

DISCUSSION – SESSION II

Chairmen: J. G. Evans

S. Kanowski

Sex-related use of hypnotics

Professor Kanowski said that more women than men used hypnotics. He did not know of data on dosage levels as distinct from frequency of use. *Professor Evans* speculated that women might develop a habit of using hypnotics during a phase of sleep disturbance associated with the menopause. *Professor Kanowski* thought that a greater prevalence of depressive and psychoneurotic symptoms in elderly women was a major factor explaining their frequent use of hypnotics.

Dr Ather noted the considerable individual variation in response to chlormethiazole and thioridazine, but he said that no analysis had been made to see if either drug was more predictable in its first-time effects. Nor had he examined the possibility of sex-specific differences in response to drugs. Most studies of treatment in elderly groups inevitably enrolled a majority of women.

Ethics of study design

The problem of the Hawthorne effect obscuring the specific effects of drugs in therapeutic trials among chronically mentally impaired patients raised several questions. *Professor Kanowski* commented that the inclusion of a placebo washout period was ethically justifiable, because it was common for elderly patients to show improvement following the withdrawal of long-term psychotropic medication. However, he thought that the management of agitated and distressing behaviour with placebo raised serious problems of ethics and of obtaining the cooperation of nursing staff. He felt that the only acceptable study design was to test a new drug against a generally established treatment as standard.

Professor Dehlin suggested that there might be a specific nosological entity of primary chronic insomnia that would justifiably be treated with hypnotic drugs. *Dr Swift* considered that if such an entity existed, perhaps reflecting age-associated physiological changes, it would be important to measure the balance of benefits and disadvantages arising from a policy of treating it with hypnotic drugs. *Dr Scott* questioned the suitability of the traditional prescribing policy for chlormethiazole of starting with the lowest dose and increasing it as necessary. This could result in patients experiencing side-effects, specifically nasal irritation, without the desired sedation. *Dr Swift* thought that the dangers of over-sedation in older patients justified a cautious approach to dosage.

Professor Kanowski commented that memory impairment had been documented as a side-effect of some benzodiazepines. *Dr Swift* had not included memory assessment in his research protocol, as he had not found a reliable method for detecting memory impairment following single doses of a hypnotic drug.

Side-effects of chlormethiazole

Dr McCarthy noted that he had not seen evidence of clinical dependence on chlormethiazole among elderly patients. *Dr Swift* commented that among a large series of elderly patients he had observed clinical dependence on benzodiazepines but not on chlormethiazole. He speculated that this may be related to the different receptor binding patterns of the drugs. *Dr Campbell* had not seen dependence on chlormethiazole among obstetric patients.

Dr Glatt noted that the low risk of

dependence associated with chlormethiazole prescribed for the elderly contrasted with reports of addiction among some young adult subjects. Could this reflect on the organic origin of the sleep disturbance in older patients, compared with a higher prevalence of neurotic causes in young adults, associated with a higher risk of drug abuse? Another suggestion was that addiction in young alcoholics occurred through excessive prescription of chlormethiazole.

Professor Dehlin had not shown metabolic tolerance developing during chlormethiazole administration, but *Dr Khanna* said experimental evidence showed that chlormethiazole can induce its own metabolism.

Dr McCarthy commented that the importance of vasoactive effects of sedation among the British elderly lay partly with the low bedroom temperatures common in British homes. A sedative which caused postural hypotension leading to nocturnal falls and which impaired body heat conservation by preventing vasoconstriction could be an important cause of hypothermia. At least 4% of people aged 65 and over admitted to Oxford hospitals during the winter had hypothermia.

Professor Kanowski considered that respiratory complications of chlormethiazole were only a danger with intravenous administration. Special care was necessary in treating patients with pulmonary disease.

Dr Swift noted that nasal irritation as a side-effect of chlormethiazole was much less common in older than in younger patients. *Dr McCarthy* commented that nasal irritation had not occurred as a side-effect of chlormethiazole among the elderly participants in his study.

Opinion varied about the frequency and severity of nasal irritation caused by chlormethiazole in young patients which might inhibit its use (even though the problem usually diminishes after a few days of treat-

ment). The frequency of nasal irritation might also be less in alcoholics. *Dr Shaw* suggested this might be due to cross-tolerance between alcohol and chlormethiazole.

Sleeping patterns

Dr Bayer explained that in his study the nurses' assessments were carried out at fixed times during the night and were based on observation rather than systematic evaluation of respiration or movement patterns. *Dr McCarthy* commented that EEG patterns from sleep laboratory data supported the view that patients' reports of their sleeping time were unreliable, but nurses' assessments of sleeping patterns were usually accurate. *Dr Bayer* noted that although a longer period of observation following cessation of drug administration in his trial might have been desirable because long delayed effects of benzodiazepine withdrawal sometimes occurred, the data did not suggest any residual or incipient effects after 5 days without active treatment.

Bioavailability

Professor Dehlin said it had not been possible from his data to determine whether the hypnotic effects of chlormethiazole were correlated with plasma levels, nor whether individual variation in the pharmacokinetics of the drug could be partly attributable to concurrent drug treatment. *Dr Scott* had described the great individual variations in blood levels that may be seen during the first hour after administration. *Professor Dehlin's* study had attempted to standardize the administration of the chlormethiazole capsules with a drink of water, but oesophageal delay and differences in absorption from the stomach due to posture, may affect early blood levels.