States, apart from that afforded by the asylums themselves, or agencies for relief of the poor. Information, however, on this subject would be interesting. In Switzerland some organized "After-Care" Treatment exists, or is being promoted.

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4. *Therapeutic Retrospect.*

By Harrington Sainsbury, M.D.

Ethylene or Ethene Bromide, $C^2H_4Br_2$, *a new remedy for Epilepsy.* "Therap. Monatsh.," June, 1891.

Dr. Julius Donath, of Budapesth, brings before our notice on p. 335 of the above journal his own experience with this compound. Reviewing the action of bromides in epilepsy, Dr. Donath holds that it can scarcely be doubted from clinical evidence that the effective agent in the bromides is bromine. Thus the bromides of potassium, sodium, and ammonium act alike in this disease, and moreover the same is found to hold of the recently introduced Rubidium-ammonium bromide (Prof. Laufenauer). The prolonged use of the bromides of the alkalies, is, however, liable to be followed by a train of toxic symptoms: Mental torpor, slow speech, unsteady gait, tremor, ataxia, in some cases mental derangement (delirium, maniacal attacks), further anæmia, wasting, skin eruptions, intestinal and bronchial catarrh. Of these, with the exception of the skin eruption, the cause, according to Dr. Donath, is the prolonged use of the alkalies, for other salts of potassium, for instance, may bring about the same results. Accordingly, Dr. Donath sought for some compound of bromide with more harmless base, and he thought to find amongst the organic compounds one such whose base, being burnt up in the body, would liberate an exceptionally active bromine, since it would act in *statu nascendi*. Amylene bromide was first thought of, but discarded, because of the difficulty of preparing a chemically pure compound, *i.e.*, free from isomeric varieties. Ethylene bromide, $C^2H_4Br_2$, which is readily obtained in purity, was ultimately selected. The compound is a slightly brownish liquid, having the odour of chloroform, and a sweet burning taste. At 0° C. it becomes a white crystalline solid; at 131° C. it boils. In water, the heavy liquid, Sp. gr. 2·163, is insoluble, and sinks to the bottom, but it mixes in all proportions with rectified spirits, and in fixed fatty oils, *e.g.*, the oil of sweet almonds, it dissolves to form a clear solution.

For internal administration an oily emulsion is best, *e.g.*:—

℞	Bromide of ethylene	... ...	5 pts.
	Oily emulsion	... ...	100 pts.
	Oil of peppermint	... ...	2 drops.

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Of this emulsion adults should take 20-30 drops twice daily, in ½ tumbler of water or eau sucrée. Every third day the dose may be raised till it has reached about 70 drops. Dr. Donath has not exceeded this dose thrice daily. These doses correspond to 1·5-3 grains of ethylene bromide twice or thrice a day. Children of 8-10 years should begin with 10-20 drops. The dilution of the emulsion with water (½ tumbler) or with milk is absolutely necessary, to prevent gastric irritation.

Used after the above method, the author has never seen more than slight signs of stomach irritation rarely amounting to nausea or vomiting, and readily yielding to a diminution of the dose or on the addition of a small dose of opium to the emulsion. No toxic effects after absorption have been seen, notably no eruption.

Other formulæ for the administration of the drug are:—

℞ Rectified spirits of wine } of each 5 pts.
Ethylene bromide }
Oil of peppermint ... ... 2 drops.

Of this 5-10-15 drops are to be taken, well shaken up in ½ tumbler of milk, twice or thrice daily.

Or the bromide mixed with oil of almonds, may be given in gelatine capsules

℞ Ethylene bromide ... ... 3 drops
Oil of almonds ... ... 6 „
2-4 capsules twice or thrice daily.

For hyperdermic use oily solutions might be employed.

Dr. Donath employed ethylene bromide in 21 cases of genuine epilepsy. Ten of these cases gave definite results, the other eleven either on account of the shortness of the time during which they had been under observation, or because of the long intervals between the attacks, could not be utilized.

