Abstracts of Submitted Presentations

S13

Assessing the Economic Value of Combination Vaccines

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Background. An operations research vaccine selection algorithm was previously developed for vaccine purchasers to assemble formularies that satisfy the immunization schedule at the lowest overall cost to payers or to society. It takes into account distinguishing features of economic consequence among competing vaccines. We "reverse engineered" the algorithm to solve for the price of hypothetical pentavalent and hexavalent vaccines that would permit each to "win a place" in best-value formularies in competition with existing vaccines.

Methods. Iterative bisectional search by integer programming found the *inclusion price* of four non-US-licensed vaccines. Licensed products (n=15) for the same diseases were set at March 2000 prices. Injection costs varied from $5 - $45 per dose. Preparation costs were 25¢ for pre-filled syringes, 75¢ for liquids, $1.50 for lyophilates.

Results. Inclusion prices ranged from $9 to $129 per dose, depending on cost assumptions and usage frequency. **DTPa-HIB-HBV** ranged from $27 to $68 at optimal utilization to avoid extravaccination, with similar ranges for **DTPa-HIB-IPV** ($28 to $75) and **DTPa-HBV-IPV** ($35 to $76). Comparable inclusion prices for hexavalent **DTPa-HIB-HBV-IPV** were higher than for pentavalents ($40 to $123).

Conclusions. The vaccine selection algorithm provides a tool for rational pricing decisions for new combinations entering the market.

S14

INEFFECTIVENESS OF THE CURRENT STRATEGY TO PREVENT HEPATITIS A IN TRAVELLERS

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Introduction: Each year, a large number of Canadians travel to regions of the world where hepatitis A remains endemic. Many of these travelers are not immune and the current preventive strategy relies wholly on self referral to a travel clinic. All the costs associated with such a visit are assumed by travellers. We estimated the effectiveness of this strategy.
Method: We conducted a case-control study which included 108 travel-related hepatitis A cases with onset of disease between 1997 and 1999 and 620 controls who traveled during the same period.
Results: Hepatitis A was strongly associated with high-risk travel (OR=7.2; 95% CI: 1.76-29.4), although only 7% of cases were found in this category. The risk of Hepatitis A was 5 times lower in travellers who did visit a travel clinic than in those who did not (80% efficacy). As only 14% of the controls visited a travel clinic prior to their trip, the effectiveness of the current strategy was 11% (80% x 14%).
Conclusions: Hepatitis a in travellers can be prevented effectively by attendance at a travel clinic. Unfortunately, most travellers do not visit such clinics prior to departure. Even if all high-risk travellers were to visit a travel clinic, this would have a negligible impact on the number of travel-related HA cases (~7% reduction). The current strategy for the prevention of hepatitis A in travellers is ineffective and should be reexamined.

S15

Efficacy, immunogenicity and safety of the malaria vaccine RTS,S/SBAS02: an overview

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Objectives: A safe and effective vaccine against malaria can significantly contribute to conventional measures to prevent and control malaria. The candidate vaccine, RTS,S/SBAS02, has shown promising results in several phase I/II trials **Methods**: RTS,S/SBAS02 is a pre-erythrocytic malaria vaccine based on the circumsporozoite surface protein of *P falciparum* fused to hepatitis B surface antigen formulated on the SBAS02 adjuvant, an oil-in-water emulsion containing 3D-MPL and QS21. Safety and efficacy was initially evaluated via sporozoite challenge studies conducted at the WRAIR which evaluated various dosing and schedules of the vaccine. Subsequent, a proof of concept field efficacy study has been conducted in The Gambia after 3 doses of vaccine in semi-immune men during a first malaria transmission season. A booster dose was given during the following malaria season. Controls received a rabies vaccine. Reactogenicity and safety were evaluated via diary cards. **Results**: The challenge studies in healthy volunteers consistently demonstrated protective efficacy ranging between 42-86% when given according to 2-3 dose schedule and significant prolongation of the pre-patent period. Vaccine efficacy against parasitaemia and adjusted for covariates over a malaria transmission season in the field, was 71% (95% CI 46-85%) during the first 2 months after vaccination but decreased to 0% during the last 2 months of surveillance. After the booster dose (given ± 19 months after the first dose), a vaccine efficacy of 44% (95% CI 1-69%) was observed during the 9 week surveillance period. There were no safety issues and the vaccine showed acceptable reactogenicity in all volunteers. **Conclusion**: The RTS,S/SBAS02 malaria vaccine is safe and well tolerated by malaria-naïve and semi-immune adult volunteers. 2 or 3 doses consistently protect against *P falciparum* sporozoite challenge. The field efficacy results show that an effective but short-lived protection can be established. The booster study confirms the immunogenicity of the vaccine. Partial efficacy, similar to the effect of bednets, may lead to significant protection against severe disease and death in the main target population and studies are planned in children in endemic areas.

S16

YELLOW FEVER (YF) 17D VIRUS AS A LIVE VECTOR FOR NOVEL CHIMERIC VACCINES (CHIMERIVAX™): PRECLINICAL AND CLINICAL EXPERIENCE.

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YF 17D- a live, attenuated vaccine with a long history of safe and efficacious use - is an ideal vector for genes encoding protective antigens of heterologous flaviviruses. The envelope prM and E genes of YF 17D are replaced with the corresponding genes of the target for vaccine development. The E protein of the donor contains protective antigens, while genes for replicative enzymes are provided by YF. The vaccines were less neurovirulent than YF 17D virus. Monkeys given doses as low as 2 logs rapidly developed high neutralizing antibody titers and were fully protected against challenge. Simultaneous immunization of monkeys with multiple ChimeriVax™ vaccines against all 4 dengue serotypes was successful. ChimeriVax™-JE and dengue viruses were markedly restricted in their ability to replicate in mosquitoes. A Phase I/II clinical trial of ChimeriVax™-JE was conducted in yellow fever immune and non-immune adults. The vaccine was well-tolerated, with no difference in minor adverse event rates from controls given YF 17D vaccine. 100% of the subjects seroconverted to JE by neutralization test. Prior yellow fever immunity did not impair immune responses, and in fact enhanced the JE antibody response. ChimeriVax™ technology is expected to provide new single-dose, low-cost vaccines against JE, dengue, West Nile and tick-borne encephalitis having a safety and efficacy profile similar to YF 17D.