doubts will exist about the causation of antenatal injuries and vaccination injuries, for which the commission supports a cause of action. The question is one of drawing a line, and the fact that it may not be easy in some cases is no ground for refusing a remedy in all cases. In New Zealand the problem has been dealt with by placing a restrictive interpretation on the words "medical misadventure" so that compensation does not result every time medical treatment fails: no compensation was paid when an embolus developed in a leg operation, on the grounds that such an operation has always entailed the risk of blood clotting. In Sweden, too, the system seems to work satisfactorily, actually protecting doctors from the likelihood of being sued in tort and giving compensation to many more than could ever have recovered it previously.

Only in relation to medical experiments does the commission make an exception. Here they cite an instance where the Medical Research Council made an ex gratia payment to a volunteer who developed a neurological lesion shortly after receiving live attenuated influenza vaccine. Lord Pearson recommends that there should be strict liability for any volunteer in medical research who suffers severe damage as a result. Ironically, the commission ignores the point that this would not have availed the volunteer in the MRC trial, since in his case a causal connection could be neither proved nor disproved.

The commission's voluminous recommendations deserve the same painstaking study as brought them into being. In particular, the medical profession and the pharmaceutical industry will have to think deeply about the recommended strict liability for dangerous drugs. The long shadow cast by practolol, which continued to be prescribed after being withdrawn by ICI, has led to the commission's recommending that proof that the manufacturer withdrew or tried to withdraw the product should not be a defence. Doubts may be raised about the justice of that, just as questions may be asked about the long-term wisdom of not permitting a defence of development risk to pharmaceutical companies, especially since the commission proposes no ceiling on the producer's liability. Nor does the commission think that it should be a defence that the Committee on Safety of Medicines sanctioned the sale of the drug. There is much to be discussed before the commission's recommendations reach the stage of legislation before Parliament.

[1] *Royal Commission on Civil Liability and Compensation for Personal Injury* (chairman Lord Pearson). London, HMSO, 1978, cmnd 7054-1, 2, and 3.
[2] *British Medical Journal*, 1975, **1**, 635.
[3] *British Medical Journal*, 1975, **4**, 714.
[4] Cooper, J, *New England Journal of Medicine*, 1976, **296**, 1268.

Whooping-cough vaccines

Two important points about whooping-cough vaccines are clearly made in an article by Dr A H Griffith on page 809 of this issue. Firstly, in the past these have differed appreciably one from another in respect of their toxic effects, as judged by tests in mice; their content of agglutinogens; their potency; and their protective efficacy in children. Their liability to produce adverse reactions was probably equally variable. These points, though well established and known to experts, seem not to be generally appreciated and have certainly not been prominent in the public discussions of adverse reactions after whooping-cough vaccination. Secondly, Dr Griffith's study shows that any manufacturer who accepts his obligation to collect, record, and consider the incidence of reactions to his vaccine faces a frustrating and indeed nearly impossible task.

These conclusions emerged from the efforts made by the Wellcome Foundation to ascertain the incidence of severe reactions after administration of its whooping-cough vaccines. The Wellcome product, it is important to emphasise, was shown by the five-year survey of the Public Health Laboratory Service[1] to be superior in protective efficacy to another British vaccine. During the past 25 years the Wellcome vaccine has invariably been produced on solid medium containing charcoal, a procedure intended to absorb the bacterial toxins from the surface cultures. This method of production is more troublesome and more expensive than that of culture in fluid medium in deep tanks, which was used—at least for a time—by certain other manufacturers of whooping-cough vaccines. Although fluid-culture vaccines can be and are made to meet all the required specifications of the appropriate licensing authorities, Wellcome have taken the view that such vaccines tend to be more toxic in some animal tests than are solid-culture vaccines and that their potency (in terms of standard international units) may have to be reduced to ensure that they pass the toxicity tests.

