paralysis. The severity of the disease and the lack of causal therapy emphasize the need for prevention of tick borne encephalitis (TBE) by vaccination. Inactivated, whole virus TBE vaccines (FSME IMMUN, Baxter and Encepur, Novartis) are widely used in Europe. In recent years a full clinical development program, including safety, immunogenicity and seropersistence studies has been conducted for FSME-IMMUN in all age groups. Antigen doses of 2.4 μg and 1.2 μg were identified as optimal for adults and children, respectively. In an ongoing study, the safety and immunogenicity of FSME-IMMUN 0.25 ml Junior and Encepur 0.25 ml Children are being investigated in children 1 to 11 years of age. A total of 150 and 152 subjects were enrolled in the FSMEIMMUN and Encepur group, respectively. Immunogenicity was assessed by two different ELISA assays using antigens homologous to the TBEV strains of either FSME IMMUN (IMMUNOZYM[1]), or Encepur (Enzygnost[2]). Four weeks after the second vaccination, in the FSME-IMMUN group, 100% of subjects were seropositive in both the IMMUNOZYM- (>126 VIEU/ml) and the Enzygnost ELISA (>10.32U/ml) compared with 94.0% and 96.7% respectively, in the Encepur group. Geometric mean concentrations (GMC) measured by IMMUNOZYM ELISA were 3026 in the FSME-IMMUN and 678 in the Encepurgroup. GMCs measured with the Enzygnost ELISA were 163.3 (FSME-IMMUN) and 93.7 (Encepur). Local reactions after the 1st vaccination occurred in 12.7% with FSME-IMMUN and in 28.9% with Encepur. The rate of systemic reactions was comparable: 9.3% (FSME-IMMUN) and 11.8% (Encepur). The presently marketed TBE vaccines represent highly effective tools for the prevention of this continuously spreading disease.

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**37.003**

**Strategies for the Development of New Vaccines**

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The reputation of vaccination rests on a two hundred year old history of success against major infectious diseases. In general, two achievements have been crucial to the success of vaccines: the induction of long-lasting immunological memory in individuals and the stimulation of a herd immunity that enhances control of infectious diseases in populations. However, when one reviews the vaccines now available it is apparent that most successes have been obtained when the microbe has a bacteremic or viremic phase during which it is susceptible to the action of neutralizing antibodies, and before replication in the particular organ to which it is tropic.

Success has also been achieved against some agents replicating on respiratory or gastrointestinal mucosae, against which it has been possible to induce immune responses acting locally as well as systemically.

[1] IMMUNOZYM FSME IgG, Progen.
[2] Enzygnost TBE, Dade Behring.

and modern efforts are directed towards pathogens against which cellular immune responses are critical.

Newer approaches in vaccine production such as nucleic acid immunization, vectors, reverse genetics and additional routes of administration may circumvent prior difficulties. The target of vaccination will shift towards adolescents, adults, patients in hospital and those with chronic diseases and possibly will extend to therapy as well as prevention. The major scientific problems to be solved are maintenance of immune memory, immaturity and post-maturity of the immune system, and adjuvants capable of stimulating selective cell types.

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**37.004**

**New Technology Update: Cell Culture derived seasonal and pandemic flu vaccine**

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The Vero cell line is the most widely accepted continuous cell line by regulatory authorities and has been used since decades for the production of, e.g. polio-, rabies- and rotavirus vaccines. Here we report on the clinical characterization of Vero cell derived inactivated pandemic- and seasonal influenza vaccines.

A whole virus H5N1vaccine based on (Vietnam/1203/2004/H5N1, clade 1) was demonstrated to be safe and had an excellent tolerability profile. A dose of 7.5 $g of a non-adjuvanted vaccine formulation was highly immunogenic and induced antibodies neutralizing homologous strains as well as viruses from other H5N1 clades. A booster dose of a heterologous (clade 2) H5N1 vaccine 12-17 months later resulted in enhanced antibody responses against both the original (clade 1) and the booster (clade 2) strain, indicative of .cross-protective memory.

A vaccine against the current pandemic H1N1 strain is being studied in adults and children. In adults, two doses of 7.5$g antigen induced seroprotective HA antibody titers in 89% - 91% of subjects. An ongoing pediatric study demonstrated that after the second dose 100% seroprotection (HI assay) was attained in the 3-8 and 9-17 year old cohorts.

Vero cell derived trivalent seasonal influenza vaccines (split virion), using wildtype virus seed stocks were developed and extensively tested in human studies. Their immunogenicity met all licensure criteria, clinical efficacy was demonstrated and safety profile was comparable to egg derived vaccines[1].

