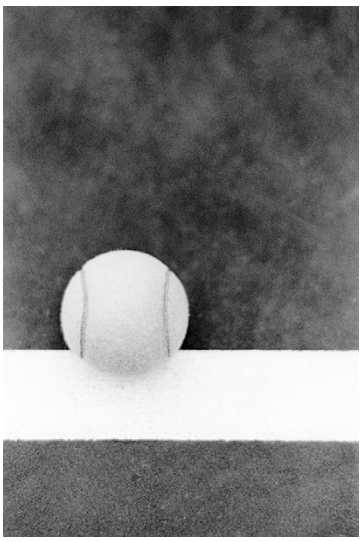
HIV

Set-point — the virus adapts?

Understanding the relationship between viral load and transmission is of vital importance for the treatment, and eventual elimination, of HIV. It is well known that individuals who have high levels of HIV in their blood are the most infectious. However, a new paper published in the *Proceedings of the National Academy of Sciences USA* now suggests that individuals who have an intermediate viral load actually make the greatest contribution to the transmission and spread of HIV-1.

During the asymptomatic period of infection, HIV-1 viral load tends to fluctuate around a value that is known as the set-point, which varies widely between patients. In this study, Fraser and colleagues analysed existing data on the viral load and duration of the asymptomatic infectious period of untreated HIV-1-infected individuals, to assess the impact of different set-points on viral transmission.

They initially focused on data that were collected between 1982 and 1993 from a cohort of 123 males from the Netherlands, who were recruited prospectively prior to their infection. As expected, the viral load and duration of asymptomatic



infection were negatively correlated. Data were then analysed from studies conducted in Uganda and Zambia between 1994 and 1998 of more than 900 HIV-1-positive individuals who had HIV-1-negative sexual partners. The annual transmission rate was calculated and it was found that those with a high viral load (10,000 copies per millilitre of blood) were over 10 times more likely to infect their partner than those with a low viral load (1,000 copies per millilitre of blood). However, combining the two analyses showed that over the entire infectious period it was individuals who had intermediate viral loads that had the highest 'transmission potential'. Notably, this intermediate value was remarkably close to the most common value for both experimental cohorts. The authors propose that this is a result of adaptation, by which the virus produces lower viral loads to maximize transmission and, consequently, survival. The evidence presented, although consistent with this interpretation, is not conclusive, as the authors acknowlege and discuss.

This study has implications for treatment regimes that target antiretroviral agents at those patients who are most responsible for transmission, which is clearly not those who have the highest viral loads. The authors warn that interventions that alter the relationship between viral load and infectivity could come at the cost of an increase in the virulence of HIV-1.

Gillian Young

ORIGINAL RESEARCH PAPER Fraser, C., Hollingsworth, T. D., Chapman, R., de Wolf, F. & Hanage, W. P. Variation in HIV-1 set-point viral load: epidemiological analysis and an evolutionary hypothesis. *Proc. Natl Acad. Sci. USA* **104**, 17441–17446 (2007)