AIDS casts a longer shadow

The good news is of rapid progress in describing what seems to be a new virus — the bad news, proof of heterosexual transmission and of the mounting prevalence of antibodies.

WHILE no patient has yet been cured of the disease called AIDS (for acquired immune deficiency syndrome), it is proper that there should be full-hearted celebration at what has been done to understand the mechanism of this infection. That is one legitimate response to the appearance of the latest contribution from Dr Robert Gallo, at the National Cancer Institute, and his associates there and elsewhere, in France as well as in the United States (see page 166, this issue). The latest development is that Gallo has been able to clone DNA copies of the RNA genome of the virus, called HTLV-III (for human T-cell leukaemia virus), which was identified as the causative agent of AIDS only a few months ago. Presumably it is now a matter of weeks, not months, before the full nucleotide sequence of the 10,000 or so bases in the genome is known. Quite soon, it should also be known whether the vaccines against AIDS will be effective.

So quick has been the succession of events in this saga that it is easy to forget that the disease was first recognized only as recently as 1981. Inevitably, hindsight showed that the disease was not entirely novel — people had been dying from it for at least a couple of years. The chilling feature of AIDS was, and remains, the high mortality among those affected. In advanced societies, there is still no basis on which to deny that those frankly infected will in due course die, usually of some other infection or from Kaposi's sarcoma. That the disease, for the time being, is largely confined to a few groups of people (male homosexuals, those who inject themselves with narcotics and those dependent on blood transfusions, haemophiliacs especially) does not make the social problem less serious or even allow those not in one of the groups at risk to congratulate themselves that they will never come to harm. If, as is probable, HTLV-III is a virus to which the populations of advanced societies are still naive, it is understandable that it should first infect those to whom transmission is easiest. By the same logic, spread will eventually be more general. AIDS should be everybody's worry.

That is another reason for marvelling at the speed with which so much has been learned about the virus, and at the luck that AIDS did not strike ten years earlier, when it would have been much more difficult to disentangle what is going on. One of the crucial steps in characterizing the disease has been the recognition that an almost invariable accompaniment of overt AIDS is an altered balance between the T lymphocytes called "helpers" and "suppressors". (There are fewer helpers.) These white blood cells are concerned with the regulation of the immune response in ways that are by no means clear. But ten years ago, even the distinction between helper and suppressor cells had not been established.

For the rest, the development of the present understanding of AIDS, and the description of HTLV-III, has followed the path that would have been expected of classical virology — but at an enormously accelerated pace. Gallo's group was able, in 1981, to hit the ground running because of the experience it had acquired in its investigation of the virus now known as HTLV-I, responsible for the disease called adult T-cell leukaemia, first recognized in south-west Japan but then among Caribbean and some African populations. That also upsets the balance between helper and suppressor cells, so that it is not surprising that Gallo and his associates can now also report that the genetic structures of the two viruses have much in common but are also distinct. If that investigation had not been fresh in their minds, it is hard to think that Gallo's group could have made such rapid progress.

But Gallo has not been the only investigator in the field. Professor Louis Montagnier's group at the Institute Pasteur in Paris was formally the first to announce that AIDS is caused by a distinctive virus, in May 1983. That virus, christened LAV, has now been shown to be indistinguishable from HTLV-III, and is also being produced by an infected cultured cell-line. There is even said to be some tension between the two groups. In August this year, Professor Montagnier wrote (see *Nature* **310**, 446) in terms suggesting that he and his associates feared they would be overlooked in all the attention being paid to Gallo's fast-moving high-tech enterprise. That would be absurd as well as unjust, for in spite of what has been learned, so much remains to be learned about the biology of AIDS that everybody's energies will be needed before we are safe.

Mercifully, there is movement even towards that goal. Gallo and his associates have reported (*Science* **226**, 447; 1984) the presence of HTLV-III in the saliva of apparently healthy male homosexuals and in that of people suffering from what is called ARC, or AIDS-related complex (which may or may not be an early form of the disease). They have also recovered HTLV-III from the semen of two AIDS patients (*ibid.*, p.449). Guesses at the method of transmission by male homosexuals are thus confirmed; the bad news is that apparently healthy people can be carriers (and presumably transmitters).

It remains perplexing that so little can at present be made of the prevalence of antibodies against HTLV-III among apparently healthy people. Most AIDS patients carry antibodies against the virus, suggesting that their first response to infection was normal, but that their immune system was eventually overwhelmed. There seems to be abundant evidence (little of it published as yet) that the presence of antibodies is widespread among the groups at risk. Only a proportion of those infected by HTLV-III may succumb to AIDS, but, with the long lapse of time (perhaps four years) between infection and overt disease, it is not yet possible to tell how many of them will develop AIDS. Only prospective studies can serve.

Montagnier and the other members of a Franco-Belgian team have made an indirect and preliminary start on this part of the problem, Working in Zaire (once part of the Belgian Congo), they have traced the origin of the first AIDS cases presenting themselves at hospitals in Belgium in 1981. It now emerges (Brun-Vezinet *et al.*, *Science* **226**, 453; 1984) that as much as five per cent of the population of Zaire may carry antibodies. By using sera kept in hospital refrigerators from earlier investigations, it has been possible to date one case of AIDS to 1977. The same team (Piot *et al. Lancet* **ii**, 65; 1984) has found unambiguous evidence of heterosexual transmission — and an annual incidence of AIDS as high as 20 per 100,000.

On the face of things, AIDS is nevertheless a new disease. Its nearly simultaneous appearence in Zaire, Haiti and the United States suggests that HTLV-III itself is a novel virus, presumably derived from something like HTLV-I. But how? And why does infection have a profound effect on only one class of T cells? Why should Kaposi's sarcoma, normally rare, be such a common sequel?

For the time being, these questions are wide open. But we are fortunate that Gallo and Montagnier were so quick off the mark, and that they and others now have the techniques they need. **John Maddox**