A criticism of the use of tricyclic antidepressant drugs in the treatment of childhood enuresis

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Doctors under pressure are inclined to accede to their patients' demands for drug treatment simply because an attempt at health education is time-consuming and often the advice given is unheeded. Tricyclic antidepressant compounds are being used in increasing amounts in both the treatment of adult depression and the treatment of childhood enuresis. Their use in the former may not be in doubt, but considerable doubt must now be expressed about their use in enuresis.

Recent experience in hospital practice of dealing with cases of poisoning in children with these drugs, made me aware of the severe effects of a potentially lethal drug on otherwise healthy children.

Effectiveness of tricyclic compounds

The drug manufacturers claim that a large percentage of enuretic children may be expected to be completely dry or greatly improved soon after starting treatment with imipramine or amitriptyline. This statement is based on studies which have involved relatively small numbers of children.

In addition, the children involved had been very carefully followed-up by doctors particularly interested in this subject and the role of the doctor is as important as the drug in the treatment of enuresis. Noack (1964) found only 14 out of 44 enuretic children dry after a year's treatment with a tricyclic compound. Poussaint and Ditman (1965) in a study of 50 outpatient enuretic children, found that 14 (28 per cent) failed to benefit at all from treatment with imipramine. In addition, only 11 out of 47 cases treated with imipramine remained dry after two months' medication and they were followed-up for only one to three months. Shaffer *et al.* (1968) found that 20 out of 56 children became dry while on the drug, but only two remained dry after its withdrawal.

Dische (1971) emphasises the chart in itself has a therapeutic role and it is significant that drug companies produce 'star charts' which may have as much effect as the drug itself.

Increase in prescribing of tricyclic compounds

Parish (1971) has reported the large increase in prescribing of tricyclic compounds in adults. In England and Wales in 1962 there were 0·7 million prescriptions for imipramine and 0·3 million prescriptions for amitriptyline. The comparative figures in 1968 were 1·2 million for imipramine and 2·4 million for amitriptyline.

Prescriptions for these compounds to children under the age of 15, show a similar increase. In the practice in which I am working, during the two-year period 1969–1970, 92 children with enuresis were treated with tricyclic compounds and received a total of 230 prescriptions for imipramine and 31 prescriptions for amitryptyline.

In addition, it was significant to note that 58 (62 per cent) of the 92 mothers of these children during that two year period, had on one or more occasions, received treatment with sedatives, tranquillisers or antidepressants. Nineteen (20 per cent) of the mothers had actually been taking imipramine or amitriptyline at the same time as their children.

Obviously where additional anxiety exists in the home, the child is unlikely to benefit from drug therapy and unfortunately many enuretic children come from an environment where unsatisfactory control of drug consumption co-exists.

The ease of access of children to these compounds, prescribed both for their own enuresis and for their parents' depressive illnesses, suggests that more careful consideration should be given to the use of these drugs in unsuitable home conditions.

Dangers of accidental ingestion

The first case of imipramine poisoning was described by Noack (1960). The danger to children of accidental ingestion has become increasingly recognised in recent years (Giles, 1963; Steel *et al.*, 1967; Penny, 1968; Teitelbaum, 1969; Young and Galloway, 1971). In 1968 there were only 17 recorded cases of poisoning by tricyclic compounds in children, by 1970 36 cases had been reported.

The effects of poisoning are severe. The toxic effects simulate atropinism and include hyperpyrexia, convulsions, agranulocytosis and allergic reactions. Some of the most severe effects occur in the cardiovascular system. These include hypotension, atrioventricular dissociation, atrial fibrillation, intraventricular conduction defects and myocardial infarction.

Amitriptyline and imipramine are absorbed quickly from the intestinal tract and are largely bound to plasma proteins and this means that in cases of overdose treatment must be initiated fairly quickly after ingestion of the drug. There is no specific antidote; treatment of acute poisoning is mainly supportive.

Tricyclic compounds are now second only to salicylates as a cause of death due to self-poisoning in children. The causes of death in children under ten years in England, Wales and Scotland from accidental ingestion of poisonous substances, for the period 1965–69, are as follows (Registrar General, 1969):

Salicylate poisoning	39
Tricyclic antidepressant poisoning	22
Medicinal iron poisoning	17
Barbiturate poisoning	14

Fraser (1971) collected information on the circumstances of 20 children's deaths from imipramine poisoning. Most of the children were one, two or three years old. For whom had the drug been prescribed?

for the mother	12 cases
for a grandparent	3 cases
for adults unrelated to the child	2 cases
for an aunt	1 case
for an enuretic sibling	1 case
for the child who died (for enuresis)	1 case

Thus the hypothesis that fatal antidepressant poisoning might often be due to the use of these drugs for the treatment of enuresis was not upheld. However, a large number of children are now being admitted to hospital with poisoning due to tricyclic compounds and many of these children have ingested the drug, which had been prescribed for their own enuresis or that of a sibling. In the Royal Hospital for Sick Children, Edinburgh, in 1968, there were seven recorded cases of poisoning by tricyclic compounds and by 1971 there were 20 cases. Similar increases in cases of Tricyclic poisoning have been noted by other hospitals. Are we going to reach the stage when there will be reports headed; 'Deaths due to enuresis?'.