There was good reason, therefore, for Wellcome to try to ascertain whether their whooping-cough vaccines caused fewer adverse reactions as well as conferring significantly better protection on immunised children. Given the whole picture presented in the public campaigns against whooping-cough vaccines, the details described and assessed in Dr Griffith's paper certainly suggest very strongly not only that deaths and persistent neurological damage were uncommon with the Wellcome vaccine but also that such reactions are difficult to attribute with certainty to the immunisation. After all the relevant information had been collected from the authors of published papers, from hospital records, and from the Committee on Safety of Medicines there seemed to have been only six deaths between 1964 and mid-1977 after administration of Wellcome vaccine. At least three of these were not the result of the vaccine. In addition, five or possibly six cases of persistent neurological damage were recorded after but not necessarily due to administration of the vaccine. Alternative causes were apparent in some of the cases.

Beyond question, therefore, despite some missing pieces of relevant but unobtainable information, there is a prima facie case for investigating whether or not the Wellcome vaccine caused fewer reactions than the others in use at the same time or whether equally detailed investigations of other vaccines would have shown comparably low rates of serious adverse reactions. We need to know whether vaccines made in different ways vary in their toxicity as well as in the protection they provide. Surely it is not beyond our resources and ingenuity to devise a way in which the full details of every protective immunisation are accurately recorded and stored in a national computer. Only in this way could we deal with several important problems at present complicating the immunisation campaign. This campaign is one of our most beneficial efforts in preventive medicine, but it is now frustrated and bedevilled by allegations that cannot be properly assessed by reason of incomplete information.

Whooping-cough vaccines are not our only concern. Some years ago there was an influenza vaccine with an oil adjuvant which had to be withdrawn because it might induce neoplastic changes. How could an effective follow-up to assess such a long-term anxiety be effective without full details of the

identity of those at risk and the batch number of the agent used? How many unnecessary and dangerous doses of tetanus antitoxin are given because the family doctor or casualty department cannot check with a computer to find whether the injured patient has or has not received a full course of immunisation with tetanus toxoid?

Against the proposal to put this information on a computer objectors complain that everyone would require to be given a number. Need this really conjure up visions of a 1984-type of police state—or of dangerous risks of breaches of confidentiality about a person's health record? Surely it is not impossible to devise a system that ensures complete medical confidentiality and does not frustrate such an important objective as the collection and storage of the complete and accurate information we need to assess every aspect of our immunisation campaign.

[1] Final Report to the Director of the Public Health Laboratory Services by the Public Health Laboratory Service Whooping-cough Committee and Working Party, *British Medical Journal*, 1973, **1**, 259.

Genital herpes and cervical carcinoma

The notion that herpes simplex viruses might be responsible for carcinoma of the cervix was first voiced by Nahmias *et al* at the First International Congress for Virology in 1968[1] and later that year in *Science* by Rawls *et al*.[2] Since then, countless papers and reports both supporting and rejecting an oncogenic role for herpes simplex viruses have fanned the controversy—and, incidentally, stimulated worldwide interest in these viruses. A decade later two questions have yet to be answered: how convincing is the evidence that herpes simplex viruses cause cancer? And are the data sufficient to warrant preventive measures?

Given the limitations on human studies and the difficulties attendant in relating a common virus infection with a relatively infrequent event—cervical carcinoma—progress on the first of these questions has been slow but encouraging.[3] Several laboratories have reported that sera from patients with cervical cancer contain antibody that reacts with poorly defined viral antigens,[4–7] while sera from control patients do not react in this way. Confirmation has come[8] of the report by Frenkel *et al*[9] of the presence of herpes simplex virus nucleic acid sequences in tumour cells. The epidemiological aspects, however, remain vague: the concept of the onset of sexual activity at an early age as the prime risk factor does not fully account either for the infected woman who does not develop carcinoma or for the patient with carcinoma but with no evidence of virus infection.[3]

