# Brief Reports

## SEASONAL VARIATION IN RESPIRATORY SYNCYTIAL VIRUS EPIDEMICS IN THE GAMBIA, WEST AFRICA

**Respiratory syncytial virus outbreaks tend to occur seasonally and are a major cause of childhood morbidity. In The Gambia a regular pattern of outbreaks during six consecutive annual seasons was disrupted by 2 years of irregular outbreaks, followed by another 2 years of regular seasonal outbreaks. Improved understanding of the transmission dynamics of respiratory syncytial virus is essential to design and test effective interventions.**



Respiratory syncytial virus (RSV) is recognized as the most common viral cause of severe lower respiratory tract infections in infants and young children worldwide.[1, 2] Virtually all children are infected during the first 2 years of life. About 1 to 2% of infants infected with RSV are hospitalized. Besides acute morbidity severe RSV infection in early life is associated with subsequent wheezing and higher prevalence of pneumonia in childhood; an association with atopic disease in later life has been suggested.[3, 4]

RSV is now recognized as an important pathogen in the general adult population as well, particularly in the elderly, in whom the infection can have variable and less distinctive clinical symptoms.[5]

Currently treatment for an acute infection is mainly symptomatic and supportive, including oxygen therapy and nasogastric feeding.[6] Prevention is hampered by the absence of a protective vaccine, and a limited understanding of the transmission dynamics that trigger the development of subsequent epidemics.

RSV infections occur primarily in seasonal epidemics. In temperate climates the infection is most frequent during the cold and wet season, whereas in tropical climates cases tend to cluster during the hot and wet season.[2] The driving force behind this seasonality is not known, although climatic factors are assumed to be more relevant than social factors[7]; seasonal transmission of most microbes is related to humidity. It is still debated whether differences in circulating strains contribute to differences in seasonality. The relative proportions of different genotypes vary from year to year with steady replacement of the dominant genotype each year, suggesting that herd immunity may play a role in the abundance of a particular genotype in a particular epidemic.[8]

**Methods.** The Gambia is a small West African country, situated on the edge of the arid Sahel belt. It has one rainy and hot season, which usually peaks between July and September. Since October 1993 a nasopharyngeal aspirate for RSV surveillance has been collected in all children younger than the age of 2 years who were admitted with a diagnosis of an acute respiratory tract infection in either of the two referral hospitals in the periurban region near the capital Banjul. The nasopharyngeal aspirates were analyzed by immunofluorescence microscopy for the presence of RSV. There were no methodologic or technician changes over the study period. Testing was done on a daily basis, excluding weekends and public holidays, and was approved by the joint Gambia Government/Medical Research Council Laboratories Ethics Committee. The epidemiology and clinical spectrum of disease have been described elsewhere.[9]

**Results.** During the first 6 years of surveillance, regular epidemics occurred during the rainy season, from August to November, which coincided with a larger number of acute respiratory tract infection admissions. The magnitude of the outbreak varied from one year to another. In 1997 and 1998 relatively small RSV outbreaks occurred, whereas in 1999 no outbreak occurred during the rainy season. Thereafter an unusual epidemic occurred from December 1999 to October 2000, with one peak in March (in the middle of the dry season). The epidemic did not subside as usual, and another peak occurred 5 months later in August 2000. In 2001 and 2002 regular seasonal epidemics occurred, once again coinciding with the hot, rainy season as expected. Figure 1 shows the absolute number of RSV cases diagnosed per month and the percentage of children diagnosed with RSV on the total of admitted children screened.

Data on monthly rainfall and relative humidity were obtained for the two weather stations (Banjul in the west, Yundum in the middle/east), which covered most of the study area. There were no major disturbances of the pattern during the years studied. A regular rainy season occurred between June and October each year, although with fluctuations in the total amount of rain and the actual distribution during these months. Total rainfall in the two stations was highest in 1999, closely followed by 2000 and 1994, and lowest in 2002, followed by 1993 and 1996. Relative humidity was highest at the end of the rains, and lowest from December to March (Fig. 2 appears on the PIDJ website, *www.pidj.com*). There were no obvious changes in social factors either, which could be linked to the disturbed seasonality in 1999 and 2000.