Alternatives to drug therapy

Brazelton (1962) has described a child-orientated training scheme where mother and child are involved at an early stage in discussion about toilet training. Basically the matter must be dealt with under the umbrella of health education. In large group practices, there is an argument for enuretic clinics where one of the group takes a special interest in this subject and certainly a well-motivated and interested practitioner can do a great deal for the enuretic child. Naturally not every general practitioner is interested in enuresis but seeing a child for five minutes and issuing a prescription is not the answer.

The results of buzzer training (Young, 1965) show that with adequate supervision by parents and doctors at least 75 per cent of bedwetters should become dry with this method. There are few factors which form outright contra-indications to buzzer training. It seems ironical that the 'buzzer alarms' are scarce and yet potentially dangerous drugs are readily prescribed. A recent report (Dische, 1971) showed that a good measure of success was achieved with sympathetic handling alone and the use of drugs was questioned.

Summary

The increasing use of tricyclic compounds in the treatment of childhood enuresis is questioned. The dangers of overdose are emphasised and the prescribing of these drugs where unsatisfactory home conditions prevail is not recommended.

It may be that many practitioners do not have the time to discuss with mothers the management of their children's enuresis. I have encountered parents who have increased the dosage on their own initiative and they had been totally unaware of the dangers of overdose. I have also met mothers who have allowed their children to take their own medicine at night. Imipramine and amitriptyline syrup are both pleasant to taste and the tablets are small and inviting to the young child. It is therefore essential to warn parents of the dangers of these drugs, but are drugs going to be successful when parents are unsure of their safety?

Doctors must consider the justification for continuing to prescribe vast quantities of these compounds in circumstances where children may have easy access to them and where the children themselves may be taking the drug unnecessarily. The relatively low therapeutic indices of these drugs, especially in children, should be borne in mind by those who prescribe them. There must be a lesson to be learned from the fact that tricyclic compounds are now second only to salicylates as a cause of death in children due to self-poisoning. "The drug treatment of enuresis requires caution. Not infrequently and despite the arguable evidence of its efficacy the doctor has accepted the idea of drug treatment, perhaps because to do so seems to save his time, perhaps to comfort the family and play for time while the child recovers" (Apley and Mackeith, 1969).

I do not presume to know the answers to the problem of childhood enuresis, but I am of the opinion that tricyclic compounds have a limited role to play in the treatment of this condition. They are not so effective as some would have us believe and the relapse rate is high.

REFERENCES

Apley, J. & MacKeith, R. (1968). *The Child and his Symptoms*. Second ed. Oxford: Blackwell Scientific Publications.
Brazelton, T. B. (1962). *Paediatrics*, **29**, 121–128.
Dische, S. (1971). *British Medical Journal*, **2**, 33–36.
Fraser, M. S. (1972). *Practitioner*, **208**, 203–211.
Giles, H. McC. (1963). *British Medical Journal*, **2**, 844–846.
Noack, C. H. (1960). *Medical Journal of Australia*, **2**, 182.
Noack, C. H. (1964). *Medical Journal of Australia*, **1**, 191–192.
Parish, P. A. (1971). *Journal of the Royal College of General Practitioners*, **21**, Suppl. 4.
Penny, R. (1968). *American Journal of Diseases of Children*, **116**, 181–186.
Poussaint, A. F. & Ditman, K. S. (1965). *Journal of Paediatrics*, **67**, 283–290.
Registrar General. (1969). Statistical Review of England and Wales. London: H.M.S.O.
Shaffer, D., Costello, A. J. & Hill, I. D. (1968). *Archives of Disease in Childhood*, **43**, 665–676.
Steel, C. M., O'Duffy, J. & Brown, S. S. (1967). *British Medical Journal*, **3**, 663–667.
Teitelbaum, D. T. (1969). *Journal of Paediatrics*, **75**, 523–524.
Young, G. C. (1965). *Developmental Medicine and Child Neurology*, **7**, 557–562.
Young, J. A. & Galloway, W. H. (1971). *Archives of Disease in Childhood*, **46**, 353–355.

ORAL PENICILLING IN URINARY INFECTIONS

A detailed case-report and a clinical trial of oral penicillin G in the treatment of urinary infection are reported. Six general practitioners and 530 patients were involved in the trial, part of which was 'double-blind'. It was found that oral penicillin G at a dose of 500 mg six-hourly for two weeks was as satisfactory as established regimens for treating this common condition.

Hulbert, J. (1972). Gram-negative urinary infection treated with oral penicillin G. *Lancet*, **2**, 1216–1219. Author's summary.