Influenza A and Parvovirus B19 Seropositivity Rates in Gabonese Infants

Julian J. Gabor, Norbert G. Schwarz, Meral Esen, Peter G. Kremsner, and Martin P. Grobusch*

Medical Research Center (CERMEL), Lambaréné, Gabon; Institute for Tropical Medicine, University of Tübingen, Germany; Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany; Center for Tropical Medicine and Travel Medicine, Department of Infectious Diseases, Division of Internal Medicine, Academic Medical Center, University of Amsterdam, The Netherlands

Abstract. Clinical and epidemiological data from Central Africa on influenza A and parvovirus B19 infections are limited. We analyzed 162 blood samples of infants 3, 9, 15, and 30 months of age for IgG antibodies against both pathogens. Antibody responses were 0, 3.7%, 12.3%, and 20.4% against influenza A; and 1.2%, 2.5%, 3.1%, and 9.3% against parvovirus B19, respectively. Seropositivity rates were 89.5 (95% confidence interval [CI]: 59–120.1) and 38.2 (95% CI: 18.9–57.6)/1,000 person-years at risk for influenza A and parvovirus B19, respectively. Our data add to the understanding of the epidemiology of both conditions.

Over the past decades, combating major infectious diseases in Africa such as human immunodeficiency virus (HIV), tuberculosis, and malaria rightfully enjoyed priority; other causes of fever were not in the focus of medical research. Consequently, clinical and epidemiological data on viruses such as influenza virus A and parvovirus B19 from (among other regions) Central Africa is limited, particularly for young children. However, the policy of administering an artemisinin combination therapy after confirmation of malaria by rapid diagnostic testing/randomized controlled trial (RDT-RCT) has led to the recognition that febrile disease episodes in patients suspected of malaria on clinical grounds are often a result of other causes. The burden of influenza in sub-Saharan Africa (sSA) is mainly assessed by passive case detection on hospital admission or at outpatient clinics and thus probably often yields underestimates. Available data indicate that the burden of influenza is comparable to other areas in the world.^{1–3} Influenza A (H1N1), A (H3N2), and B viruses have been found circulating in the human population of Central Africa, with first evidence of the emergence of oseltamivir-resistant A (H1N1) strains.⁴ Apart from the elderly, young children are at risk to develop severe disease often associated with complications. Children also serve as sources of secondary infections in households and communities. In our study area, van Riet and colleagues⁵ found pre-vaccination antibodies against A and B influenza viruses, with those against A-H3N2 being highest. The epidemiology of parvovirus B19 is by and large unknown in sSA. In Central Africa, infection with homologues of human parvoviruses in primates is common, thus constituting a potential reservoir⁶; for parvovirus 4, positive antibodies have been found in 35% of the adult population in the Democratic Republic of Congo.⁷ Although infections in immune-competent individuals are usually mild, parvovirus B19 can cause increased morbidity and even mortality in a population with a high prevalence of hematologic disorders, chronic parasitic infections, and HIV.^{8–11} In this study, we assessed immunoglobulin G (IgG) serum antibodies against influenza A and parvovirus B19 in young Gabonese children to estimate the potential burden of disease in early childhood.

The ethics committee of the International Foundation of the Hôpital Albert Schweitzer approved the study. Venous blood samples were obtained from infants participating in the Intermittent Preventive Treatment in Infants study (IPTi) in Lambaréné, Gabon^{12,13} (clinical trials registration no. NCT00167843). The study was conducted between December 2002 and April 2007 to provide data about the efficacy of sulfadoxine/pyrimethamine as an intermittent preventive treatment against malaria. Study participants were recruited at birth from December 2002 to February 2005 at two hospitals in the town of Lambaréné. Study procedures were the same for all 1,189 IPTi-infants. Selection criteria for the 162 infants described in this sub-cohort were recruitment in the first 12 months of the IPTi trial and complete blood collection on all four study visits at 3, 9, 15, and 30 months of age. After blood collection, EDTA-plasma samples were stored at –80°C.

Anti-influenza A IgG antibodies were determined by a commercial enzyme-linked immunosorbent assay (ELISA) test (VIRCELL, Santa Fe, Spain) with a sensitivity/specificity of 95/89%. The ELISA uses influenza antigen of strain A/Victoria/3/75 (H3N2). It is not directed against a specific influenza A strain, but rather indicating presence of human anti-influenza A IgG. Anti-parvovirus B19 IgG were determined by ELISA (VIRCELL) with a sensitivity/specificity of 98/95%.

To avoid recording seropositivity caused by maternal antibodies in the first months of life, all month-30 specimens were tested first. In case of seropositivity, analysis continued with samples from the next-earlier time point backwards, and so on. Statistical analysis was performed with R 2.14.2 (www.r-project.org). From birth onward the midpoint between time intervals of being seronegative and becoming seropositive was taken as the proxy time point of infection to calculate cases/person-years. Observation time for cases/person-years stopped at the time point of the calculated seroconversion. At birth, information such as the numbers of siblings and vaccination status was noted and reassessed at each time point of blood draw.

