Drug Treatment of Disease

MIGRAINE: PART II*

BY

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DRUGS TO REDUCE FREQUENCY AND SEVERITY OF ATTACKS (cont.)

5. Hormones

As one would expect, there is hardly a hormone which has not been tried in migraine or which has failed to elicit laudatory claims. Cortisone is sometimes useful to offset the nausea induced by ergotamine, but otherwise the only hormones which may be expected to be helpful are the progestogens, and these only in one type of the disease—premenstrual migraine. Their use in this fairly common form of migraine has been fully described by Greene and Dalton (1953). In brief, if attacks of migraine occur consistently at the time of ovulation or during the last 10 days of the menstrual cycle or both, progesterone should be given intramuscularly in a dose of 25 mg. or more on alternate days for a week before the expected attack. The injections are continued until the day before the expected onset of menstruation. The treatment is successful in about 80% of cases, but it is often necessary to repeat it regularly month by month. Experiments are now in progress to determine whether 19-norethisterone, which is active when given by mouth, may be used to replace parenteral progesterone. Ethisterone (10 mg. three times a day by mouth) has been found beneficial in a minority of cases.

The mechanism of action of progestogens is still uncertain. The current hypothesis, which does not account for all the facts, is that an unduly high oestrogen:progestogen ratio, present at the time of ovulation and in the premenstrual phase, induces retention of water, perhaps by causing retention of sodium. The water retention causes sufficient cerebral oedema to act as a "trigger" in women in whom a constitutional tendency to migraine is present.

6. Antihistamine Drugs

Histamine, a powerful vasodilator, can cause headache in healthy people by dilating the cranial arteries, and it appears that some patients are peculiarly sensitive to histamine. Some physicians have held that the dilatation of the cranial arteries which accompanies the painful phase of migraine is a "histamine effect," and in consequence many antihistaminic drugs have been tried in this affliction, and isolated successes have been reported. I am not aware of a large controlled trial. The antihistamine drugs are very numerous and cannot all be described here.† Their hypnotic properties are a disadvantage when treating this type of headache.

*Part I appeared last week; Part II concludes the article.

†The pharmacology of the antihistamines was reviewed by Professor J. H. Burn, F.R.S., in an earlier article in this series (*Journal*, October 4, p. 845).

7. Histamine and Neostigmine Desensitization

Histamine desensitization can be achieved by the subcutaneous injection of gradually increasing doses, but it has not been conclusively proved that the method has prophylactic value in true migraine, and it is troublesome to carry out. Similar doubts arise in considering the procedure of neostigmine desensitization, which is based on the hypothesis that the arterial dilatation is due to acetylcholine. As neostigmine inactivates cholinesterase, the injection of gradually increasing quantities might accustom the body to the action of acetylcholine. The value of the method remains questionable. Desensitization to specific allergens has, perhaps, a sounder foundation, but is also of unproved value.

8. Miscellaneous

All or almost all the vitamins, thiocyanate, calcium, potassium perchlorate, belladonna, and numerous vasodilators and vasoconstrictors have been suggested. It is noticeable how often an author has described his success in a few cases and has failed to publish later the results of a more extended trial. "Let us use these new drugs while they still work." Of late, hydantoines such as phenytoin sodium B.P. ("epanutin") have been tried, but I have heard of no controlled investigation and have no experience of them.

DRUGS WHEN AN ATTACK THREATENS

1. Analgesics

Migraine is not invariably accompanied by severe pain, and in mild cases satisfactory relief may often be obtained by the use of common analgesics such as aspirin and amidopyrine. It is hardly ever justifiable to use more powerful analgesics such as pethidine or opium alkaloids. Migraine is a not uncommon cause of drug addiction.

2. Barbiturates

Even in more severe attacks, barbiturates may be useful, especially for their capacity to allay the accompanying fear. Many patients find "veramon," a combination of amidopyrine, 286 mg., with barbitone, 114 mg., an excellent remedy, but the danger of agranulocytosis from amidopyrine, uncommon though it is, must not be forgotten.

3. Hormones

Progesterone, so valuable as a prophylactic in true premenstrual migraine, is useless in the treatment of an acute attack. On the other hand, cortisone, which is both useless and, because of its side-effects, inadvisable as a prophylactic, may in an occasional case entirely abort an attack. It should be given by mouth at the very beginning in a dosage of 50 to 200 mg. If vomiting is an early symptom it may be given intramuscularly.

Even when it fails to prevent headache, it may reduce the nausea and vomiting caused by ergotamine. A.C.T.H. (25 to 100 mg. by injection) has a similar effect, which is slower in onset but more durable.

