

Richard K. Root Memorial Lecture

35.001

Transmission and Prevention of Transmission of HIV: Clues from the Early 21st Century

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HIV is transmitted by blood and blood products, from HIV infected mothers to babies (before and during birth, and through breast milk) and by anal and vaginal intercourse. The sexual transmission of HIV has led to the majority of infections worldwide and this route of transmission has great variability in efficiency (~1/10-1/1000 transmission events/sexual exposure). Transmission variability reflects viral concentration in the genital secretions of the infected host, inflammation in the index case or partner, and the sexual acts chosen. HIV prevention depends on complimentary behavioral and biological strategies. Condoms and male circumcision reduce the risk of HIV acquisition. No preventive vaccine has been developed, but a recent trial in Thailand has suggested potential limited protection from infection, albeit for a brief period of time. To date all first and second generation topical vaginal microbicides have failed to provide reliable and significant protection from HIV infection, but trials with antiretroviral agents are in progress. The use of oral or topical antiretroviral agents for HIV prevention is considered pre-exposure prophylaxis (PrEP). More than 20,000 study subjects are enrolled in trials with oral antiviral agents, especially the combination of tenofovir and emtricitabine. It is likely that HIV infected patients receiving antiretroviral therapy are less contagious and a large randomized controlled trial (HPTN052) has enrolled more than 1500 HIV discordant couples to address this question directly. The enthusiasm for ART as prevention has led to a "seek, test and treat strategy" now called "TLC PLUS"...which requires wider HIV testing (T), linkage (L) to medical care and delivery of ongoing care (C), PLUS emphasis on combined behavioral and biological prevention strategies for HIV positive people. Several pilot studies designed to implement TLC PLUS are underway worldwide. HIV transmission has been well-studied and prevention strategies are likely to be increasingly successful in the coming years.

doi:10.1016/j.ijid.2010.02.1856

36.001

Growing burden of dengue in Latin America: A public health challenge

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The evolution of dengue fever and dengue hemorrhagic fever in the world in the last 50 years shows the lack to effective vector control. The re-emergence of dengue fever and the new dengue hemorrhagic form in The Americas has epidemiological, clinical, ecological, political and socio-economic implications. Insufficient political commitment, inadequate financial resources, increased globalization and urbanization growth have contributed to change the dengue situation after 19 Latin American were certified to have eradicated *Aedes aegypti*. Difficulties begin with diagnosis (clinical and laboratory), which includes asymptomatic infections, undifferentiated febrile illness and differential diagnosis with other hemorrhagic diseases. Collection of appropriate epidemiological data and a true appreciation of the social and economic impact of dengue are essential to securing social, political and economic commitment for dengue control efforts, as well as increased scientific and social awareness. In addition, the estimation of cost-effectiveness is necessary in order to define the optimal division of resources between traditional dengue vector control and the eventual introduction of dengue vaccines. Furthermore, anticipating the coordination of all the efforts to facilitate the regulatory requirements and to develop vaccination strategies is essential.

doi:10.1016/j.ijid.2010.02.1857

36.002

Clinical development of tetravalent dengue vaccine for endemic areas

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A vaccine to protect against dengue disease is sorely needed, particularly for children living in endemic areas who are most affected by the disease. The safety and immunogenicity of a tetravalent live attenuated dengue vaccine containing 5 log₁₀ TCID₅₀ of chimeric yellow fever (YF)/DEN1,2,3,4 viruses (TDV) was tested in children in the Philippines, where dengue is endemic, and in a region of Mexico, where dengue is non-epidemic.

In each of two randomized controlled blind-observer phase 1 trials (one per country), 126 subjects 2-45 years old were enrolled, including 72 2-11 yr olds/study. Subjects were divided into two groups receiving 1) 3 doses of TDV 2) 1 dose of either Stamaril® YF vaccine (Mexico) or Typhim Vi® (Philippines) followed by 2 doses of TVD. Vaccines were administered at months 0, 3-4, and 12. Baseline flavivirus serostatus was determined. Vaccine safety and immune response were evaluated after each vaccination.

