monia pathogens, especially respiratory viruses. Indeed, because of these methods, it is now much easier to confidently diagnose a viral than bacterial cause of a respiratory tract infection. Diagnosing a bacterial aetiology of pneumonia remains problematic, although may be improved with use of quantitative approaches that are the focus of ongoing research. There is a pressing need for completely new approaches to pneumonia diagnostics, particularly approaches that can distinguish colonising from infecting microorganisms, that can distinguish recent from past infection, that account for host responsiveness, and can utilise samples that are easy to obtain.

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Date: Thursday, April 3, 2014
Time: 15:45-17:45
Room: Auditorium 2

Clinical spectrum and complications of childhood pneumonia in the era of bacterial conjugate vaccines

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Pneumonia remains a leading cause of under-5 childhood mortality, particularly in low and middle-income countries. The rollout of conjugate bacterial vaccines, including *Haemophilus influenzae* type b conjugate vaccine (HibCV) and particularly pneumococcal conjugate vaccine (PCV), into national immunization programs recently, has been associated with dramatic decline in all-cause pneumonia hospitalization in many developed countries where PCV immunization has been implemented. Also, PCV immunization has variably been associated with changes in incidence of hospitalization due to influenza virus and RSV-associated pneumonia in some settings. There is, however, limited data from low and middle-income countries on the effectiveness of PCV against pneumonia once introduced into immunization programs. A broader diversity of serotypes associated with pneumococcal disease and higher prevalence of underlying risk factors for pneumonia such as greater prevalence of malnutrition, HIV-infection and tuberculosis may affect the impact of PCV on all-cause pneumonia morbidity and mortality in children. Furthermore, early experience from few studies in developed countries with 7-valent PCV, suggested a temporal association between PCV-7 introduction and an increase in complicated pneumonia including that due to empyema due to few serotypes not included in PCV7, but which are now included in the 10 and 13-valent PCVs formulations currently used. The global public health value of PCV will be measured by its success in reducing all-cause childhood pneumonia morbidity and mortality in low and middle-income countries. Results on the impact of PCV immunization in early-adopting low and middle incoming countries are imminent and will contribute in determining the potential of PCV in improving child health globally.

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Future *Streptococcus pneumoniae* vaccines

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The goal of PATH's pneumococcal vaccine project is to accelerate the development of promising new pneumococcal vaccines that are safe and effective in young children, and to ensure their affordability, availability, and use in developing countries. As part of this project, we are developing a portfolio of vaccine candidates with a particular emphasis on common protein vaccines. Vaccines containing proteins that are common to all pneumococcal serotypes could provide broad and affordable protection to children worldwide. Our lead protein vaccine strategy involves the development of an inactivated, whole cell vaccine (SPWCV) designed to offer broad serotype-independent coverage coupled with low manufacturing costs. Preclinical studies have demonstrated protection against both nasopharyngeal carriage (T-cell mediated) and invasive disease (antibody mediated). We recently completed a randomized, double blind, placebo-controlled Phase 1 study designed to assess the safety, tolerability and immunogenicity of SPWCV formulated with aluminum hydroxide (PATH-wSP) in healthy adults. PATH-wSP was found to be safe and well tolerated. PATH-wSP elicited significant immunoglobulin G responses to pneumococcal antigens, including pneumococcal surface protein A (PspA) and pneumolysin, as measured by a variety of immunoassays, including enzyme-linked immunosorbent assay (ELISA) and Meso Scale Discovery (MSD) multiplex assay. Functional antibody responses were detectable by either passive transfer of protection to mice or elicitation of pneumolysin toxin neutralizing antibodies. Significant increases in T-cell cytokine responses, including IL-17, were seen among subjects receiving the 600 μg dose level of PATH-wSP.

We are also exploring strategies to incorporate common protein antigens into a limited-valency pneumococcal conjugate vaccine (PCV). This hybrid approach is designed to take advantage of the regulatory path established for licensure of new PCVs and to offer the further benefit of broader coverage by adding a pneumococcal protein antigen. Overall, pneumococcal protein vaccines offer considerable promise, either alone or in combination with PCVs; yet the clinical and regulatory challenges for eventual licensure are considerable.

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