



PRESCRIBING INFORMATION

INDICATIONS

ATROMID-S is indicated where reduction of serum lipids is desirable; e.g., patients with hypercholesterolemia and/or hypertriglyceridemia.

Patients with hyperlipemic states involving elevation of both serum triglycerides and serum cholesterol generally have a more favorable response than those with primary hypercholesterolemia and normal triglyceride levels. However, since response is unpredictable, a therapeutic trial with ATROMID-S should be undertaken in patients with hypercholesterolemia.

In patients with essential hyperlipemia and xanthomatosis, frequently the skin lesions have regressed on ATROMID-S therapy.

CONTRAINDICATIONS

While teratogenic studies have not demonstrated any effect attributable to ATROMID-S, it is known that serum of the rabbit fetus accumulates a higher concentration than found in the maternal serum. Presumably, the fetus may not have developed the enzyme system required for the excretion of ATROMID-S. Young women with familial hyperlipemia should not be deprived of this drug, and its use in nonpregnant women of child-bearing age may be undertaken in patients exercising strict birth control procedures. In patients who then plan to become pregnant, the drug should be withdrawn several months before conception.

As pregnancy may occur despite birth control precautions in patients taking ATROMID-S, the possible benefits of this drug to women of childbearing age must be weighed against possible hazards to the fetus. Since it is not known whether ATROMID-S is secreted in human milk, the drug should not be given to lactating women.

This drug is not, as yet, indicated in children since studies in children have been insufficient.

It is not recommended for patients with impaired renal or hepatic function. For Precautions and Adverse Reactions, see Compendium of Pharmaceuticals and Specialties.

DOSAGE AND ADMINISTRATION

For adults only.
The recommended dose is one capsule (500 mg) four times daily.

AVAILABILITY

No. 3243 — Each capsule contains 500 mg clofibrate, in bottles of 100.
Further information, references, and scientific brochure available on request.

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M-2442/10/69

Delirium from Misuse of Dimenhydrinate

We here report a case of severe delirium, closely resembling atropine poisoning and with possible extrapyramidal symptoms, following ingestion of an overdose of dimenhydrinate taken by an 18-year-old man as a substitute for marijuana or lysergide.

REVIEW OF LITERATURE

Dimenhydrinate (Gravol; Horner) may be purchased in Canada without prescription. It is recommended for the prevention and relief of nausea, vertigo and vomiting in motion sickness and other clinical disorders.¹ Pharmacologically it is classed as an antihistamine.²

Apart from a single newspaper report³ we have been unable to find a report of toxic psychosis due specifically to dimenhydrinate, or of its use for "kicks".

Over the past year, however, there have been reports of the use of other antihistaminic drugs by young people to obtain a "high". Gott⁴ described the use of cyclizine (Marzine; Burroughs Wellcome) by a group of youths. Nigro⁵ reported a toxic psychosis due to diphenhydramine hydrochloride (Benadryl; Parke Davis); his patient, a 16-year-old girl, had taken an overdose after being disciplined for some acting-out behaviour, and had probably swallowed 10 capsules of 50 mg. each. She developed a hallucinatory delirious state with marked signs of cholinergic hypofunction. Her mental state reverted to normal 29 hours after ingestion of the drug. The initial symptoms were thought to resemble an acute schizophrenic reaction, with loosened association, autism, affective blunting, inappropriateness, ambivalence and visual hallucinations.

The effects of overdosage with antihistamines have been reported previously. Waldman and Pelner⁶ reported two patients with toxic delirium, dry mouth, fever and mydriasis after prophenpyridamine (Trimeton) ingestion. They suggested the use of neostigmine in the therapy of this type of reaction. Wyngaarden and Seevers⁷ reviewed the toxic effects of antihistaminic drugs, and analyzed 11 fatal and 18 non-fatal cases of overdosage. They listed 66 symptoms of acute toxicity, grouped according to the system affected; these included various symptoms of toxic psychosis, atropine-like effects and central nervous system effects. The latter are quite varied, but do not include extrapyramidal symptoms. These authors also listed a number of "unusual reactions", e.g. narcolepsy, shock-like states, labyrinthitis, cardio-spasm and syncope. They stated, incidentally, that the pupillary dilatation caused by diphenhydramine could be abolished by thiopental, which would suggest that this effect is a direct central action of the antihistaminic drugs rather than a peripheral atropine-like action.

Gott⁴ states that antihistamines, as well as non-prescription medications containing scopolamine or stramonium, are potential hazards because of their ready availability to irresponsible persons. Nigro⁵ states that patients taking diphenhydramine warrant close observation for behavioural aberrations, and that the onset of an acute psychosis demands a search for a possible drug etiology, including diphenhydramine.

