In this paper a case of human onchocerciasis in Portugal is presented in order to increase awareness of medical doctors of its diagnosis, clinical manifestations and treatment. A 33 years-old white Portuguese male presented with oedema and pruritus of the hands, arms and neck, one year after returning from six months working in Congo. Results of physical and opthalmological examinations were normal except for pruriginous, subcutaneous oedemas in the hands, arms and neck. Blood smears were examined for microfilariae but were all negative. However, blood samples were positive for filariae using ELISA and IED tests based on *Dirofilaria immitis* antigen. Eosinophil counts were high. Two skin biopsies were taken from the iliac crest and scapular region and both found to be positive for *Onchocerca volvulus*. Ivermectin was then prescribed and repeted six months later. Following treatment the symptoms disappeared, the eosinophil count returned to normal and IED precipitation lines and ELISA values were reduced. Despite the close relationship between Portugal and Africa only a few cases (three) of onchocerciasis have been diagnosed in our laboratory and no report of imported cases of this parasitic disease has been made so far. It is possible that more cases are occurring in our country, but physicians are not familiar with the disease and its elective treatment is not available in Portugal.

80 LARGE OUTBREAK OF CEREBROSPINAL MENINGITIS IN NIGERIA, 1996. Nasidi A, Mohammed I, Oyewole F, Usman A, Yakubu M, Qabasiu M, Coker EBA, and Abdullahi S. Federal Ministry of Health, Lagos, Nigeria.

In 1996, an outbreak of cerebrospinal meningitis occurred in Nigeria, a country of more than 105 million people and 31 states, which is situated in the "meningitis belt" of subSaharan Africa. The outbreak was investigated and controlled by the Federal Ministry of Health supported by international teams from the World Health Organization, UNICEF, Medicins Sans Frontiers/Epicentre, the International Federation of the Red Cross and the Centers for Diseases Control and Prevention. The first cases were identified in Kebbi and Sokoto states in the eastern part of the country in later 1995. By the end of the epidemic, thirteen states (population >40 million) in the north of the country had experienced epidemic disease. From November 1995 to June 1996, 100,272 cases were recorded with an overall 10.9% case fatality rate, range 5.4%-24.4%. A local government area in Yobe State had the highest attack rate with 1059 cases per 100,000 people. The highest attack rate was among people aged between 6 months to 15 years. The causative agent was identified by Central Public Health Laboratory in Yaba and confirmed by the WHO Collaborating Center in Norway as *Neisseria meningitides* serogroup A, 111-1 clone. People between I and 30 years of age were targeted for vaccination because of lower vaccine efficacy in young children and lower attack rate among older individuals. Overall, 10.8 million doses of polysaccharide meningococcal vaccine were distributed. Immunization coverage achieved ranged from 25 - 75% in rural and densely populated urban areas of the affected and contiguous states; however, these levels were reached late in the epidemic and only in limited areas. This large outbreak of meningitis occurring despite the availability of an effective vaccine demonstrates the danger posed by reemerging diseases and the need to improve emergency preparedness. The development of a more effective vaccine prevention strategies and long term plans of action for the African continent, in particular and for the whole meningitis belt as a whole has become a matter of great importance and urgency. This paper describes the outbreak in details and shall also propose effective control strategies.

Jean - Philippe

X 81 DEVELOPMENT OF A MENINGOCOCCAL A/C CONJUGATE VACCINE. Campagne G, Garba A, Boulanger D, Schuchat A, Fabre P, Ryall R, and Chippaux JP*. Centre de Recherche sur les Méningites et les schistosomiases, Niamey, Niger; Centres for Diseases Control, Atlanta, USA; Pasteur Mérieux Connaught, Marnes-La-Coquette, France; and Pasteur Mérieux Connaught, Swiftwater, PA.

Meningococcal meningitis remain an important public health problem in sub-Saharan Africa, primarily affecting children and young adults. Periodic outbreaks are associated with a high mortality. *Neisseria meningitidis* A:4:1.9 clone III-1 which currently circulates in Africa and has caused most African epidemics since 1988, is notably responsible for more than 110,000 cases and 11,000 deaths, during the first five months of 1996. Limitations in currently available polysaccharide vaccine suggest that development of a conjugate meningococcal vaccine is appropriate, in order to improve meningitis control by producing lasting protection in immunized infants. We conducted a preliminary trial with a meningococcal A/C conjugate vaccine (MenD) in Niamey. The A and C polysaccharide antigens (PS) of *N. meningitidis* were each covalently bound to diphtheria toxoid. Trial objectives were (i) to compare the immunogenicity of different vaccine doses (1, 4 and 16 (u)g PS) administered with the routine Expanded Programme on Immunization (EPI) schedule for DTP and (ii) to evaluate their respective reactogenicity. Two control groups were studied, the first vaccinated with the polysaccharidic vaccine (PSV) and the second with the conjugate Haemophilus influenzae type b (Hib). We randomized 180 infants aged 4-8 weeks in five equal groups. All subjects were examined at home for 5 days after each injection to evaluate short-term reactions. A blood sample was obtained before the first injection and one month after the third injection. There were 172 evaluable subjects (95.6%). Local reactogenicity was somewhat more common among infants receiving MenD but no differences in systemic reactogenicity were observed between different doses of MenD and either control vaccine. Antibody titers (ELISA) and bactericidal activity suggested good immunogenicity with both the 4 and 16 (u)g dose of

both A and C antigens. Nine months later, we determined antibody response to a PSV injection among infants previously vaccinated with either MenD or PSV, to stimulate natural infection with N. meningitis. After selection of the best dose of antigen to obtain efficient antibody titers, we will proceed to a larger trial designed to identify the optimal infant vaccination schedule with the longterm goal of including the MenD in routine infant immunization.

