From *Pan* to pandemic

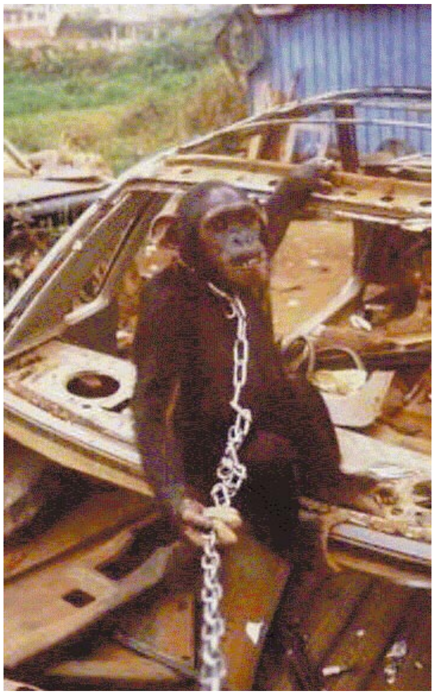
Robin A. Weiss and Richard W. Wrangham

Further evidence that HIV-1 originally came from chimpanzees bears on a variety of issues — the evolution of AIDS viruses, disease transmission from animals to humans, and chimpanzee conservation and welfare.

The origin of human immunodeficiency virus type 1 (HIV-1), the retrovirus that is the main cause of AIDS, has been a puzzle ever since it was discovered by Barré-Sinoussi and her colleagues[1] in 1983. On page 436 of this issue[2], Gao *et al.* provide the most persuasive evidence yet that HIV-1 came to humans from the chimpanzee, *Pan troglodytes*, which harbours a related simian immunodeficiency virus, SIVcpz. Moreover, by genetic typing of mitochondrial DNA, it is clear that the three strains of SIVcpz most closely related to HIV-1 come from a single subspecies, *Pan troglodytes troglodytes*, which lives in the same part of central Africa where AIDS is thought to have arisen.

There are three principal groups of HIV-1: the main (M) group comprises the majority of subtypes that have spread across the world; an outlier (O) group is found in Cameroon, Gabon and Equatorial Guinea; and a new group (N) was last year identified in two people in Cameroon[3]. HIV genetic sequences from a Congolese serum sample, originally taken in 1959, showed that the diversification of all the M subtypes has occurred in very recent times, say the past 50 years[4]. Gao and colleagues' evolutionary analysis of the M, N and O groups in comparison to SIVcpz isolates indicates that these HIV-1 groups represent three separate transfers from chimpanzees to humans (such inter-species transmissions of infectious disease are known as zoonoses).

It has been shown[5,6] previously that several strains of HIV-2 in West Africa were independently derived from SIVsm, the virus endemic in the sooty mangabey monkeys of that region. The other human retroviral pathogen, human T-lymphotropic virus type 1 (HTLV-1), has also originated more than once from related simian viruses, including STLV-1 of chimpanzees[7,8]. And a new paper[9] reporting a parallel zoonosis to that of Gao *et al.*[2] has demonstrated that human pygmies in Gabon are infected with a strain of HTLV-1 that is virtually indistinguishable from STLV-1 of mandrills living in the same forest. Finally, a survey of people who handle primates in captivity recorded several instances of foamy retrovirus transmission and one transfer of SIVmac[10], the strain that causes AIDS in macaques.



KARL AMMANN

Figure 1 **Chimpanzee orphan, chained in a junk car lot in Cameroon. The rest of its family had been shot and butchered for the bushmeat trade.**

So cross-species transmission of primate retroviruses to humans through hunting or husbandry probably occurs relatively frequently, although — thankfully — the subsequent epidemic spread in the human population is a much rarer event. Such zoonoses have heightened the concern that retroviruses might also cross to humans from more distant species, such as pigs, if their tissues were used for xenotransplantation[11].

Gao *et al.*[2] also show that a chimpanzee called Noah, from which a highly divergent strain, SIVcpzANT, was isolated, actually belongs to the different subspecies *Pan troglodytes schweinfurthii* (the names and distributions of all four subspecies are shown in the map on page 438). Gao *et al.* argue that SIVcpz is an ancient chimpanzee infection that has co-evolved with its host during subspeciation. They previously followed the same logic for the diversification of SIVagm among the various subspecies of African green monkey[12]. But these monkeys, like the chimpanzee subspecies, have largely non-overlapping habitats, so it is also conceivable that SIVs were more recently introduced and owe their diversity to geography rather than co-evolution.

Indeed, the ability of SIV to jump host species, together with the demonstration by Gao *et al.* that one strain of SIVcpz is (like HIV-1E in Thailand) derived from genetic recombination between two distinct parent strains, suggests that the co-evolution hypothesis needs to be viewed with a little caution. To bolster Gao and colleagues' conclusion that chimpanzees are a natural reservoir population for the precursor of HIV-1, serological surveys for the prevalence of SIVcpz infection are required in wild populations in Africa.

