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## Challenges in management of sexual transmission and pathogenesis of HIV due to host and pathogenic variation

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Poor proof reading activity of Human Immunodeficiency Virus (HIV) results in to presence of distinct viral variants in different cells and secretions of the same individual. These viral variants may influence the affinity to different host cell CD4 dependent and independent receptors. Sexually HIV has been transmitted by binding to human Mannose Receptor (hMR) on human sperm, vaginal epithelial cells which are devoid of conventional CD4 receptor. HIV binding to hMR induces Matrix Metallo-proteinase 9 which weakens the cell surface and therefore increases the risk for sexual transmission of HIV. Further the localization of hMR was found to be in lower number of vaginal epithelial cells of HIV negative female partner of serodiscordant couples as compared to normal females suggesting the association of hMR in sexual transmission of HIV. Genotypic characterization of C2-V3 region of HIV1 C env gene in PBMCs, sperm, vaginal epithelial cells and cervical cells showed presence of distinct variants in the same individual with variable infectivity and different numbers of N-linked glycosylation sites suggesting variation in co-receptor affinity in different cells of the same individual which may influence disease progression and risk of sexual transmission of HIV. Additionally genotypic characterization of HIV1 gp41 by next generation sequencing showed presence of multiple variants in blood of the same individual. Presence of distinct and multiple HIV variants in PBMCs and urogenital cells may influence the viral affinity to host and immune cells and therefore may affect the transmission, infectivity, pathogenicity and response to ART.

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## Why concern about influenza world wise?

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A disease known almost from the time civilization begun high morbid and mortality has been associated with influenza. Record suggested the reason to stop WW 1; one was the disease influenza which had devastating effect in human as well as in swine. The H1N1 virus was highly pathogenic to man as well as swine. This influenza pandemic estimated to have killed 40-50 million human lives, more than the WW 1. Past century has seen two more influenza pandemics with equally devastating effect. In 1918-1919, the virus affected both human & swine. The influenza pandemic started with Swine in Mexico (2009) causing infection in human there spread very fast to USA and all over the world in just 3-months. A pandemic was declared by WHO. The virus responsible for this had three mutation received genes from swine, human as well as birds (H1N1) although very invasive but had low pathogenicity and the deaths recorded was very few as compared to other influenza pandemics, world has seen. Interestingly, this virus has replaced the old H1N1 from the influenza preventive seasonal vaccine as not seen in circulation. The main concern today is that although human influenza strains are few but today human lives under a threat of influenza from other hosts mainly the bird influenza. Domesticated and the wild birds have all the influenza viral strains known till today in all combinations of H & N. The threat started when 18 farm persons got infected in 1997 from birds and 6 died making this virus as most pathogenic and the infection was directly from the diseased birds. This was unknown. Till then, there used to be one intermediary host working as biological incubator. Total killing of the bird population contained the infection but since 2003-04 human cases have been observed in South East Asian Countries. A pandemic due to H5N1 has been in waiting to take place and could be started anywhere. But this is not the only bird influenza virus posing pandemic fear in human; today several other avian (HPAI) are lurking around to become pandemic human stain. Preventive human seasonal vaccine is available but no pandemic vaccine since the influenza pandemic remains unknown.

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