Rabies virus, paralytic and classical

SIR,—The report by Dr Lopez and colleagues (Feb 15, p 408) supports the notion that the paralytic and classical (or hydrophobic) types of rabies may result from different forms of rabies virus.[1]

Localised outbreaks of a single clinical type of rabies have occurred in animals and man, a situation unlikely to arise if host factors alone are responsible for the clinical type of rabies. An epidemic of paralytic rabies spread by vampire bats occurred in Trinidad in the 1920s and 1930s. Several thousand livestock cases and more than 70 cases in people of different races were reported. Remarkably, there were no cases of the generally much more common classical rabies in the same period, although a few of the paralytic cases eventually showed some hydrophobic manifestations.[2,3] In 1953 a smaller outbreak of 9 cases of paralytic rabies transmitted by vampire bats occurred among miners in British Guiana;[4] although clinical details are sketchy, all cases apparently had acute ascending myelitis. Two dogs died in camp during the same period after developing paralysis of the hind legs. In 1973 and 1974, an outbreak of paralytic rabies, possibly spread by rats, occurred in Surinam.[5] 7 children were affected, 5 with paraparesis and 2 with facial paresis; no manifestations of classic rabies were reported. In Peru in 1990, Lopez and colleagues have identified an outbreak of classical rabies probably transmitted by vampire bats. Although complete clinical information was not given, paralytic manifestations arose in, at most, 2 of the 29 cases.

In human-to-human transmission of rabies, such as the four cases transmitted by corneal transplant, the clinical type has been the same in primary and secondary cases; this suggests that some characteristic of the virus is responsible for the clinical type of rabies. In the reports from the USA[6,7] and France,[8] the donors and recipients had paralytic rabies; in the report from Thailand,[9] the single donor and both recipients had classical rabies. Rabies virus isolated from the paralytic cases differed antigenically from other human isolates studied.[10]

Further study is needed of the relation between clinical type of rabies and the antigenic characteristics of the rabies virus isolates. Host factors, severity of the bite, size of inoculum, postexposure prophylaxis, and other factors may also modify the clinical manifestations of rabies and may confound the relation between virus strain and clinical type.

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Psychotic reactions to zolpidem

SIR,—Zolpidem, an imidazopyridine derivative, is a novel, rapid-onset, short-acting hypnotic drug lately marketed in several European countries.[1] Chemically unrelated to benzodiazepines, zolpidem is thought to have fewer adverse effects, especially with respect to residual sedation, amnesia, and potential for rebound insomnia and dependence.[1,2] We have seen two cases of psychotic reactions to zolpidem that were similar to previous reports for triazolam[3-5] and that suggest that zolpidem may have side-effects in common with short-half-life benzodiazepines.

Patient 1—A 27-year-old female doctor took 1 tablet of zolpidem 10 mg at 0100 h because she felt nervous. She did not drink alcohol and was not on addictive or other drugs. 30 minutes later, while still awake, she began to experience psychotic symptoms. She told her husband that walls were moving and coming closer. She saw marbles rolling on the ceiling and falling. She pointed to objects that approached her and changed size. During this period, which lasted about 30 min, she looked hypervigilant. She then fell asleep until 0800 h. She felt normal when she awoke and had no memory of these events. She was in excellent physical and psychological health and had not taken zolpidem before. She occasionally used lormetazepam 1 mg, but the last intake had been more than one month previously.

Patient 2—A 26-year-old nurse took 1 tablet of zolpidem 10 mg at 0730 h after returning from her first day of night-shift (2200 h to 0700 h). She had not had any alcoholic beverages or drugs and had been fasting since 0400 h. 20 minutes later, she had the feeling that her bed was pitching and that she was on a sailboat. She called her husband and said that she saw a crowd of at least 25 unknown people around her and that she felt she was suffocating. She also saw spots of various colours. These experiences lasted around 15 min, after which she felt asleep. When she awoke 8 h later she felt perfectly normal and did not remember these events. She was in very good health and had not taken zolpidem in the past. She usually used alprazolam 0·25 mg on the first day after a change of shift. She was not on other medication and did not use alcohol, or addictive drugs.

In these two cases psychotic symptoms appeared after the first intake of zolpidem at the recommended dose. It is noteworthy that neither subject had such reactions to the benzodiazepine that they had taken previously. Nor had they any memory of the adverse reaction reported by their husbands. Similar amnesic events have been described for several benzodiazepines, particularly triazolam.[3-5] Zolpidem and triazolam share pharmacokinetic profiles, with rapid absorption (t_{max} 1·8 h[1] and 1·5 h,[6] respectively, and a very short elimination half-life (2·2 h and 2·3 h, respectively[1,6]). Although chemically unrelated to benzodiazepines, zolpidem acts through benzodiazepine receptors.[7] However, several experimental findings suggest that zolpidem binds selectively to the benzodiazepine receptor type 1 but not to type 2 or type 3.[7] The safety profile of zolpidem has been related to this selective binding.[1,2,7] Our two cases suggest that amnesic psychotic reactions could depend more on the pharmacokinetic profile of the hypnotic drug than on specific binding to benzodiazepine receptor subtypes.

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Retrograde acute lymphangiitis

SIR,—Acute lymphangiitis is classically described as a disorder caused by streptococci (occasionally staphylococci) entering through a peripheral lesion and giving rise to an ascending infection along lymphatic vessels, and which presents as red streaks extending to enlarged and tender regional lymph nodes. Over three weeks one of us (C. B.) occasionally noted tenderness in the left axilla in the morning. The pain extended some way into the arm and was aggravated on extension. No physical signs were present and the pain usually subsided after an hour or two. One day the pain did not go away but increased and spread to reach the dorsum of the hand—and that evening a typical red streak developed along the