we present the clinical description and results of immunodiagnostic investigations in three cases of human infection with pseudorabies virus.

A 52-year-old man (case 1) spent his holidays on the island of Bornholm, Denmark, in 1983. There he took care of a cat which had a bloody discharge from the ears and showed fits of suffocation and choking. He cut his left thumb when washing the cat's dishes and a week later the thumb started to swell and became sore and inflamed. He felt weak, feverish, and sweaty. He noticed dysphagia, dysgeusia, burning and piercing pain in the tongue, dryness and tension in his nose, mouth, and throat, and hypersalivation during meals. Several weeks later he complained about loss of appetite, loss of weight (10 kg), intermittent headache, tinnitus, muscle and joint pain, paraesthesia and loss of tactile sense in hands and feet, and a feeling of inner tension. With slowly decreasing intensity and several relapses the illness lasted for almost a year.

The clinical history suggested infection but routine virological, bacteriological, parasitological, and immunological investigations were negative. He had several thorough check-ups and a year later a neurological examination, including encephalography, electromyography, and electroneurography, was done; all findings were normal. When the patient returned to Bornholm he was told that many cats had died without obvious reason at the time of his first visit and the symptoms described in the cats led us to suspect an epidemic of pseudorabies.

In January 1986 we saw two similar cases—a 43-year-old man and his 41-year-old wife (cases 2 and 3) who had toured the south of France in August, 1985. They also recalled close contact with cats and other domestic animals. However, they did not know if any of these animals were ill. Both had fallen ill at the end of the journey with tiredness, fever, profuse sweating, mild diarrhoea, and painless generalised lymph-node enlargement. They complained of dysphagia, a sensation of dryness and tension in the nose, throat, and mouth, and perception of strange smells and tastes. When we saw them most symptoms had disappeared. The man reported occasional dysphagia; his wife was still weak, with tiredness, slight dysphagia, and tingling sensations. Several months later both had recovered completely. Clinical and neurological examination and laboratory investigations were normal.

Pseudorabies antibody studies were done in all three cases, by virus neutralisation and immunoprecipitation tests.[6] When first tested, 5–15 months after the onset of clinical illness, all three patients were antibody positive with inverse titres of 8 to 16. 2–24 months later the patients were seronegative.

In no previous suspected case of human pseudorabies[2-4] has clinical observation been supported by virus isolation or detection of antibodies. Our three cases strongly indicate that pseudorabies can occur in man. The three patients had had contact with animals and the route of transmission may be by inoculation via the skin or through mucous membranes. The symptoms may start 1–3 weeks after infection, with fever, sweating, weakness, and tiredness. Later central nervous system involvement predominates, especially in cranial nerves I, V, and IX. The symptoms may suggest a psychosomatic syndrome. Infection can be confirmed by assay of neutralising antibodies to pseudorabies virus.

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INTRAVENOUS STREPTOKINASE GIVEN WITHIN 0–4 HOURS OF ONSET OF MYOCARDIAL INFARCTION REDUCED MORTALITY IN ISIS-2

SIR,—The Second International Study of Infarct Survival (ISIS-2) is a large (target about 20 000 patients by Dec 31, 1987 randomised placebo-controlled trial of intravenous streptokinase (1·5 megaunits 'Streptase' infused over 1 h) in acute myocardial infarction. Because the delay from onset of pain to treatment may influence the effects of treatment, the protocol anticipated separate study of patients entered "early" (0–4 h), "intermediate" (5–12 h), and "late" (13–24 h); so far, 45%, 40%, and 15% of entrants, respectively, have been randomised in these periods.

During the period of recruitment, interim results are reviewed confidentially by an independent data monitoring committee. ISIS-2 will eventually monitor post-discharge survival (at 5 weeks and long-term), but at present only mortality in hospital is available (10% dead, average follow-up 1–2 weeks). In January, 1987, the data monitoring committee informed us that among the nearly 4000 "early" patients for whom data were available there was, in their opinion, "proof beyond reasonable doubt" that streptokinase reduced mortality in hospital (from about 12% among placebo-allocated patients to about 8% among those allocated streptokinase).

This difference was considered too large to be due just to the play of chance; moreover it is reinforced by results from other trials of streptokinase.[1-3] It is, however, not yet known how long after discharge this mortality difference will persist, nor whether there are identifiable categories of patient who will, and who will not, gain significant benefit from intravenous streptokinase. Hence, some uncertainty may remain as to who to treat. For example, many physicians do not give streptokinase to myocardial infarction patients aged over 70 (even if they present early), and there may be other categories of "early" patients—defined, perhaps, by electrocardiography, by clinical history, or by clinical judgment—in which it is still not considered clear that streptokinase is definitely indicated.

Most patients with acute myocardial infarction do not present within 4 h of pain, and for "intermediate" or "late" patients there is still wide uncertainty about the effects of treatment. Consequently, ISIS-2 will continue throughout 1987 and patients (whether within 0–4, 5–12, or 13–24 h of pain onset) can be randomised if the responsible physician remains, in the light of this and other evidence, uncertain as to whether streptokinase is indicated.

Reports of completed clinical trials should be refereed, and should involve a full description of methods plus extensive tabulations of results (eg, ISIS-1[4]). This enables doctors to evaluate the evidence critically and assess its implications for medical practice. The need for full details is, if anything, greater rather than less for a trial reported before completion (especially if, as here, only one subgroup is reported prematurely). Until these further details are available, however, this provisional result may be of some practical value, and is presented on behalf of the doctors and nurses who have treated these patients in the 400 collaborating hospitals worldwide. Copies of the protocol are available on request.

Members of data monitoring committee: Sir Richard Doll, Prof P Armitage, Dr D. Chamberlain, Prof D. Julian, Prof P. Meier, and Prof L Wilhelmsen. The manufacturers of 'Streptase' (Behringwerke/Hoechst fund ISIS-2 but are not involved in its conduct or monitoring.

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