coccidioides brasiliensis, which in their saprophytic mold form and under certain environmental conditions produce microconidia (< 5 mμ). These propagules become air-born and are accidentally inhaled by man; once in the lungs they convert to the tissue e forms. Most patients are adult males engaged in aerosol-generating activities (agriculture, forestry, masonry, speleology), with women and children being afflicted less often. The three mycoses initiate their pathologic expression in the lungs but extra-pulmonary dissemination is common mainly to mucous membranes, skin, lymph nodes, liver, spleen, adrenals, bones, CNS and others; these entities are systemic and one-organ affection is rare. Signs and symptoms may be related to the respiratory tract but are more often referred to secondary lesions making it difficult to confirm suspicion on clinical evidence alone. Image studies vary depending on the diseases' course and include infiltrates, nodules, cavities, pleural retraction, fibrosis and calcifications. Definitive diagnosis is established only on mycological grounds through biopsies, direct examinations and cultures. The three etiologic agents' differential characteristics under the microscope plus the type of propagules produced in cultures, allow their precise identification. Availability of several indirect tests to determine circulating antibodies and antigens and also of several DNA-based tests serve to confirm diagnosis and facilitate follow-up studies. These mycoses are difficult to treat requiring prolonged courses and careful medical supervision. Treatment has greatly improved with the advent of the new triazoles (itraconazole, voriconazole, posaconazole) but amphotericin B remains a major therapy; recovery is contingent on prompt diagnosis, patient's immune status and stage of the mycosis at therapy initiation.

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15.003

Fungal Skin Infections in the Tropics

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The main challenges confronting us in the tropical mycoses are 1) rapid and accurate diagnosis 2) the availability of appropriate therapy and 3) a rising incidence of certain infections. Diagnosis is dependent on the logical association between the clinical appearances and appropriate laboratory steps. However key features of fungi that aid their recognition are their size and the simple cultural and histological techniques used to detect them. Use of conventional histopathology or immunopathological techniques is highly effective in many cases but molecular tools are now used for some conditions including dermatophytosis and sporotrichosis. With some mycoses the process is simpler. In mycetomas, for instance, histological or cultural evidence can be obtained directly from sinuses or by biopsy.

Most new antifungals have not been profiled with tropical mycoses in mind and there are few evidence-based clinical trials to establish usage or duration of therapy. The commonest of these infections that present major therapeutic problems are the mycetomas and chromoblastomycosis. Fungal mycetomas seldom respond to normal doses of antifungals; whereas those caused by bacteria, actinomycetomas, respond to a range of antibacterials such as dapsone, amikacin, fusidic acid, imipenem etc unless they are very extensive. There is only limited reporting of the use of newer azoles, posaconazole and voriconazole in these mycoses. Mycoses where there have been changes in epidemiology, suggesting, spread include tinea capitis. Spread of *Trichophyton tonsurans* infections to South America and West Africa are examples. Whereas HIV in many countries is controlled through the use of antiretrovirals in infected individuals late recognition is a feature in many areas of the tropics and therefore there is a continuing risk of systemic fungal infections presenting with skin lesions as their first and most obvious clinical manifestation. Being alert to these changes provides a rapid means of dealing with these infections.

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15.004

Prevention and Treatment of Nosocomial Candidiasis

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Candidemia is an important nosocomial infection, with high incidence and mortality rates. Strategies for the management of candidemia include prophylaxis and treatment of established infection. Prophylaxis is more likely to benefit groups of patients with high incidence of candidemia, such as premature neonates, allogeneic hematopoietic stem cell transplant recipients and high-risk liver transplant recipients. For the treatment of candidemia, various studies have been conducted comparing different drugs, such as fluconazole, voriconazole, deoxycholate and liposomal amphotericin B, and the echinocandins caspofungin, micafungin and anidulafungin. In general, the echinocandins represent the best option for the initial treatment of candidemia. In addition to prophylaxis and treatment, attempts to define a group of patients that may benefit from early empiric or preemptive have been developed. These include the development of prediction rules and the use of serum biomarkers such as 1,3-beta-D-glucan and polymerase chain reaction-base techniques.

