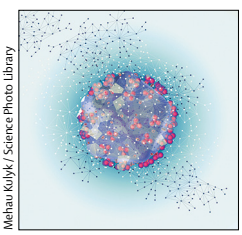
Global molecular epidemiology of HIV-1: the chameleon challenge



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For more on **HIV-1 recombinants** see http://www.hiv.lanl.gov

HIV-1 is characterised by extensive genetic heterogeneity that has implications for diagnosis, vaccine development, and clinical management of HIV infection.[1] Group M, which is responsible for most of the HIV-1 infections globally, has been classified into nine distinct phylogenetic clusters named after subtypes (A–D, F–H, J, and K) and intersubtype recombinant forms. The latter are further classified into circulating recombinant (CRFs) and unique recombinant forms (URFs). CRFs are recombinant viruses that have been spread to more than three epidemiologically unrelated people living with HIV (PLHIV). The number of CRFs and URFs has been increasing since discovery and, to date, 96 CRFs have been detected.

In *The Lancet Infectious Diseases*, Joris Hemelaar and colleagues[2] report the global prevalence of different HIV-1 subtypes and recombinants on the basis of a large collection of data. They did a systematic review and global survey using 383 519 samples collected during 1990–2015 to estimate the global and regional distribution and trends of the HIV-1 clades (subtypes and recombinants). Notably, they also inferred the prevalence of HIV-1 subtypes and recombinants after weighting the regional distributions of HIV-1 clades with the UNAIDS estimate of the total number of PLHIV in each country.

Hemelaar and colleagues report that, during 2010–15, subtype C was the most prevalent clade (46·6% of global HIV-1 infections), followed by subtype B (12·1%), subtype A (10·3%), CRF02_AG (7·7%), CRF01_AE (5·3%), subtype G (4·6%) , and subtype D (2·7%). The combined prevalence of subtypes F, H, J, and K was 0·9%. The global contribution of recombinants, including CRFs and URFs, was 22·8%. The distribution of the HIV-1 clades reflects the regional prevalence of HIV-1. Subtype C had the highest prevalence, which is unsurprising given that it dominates in southern Africa where the proportion of PLHIV is greatest.

Subtype C showed a decreasing trend in 2010–15 versus previous years (2000–09), when its prevalence had increased. The proportions of infections due to subtypes A, D, and G declined; by contrast, the prevalence of subtype B increased throughout 2000–15. Among the recombinants, the proportions of CRF01_AE, other CRFs, and URFs increased over the study period, leading to an overall increase for CRFs, URFs, and recombinants. For subtype B, which accounted for almost all HIV-1 infections in middle-income and high-income countries at the beginning of the epidemic,[3] Hemelaar and colleagues reported a decreasing trend for western and central Europe and north America during 2010–15.

Notable differences in regional distributions of HIV-1 subtypes were seen in eastern Europe and central Asia, where the proportion of subtype A declined from 91·3% in 2005–09 to 52·8% in 2010–15, with a concomitant increase in the prevalence of subtypes B, C, and CRFs (mostly CRFs other than CRF01_AE and CRF02_AG). The large increase in CRFs is due to CRF63_02A1 affecting mostly people who inject drugs in central Asia and Russia. In the Middle East and North Africa, the proportion of CRFs (mostly CRF35_AD) is increasing over subtype B. Southeast Asia had the highest prevalence of CRF01_AE (peaking at 72·8% in 2010–15), with a decreasing trend over the previous 5 years.

Although the global and regional distribution of HIV-1 depends on many factors—such as HIV-1 prevalence, global mobility, socioeconomic factors, differences in the characteristics of diverse strains, and differences in access to antiretroviral treatment and clinical care—in several cases, the proportion of recombinants increases over different subtypes. This increase could be due to differences in transmissibility or replicative capacity of recombinant viruses versus the so-called pure subtypes.[4]

Understanding the global and regional molecular epidemiology of HIV-1 infection is important for several reasons. First, research on vaccine development is based on the distribution of HIV-1 clades. For example, one of the ongoing vaccine trials that is in progress in South Africa, has used immunogens modified according to the locally circulating strains of subtype C.[5] Second, knowledge about the distribution of HIV-1 genetic diversity has been useful because it informs investigations into the changing patterns of the global epidemic and the potential implications for diagnosis and clinical management. In the past few years, molecular epidemiology has also been the

centre of interest for public health purposes.[6] Finally, the decline in the global prevalence of subtype C, which dominates in South Africa, raises hope about the potential to eliminate new transmissions through the implementation of the UNAIDS 90-90-90 global target.

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Pneumococcal vaccines in Nepal

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Worldwide, pneumococcal conjugate vaccines (PCV10, PCV13) are included in many national immunisation schedules to prevent severe pneumococcal disease, particularly meningitis and pneumonia. PCV schedules vary from country to country.[1] A 2012 WHO Position Paper on PCV endorses either a 2+1 (two primary, one booster) or 3+0 (three primary, no booster) vaccination schedule depending on disease epidemiology, coverage, and timeliness of immunisation.[2] Many countries have adopted a 2+1 schedule, with the first two doses administered early in infancy, approximately 8 weeks apart, and the third dose given late in the first year or early in the second year of life. The rationale for this approach is that two PCV doses are likely to offer similar protection for infants to three doses in the first year of life,[3] with the booster dose offering longer lasting immunity and therefore protection, and better indirect protection. The effectiveness of this schedule has been shown in many settings.[4]

Studies of PCV7 have shown that two doses have similar immunogenicity to three doses for most serotypes, exceptions being serotypes 6B and 23F.[5] Many African countries continue to use a 3+0 schedule which has been shown to be effective in the two African efficacy trials of a nine-valent PCV, which was a precursor of PCV13.[6,7] In the trials, the vaccine was immunogenic for serotype 1, the dominant cause of pneumococcal disease in less developed countries, but surprisingly showed little efficacy against serotype 1 disease. Data from South Africa, which has implemented a 2+1 schedule, suggests that this schedule might provide better long-lasting protection and better herd protection especially for serotype 1, which is more prevalent in older children.[8]

As part of the Global Polio Eradication Initiative, WHO now recommends that countries using oral polio vaccine should add a single dose of inactivated polio vaccine (IPV) at or after 14 weeks of age. For many countries, this has necessitated the administration of three injectable vaccines (PCV, IPV, and diphtheria, tetanus, whole-cell pertussis, hepatitis B virus, Haemophilus influenzae type B) at a single clinic visit at 14 weeks. The Nepali Ministry of Health was concerned about the acceptability of this policy. To address this concern, Rama Kandasamy and colleagues[9] did an open-label randomised clinical trial of two different 2+1 PCV10 schedules to compare the immunogenicity of the second dose of PCV10 given at 10 weeks of age (6+10) with that given at 14 weeks of age (6+14).

The authors found that for six of the ten serotypes in the vaccine, immunogenicity was inferior in the 6+10 group by one or both of the standard measures. The most substantive differences were seen for serotypes 6B and 23F, and these were largely corrected by the time the booster was due at 9 months. Following the booster there were no significant differences between the groups. The clinical relevance of these findings is not known. The risk of pneumococcal disease is age dependent. Giving the second dose at 10 weeks would provide protection earlier, but the level of protection might be less for up to six serotypes