No related serious adverse events were observed. The reactogenicity profile was comparable to that of the control vaccines. No increase in reactogenicity was observed: in children compared with adults, or after the second or third dose compared with the first. In both non-endemic and endemic populations, immune responses increased incrementally after each of the 3 doses of TDV and were balanced against the 4 serotypes after 3 doses.

TDV was well tolerated and immunogenic in children in both endemic and non-endemic areas with a 3 dose schedule.

doi:10.1016/j.ijid.2010.02.1858

36.003

Pertussis surveillance and testing: Recommendations from the GPI

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The Global Pertussis Initiative (GPI) was established in 2001 to evaluate the ongoing problem of pertussis worldwide and to recommend appropriate pertussis control strategies. In addition to primary vaccinations, the GPI currently recommends pertussis booster vaccination to pre-school children, adolescents, and those adults at risk of transmitting *Bordetella pertussis* infection to infants. The GPI actively encourages efforts toward global standardization of pertussis disease clinical definitions and diagnostics. At a meeting in Paris in January 2010, GPI members discussed pertussis surveillance and testing, and prepared recommendations on the implementation and utilization of these activities. Issues and projects discussed included:

- Advantages and limitations of various national surveillance systems;
- Seroprevalence studies;
- Ideal surveillance methodologies;
- Ongoing efforts in standardization of real time PCR, culture, serology and sample treatment;
- Likely future advances (eg, antibody detection in saliva).

Previous regional meetings of the GPI have confirmed that many countries have limited laboratory facilities for the detection of pertussis. The GPI hopes that the future introduction of increased laboratory capabilities and greater harmonization of clinical definitions and detection methods will lead to enhanced surveillance and a better estimate of the burden of pertussis infection worldwide.

doi:10.1016/j.ijid.2010.02.1859

36.004

Adolescent and adult Pertussis vaccination programs: Are they having an impact?

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Pertussis disease in infancy remains a significant problem, with a high risk of serious morbidity and mortality

in both developed and developing countries. Improved disease prevention strategies are imperative. In countries with established childhood vaccination programs, studies have shown that adults are the predominant source of infection for infants. Therefore strategies to protect infants now emphasise vaccination of adults, particularly those (eg, parents, close household contacts and health-care workers) at high risk of transmitting infection to infants. A cocoon strategy, in which all potential adolescent and adult contacts of infants are vaccinated, is probably the most cost-effective solution.

Postpartum vaccination program of new mothers are ongoing in the US. The introduction of booster doses in adolescents has been an important step toward decreasing disease burden. For example, in areas of Canada where Tdap vaccine has been administered to 14- to 16-year-olds, marked reductions of pertussis have been observed in adolescents and younger age groups, possibly due to herd immunity.

Adult disease in itself is a concern, with the true adult burden estimated at more than 600,000 cases annually in the United States. Adults commonly have a persistent cough for up to 4 months, often requiring medical treatment for the associated morbidity and to reduce the risk of infection to others. Furthermore, it can have significant financial implications for the patient and society. Evidence suggests that implementation of adult vaccination programs could be highly cost-effective and even cost-saving. This presentation will review available data on pertussis vaccination of adults and adolescents, and assesses the potential impact of such vaccination, both now and in the future.

doi:10.1016/j.ijid.2010.02.1860

Infectious Disease and Vaccines Development (Invited Presentation)

37.001

Meningococcal C in Latin America

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NO ABSTRACT RECEIVED

doi:10.1016/j.ijid.2010.02.1861

37.002

Tick-borne encephalitis: Clinical Development of vaccines for Children and Adults

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Tick-borne encephalitis virus (TBEV), a member of the family Flaviviridae, causes substantial morbidity and even mortality in endemic areas. The distribution of TBEV covers many countries in Europe and large parts of central and eastern Asia. Although most infections with TBEV are asymptomatic, more than 10,000 severe cases are reported annually, and the incidence has increased considerably during the last few decades. Up to 46% of patients are left