipah virus was first discovered in an outbreak of acute encephalitis in Malaysia in 1998, in which 39% (109) of 283 people with recognized infection died. Using diagnostic tests developed as part of the first investigation, Nipah virus outbreaks have been recognized nearly every year in Bangladesh since 2001, and occasionally in neighboring India. Over 70% of people infected with Nipah virus in South Asia have died (Luby et al., 2009a). One-third of survivors have permanent neurological deficits (Sejvar et al., 2007). Several outbreaks have included short chains of person-to-person transmission among persons who contact secretions from Nipah patients. The ability of Nipah virus to spread to patient caregivers has raised concern that the virus might adapt to more efficient human-to-human transmission. This paper examines the potential of Nipah virus to cause an expanding epidemic, describes epidemiological patterns observed to date, summarizes relevant research and suggests measures that should be taken for surveillance, prevention and infection control.

2. Nipah virus: pathogen and clinical onset

Nipah virus is a paramyxovirus (genus Henipavirus) whose wildlife reservoir is bats of the genus *Pteropus* (Halpin et al., 2011). Nipah virus does not cause any apparent disease in infected bats (Middleton et al., 2007) and likely co-evolved with these bats. The ephrin-B2 and ephrin-B3 molecules which Nipah virus exploits to enter epithelial cells are widely conserved across mammals, and many mammals are therefore susceptible to Nipah virus infection (Bossart et al., 2008).

In humans, Nipah virus infection causes a widespread vasculitis (Wong et al., 2002). The brain and lung are the most commonly affected organs (Wong et al., 2002). Most patients present with fever and headache; a reduced level of consciousness, focal neurological signs and cough are commonly observed (Goh et al., 2000; Hossain et al., 2008; Paton et al., 1999). Most people infected with Nipah virus develop severe disease. A serological study of 612 contacts of Nipah cases in Bangladesh identified 15 people who developed Nipah infection. Eleven of the 15 (73%) developed severe illness, while four had only fever (Hossain, 2010).

3. Epidemiology of Nipah virus infection

The large outbreak in Malaysia began in 1998 when Nipah virus spilled over from bats to pigs. Within an industry in which large numbers of pigs were raised in close proximity, Nipah virus was widely transmitted from pig to pig (Chua, 2003). Many people who had close contact with sick pigs, especially those in contact with respiratory secretions and urine, became infected (Parashar et al., 2000). Among 283 recognized human infections, 109 people (39%) died (Chua, 2003).

* Tel.: +1 650 723 4129; fax: +1 650 725 3402.
E-mail address: sluby@stanford.edu

0166-3542/$ - see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.antiviral.2013.07.011

Since the virus was discovered and diagnostic assays became available, outbreaks have been identified nearly every year in Bangladesh and occasionally in neighboring India (Fig. 1). Outbreak investigations in Bangladesh have identified consumption of raw date palm sap as the primary route of transmission of Nipah virus from *Pteropus* bats to people. Date palm sap is harvested in the winter in Bangladesh by shaving the bark from the sugar date palm tree (*Phoenix sylvestris*) and collecting the sap into open clay pots (Nahar et al., 2010). *Pteropus* bats that occasionally shed Nipah virus in their saliva (Middleton et al., 2007; Reynes et al., 2005; Wacharapluesadee et al., 2005), frequently visit the trees during sap collection and lick the sap as it is running into the pot (Khan et al., 2010; Rahman et al., 2012). Although most date palm sap in Bangladesh is cooked into molasses (Halim et al., 2008), raw sap is a local seasonal delicacy (Luby et al., 2006), and it is consumption of this raw sap that has been repeatedly implicated in human outbreaks (Luby et al., 2006; Rahman et al., 2012; Sazzad et al., 2013).

Some human Nipah virus infections in Bangladesh have followed contact with sick animals (Luby et al., 2009b), but this is a much less important source of human infection in Bangladesh than date palm sap. In contrast to Malaysia, where large commercial farms raised thousands of pigs in close quarters that facilitated amplification of the epidemic (Pulliam et al., 2011), pigs, cattle and goats in Bangladesh are raised by scattered small producers at much lower densities. In both Bangladesh and India, Nipah patients occasionally transmit the infection to other people, though sustained person-to-person transmission beyond 5 generations has not been recognized (Chadha et al., 2006; Gurley et al., 2007a; Homaira et al., 2010; Sazzad et al., 2013). People providing direct care for fatally infected patients with prominent respiratory symptoms are at greatest risk of becoming infected (Gurley et al., 2007a; Luby et al., 2009a).

