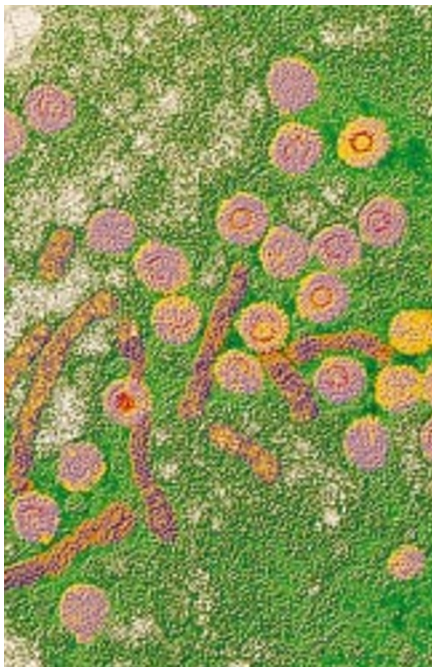

Figure 1 **Coloured transmission electron micrograph of hepatitis B virus particles. The orange spheres are the complete, active virus; brown rods are part of the disassembled virus coat, without a core, and they are inactive.**

invoke Koch's postulates, but these are often unhelpful in chronic diseases because most causal factors are neither necessary nor sufficient for those diseases to occur. Moreover, experimental inoculation of animals is often impossible, or it is irrelevant to human disease. For example, the link between *H. pylori* and peptic ulceration was demonstrated by randomized clinical trials, and the human immunodeficiency virus was shown to cause AIDS by observational epidemiology, rather than by fulfilment of Koch's postulates.

Trials of anti-infective treatments are useful for testing hypotheses about the roles of infection in disease, and their findings have led to the routine use of antibiotics in the treatment of peptic ulceration, Lyme arthritis and, in some cases, even B-cell gastric lymphomas. Vaccines and antibiotics are also being tested in studies for the prevention of liver cancer (hepatitis B vaccine)[9], gastric cancer (*H. pylori* eradication regimens)[10] and cervical cancer (human papillomavirus vaccines)[11].

When the development of an infection may not be preventable, or its effects cannot be fully or rapidly reversed by such treatments, observational epidemiology can be useful in predicting the likelihood of causality. The numerical strength of epidemiological associations provides a particularly good indicator — for example, lung cancer is 20 times more common in cigarette smokers than in non-smokers. Yet, for some persistent infections, epidemiological studies have reported greater than 100-fold associations, such as for hepatitis B virus (Fig. 1) and liver cancer[12], or human herpesvirus-8 and Kaposi's sarcoma[13]. Moreover, human papillomavirus types 16 or 18 are about 30 times more common in women with cervical cancer[14], and *C. pneumoniae* is around ten times more common in atherosclerotic plaques than in disease-free blood vessels.

What diseases might next be linked to persistent infections? Because most chronic diseases tend to have long induction periods, and most persistent infections behave insidiously, few clinical or epidemiological features can be used as definite guides. But certain features of disease may offer clues. These include a high incidence of disease in people who are prone to infections (such as the immunosuppressed); large variations in incidence by geographical region or other patterns of clustering; apparent improvement with antimicrobial treatments; and strong correlations with markers of poverty. On the basis of these and other features, diseases that have been suspected of being (at least partly) caused by infectious agents include Crohn's disease, rheumatoid arthritis, multiple sclerosis, chronic obstructive lung diseases, multiple myeloma, certain leukaemias and lymphomas, and melanoma[7,15–17].

All of these discoveries make a case for a coordinated effort by microbiologists, virologists, molecular biologists, clinicians and epidemiologists to search for new — as well as known — infectious agents in human tissues, and to study their possible correlations with clinical disease. Many human pathogens have the potential to cause chronic diseases, and new technology, combined with modern epidemiology, has made the discovery of new associations more feasible than ever before. □

John Danesh is in the Clinical Trial Service Unit and Epidemiological Studies Unit, University of Oxford, Oxford OX2 6HE, UK. Robert Newton and Valerie Beral are in the Imperial Cancer Research Fund Cancer Epidemiology Unit, Oxford OX2 6HE, UK.

