3. *Therapeutic Retrospect.*

By HARRINGTON SAINSBURY, M.D.

The Sedative and Hypnotic Action of Atropine and Duboisine.—Dr. Nicolaus Ostermayer (Budapesth) reports an undoubted sedative action as belonging to atropine, also, indirectly, a hypnotic action, in that the drug by lessening reflex irritability predisposes to sleep. In this latter action atropine would, according to the author's view, resemble the bromides, sleep being favoured by rendering the organism less susceptible to disturbing influences. The author regards atropine as decidedly less certain and less powerful than hyoscine, but as free from the danger of causing collapse. With continued use the dose must be raised. Disagreeable by-effects were witnessed in one case, viz., diarrhœa and vomiting. Atropine may be tried in cases in which morphine and hyoscine have proved ineffectual; it is scarcely a drug to have recourse to in the first instance. The dosage employed was 1-2 mg. ($\frac{1}{70}$-$\frac{1}{35}$ grain) pro dosi, injected subcutaneously. The largest dose pro die was 3 mg. (about $\frac{1}{21}$ grain).

Duboisine, the sulphate, is a prompt and powerful hypnotic and sedative in the stage of excitement of psychic disease. The effects of the drug generally appear in from 10-15 min., and sleep is produced in about 20-30 min. The dose in cases of much excitement should be 2-3 mg. ($\frac{1}{35}$-$\frac{1}{25}$ grain), but in sleeplessness without motor unrest half this dose. No serious toxic symptoms or bad after-effects follow these doses. Habituation shows itself with prolonged use. The author recommends the use of duboisine in place of hyoscine, especially in cases of circulatory trouble. Duboisine is much cheaper than hyoscine.

Dr. Serger, of Sachsenberg, reports unfavourably of the use of hyoscine in the treatment of mental diseases; in this he agrees with Gnauck. The inconstancy of the action of hyoscine and the very unpleasant by-effects, *e.g.*, dryness of the throat, difficult swallowing, hebetude and lassitude, but above all important circulatory symptoms, these render the drug unsuitable as a hypnotic and sedative.—"Therap. Monatsh.," Mch., 1891.

These results, apart from their practical significance, are of interest as indicating that these alkaloids, hyoscine, atropine, and duboisine, must be isomers of and not identical with each other.

Sulphonal.—A new method of administering this compound is recommended by David D. Stewart in the "Medical News" for 1891, No. 5. The sulphonal is to be *dissolved* in boiling water, say about 6 oz. ($\frac{2}{3}$ tumbler), agitation accelerates the solution, then cold water is to be added carefully, so as to cool the drink just sufficiently to enable it to be swallowed. Some flavouring agent,

e.g., peppermint, may be added to cover the bitter taste of the drug. Taken thus sulphonal acts much more promptly and more efficiently.—"Lancet," Feb. 21, 1891, and "Therap. Monatsh.," Mch., 1891, p. 216.

Piperazidine in Mental Affections.—In the April number of the "Therap. Monatshefte" Drs. Schultze and Umpfenbach report on experiments with piperazidine in the asylums of Bonn and Andernach. In the last number of this Journal we referred to experiments made with piperazidine, and we drew attention to the contrast between its action and that of the spermine of Professor Poehl, with which piperazidine was at first thought to be identical. The present observers confirm the negative aspect of the subject which we then recorded, for they fail to find in piperazidine the powerful tonic action claimed for spermine by Poehl and other observers. Schultze employed the subcutaneous injection of the drug in doses of from 1 centigramme to 1 decigramme (¼ grain-1½ grains); he records over 200 injections. The injections were painful, so much so in some cases that they had to be discontinued; they were frequently followed by a weal at the site of the injection, with surrounding hyperæmia, but never was an abscess occasioned. Thirty-three patients received the injections, and of these 11 suffered from melancholia, 4 from stupor, 3 from senile dementia, and 4 from general paralysis. Schultze was unable to detect, either by the finger or sphygmograph, any signs of a more vigorous circulation after the injections. Of sixteen patients whose muscular power was tested by the dynamometer as carefully as the method admits of, only one showed a decided increase of strength. The method, however, is obviously a very coarse and uncertain one, and could only be used advantageously on a large scale. Subjectively, several patients maintained that they felt much stronger after the injections, and that they had slept unusually well; but injections with sodium chloride proved equally beneficial with one exception, that of a case of delirium tremens, who in the convalescent stage suffered much from restless nights and during the day was very fidgety. This patient expressed his sense of improvement after the injections of piperazidine only.

