RCTs. On the other hand, RCTs will soon establish whether Pre-EP is an effective means of HIV prevention. If Pre-EP is proven effective, there will be substantial challenges in formulating a policy framework to guide its use.

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62.004

Antivirals for HIV Prevention

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The possibility that antiretroviral drugs may be useful for HIV prevention has been suggested by animal studies that have documented that if these medications are used before or after a retroviral challenge, they can protect against the development of HIV infection. Epidemiological studies in HIV discordant couples suggest that individuals with lower plasma RNA levels are less likely to transmit HIV to their sexual partners. These findings have lent support to new HIV prevention approaches that include the evaluation of the use of pre- and post-exposure prophylaxis (PrEP and PEP) in high risk HIV-uninfected persons, and studies of the use of antiretroviral drugs to lower plasma RNA in people who are in discordant couples, in order to decrease the likelihood of HIV transmission. Questions that remain to be addressed include whether the benefits of decreasing HIV transmission are offset by behavioral disinhbition, drug toxicities, and costs. An additional set of important considerations include the timing and duration of antiretroviral drug use and whether these compounds are best used as topical microbicides applied to the cervicovagingal or rectal mucosa, or whether oral chemoprophylaxis is more effective. Over the next few years, several thousand at risk persons will be evaluated in efficacy trials to address the optimal uses of antiretroviral medications for HIV prevention.

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Emerging Rickettsioses in Asia (invited)

63.001

Spotted Group Rickettsioses in Asia

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Tick-borne rickettsial diseases are usually called spotted fevers. Their agents, rickettsiae from spotted fever group (SFG), are obligate intracellular bacteria widespread in nature and associated with parasitic blood-feeding arthropods. Ixodid ticks are common human parasites and they may host different microbial pathogens that are often transmitted via ticks feeding on humans. Humans are not natural hosts in rickettsial lifecycle, but due to high frequency of tick bites, the incidence of tick-borne diseases, including rickettsiosis, may be very high. A vast Asiatic territory with different biotopes harbors lots of natural foci of multiple tick species. For the moment, 9 rickettsial diseases are more or less regularly reported in Asia and 2 more rickettsial species potentially associated with human illnesses were found. Rickettsiae recognized as human pathogens are *R.conorii indica*, agent of Indian tick typhus (India), *R.sibirica sibirica*, agent of Siberian tick typhus (Eastern Russia, Mongolia, China), *R. heilongjiangensis*, agent of Far Eastern tick-borne rickettsiosis (Eastren Russia, Nothern China), *R. japonica*, agent of Japanese spotted fever (Japan, Korea), *R.sibirica mongolitimonae* (Nothern China), agent of LAR (Lymphangitis-associated rickettsiosis), *R.aeschlimannii*, unnamed spotted fever (Kazakhstan), *R. raoultii*, unnamed rickettsiosis (Eastern Russia), *R.honei*, Thai tick typhus (Malaysia, Thailand, Laos) and *Candidatus* Rickettsia kellyi, unnamed rickettsiosis (India). Suggested pathogenicity were reported for *R. helvetica* found in Japan and *R.tamurae* (Japan, Laos). Studies show that in some regions, the seropositivity rate for SFG is as high as 57% for certain population groups. The real role of tick-borne rickettsiosis in human pathology also may be shaded by lack of diagnostic facilities and methods in some countries, misdiagnosing with scrub typhus, murine typhus, dengue fever and other clinically resembling entities.

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63.002

Scrub Typhus

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Scrub typhus is recently recognized as a common cause of acute fever in rural Asia. Clinical presentations of scrub typhus vary widely from acute flu-like syndrome, with or without signs of organ dysfunction such as jaundice or renal insufficiency, to multi-organ dysfunction mimicking sepsis syndrome. Acute undifferentiated fever (AUF) with or without organ dysfunction is the major clinical presentation of scrub typhus. The incidence of scrub typhus ranged from 1.1 to 19.3% in various studies conducted in indigenous patients who presented with AUF in rural hospitals in Malaysia, Indonesia and Thailand. The incidence of scrub typhus, murine typhus, and SFG rickettsioses was 7.8%, 2.4%, and 5% respectively in a recent study conducted in patients with AUF who presented with severe manifestations in Thailand. Jaundice, renal dysfunction, abnormal chest radiography on admission occurred in 21%, 35.7%, and 50% respectively in patients with severe scrub typhus. Multiorgan dysfunction or sepsis occurred in 14%. Clinical spectrum of severe murine typhus and SFG rickettsioses were similar to scrub typhus. The reported mortality of severe scrub typhus varied from 2.4%to 16.7%.

Awareness that scrub typhus is one of the common cause of AUF in adults in rural Asia improves the probability of an accurate clinical diagnosis. Early recognition and appropriate treatment reduce morbidity and mortality. Results from recent clinical studies from Thailand indicate that rational antimicrobial therapy would be doxycycline in mild cases and a combination of either cefotaxime or ceftriaxone and doxycycline in severe cases. Azithromycin could be considered as an alternative treatment when ever doxycycline