82 CLONING OF THE *SCHISTOSOMA MANSONI* DIAGNOSTIC PROTEINS, UPPER AND LOWER GP30. Hancock K* and Tsang V. Division of Parasitic Diseases, Centers for Disease Control and Prevention, Atlanta, GA.

For antibody diagnosis of *Schistosoma mansoni* infection, our laboratory has used the criteria of reaction with two genus-specific proteins, upper and lower gp30, of mansoni adult microsomal antigen (MAMA)in a western blot assay. In order to eliminate the need for adult worms and the extensive fractionation required to obtain the antigen and to simplify the assay format, we targeted upper and lower gp30 for cloning. Upper gp30 was purified by further fractionation of MAMA using continuous elution electrophoresis. The fractions containing upper gp30 were separated by SDS-PAGE and a single band of molecular weight 29.4 kDa was sequenced. Lower gp30 was purified by extraction of the microsomal fraction from adult worms into the detergent phase of Triton X-114 followed by lentil lectin affinity chromatography. The bound fraction was separated by SDS-PAGE and a single band of 25.9 kDa was sequenced. Protein sequence was obtained on two internal peptides from both upper and lower gp30. The two peptide sequences obtained from upper gp30 aligned with three, overlapping *S. mansoni* sequences in the EST database. Together these sequences formed an open reading frame encoding a 28.4 kDa protein. The two peptide sequences obtained from lower gp30 matched a previously described *S. mansoni* protein, Sm25. Using the GenBank sequences, both proteins have been cloned. Expression studies are under way to confirm the antigenic characteristics of the recombinant proteins.

83 CORRELATION OF RESISTANCE TO INFECTION OF *SCHISTOSOMA MANSONI* WITH IMMUNOLOGICAL REACTION INDUCED BY CANDIDATE VACCINE ANTIGENS. Al-Sherbiny.

Over the past six years, a cohort of rural Egyptians living in an area with high *Schistosoma mansoni* prevalence (70%), well delined in terms of *S. mansoni* infection were enrolled in this study and their treatment and reinfection history was documented. Blood, urine and stool samples were collected before, 3 and 12 month after treatment with PZQ. PBL were tested, *in vitro*, against selected vaccine antigens namely, Paramoycin, Irv-5, P-28, SG3PDH, MAP4, MAP3, Sm-14, PN-18, PL-45 and PR-52 to determine their proliferative responses. The ability of these antigens to induce Th1 and Th2 cytokine responses was also determined namely, IL-2, IL-4, IL-5, IFN-γ. Total antibody and specific isotypic responses to candidate vaccines were determined by FAST-ELISA pre-, 3 and 12 month post-PZQ treatment. The percentage of responders and the magnitude of response for each vaccine were evaluated for each parameter tested. In the prospective analysis, immune responses induced by each antigen were correlated with reinfection over a 12 month period. With continuous exposure to infested water, a subset of our study cohort remained free of infection till 1997 after a parasitological cure in 1991, "resistant" subjects. Others became repeatedly reinfected after parasitological cure with PZQ in 1991 till 1997, "susceptible" subjects. Accordingly, the immune responses induced by each antigen, which significantly correlated with resistance to human schistosomiasis were determined. The study demonstrated that candidate vaccine antigens induced characteristic immunological reactions that significantly correlated with resistance to reinfection (prospectively and retrospectively) and that the basis for the conducting human phase I and II clinical trials in the near future is feasible.

84 MOLECULAR IDENTIFICATION OF THE *SCHISTOSOMA JAPONICUM* (PHILIPPINE STRAIN) 22.6 -kDa TEGUMENTAL ANTIGEN AS A TARGET OF THE HUMAN IgE RESPONSE. Santiago ML*, Hafalla JC, Kurtis JD, Wiest PM, Olds GR, Dunne DW, and Ramirez BL. Research Institute for Tropical Medicine, Manila, Philippines; International Health Institute, Brown University, Providence, RI; Department of Medicine, MetroHealth Medical Center, Case Western University, Cleveland, OH; and Microbiology and Parasitology Division, Department of Pathology, Cambridge University, Cambridge, UK.

Rational design of a vaccine against human schistosomiasis would need to consider potential correlates of human immunity. In *Schistosoma mansoni* and *S. haematobium*-endemic communities, resistance to reinfection has been shown to correlate with older age and elevated IgE levels against soluble adult worm antigens. Recent findings of an age-dependence of the human IgE response in field studies in the Philippines provide evidence for a similar immuno-epidemiologic pattern in *S. japonicum*-endemic populations. Thus, in an effort to identify potential vaccine candidates against human schistosomiasis japonica, we identifed older, high-IgE responders from a cohort of 179 infected individuals in Leyte, the Philippines and show that their IgE antibodies recognized a dominant 22-kDa antigen. The molecular nature of the antigen was determined by double-immunoscreening 5 x 10^5 l-ZAP clones

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