In two cases—one of dementia in a woman, the other a paralytic, a man—the effects, whether post or propter, were harmful. The woman became very restless and garrulous, and in the end had to be transferred to the quarter for restless patients. After improvement, a repetition of the drug in half-dose brought a return of the unrest. The paralytic suffered from an epileptiform attack within twenty-four hours after each of two injections, though for some six weeks before and twenty days after no attacks occurred.

The four cases of stupor were in no wise benefited.

These observations suggest that in piperazidine we have a base which differs from the spermine of Poehl, and, indeed, MM. Majert and Albrect-Schmidt, of the Schering Laboratory, come to this

same conclusion on the ground of the chemical reactions of the two bodies.

Dr. Umpfenbach, working with the same product, viz., Schering's pure piperazidine and the hydrochlorate of piperazidine, administered it by the mouth in doses of 7·5 grains several times per diem, and subcutaneously to the extent of about 4·5 grains pro die. (The watery solutions of these salts do not keep very well, they become turbid.) He records that some pain is excited by the injections, and that induration may follow and persist for some weeks.

Umpfenbach experimented on some sixty cases. In three cases out of eighteen, marked by anergic stupor, there appeared to be some stimulation of the faculties. In melancholiacs no benefit resulted. In three cases of dementia (Blödsinn) an unusual restlessness developed, and in the case of a melancholiac woman with hallucinations the unrest and anxiety were much increased.

In certain cases of nervous affection, *e.g.*, disseminated sclerosis, hereditary chorea, epileptic tremor, tabes dorsalis, piperazidine was tried, but without noteworthy effect.

Umpfenbach concludes that piperazidine does not show any decided effects as a nervine tonic.

A few cases which he records show a decided influence upon the kidneys, the flow of urine being notably increased, and in one case of albuminuria the loss of albumen much diminished. The experiments in this direction are but few.

Somnal is reported on by Dr. Umpfenbach in the May number of the "Therap. Monatsh." p. 289. He leaves open the question of the chemical constitution of the body, viz., whether it is a simple mixture of chloral hydrate and urethane in solution in alcohol, or whether it is a definite compound. He employed it in doses of 2-4 grms. at night, rarely 6 grms. (30-60 grains, rarely 90 grains). It was given in water with a little syrup.

On healthy people, attendants, etc., it for the most part gave good results in simple insomnia; in insomnia from pain it did not serve.

In mental cases it was tried on 70 individuals, ranging between the ages of 15-76 years. Twenty-eight of the cases were acute, the remaining 42 were treated during periods of excitement and noisiness; in a few cases only was there simple insomnia. The desired effect was attained permanently in 33 cases, temporarily in 13 cases; in 24 cases it was absent.

Strangely, Umpfenbach finds a very striking difference between the effects of the drug on men and women. It is far more effective with the former. The differences in his results are so marked that according to them somnal would be a bad hypnotic for women, but a good one for men (of the 70 cases, 36 were women, 34 men). Where somnal was effective it acted in from $\frac{1}{2}$-$\frac{3}{4}$ hour, some five hours' good sleep were obtained, and no bad effects followed, with few exceptions. In these latter, headache, confusion, unrest,

vomiting were among the symptoms, but they were not prominent. No case of eruption occurred. The effect of age was not obvious. The general nutrition of the patients did not suffer.