The ramifications of the new findings[2] extend well beyond the evolution of HIV-1, and zoonotic transmission of disease, to chimpanzee conservation and welfare. Like the other great apes, chimpanzees are in trouble. In most of the 21 African countries where they live in the wild, their numbers are plummeting — partly because of habitat loss, and partly because ape-hunting has become big business (Fig. 1). Hunters are paid by timber companies to provision logging camps, while the kills of freelance hunters are traded as far as the cities. Ape meat can fetch premium prices in middle-class restaurants.

This 'ape bushmeat crisis' cannot last long. Numbers are hard to come by, but some estimates of the annual chimpanzee kill are in the thousands, which is an unsustainably high figure when as long as a decade ago the world population was estimated at around 200,000. In the face of such an onslaught, populations of the large, slowly reproducing apes will be swiftly eradicated[13].

Hunters dismember chimpanzees with primitive butchery, and so expose themselves to the risk of zoonotically transmitted disease. Conservationists, therefore, are debating the merits of a campaign that would publicize the disease-transmitting dangers of treating apes as food. Some are concerned that this could backfire, and result in intensified slaughter of the primates, whereas others think the situation could hardly get worse. Later this month, a meeting hosted by the American Zoological Association aims to turn discussion into action. In the long term, apes will survive in the wild only where they are not eaten, a prospect that depends on the acceptance of new values by which apes are treated as too human-like to kill or eat. Many believe that new ethics are also needed in the scientific world. To some AIDS researchers, the use of chimpanzees is constrained merely by their high cost and scarcity[14]. By 1996, 198 chimpanzees had been experimentally infected with HIV in six of the major research institutions in the United States[15], although HIV seldom causes disease in these animals.

Worldwide, there are now about 35 million carriers of HIV-1, and with the increased evidence that the virus is linked to SIVcpz there may be calls for more use of chimpanzees in AIDS research. But according to a growing constituency, evidence of ape possession of human-like cognition and emotions should reduce our willingness to infect them, and condemn them to solitary confinement for life (which lasts for 60 years or more)[16].

The approach of Gao *et al.* may prompt fresh thinking. Fieldwork with free-living apes provided information for the evolutionary history of chimpanzee subspecies that was critical to their results. Further fieldwork linking demographic data to biomedical monitoring could be even more productive. The four chimpanzee subspecies have deep evolutionary roots, and may yield further types of SIV beyond the two already identified. These are best studied in the place where the host–virus systems evolved. Chimpanzees in captivity are mostly taken from the wild before they become sexually active, and so rarely harbour SIV. Infection can be expected at higher frequencies in wild adults[17], and such individuals would offer research opportunities that simply do not pertain in captivity, where experimenters cannot know how virus strains match to genetic lineages.

Two other ways forward are these. Field researchers intermittently find fresh corpses of individual apes, often with well-documented life-histories, which offer untapped possibilities for virological analysis. And DNA studies of faeces might allow non-invasive monitoring of virus infection.

Biomedical researchers have the prospect of collaborating with fieldworkers in a synthesis that would benefit conservation. The link between HIV-1 and SIVcpz may open a door for research that helps both humans and apes. □

Robin A. Weiss is in the Windeyer Institute, University College London, 46 Cleveland Street, London W1P 6DB, UK.
e-mail: robinw@icr.ac.uk
Richard W. Wrangham is in the Department of Anthropology, Harvard University, Cambridge, Massachusetts 02138, USA.
e-mail: wrangham@fas.harvard.edu

1. Barré-Sinoussi, F. *et al. Science* **220,** 868–871 (1983).
2. Gao, F. *et al. Nature* **397,** 436–441 (1999).
3. Simon, F. *et al. Nature Med.* **4,** 1032–1037 (1998).
4. Zhu, T. *et al. Nature* **391,** 594–597 (1998).
5. Gao, F. *et al. Nature* **358,** 495–499 (1992).
6. Chen, Z. *et al. J. Virol.* **71,** 3953–3960 (1997).
7. Koralnik, I. J. *et al. J. Virol.* **68,** 2693–2707 (1994).
8. Voevodin, A. *et al. Virology* **238,** 212–220 (1997).
9. Mahieux, R. *et al. J. Virol.* **72,** 10316–10322 (1998).
10. Heneine, W. *et al. Nature Med.* **4,** 403–407 (1998).
11. Weiss, R. A. *Nature* **391,** 327–328 (1998).
12. Sharp, P. M., Robertson, D. L. & Hahn, B. H. *Phil. Trans. R. Soc. B* **349,** 41–47 (1995).
13. Wilkie, D. S. & Carpenter, J. *Biodivers. Conserv.* (in the press).
14. Letvin, N. L. *Science* **280,** 1875–1880 (1997).
15. National Research Council *Chimpanzees in Research: Stategies for their Ethical Care, Management, and Use* (NRC, Washington, DC, 1996).
16. Singer, P. & Cavalieri, P. (eds) *The Great Ape Project* (St Martin's, New York, 1994).
17. Jolly, C. J. *et al. J. Med. Primatol.* **25,** 78–83 (1996).