Of the 162 included infants, 83 were female and 79 were male. Among all study participants, 20.4% acquired IgG serum antibodies against influenza A and 9.3% against parvovirus B19 during their first 30 months of life. The rising proportions of seropositive infants across the four time points are given in Table 1. Median age on blood collection at 3, 9, 15, and 30 were 3.0 months; 9.1 months; 15.2 months;

* Address correspondence to Martin P. Grobusch, Center for Tropical Medicine and Travel Medicine, Department of Infectious Diseases, Academic Medical Center, Meibergdreef 9, 1100 DD Amsterdam, PO Box 22660, University of Amsterdam, The Netherlands. E-mail: m.p.grobusch@amc.uva.nl

TABLE 1

IgG antibodies against influenza A and parvovirus B19 in 162 infants at 3, 9, 15, and 30 months of age in Lambaréné/Gabon, 2003–2007, and corresponding estimates of infection rates in the first 30 months of life

	3 months	9 months*	15 months*	30 months*	Cases/1,000 person-years (30 months)
Influenza A	0	3.7% (6)	12.3% (20)	20.4% (33)	89.53
Parvovirus B19	1.2% (2)	2.5% (4)	3.1% (5)	9.3% (15)	38.22

*Including all infants positive at this age.

and 30.1 months, respectively. The estimated incidence of infection during the first 30 months of life were 89.5 cases/1,000 person-years (95% confidence interval [CI]: 58.98–120.1) for influenza A and 38.2 cases/1,000 person-years (95% CI: 18.9–57.6) for parvovirus B19. Two study participants were already positive for parvovirus B19 at 3 months of age. In summary, 21.7% of female and 19% of male subjects were positive for influenza A at 30 months of life and 8.4% and 10.1% for parvovirus B19. For both influenza A and for parvovirus B19, the proportion of seropositive children at 30 months of age did not differ significantly between boys and girls (data not shown). As well, no association was found between the number of siblings and seropositivity (data not shown). As a result of the intervals of blood collection with 6 and 15 months, a correlation analysis regarding possible seasonality was not feasible.

More than 20% of the children tested had contact with influenza A before 30 months of age; van Riet and others (2007) showed that in the study area, at the median age of 9 years, all children had antibodies against at least one influenza A strain.⁵ These results highlight the considerable risk of infection with influenza A in Gabon. Pre-school children belong to the most endangered group for influenza-associated complications.¹⁴ Furthermore, infected children serve as contractors and spread the disease to household contacts; for example, to elderly individuals who are more susceptible to influenza-associated complications. Influenza vaccination, in Africa as elsewhere, reduces overall morbidity in children and adults and illness-related economic and medical consequences, like work days lost, visits of health care providers, or use of antibiotics.¹⁵ In the United States, the Centers for Disease Control and Prevention (CDC) recommends influenza vaccination already for children > 6 months of age. Gabon has an operative Expanded Program on Immunization (EPI), therefore it appears in principle to be feasible to implement influenza vaccination for infants. However, in view of the logistical problems and costs in relation to the potential disability-adjusted life years saved, implementation of such a program appears to be not feasible in most resource-poor setting at this point in time.

The missing correlation between siblings and infection rate observed is possibly attributable to the predominant local family structure, where different generations of various degrees of kinship live in households together. In this study, we focused on the more common influenza A because of its potential to cause more severe illness and pandemics in comparison to influenza B and C, and in view of the results of a previous study indicating influenza A (H3N2) as the highest prevalent.⁵ More than 9% of children examined were anti-parvovirus B19 IgG seropositive at 30 months of age. This is comparable with other reported seroprevalence rates for parvovirus B19.⁸ Parvovirus B19 infections during pregnancy

cause hydrops fetalis, fetal anemia, and fetal death. In healthy immune-competent individuals parvovirus B19 causes mild disease, or the infection remains asymptomatic. However, persons with hematological disorders resulting in decreased erythrocyte production or erythrocyte loss are at risk of an aplastic crisis caused by parvovirus B19 infection. Glucose-6-phosphate dehydrogenase deficiency, thalassemia, and sickle cell disease or anemia resulting from malnourishment, chronic hookworm infestation, or malaria, are highly prevalent in Central African populations predisposing for increased morbidity of parvovirus B19 infections. Parvovirus B19 may also induce chronic or severe anemia in HIV-infected persons.

Limitations of this study are that we were limited to a choice of possibly relevant disease-causing viruses; furthermore, we did not systematically record clinical data. Therefore, we could not assess to what extent seropositivity correlated with disease. To investigate seasonal incidence of influenza, it would be necessary to perform a prospective study and to include investigation of seasonal influenza strains by hemagglutination-inhibition testing. That notwithstanding this, our data are providing an insight into the regional epidemiology of the two viruses, influenza A and parvovirus B19 are notably present in Gabon. Against a backdrop of concomitant and underlying conditions such as hemoglobinopathies and HIV infections, both pathogens may not only lead to significant morbidity in the Central African setting on their own but as well lead to aggravated disease, and should be taken into account as conditions of public health relevance in the area.

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Authors' addresses: Julian Gabor, Meral Esen, and Peter G. Kremsner, Institute of Tropical Medicine, Infectious Diseases, Tuebingen, Germany, E-mails: julian.gabor@gmx.de, meral.esen@uni-tuebingen.de, and peter.kremsner@uni-tuebingen.de. Norbert G. Schwarz, BNI, Epidemiology, Hamburg, Germany, E-mail: schwarz@bnitm.de. Martin P. Grobusch, Academic Medical Center, University of Amsterdam, Infectious Diseases, Tropical Medicine and AIDS, Amsterdam, The Netherlands, E-mail: m.p.grobusch@amc.uva.nl.

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