TODAY'S DRUGS

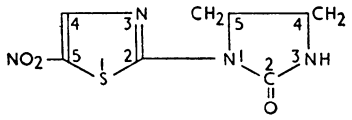
With the help of expert contributors we publish below notes on a selection of drugs in current use.

Niridazole

This drug is manufactured by Ciba Laboratories Ltd. and is marketed overseas under the name Ambilhar. It has been introduced principally for the treatment of schistosomiasis, but is also active in amoebiasis and in Guinea-worm infection.

Chemistry and Pharmacology

Niridazole is 1-(5-nitro-2-thiazolyl)-2-imidazolidinone.



It was synthesized in the course of studies on the pharmacological and therapeutic properties of nitro-derivatives of various heterocyclic compounds. Chemical methods of assaying the drug in body fluids have not so far been evolved, but a good deal of work has been done on its metabolism by labelling the carbon atom at position 4 of the imidazoline ring with carbon-14. These studies have shown that the compound, which is given by mouth, is absorbed over a period of several hours. It passes in the portal blood to the liver, where it is largely broken down into metabolites at its first passage. Because of slow absorption and rapid breakdown a low but therapeutically active concentration is maintained in the blood when the drug is given at 12-hourly intervals. The metabolites attain a high concentration in the blood, and are slowly excreted in the faeces and in the urine, which is coloured dark brown. The metabolites seem to have no effect on either host or parasite, but the worms absorb the drug itself and are unable to excrete the metabolites. Experimental work has shown that the initial effect of the drug upon the worms is to impair egg-production in the females, which then die and are eventually absorbed. The male worms are less sensitive, but they also are killed.

Clinical Trials

Clinical trials[1-3] of niridazole have been made in many parts of the world. Before its introduction the therapy of schistosomiasis had been very largely based on trivalent antimony compounds. These have serious disadvantages—they must be given by injection, often slowly intravenously, and they leave a much smaller margin between effective and dangerous dosage than is desirable. In short, they are for the most part unsuitable for the mass treatment of a disease which affects some 200 million people throughout the world. Niridazole has an initial advantage over the antimonials in that it is given by mouth. It has been long known that infections with *Schistosoma haematobium* are more readily cured than those with *S. mansoni,* which in turn is more susceptible than *S. japonicum.* The results with niridazole fall into this pattern. Nearly all cases of *S. haematobium* seem to be cured by a single course of treatment ; *S. mansoni* cases are more resistant and the reported success rates vary from 47% to 100% ; published results in *S. japonicum* infections are few and so far indicate amelioration rather than cure. Here the point should be made that "cure" in schistosomiasis means different things to different people. Some workers maintain that no demonstrable eggs should be excreted four months after the completion of treatment if a complete parasitological cure is to be claimed. Others hold that the excretion of black, unhatchable, and apparently dead eggs may continue for four months after treatment without excluding possible cure. Furthermore, the effect of treatment on the numbers of eggs excreted is of importance, as a substantial fall in numbers indicates the destruction of a corresponding proportion of female worms and a corresponding reduction in consequent damage to the host's tissue. There seems to be no doubt that niridazole, even when it fails to kill all the worms, none the less kills a large proportion of them as judged by subsequent egg-counts.

Amoebiasis

The action of niridazole on amoebic dysentery and amoebic liver abscess has been shown to be usually curative. It has been pointed out that niridazole is the only drug currently available which will act upon *Entamoeba histolytica* both in the tissues and in the lumen of the large intestine. Nevertheless, the available methods of treating amoebiasis are so satisfactory that niridazole is perhaps unlikely to replace them as the first line of treatment.

Guinea Worms

Guinea-worm infections, though of minor importance compared with schistosomiasis and amoebiasis, are none the less responsible for much discomfort and disability and sometimes for permanent crippling. Hitherto there has been no satisfactory way of dealing with these parasites. Now it has recently been shown that a seven-day course of niridazole is lethal to the worm, which is either spontaneously discharged from the ulcer or can readily be withdrawn.

Toxic and Side-effects

The common side-effects of niridazole are minor in character and include slight nausea, occasional vomiting, headaches, and drowsiness. Less usual are psychic disturbances, which are worse at night and take the form of confusion, apprehension, and hallucinations. A rare but serious side-effect is the occurrence of epileptiform convulsions, which have led to death on one occasion.[4] Convulsions are a clear indication for cessation of treatment ; the other side-effects are not, and cease within a few hours of completing the course.

Dosage

The daily dose is 25 mg./kg. body-weight, given at intervals in two or three equal amounts. 0.5 g. eight-hourly is an average adult dose. It should be given for seven days in Guinea-worm infections and urinary schistosomiasis and for 10 days in amoebiasis and intestinal schistosomiasis.

Price

Niridazole is not yet marketed in Britain.

REFERENCES

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3 McMahon, J. E., and Kilala, C. P., *Brit. med. J.*, 1966, **2**, 1047.
4 Nicholson, N. G., and McMahon, J. E., ibid., 1261.