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Plenary 4 (Invited Presentation)

16.001

The Changing Patterns of Global Migration and the Impact on Infectious Diseases

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Human migration has always been associated with disease translocation. Over the last century the speed and volume of international travel and migration has reached unprecedented levels bringing the impact of globalization into every sector of society- economic, environmental, political, socio-cultural, and health. As a consequence, the

threat of geographic expansion from emerging and traditional infectious diseases has increased. UNESCO defines an international migrant as a person living outside their birth country for >= 12 months. The global patterns of human migration have changed substantially in the last half century: 1) increased # countries sending and receiving migrants, 2) accelerated rates of migration, 3) bi-directional migration and migration transitions, 4) diversification of migrant types, and 5) changes in gender patterns of migrants. Along with these profound changes in demography, volume, speed, and purpose of migration come unique challenges in detection, diagnosis, response and management of infectious diseases. Even in the 21st Century infectious diseases account for ~25% of the global mortality burden as well as substantial morbidity. Increasingly these diseases are blind to geopolitical borders. Cyclical pandemics like influenza traverse the globe more rapidly than ever; newly emerged pathogens like SARS represent a constant challenge to public health preparedness and response. Even old diseases like tuberculosis emerge in more lethal drugresistant forms e.g. XDR-TB. These challenges demand new paradigms to global disease control in governance, surveillance and response. The 2005 International Health Regulations and a range of newly formed international networks and partnerships are a testament to the challenges posed by the new era of migration. Our success in combating these microbial threats will depend on our collective effort to organize and respond on ''supra_national'' level.

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Will the next generation end AIDS? (Invited Presentation)

17.001

Role of innate immunity in the control of HIV infection

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While the immunological correlates that contribute to slower HIV disease progression are still unknown, epidemiologic data strongly suggest that particular major histocompatibility complex (MHC) class 1 alleles (including -B27, -B57, and others that fall within the HLA-Bw4 family of HLA-class I B alleles) are highly enriched in subjects who maintain undetectable viral loads in the absence of antiretroviral therapy, Elite controllers. While these MHC molecules interact with T-cell receptors found on cytotoxic CD8+ T cells, they also interact with innate immune receptors, such as the Killer Immunoglobulin like receptors (KIR) found on the surface of innate cytotoxic Natural Killer (NK) cells. Furthermore, the protective effect of MHC class I alleles is amplified in subjects that co-express particular KIRs, with which they are able to interact, resulting in slower progression to AIDS in these individuals compared to those that only possess the KIR or MHC allele alone. Thus it is plausible that NK cells may play a central role in the control of HIV infection. NK cells expand rapidly following acute infection, and specific populations of KIR+ NK cells expand preferentially in subjects that co-express protective KIR/MHC class 1 combinations. This specific KIR3DS1+ NK cell clonal expansion persists for up to 1 year in the peripheral circulation, and is associated with more aggressive containment of HIV-viral replication in vitro, these NK cells exhibit a more polyfunctional cytokine profile, and kill MHC class 1 target cells more more aggressively than NK cells from individuals that do not have the protective KIR/HLA combined genotype. However, despite this early epansion of NK cells in the periphery, these cells do not gain access to secondary lymphoid organs, thus providing a safe haven within which the virus is able to replicate unabated by the innate immune system, potentially allowing the virus to establish a chronic infection. These data strongly suggest durable control of HIV infection is associated with an early aggressive deployment of highly licensed antiviral NK cells in the periphery that may provide specific and non-specific control of HIV viral replication in acute infection, while producing large quantities of cytokines and chemokines required for the induction of high quality adaptive immune responses that may then maintain control of HIV replication most likely in contained tissue sites.

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17.002

The Role of T Cell Immunity in the Control of HIV Infection

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The window between transmission and peak viremia, prior to the establishment of viral reservoirs, is the narrow but critical period in which a HIV-1 vaccine must control viral replication, prevent extensive CD4 T cell destruction and curb generalised immune activation. We recently published the results of T cell studies in 4 patients, showing that the first HIV-1 specific T cells detectable just prior to peak viremia can select for complete virus escape in as little as 14 days.

Mathematical modeling of these very rapid rates of T cell escape showed that the contribution of CD8+ T cell mediated killing of productively infected cells was earlier and significantly greater than previously described; calculating that T cells in acute HIV-1 kill as much as 35% of virus-infected cells per day. These first T cell responses often waned rapidly following virus escape leaving, or being succeeded by, T cell responses to epitopes that escaped slowly or were invariant. Here, we present data from an additional 10 patients that extend these observations and demonstrate that early rapid escape from primary HIV-1-specific T cell responses occurs in the majority of patients studied, suggesting that T cells are major contributors to the control of viremia in