1. Gurfinkel, E., Bozovich, G., Daroca, A., Beck, A. & Mautner, B. *Lancet* **350,** 404–407 (1997).
2. Gupta, S. *et al. Circulation* **96,** 404–407 (1997).
3. Service, R. F. *Science* **275,** 1740–1742 (1997).
4. Goodwin, C. S., Mendall, M. & Northfield, T. C. *Lancet* **349,** 265–269 (1997).
5. Melnick, J. L. *et al. Lancet* **ii,** 644–647 (1983).
6. Chang, Y. *et al. Science* **266,** 1865–1869 (1994).
7. Lorber, B. *Ann. Intern. Med.* **125,** 844–851 (1996).
8. Kingsley, G. *Lancet* **349,** 1038–1039 (1997).
9. Chang, M. H. *et al. N. Engl. J. Med.* **336,** 1855–1859 (1997).
10. Danesh, J., Forman, D., Collins, R. & Peto, R. *Lancet* **348,** 758–759 (1996).
11. McNeil, C. *J. Natl Cancer Inst.* **89,** 281–282 (1997).
12. Beasley, R. P., Hwang, L. Y., Lin, C. C. & Chien, C. S. *Lancet* **ii,** 1129–1133 (1981).
13. IARC Working Group 70–87 (1996).
14. Munoz, N. *et al. Int. J. Cancer* **52,** 743–749 (1992).
15. Krause, A., Kamradt, T. & Burmester, G. R. *Curr. Opin. Rheum.* **8,** 203–209 (1996).
16. Rettig, M. B. *et al. Science* **276,** 1851–1854 (1997).
17. Kinlen, L. J. *Br. J. Cancer* **71,** 1–5 (1995)

Daedalus

No-party democracy

A democratic election, said J. B. S. Haldane, is a way of deciding the result of a civil war without having one. He had a point. In some developing countries political parties are essentially tribal groupings, and an election is a formalized tribal fight. Even in the developed world, the parties used to stand for identifiable social blocs — the workers, the middle class, and so on — and each party favoured its own. This at least gave the voters a choice. But modern parties, as shown in the recent British election, have quite a different strategy. They 'steal each other's clothes'. Each tries to broaden its appeal by devising policies very close to those of its rivals. The result is a complex 'curd' of policies, intertwined and very similar — indeed, often identical. This is the notorious 'Maas-trick', in which all parties collude in the same policy, denying voters any way of rejecting it. But such is the logic of modern consensual politics; so Daedalus is now taking that trick to extremes.

Group decisions are best reached, he says, not by simple voting, but by the Delphi method used in technological forecasting. A secret poll discovers the spread of opinion, which is then displayed to all the voters. Those finding themselves on the extremes of the distribution tend to change their minds; those in the mainstream retain their convictions. So a second round of voting gives a narrower distribution, which is displayed again for a third round of voting. A few iterations usually produce a clear consensus.

Daedalus wants to do this for a whole nation, and the whole range of political policies. Modern media, especially the Internet, seem ideal for the purpose. With DREADCO's computing expertise behind it, a consortium of polling firms could probably do the job whenever an election loomed. All parties could then be presented with one comprehensive set of policies expressing the people's current will. They could only compete by submitting bids to carry them out for the least amount of tax.

Politicians will heave a sigh of relief at not having to invent any more damned policies. They will compete purely for power, which is all they want anyway, and will be judged on their cash flow and competence, which is all that matters in practice. But as the logic of the customer–contractor relationship sinks in, they could find themselves facing novel competition. Bill Gates or Richard Branson might put in a lower bid than any of them.

David Jones