Nutritive Enemata.—According to Huber ("Correspond. Blatt. für Schweizer, Aerzte" 29, 1890) eggs are best adapted for injection if given along with salt—for each egg 15 grains of salt. Of the egg about 12 per cent. is absorbed. Each enema should contain two to three eggs, and be given two to three times a day. An hour before the first nutritive injection a cleansing injection of simple water should be given. The injection should be thrown as high up the intestine as possible by means of a long soft tube. From time to time peptone injections should be given, milk and egg, broth and egg, etc. For the intestines also, so we read, the saying holds *variatio delectat!*—"Therap. Monatsh.," May, 1891, p. 319.

The Treatment of Epilepsy by the Combined Use of Bromides and some Agent capable of producing Anæmia of the Nervous Centres. By V. POULET, Bulletin général de Thérapeutique.

The following are M. Poulet's conclusions:—

The bromides constitute the basis of the treatment of epilepsy. Among them the bromide of gold does not possess the advantages ascribed to it by some, and must yield the palm to the bromide of potassium.

There are always a number of cases of epilepsy which though benefited by bromide treatment are not as efficiently treated as they admit of being.

In such cases the addition of one of the following drugs, calabar bean, picrotoxine, belladonna, and, in cardiac epilepsy, digitalis, will frequently bring about the desired result, viz., the suppression of the attacks. This will hold in general for epilepsy, pure and simple, as well as for many cases of Jacksonian epilepsy, though in this latter disease the search for the exciting cause, and its removal where possible, must always precede the above palliative treatment.

The sulphates of eserine (physostigmine) and atropine may replace the use of the crude drugs, calabar bean and belladonna, and digitaline may replace digitalis.

The selection from among these drugs will be in most cases haphazard.

The doses suggested by M. Poulet are: $\frac{1}{7}$ to $\frac{1}{4}$ grain of sulphate of eserine or picrotoxine, and $\frac{1}{70}$-$\frac{1}{60}$ grain of atropine sulphate in addition to the bromides, which the author gives in general to the extent of 75-90 grains to women, 105-120 grains to men. These, of course, will be pro-die doses. In place of the alkaloids about 30 drops of the tincture of calabar bean or 12 grains of the powdered bean; 30 drops of the tincture of belladonna or 7·5 grains of the powder.

In cardiac epilepsy 24-30 drops of the tincture of digitalis or about four grains of the powder may be given along with the bromides.

The doses of the tinctures will be of preparations according to the Codex Français.

Antipyrine in Mental Disease. By M. Roscioli. "Annuaire de Thérapeutique," p. 125.

The author has employed antipyrine in doses ranging between 4-7 grammes (60-105 grains) pro die in the treatment of epilepsy, with the result of diminishing the number of attacks. Antipyrine thus used acts more rapidly than bromides, but less enduringly. The mental torpidity of bromism tending even to dementia is not observed in the case of antipyrine, or rather, it should be said, that the torpidity of antipyrine is very fugitive. Antipyrine has completely failed in the hands of M. Roscioli in the treatment of mania, of melancholia, and of general paralysis, *i.e.*, it has failed as sedative and as hypnotic (*Il Manicomio moderne*).

The Insomnia of Children. "Annuaire de Thérapeutique," p. 143.

M. Jules Simon, commenting on the treatment of infantile insomnia, insists on the value of opium, which, in spite of the endeavour to proscribe it, is "the king of hypnotics." The precautions to be adopted in the case of opium are to withhold it if there be constipation, scanty urine or pruritus (?) (démangeaisons). Saving such, to administer it in half-drop doses under twelve months, and for each year above this to add one drop of opium to the mixture.

The syrup of codeine is an excellent hypnotic. Dose, one teaspoonful of the syrup in a mixture if the child be a year old, half a teaspoonful if under one year.

The bromides may be given in 4·5 grain dose at six months, 7·5 grains at one year, after this in 15 grain dose. These represent the total dose pro die; it is best given at one time, *horâ somni*. The administration should be interrupted after 5-6 days, and then resumed. Chloral may be administered in the same doses as the bromides, and best as an injection in emulsion in the yolk of an egg, along with a little camphor water. Chloral is especially indicated if convulsions threaten.

[We should be inclined to hold the dosage of chloral here prescribed as unsafe. Fifteen grains of chloral for a child of, say, 2!]