4. The threat of zoonotic diseases

Wolfe and colleagues conducted a systematic assessment and concluded that 80% of the most devastating infectious diseases in human history were zoonoses (Wolfe et al., 2007). They proposed a classification of zoonotic disease whereby stage I infectious agents are those only transmitted among non-human animal hosts; stage II agents can spill over from animals to humans, but humans cannot further transmit the infection; stage III agents can spill over to humans and cause limited outbreaks of person-to-person transmission; stage IV agents are capable of sustained human to human transmission; and stage V are exclusively human agents (Wolfe et al., 2007). Reflecting on this taxonomy, Lloyd-Smith and colleagues suggested that the zoonotic stages are best understood as progressive increases in the basic reproductive number (R_0) of the agent for humans (Lloyd-Smith et al., 2009). R_0 is the average number of people to whom one patient transmits the infection. The transition from a stage III to a stage IV zoonosis results when a pathogen's R_0 changes from <1 to >1. Stage III zoonotic pathogens display stuttering chains of transmission where occasional individuals transmit to a few people, but the chains of transmission are not sustained.

Most Nipah patients do not transmit infection to anyone. Among patients in Bangladesh only 7% transmit the infection (Luby et al., 2009a). Most commonly, person-to-person Nipah transmission occurs as a single case followed 1–2 weeks later by a cluster of infections among the index patient's family care providers.

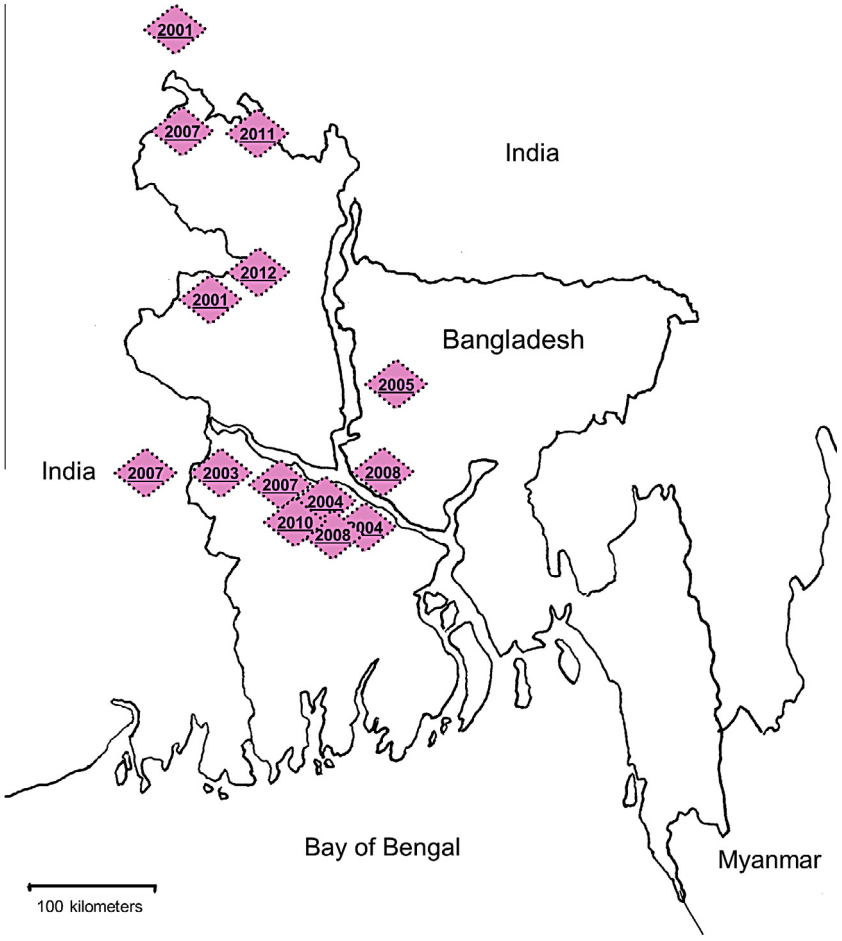

Fig. 1. Nipah virus outbreaks in Bangladesh and India from 2001 to 12.