**Discussion.** Although the occurrence of large annual epidemics is often seen as a hallmark of RSV infection, our data show that the seasonal variation in outbreaks is more complicated than can be assessed on the basis of a relatively short period. Surveillance data for severe RSV disease have been reported from a wide geographic and socioeconomic range of countries. Nonseasonal transmission patterns or changes in seasonality similar to the one observed in our study have been reported in a small number of other studies only *e.g.*[10–12] Many studies from different parts of the world reported regular seasonal epidemics, but in general surveillance for

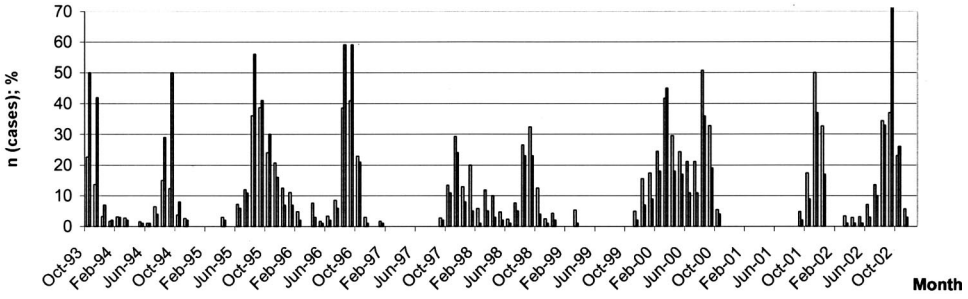


FIG. 1. Absolute numbers of RSV diagnoses, and percentage of RSV positive cases among all children ages 0 to 2 years, admitted for acute respiratory infection, by month, October 1993 through October 2002. ■, number of cases; ▨, percent positive.

these studies covered a short period of time; thus such variation can have been missed.

No persistent immunity develops after infection. Therefore reinfection is common, although usually less severe. Short term herd immunity could be responsible for the variation of dominant genotypes in subsequent epidemics. We previously described a model of RSV transmission that produced a good fit to the empiric data, taking account of gradual acquisition of immunity after repeated exposure to infection.[7] The relatively small outbreaks in 1997 to 1999 will have resulted in decreased herd immunity and a large number of susceptible children in 2000.

RSV remains a worldwide pathogen for which a vaccine is sorely needed. It is essential to explore and understand variations in the seasonality of transmission dynamics to enable the development and implementation of appropriate interventions with a lasting impact. If deviation of the regular pattern is linked to variation in strains, this will have important implications for vaccine development. No vaccine is currently available to provide active immunity against RSV, but live attenuated and subunit cloned surface protein vaccines are in development.[13] Once a promising vaccine has been identified, understanding variations in seasonality will be vital to ensure appropriate trial design.

**Authors' contributions.** MWW conceived of the idea, initiated surveillance in The Gambia and contributed to analysis and writing of the paper. MABvdS, TG and HCW contributed to surveillance, analysis and writing of the paper. MS was responsible for the processing and diagnosis of the nasopharyngeal aspirates.

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## PERSISTENT HEPATITIS ASSOCIATED WITH CHRONIC ACTIVE EPSTEIN-BARR VIRUS INFECTION

**A previously healthy boy developed persistent hepatitis without fever or lymphoproliferative disorder. Although serologic tests were not indicative, Epstein-Barr virus (EBV) genome and transcripts were detected from the liver tissue, and real time PCR detected extremely high levels of EBV viremia. EBV infection should be included in the differential diagnoses of hepatitis of unknown etiology, even with unremarkable serologic data.**

Epstein-Barr virus (EBV) causes various acute and chronic diseases, such as infectious mononucleosis, EBV-associated hemophagocytic syndrome and chronic active EBV infection (CAEBV)[1, 2]. Usually serologic examinations are used to estimate status or activity of EBV infection.[3] However, studies suggest that EBV DNA titers correlate with disease activity more accurately than serologic data.[4, 5]

We report a pediatric case of chronic active hepatitis associated with extremely high EB viral load, despite that serologic examinations were not diagnostic.

**Case report.** A 3-year-old boy was referred to Isahaya Hospital in October 2001 because of short stature that had been recognized since 1 year of age. Past medical history and family history were unremarkable. On examination his height was 91 cm (−2SD), and remarkable hepatosplenomeg-