Is the evidence sufficiently compelling to warrant preventive measures? This issue is even more controversial than the dispute about aetiology. Prevention evokes images of massive vaccination, and its opponents argue that the high cost of such a procedure, coupled with questionable effectiveness, rules it out—at least while there is so much uncertainty that herpesviruses cause cancer. The proponents argue, on the other hand, that successful prevention of infection should in fact resolve the aetiological question.[10] Skinner *et al*[11] have recently claimed that their data suggest that childhood or adolescent exposure to type 1 herpes simplex virus might offer some measure of protection against premalignant and malignant cervical lesions. Much of this argument may be irrelevant, however: for, irrespective of whether herpes simplex viruses cause cancer, there are other compelling reasons for attempting to reduce the rate of human infections with the virus. The most important of these are the genital infections of adolescents and adults, with their psychological and neurological complications, including the transmission of the virus to the newborn by the infected mother. Once considered a rare, occupational disease of prostitutes, genital herpes is now recognised as a serious, common infection.[12]

Preventive programmes are likely to fail, however, if they ignore either human behaviour or the biology of the virus. Firstly, it is unlikely that any medical campaign would have any substantial effect on sexual behaviour. Secondly, vaccination may be both impracticable and ineffective. If the virus is indeed oncogenic, the vaccine would have to be free of viral nucleic acids (which would make it costly) or would have to consist of a non-oncogenic virus strain; and lack of oncogenicity in man is impossible to prove without human experimentation. Furthermore, even the effectiveness of vaccination is in doubt because the postconvalescent, so-called immune individual is not protected from reinfection with exogenous virus or from recrudescences of viral lesions caused by virus remaining latent in the body.

The design of a successful preventive programme must rest on the fact that the virus is transmissible from person to person when lesions containing replicating virus are present. These lesions occur during primary infection and at every subsequent recrudescence of the disease. Hence the rate of virus transmission could be reduced, firstly, by abstention from sexual contact during the presence of active lesions and by measures which reduced the frequency and duration of recrudescences. Education of adolescents and young adults in the prevention of sexually transmitted diseases might help with the first aim. Secondly, infectivity might be reduced by the use of cytarabine or similar drugs from the onset of recrudescences to speed up the healing and preclude the synthesis of infectious virus. Thirdly, the possibility of stimulating cellular immune responses should be investigated further, since these seem to determine both the severity of the recurrent lesions and their duration. The unanswered questions are whether cellular immunity could be increased; what is the nature of the optimum immunogen; and how effective is the heightened immune response in preventing primary and recurrent infections.

The immediate, acute consequences of herpesvirus infections require measures to prevent them. This should be our immediate task; for if genital herpes does cause cervical carcinoma then a decrease in the incidence of genital infections should be reflected in a reduction in the cancer rate.

[1] Nahmias, A, *et al*, *International Virology*, 1969, **1**, 187.
[2] Rawls, W E, *et al*, *Science*, 1968, **161**, 1255.
[3] Roizman, B, and Frenkel, N, in *Sexually Transmitted Diseases*, ed R D Catterall and C S Nicol, p 151. New York, Academic Press, 1976.
[4] Azai, T, *et al*, *Journal of the National Cancer Institute*, 1975, **54**, 1051.
[5] Aurelian, L, and Strnad, B C, *Cancer Research*, 1976, **36**, 810.
[6] Hollinshead, A C, *et al*, *Science*, 1973, **182**, 713.
[7] Notter, M F D, and Docherty, J J, *Cancer Research*, 1976, **36**, 4394.
[8] Jones, K W, *et al*, in *Herpesviruses and Oncogenesis III*. Lyon, I A R C, 1978, in press.
[9] Frenkel, N, *et al*, *Proceedings of the National Academy of Sciences of the United States of America*, 1972, **69**, 3784.
[10] Nahmias, A, Naib, Z M, and Josey, W E, in *Oncogenesis and Herpesviruses I*, ed P M Biggs, G de-Thé, and L N Payne, p 403. Lyon, I A R C, 1972.
[11] Skinner, G R B, Whitney, J E, and Hartley, C, *Archives of Virology*, 1977, **54**, 211.
[12] Nahmias, A, and Roizman, B, *New England Journal of Medicine*, 1973, **289**, 667, 719, 781.