

### Virulence of HIV has increased since first reports of AIDS

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HIV may have evolved to become more virulent over the course of the epidemic, according to the results of a meta-analysis published in the online edition of *AIDS*.

The study estimates that six months after infection, the CD4 cell count of a person infected with HIV in 2010 was likely to stabilise at a level approximately 150 cells below that of a person infected in the early 1980s. This implies that HIV transmitted in recent years is likely to lead to more rapid development of illness compared with HIV transmitted 30 years ago.

Investigators in the USA analysed the results of studies conducted between 1984 and 2010 to see if two key prognostic markers – CD4 cell set-point and viral load set-points (the level of CD4 cells and viral load immediately after primary infection) – had changed. All the studies involved patients from North America and Europe and most were therefore infected with HIV-1 subtype B.

Increasing virulence of the virus was suggested by an annual fall in CD4 cell count of approximately 5 cells/mm<sup>3</sup> and an increase in viral load set-point of 0.013 log<sub>10</sub> copies/ml.

‘Over the course of the HIV-1 subtype B epidemic in North America and Europe there are overall trends of decreasing baseline CD4 cell counts and increasing set point viral loads,’ comment the investigators.

They calculated that these changes represent ‘a loss of 148 CD4 cells/mm<sup>3</sup> and an increase of 0.39 log<sub>10</sub> copies/ml RNA over a 30 year period (from the first CDC report of the epidemic in 1981).’ Even larger changes were observed in patients with a known date of infection with HIV.

However, there was evidence that the virulence of the virus had slowed in recent years.

Earlier research examining the virulence of HIV has produced conflicting results. Nevertheless, it is important to establish an accurate understanding of this issue as it has implications for both treatment and prevention strategies. If the virus has become more virulent, this could suggest that it is easier to transmit. Similarly, a more virulent virus would hasten the need for antiretroviral therapy.

Investigators therefore conducted a meta-analysis of studies examining trends in baseline CD4 cell counts and viral load set-points.

A total of 12 studies monitoring CD4 cell counts were identified. They included approximately 21 000 individuals, and nine studies enrolled patients with an established date of HIV seroconversion.

Viral load set-point was assessed in 8 studies involving approximately 11 000 patients. In 6 of these studies, the population comprised individuals with a documented date of seroconversion.

The studies were published between 1996 and 2009 and provided data on newly diagnosed patients over a mean of 17 years. All were conducted in Europe and North America and therefore the majority of patients were infected with subtype B virus.

The meta-analysis showed a statistically significant decreasing trend in CD4 cell count of -4.93 cells/mm<sup>3</sup> each year. When analysis was restricted to seroconvertors, the mean annual loss in CD4 cell count increased to -6.01 cells/mm<sup>3</sup>.

Viral load set-point increased by a mean of 0.013 log<sub>10</sub> copies/ml. Restricting analysis to seroconvertors showed an even larger mean increase (0.018 log<sub>10</sub> copies/ml).

‘These trends are consistent with increased virulence of HIV-1 due to viral evolution in the human population,’ suggest the investigators.

Overall, they estimate that baseline CD4 cell count has fallen by a mean 148 cells/mm<sup>3</sup> and viral load set-point has increased by a mean of 0.39 log<sub>10</sub> copies/ml since the first reports of AIDS in the early 1980s. Restricting analysis to seroconvertors showed even larger changes, with a mean reduction in baseline CD4 cell count of 180 cells/mm<sup>3</sup> with a corresponding mean increase in viral load set-point of 0.54 log<sub>10</sub> copies/ml.

They believe that their findings have both clinical significance and implications for HIV prevention. ‘A 0.3 log<sub>10</sub> copies/ml change is a clinically significant change in viral load,’ write the authors. ‘The relationship between set point and viral load disease progression predicts that an increase in set point of 0.5 log<sub>10</sub> copies/ml decreases the median time to AIDS by three years ... and will modify the per year transmission rate by 37%.’ However, the magnitude of changes in CD4 cell count and viral load set-point lessened over time.

‘Overall, our meta-analysis of trends in prognostic markers of HIV-1 disease progression suggests that HIV-1 has become more virulent over the 30-plus year history of the global HIV/AIDS epidemic,’ conclude the investigators. They call for studies in other populations and locations affected by the epidemic, especially sub-Saharan Africa, ‘to assess our findings and its future impact.’

Herbeck JT, et al. Is the virulence of HIV changing. A meta-analysis of trends in prognostic markers of HIV disease progression and transmission. *AIDS* 25, online edition, doi: 10.1097/QAD.0b013e32834db418, 2011

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## SINGLE SUTURE

Nano killer future

Forget antibiotics, let's try nanoparticles. That's according to DARPA, the US military's research arm, which says that rather than spend money on new antibiotics, which only work until bacterial strains grow resistant, ‘readily adaptable nanotherapeutics’ can fight infection instead.

The agency has called for proposals to find ways to use small interfering RNA (siRNA) to fight bacteria. The scraps of genetic code seek out their mirror image within cells, such as bacteria, and silence them. This stops protein production and leads to cell death.

DARPA is seeking ideas for adaptable nanoparticles that can be ‘reprogrammed on the fly’ by loading up specific siRNA to deal with outbreaks among troops.

As with GPS systems and the internet, this innovation might benefit the military initially, but eventually become a model for mainstream medication.

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