Condensed-matter physics

Return of the itinerant electron

David Ceperley

On page 412 of this issue, Young *et al.*[1] demonstrate magnetic polarization in a dilute, three-dimensional electron gas at a temperature of 600 K. Years of theoretical debate connect this intriguing result to a long-sought mechanism for ferromagnetism in metals first conjectured by Bloch[2], who suspected that the 'electron gas' is susceptible to magnetic ordering at low density.

What is an electron gas and why is it interesting? The idealized homogeneous gas (also known as jellium or the one-component plasma) has a long history going back to the discovery of the electron. It was used by the early quantum pioneers to model the valence electrons in a solid; they replaced the ions by a rigid uniform background of positive charge. This is arguably the most important model in condensed-matter physics because it is routinely used as a reference state in most realistic calculations of electronic structure. The valence electrons are the outer electrons of the atom, which determine how it interacts with its environment, so understanding the properties of the electron gas is significant. In most metals, the density is high enough that the electrons move almost independently and form a 'normal Fermi liquid' of mobile electrons (Fig. 1) with equal numbers of electrons with up and down spin. But at low density the potential energy dominates the kinetic energy, and the electron 'gas' freezes into the 'Wigner crystal'[3], with the electrons localized on lattice sites. This dependence on density is the exact opposite found in systems with cores, such as atoms, where it is high not low density that favours a lattice structure.

In 1929, Bloch noticed that within the 'Hartree–Fock' approximation (that is, assuming the electrons are in independent states), the spins of the electrons spontaneously align, and he suggested this as an explanation of ferromagnetism. This spin polarization should happen at a density just lower than that found in some alkali metals, such as potassium, rubidium or caesium. But at these densities one cannot ignore the fact that electrons move in a correlated way. In the Stoner model[4] introduced in the 1930s, the electron–electron Coulomb interaction is replaced by a constant repulsive energy between opposite spin electrons, to account for this correlation. The spins only partially polarize and they do so at a lower density. Many theorists have concluded from this and other calculations that the electron gas would never be ferromagnetic[5]. Calculations at an intermediate density are difficult because very small energy differences are important and any approximation has to treat the various 'phases' of the gas with equal accuracy.

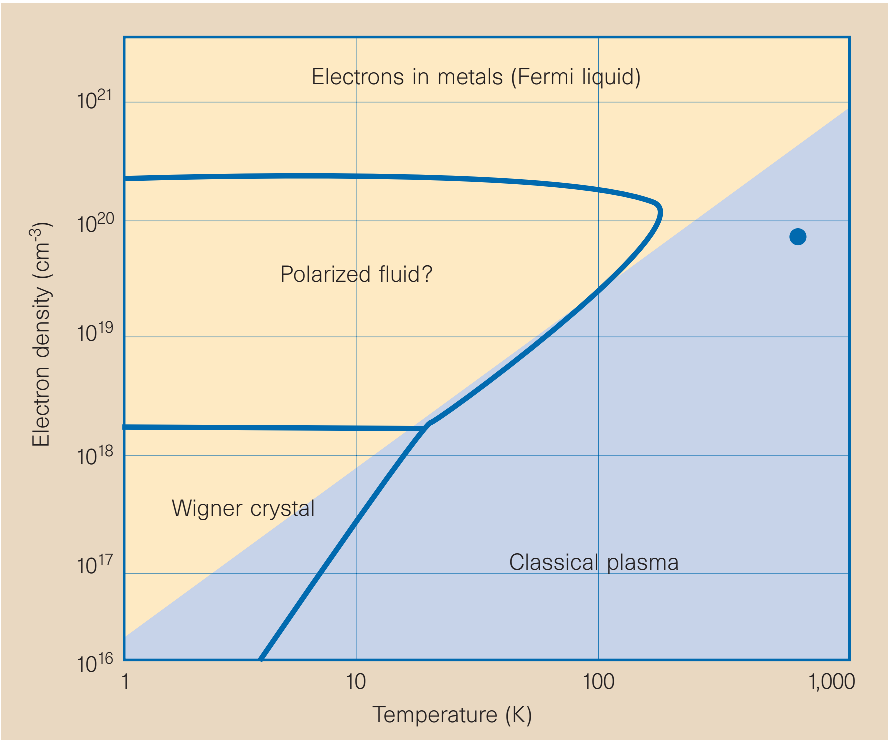


Figure 1 **Phase diagram of the electron gas. The two colours divide the classical (blue) from the quantum (yellow) regimes. The phase transition boundaries are estimates from ref. 6. The dot is the transition temperature measured by Young *et al.*[1].**