4. Miscellaneous

An immense variety of measures has been claimed as beneficial for some patients. In our ignorance of the initiating mechanism in the majority of patients, it is justifiable to try them one by one if better-attested methods have failed. Such are nicotinic acid (25 to 100 mg.), antihistaminic drugs (see above), including dimenhydrinate (50–100 mg. by injection), chlorpromazine (see above), inhalation of oxygen, the injection of procaine in the neighbourhood of the most painful area, nitroglycerin (0.3 mg.), amyl nitrite inhalations, and counter-irritants applied to the scalp. It is probable that the effect of most of these measures may be ascribed to the comforting feeling that something is being done.

5. Ergotamine Tartrate

Ergot remains the most important drug in the treatment of the acute attack.

In a small proportion of cases, ergotamine tartrate tablets, 2 mg., given very early in the attack, and repeated hourly to a limit of 10 mg., may confine the attack to the phase of vasoconstriction, the relatively tolerable phase. The patient is required, and indeed prefers, to remain recumbent in a dark room, preferably alone and free from the fussing of solicitous relations. Unfortunately, the dose needed to abort the pain is too often high enough to cause toxic effects, which to many patients are more unpleasant than an untreated attack. These are nausea, vomiting, muscle cramps, an ineffable feeling of prostration, and sometimes a phobia for the drug itself. These effects may, in some patients, be prevented by the administration (if possible even before the ergotamine) of atropine, dimenhydrinate, or chlorpromazine. Prednisolone may be extremely useful, given by mouth or, if vomiting has begun, by injection, in doses of 5 mg. to 25 mg. Some patients find that dihydroergotamine, of which about double the dose of ergotamine is needed, is better tolerated. Whichever drug is used, an effort should be made to find the minimum dose which will prevent or alleviate the headache without production of side-effects.

Ergotamine tablets are the simplest but least reliable of the preparations available. In such cases, one of the available combinations with caffeine may be tried, as described above. Other patients will require rectal suppositories (2 mg. with or without caffeine), which are often more reliable and produce side-effects in fewer patients. Severe cases usually need parenteral administration, and patients should be taught how to give the injections to themselves. It is remarkable that, though no doctor would think of treating a diabetic without teaching him the technique of injecting insulin, few make the effort when migraine is the complaint. Ergotamine tartrate is supplied in ampoules of 0.25 mg. in 0.5 ml. and may be given subcutaneously by the patient or intravenously by the doctor in emergency. But, if a doctor has to be sent for, the administration is usually too late. Again, the minimal effective dose should be found by trial and error. The dose may be repeated after an hour or two, but not more than 1.5 ml. of ergotamine tartrate or 3 ml. of dihydroergotamine methanesulphonate should be given in a day.

The contraindications to the use of ergot have been given in the description of its prophylactic use. One point should be added: the over-frequent use of ergotamine has been known to increase the frequency of attacks. It should be used as rarely as possible and in the minimal effective dosage.

The very success of ergotamine treatment in a high proportion of patients has its dangers. It is all too easy for the overburdened general practitioner to teach his patient the technique and thereafter to confine his activity to the prescription of further supplies. The disorder needs close supervision if an increase in the frequency of the attacks and the onset of chronic ergot poisoning are to be avoided. Even when the general measures outlined at the beginning of this paper have failed greatly to reduce the frequency and severity of the attacks, they should never be allowed to sink into the background of the doctor's or the patient's mind. Without them drugs are merely props.

REFERENCES

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PERSONAL MEDICAL RECORD DISKS

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The need for a personal system of recording diseases contracted, idiosyncrasies and the like, blood group, and all preventive inoculations is often mentioned in medical literature. Such a record should ideally be carried on the person: it should be shown to the doctor on request, and in certain circumstances he should look for it. The availability of the immunization history may obviate unnecessary inoculations, and may be of assistance in making a diagnosis. The record would also ensure speedy identification in cases of accident, sudden coma, or other emergency.

Cards and Other Methods of Recording

Various record cards, commonly made of cardboard, have been issued by certain commercial firms and hospitals, but have the disadvantage that they become dirty and tattered when carried in ordinary wallets or handbags. If such cards are made of plastic material or kept in plastic envelopes (which is seldom done) they should remain clean and intact much longer, and this would be a step in the right direction. An alternative procedure to carrying the records on the person is to put them away in a safe place at home; but this has the drawback that they may not be produced quickly enough to prevent an unnecessary injection of, say, tetanus antitoxic serum (Tet/Ser) for someone who has already been fully immunized with tetanus toxoid (Tet/Vac). All aspects of the prevention of tetanus in injured persons have been discussed by Parish, Laurent, and Moynihan (1957) and by Parish (1958).

Tattooing has also been suggested, mostly facetiously, for the more important inoculations and other records, but this would certainly be impracticable for repeated entries, with dates—for example, reinforcing doses of tetanus toxoid or smallpox vaccine (Var/Vac).

If tattooing, whereby the record is permanently "fixed" to the body, is out of the question, can some system of