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CASE REPORT

An 18-year-old man was brought to the Emergency Department of the Winnipeg General Hospital at 3:00 a.m. on December 28, 1968. He had left his boarding house at 9:00 a.m. on the previous day and when he returned at midnight he was incoherent, emotionally labile and violent. His landlady called the police, who brought him to the hospital and also brought three empty bottles, each of which had originally contained 25 tablets of dimenhydrinate, 50 mg. When first seen he was incoherent and violent, and four policemen were needed to restrain him. He had visual and auditory hallucinations: he imagined that a friend was present, conversed with this imaginary friend and appeared to listen to his "replies". He appeared to be out of touch with his environment, was in contact with the examiner for only fleeting moments, and did not answer questions regarding orientation and memory. His affect was one of extreme fear.

Physical examination revealed a muscular young man with long hair and marked acne, whose pupils were widely dilated and whose lips and oral mucosae were dry and parched. A brown film covered his teeth. Pulse was 128 per minute and regular, respiration 20 per minute, blood pressure 160/100. There were no other abnormal neurological signs. The urinalysis and blood count were normal; the urine was negative for barbiturates and phenothiazines.

Sedation was thought to be required and he was given a slow intravenous injection (10 minutes) of 200 mg. chlordiazepoxide (Librium; Roche), which was repeated 20 minutes later. These injections were given cautiously with monitoring of blood pressure, heart rate, respiratory rate and state of delirium.

He was much less violent at the end of this treatment, but remained restless and agitated. Over the next five hours he received two litres of 5% glucose in water and was incontinent of urine a number of times.

At 8:00 a.m. his temperature was 99.1° F., pulse 112 per minute, respirations 22 per minute and blood pressure 128/86. He was now awake, but although he had received routine oral care, he was unable to swallow or to speak clearly. He seemed, in fact, to have difficulty in moving his lips and tongue. His pupils remained widely dilated and there was still a total absence of saliva. He was flushed and restless. Because of the difficulty with swallowing and speech,

which resembled that found in drug-induced dystonic reactions which respond to antiparkinsonism drugs, he was given 2 mg. benzotropine mesylate (Cogentin; Merck, Sharp & Dohme) intravenously. After this his swallowing appeared to improve to some extent. At 11:00 a.m. he was given a further 2 mg. of benzotropine intramuscularly. He seemed to be awake and aware of his surroundings, his swallowing had improved and he was able to take oral fluids, but he still had some difficulty with speech.

By 11:00 p.m. he was quite lucid, and expressing a great deal of anger towards his landlady for having called the police. It was now possible to obtain a coherent history from him, although he had one amnesic period. He had been with a group of friends with whom he had been accustomed to take marijuana and lysergide. On a previous occasion he had taken 10 dimenhydrinate tablets (50 mg. each) but had been disappointed in the effects produced. On this occasion he thought he took between 18 and 25 tablets. Growing alarmed when he began to see smoke coming from the ears and noses of those sitting around him, he got up to go home, but has no recollection of how he got there, nor any further memory of events until he recovered in the hospital.

He has an unstable background. His parents are separated, both are alcoholics, and he has never seen his father. He has been partly brought up in foster homes, is a ward of the Children's Aid Society, and has a brief record of minor delinquency.

By December 29 he was eating well and had no hallucinations. On December 30 he was discharged to continue supervision by the Children's Aid Society and with a recommendation for psychiatric outpatient treatment.

DISCUSSION

The use of over-the-counter preparations for their euphoriant and hallucinogenic properties has been well documented. We found that the resulting psychosis in this case was indistinguishable from an atropine delirium, with the possible exception of the marked difficulty in speech and swallowing. These symptoms could have been partly explained on the basis of the extreme dryness of the mouth, but our impression was that the condition was more an inability to

move the tongue and lips, and some improvement seemed to follow the injections of benzotropine. There were, however, no other neurological signs, apart from the dilated pupils, and extrapyramidal syndromes have not been previously reported as a reaction to antihistamines.

The cautious use of intravenous chlordiazepoxide to control the agitation and prevent exhaustion in this case appears to have had no adverse effects. We were not at the time aware of the recommendation by Waldman and Pelner⁶ that neostigmine might be used in the therapy of this type of reaction, but in the only case in which they report its use the effect is difficult to evaluate. Goodman and Gilman² state that there is no specific therapy for antihistamine poisoning.

There would seem to be good reason for concern about the ready availability of a variety of medications which can be used as hallucinogenic and euphoriant agents. Many of them, as in the case of dimenhydrinate, can be obtained by the public quite legally in any quantity. Many times the normal dose is required to produce the desired effect. There is, for many of these preparations, no precise determination either of the lethal dose or of the dose required to produce euphoria and hallucinations. This double uncertainty, coupled with the tendency of those who abuse drugs to be somewhat haphazard as to the quantity they take, leads to the possibility of fatal overdosage, when the intention may be merely to produce a "high".

We acknowledge with thanks the co-operation of Dr. John Rae, Medical Director, and the Documentation Service of Frank W. Horner, Ltd., Montreal, for assistance in finding references.

This case has been reported to the Drug Adverse Reaction Program, Food and Drug Directorate, Department of National Health and Welfare.

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