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These data indicate that flexible and versatile Vero cell platform can successfully be in the production of pandemic and seasonal influenza vaccines.

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## The ill returnee from Latin America (Invited Presentation)

**38.001**

**Febrile Illnesses**

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Roughly 10% of travelers to developing countries experience a febrile illness during travel or on return. The likelihood of developing a medical condition during travel relates to an individual's past medical history, travel destination, duration of travel, level of accommodation, immunization history, adherence to indicated chemoprophylactic regimens, activities during travel, and history of exposure to infectious agents prior to and during travel. The risk for acquiring a tropical infection is primarily affected by the activities of the traveler. For example, immigrants from developing countries return home to visit friends and relatives (VFR) in their place of birth and usually don't take preventive therapy for malaria. Long-term expatriates, on the other hand, have unique risk profiles. Fever is a leading reason for post travel consultation. Careful questioning of patients about the pattern of fever and associated symptoms is useful. Several papers around the world have reported data about returning travelers with fever. The Geosentinel has reviewed its data on 24,920 travelers from 1997 to 2006. They reported that 28% of returned travelers seen at clinics presented with fever as their chief reason for seeking medical care. Fever was a marker of a serious illness requiring hospitalization. In this report, causes of fever varied by region visited and by time of presentation after travel. The exposure history is crucial to the formulation of a differential diagnosis. Knowledge of infectious disease outbreaks like the novel H1N1 Influenza pandemics in a specific region where the patient has traveled is very helpful. Travelers to Latin America can be exposed to different infectious agents that can give a systemic febrile illness. The most common ones include respiratory tract infections, mononucleosis, dengue, malaria, and typhoid fever. Sometimes no specific cause is reported. Laboratory diagnosis has to be done promptly and efficaciously to avoid delays in treatment.

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**38.002**

**Cutaneous Diseases in Returnee Travellers from Latin America**

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Cutaneous diseases are very frequent in travelers. They are ranked in the three most common causes of health problems in returned travelers. Some destinations have a higher risk of cutaneous diseases in travelers, such as the Caribbean and Latin America. The origin of most of these dermatological disorders is due to infection, but some of them are due to solar allergies and envenomization. The main cutaneous diseases observed in travelers are cutaneous larva migrans, phytophotodermatitis, complicated mosquito bites, pyodermas, miyasis and tungiasis.

Risk factors like country of acquisition, age, reason for travel, duration of the travel, gender vary according to the disease. Countries within Latin America with higher risk are Jamaica, Dominican Republic, Brazil, Belize and Bolivia. Some risk groups that have been determined for dermatological conditions include short term travelers, those with tourism as the purpose of travel, male and young travelers. Evaluation of an ill traveler with skin lesions includes very detailed questions to evaluate the history of exposure, prevention measures, immunization, previous treatment and a complete physical examination. Very rarely further diagnostic studies are needed such as blood tests, serology, skin biopsies, cultures and imaging techniques. Many cutaneous diseases related to travel can be prevented wearing closed shoes, avoiding skin contact with some fruit juices and using repellents to avoid insect bites. Use of anti rabies and anti tetanus vaccines is also recommended for some destinies and adventure travels.

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**38.003**

**Non-Enteric Helminths Including Cysticercosis**

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Segmented tapeworms of clinical importance range in size from a few centimeters (*H. nana* and *H. diminuta*) to several meters (*T. solium* and *T. saginata*) and utilize humans as definitive hosts, intermediate hosts or both. Generally, adult organisms reside and may produce disease in the gastrointestinal tract and larvae can inhabit and produce disease in any human tissue. Teniasis results from ingestion of viable metacestodes of either *T. solium* or *T. saginata*) and is often asymptomatic, but occasionally serious, life threatening illness can result. Cysticercosis is the infection by *Cysticercus cellulosae*, the larval stage of *T. solium*. Neurocysticercosis is the invasion to CNS structures that results in a variety of neurological illness. Echinococcosis is the infection by larvae of *E. granulosus* Cystic), *E. multilocularis* (Alveolar) and related species (*E. vogeli, E. oligarthus*, polycystic). Major epidemiologic and clinical differences exist. Diphyllobotriasis (*D. latum*) is frequent and is transmitted by uncooked freshwater fish. Hymenolepiasis is common in warm climates. Dipylidiasis (*D. caninum*) and sparganosis (*Spirometra*) are much less common. Advances in diagnosis, treatment and prevention of these neglected diseases will be reviewed with emphasis in neurocysticercosis.

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