AIDS, monkeys and malaria

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Could primate retroviruses have been passed on to man or other monkeys as a result of experiments with primate malarias? An answer to this question could explain the origin of the AIDS epidemic.

SEVERAL theories have been proposed to explain the origins of the AIDS epidemic[1,2]. Most have been speculative rather than testable and several have caused offence[3], particularly those which refer to sexual practices with monkey blood. The important question of the origin of human immunodeficiency virus (HIV) awaits a satisfactory answer.

Three separate outbreaks of primate lentiviruses have been recognized: HIV-1 in Europe, North America and central Africa; HIV-2 in West Africa; and simian immunodeficiency virus (SIV_{MAC}) in North American primate colonies. Both HIV-1 and -2 may have been endemic in parts of Africa for centuries and become epidemic only with the recent profound social and economic changes in these areas. Alternatively, both viruses may have recently entered the human population, in which case the likely origin of HIV-1 is the closely related SIV of chimpanzees, SIV_{CPZ} (ref. 4), and that of HIV-2 is the retrovirus of sooty mangabeys, SIV_{SMG} (ref. 5). There is little doubt that SIV_{MAC} was originally SIV_{SMG} or a close relative[5,6]. The mechanisms of cross-species transfer proposed[1,5] do not offer a plausible unifying hypothesis to explain the three outbreaks.

Direct inoculation of fresh blood is the most efficient way to transmit the AIDS virus. No one has suggested any circumstances under which fresh monkey blood could have been injected into humans in a systematic fashion, and this has not been considered as a mechanism. But the malaria literature describes many instances in which humans were injected with primate blood containing viable malaria parasites[7,8]. Most interest centred on plasmodia of Asian primates, none of which is thought to harbour SIV-like retroviruses naturally[9]. But humans have been directly inoculated with chimpanzee or mangabey blood, and macaques with mangabey blood.

In 1922, Blacklock and Adler injected themselves with fresh chimpanzee blood infected with *P.reichenowi*[10] to see if humans were susceptible to the parasite which might therefore be zoonotic *P.falciparum*. In 1939, Rodhain documented a further 12 attempts to transfer *P. reichenowi* to man[11]. Five chimpanzees were used and the volumes of blood transferred ranged from 2.5 to 15 ml. Most of the chimpanzees would have come from the Belgian Congo, now Zaire. The chimpanzee also has a quartan parasite, *P. rodhaini*, now considered synonymous with *P. malariae*. In various experiments, 6 people were given chimpanzee blood and a further 27 patients with neurosypilis were infected in sequences of up to 14 human-to-human passages [11,12].

P.schwetzi is the tertian parasite of the chimpanzee, and has close affinities with both *P.vivax* and *P.ovale* of humans. Rodhain describes ten humans challenged with chimpanzee blood infected with *P.schwetzi*[11,13]. In 1954–55, a further four adults were challenged with fresh, parasitized chimpanzee blood. Several of these people were then used as the source of blood given to a further six adults[13]. *P.schwetzi* has also been given to volunteer prisoners in the United States, by mosquito passage and direct human-to-human passage[14].

Fewer experiments have been done with *P.gonderi*, the tertian parasite of sooty and agile mangabeys (*Cercocebus atys* and *C.galeritus*) and the drill (*Mandrillus leucophaeus*). Coatney mentions two attempts to transmit this to man by direct inoculation of mangabey blood[15]. Rodhain and van den Berg infected a series of primates with *P.gonderi* originally obtained from an agile mangabey. Two humans were given blood from one macaque with a patent infection and a further neurosyphilitic patient was given parasitized blood from another infected macaque[16]. More recently, *P.gonderi* has been transmitted by blood passage to 17 rhesus macaques (*Macaca mulatta*) and to an unspecified number of *M.radiata*[8].

Thus at least 34 people have received parenteral injections of fresh blood taken from 17 chimpanzees. A further 33 received blood from people given the primary chimpanzee blood injections. Far fewer, perhaps two, are described as being given direct inoculations of mangabey blood. In addition, three people have received blood from macaques infected with mangabey malaria parasites passaged via a baboon. All these recipients of primate blood must be considered at risk of developing retroviral infections if the hosts were infected with SIV_{CPZ} or SIV_{SMG}, respectively.

It is possible, then, to propose a unifying theory to describe how primate retroviruses may have crossed species boundaries into man or other monkey species as an unforeseen hazard of primate malaria experiments. The data are by no means conclusive. There are only a few documented instances of humans having been given mangabey blood. Most of the experiments were in Europe, whereas HIV-2 probably started in West Africa. Some experiments may not have been published, particularly if they yielded negative results. The literature review may be incomplete.

But my theory is testable. It should be possible to determine more accurately the exact background to the experiments in the United States in which macaques may have been given mangabey blood, and to establish what happened to these monkeys after the project was over. The records of human volunteer experiments, particularly those involving prisoners in the United States[8], can be checked to see if any further, unpublished studies took place. Material from several of the original experiments could still exist and could be tested for the presence of retroviruses. Serum samples from some of the patients or from the original primates could have been stored, and Giemsa-stained slides could be available in slide archives. Some of the primate malarias may be cryopreserved and could even contain recoverable retroviruses. It is to be hoped that those with access to this material will test my hypothesis so that the debate about the origin of AIDS can become more scientific. □

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