Dr. Donath concludes from his experience of the drug, the records of which are given in detail in the "Therap. Monatsh." *loc. cit.*, that by its means the fits are in general diminished both in frequency and severity, that they are not infrequently replaced by the slighter forms of petit mal, *e.g.*, "absences" of mind, and sometimes by attacks of twitchings or clonic contractions, without loss of consciousness. This last was witnessed in three cases, and the author insists rightly on the extreme interest of these abortive attacks, since they further analyze the fully developed disease, and form the counterpart to the fits of mental abstraction. Thus in the attack of the grand mal we have both the convulsion and the abolition of consciousness; in the mental abstraction of the petit mal the convulsive element falls away, and now here under the influence of ethylene bromide, consciousness may remain during an attack of convulsions; artificially we thus produce a Jacksonian seizure. In certain of the cases less confusion and depression were observed after the attack; in one case the author

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is inclined to attribute to the ethylene salt the development of an aura never previously experienced. As is pointed out, it is impossible at this early stage to compare the new drug with the long-tried potassium salt, but so far as the results obtained go they are encouraging, and suggest that even if ethylene bromide should be less effective than potassium bromide, it may yet prove a valuable substitute in cases where habituation to the potassium salt has occurred, or where unpleasant by-effects have set in. In conclusion, Dr. Donath begs that this remedy may undergo a sufficient trial at the hands of those who have at their command the necessary material.

Theoretically we cannot see that the introduction of this new base can have any advantage over so innocuous a base as sodium, though it may have many over potassium and even over ammonium. There is, however, something to be said as to the possible greater efficacy of the bromine in the nascent state if this really does take place, and the organic base is actually burnt up in the organism. In any case, as Dr. Donath suggests, the efficiency of the ethylene salt in epilepsy, if established, will give further proof that the bromine is the active agent.

Chloralamide.

In the "Brit. Med. Journ." for May 16th, 1891, Dr. John Gordon furnishes us with a contribution to the study of the action of this drug. His examination is physiological, dietetic, and clinical, and has in view the determining of the value of the statements—1. That chloralamide does not depress the cardiac, respiratory, or cerebral centres, or cause marked lowering of blood pressure. 2. That it does not interfere with digestion. 3. That its action is more rapid than that of sulphonal, and is not accompanied or followed by depression, giddiness, or motor inco-ordination.

His first experiments are upon frogs, and they establish the diminution of the reflex activity of the spinal cord under the influence of chloralamide. By the method employed a stimulus of constant intensity, *e.g.*, a sulphuric acid solution (1 in 800 strength) was applied, and the time then measured up to the response to this stimulus. The experiment recorded shows very clearly the lengthening out of this interval and feebleness of the response after the injection of chloralamide.

The next experiments concern blood pressure, pulse and respiration rate; they were made upon the smaller carnivora. An illustrative experiment on a cat is recorded; the animal was under ether. The injections of chloralamide were made into the peritoneal cavity, into the femoral vein, and again into the peritoneal cavity. The quantities injected were severally 3·9 grains, 3·9 grains, 6·2 grains, and 9·3 grains, in all 23·3 grains. With the first two doses the effect on the blood pressure was not very

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marked, but after the third and fourth doses it fell to about ¼ of the original pressure. Pulse rate and rhythm were scarcely modified at all, so that in this case the quality of the pulse, not its frequence, measured the depression. The respirations fell from 60 to 24, and then ceased, whilst the pulse still numbered 144, and was regular.

The peripheral structures, motor nerve, and muscle fibre suffered decided lowering of their irritability.

Observations on the effects of chloralamide on digestion and metabolism were made on healthy people, who were kept on a carefully-regulated diet. In no case was appetite impaired, no abdominal pain, no vomiting, diarrhœa, or constipation were witnessed. There was no thirst; in fact, there were no signs of alimentary tract irritation.

On metabolism the influence was not marked. Small doses, *e.g.*, 5 grains of chloralamide appeared to stimulate, if anything, the excretion of urea, but doses of 25 grains caused a slight reduction of the urea coefficient. The phosphates excreted were slightly reduced in amount, but, oddly, the maximum of the reduction occurred with the smaller doses.

Clinical observations on the effect of chloralamide as a hypnotic were made on a number of cases of insomnia from various forms of disease. The results gained here are as follows: Pain as a cause of insomnia was not easily combatted by chloralamide, though, where the pain was moderate, the drug was fairly reliable. In painless insomnia excellent results were obtained; hypnotic action followed usually within half-an-hour. There was no tendency to deferred action, such as is not uncommonly witnessed with sulphonal. The sleep was tranquil and natural; no craving was noticed. The most reliable doses were 30 to 45 grains; excitement, giddiness, inco-ordination, headache, indeed, many of the features of alcoholic intoxication sometimes follow the use of chloralamide.

Dr. Gordon found chloralamide very satisfactory in the treatment of the insomnia of old age, hysteria, and pulmonary diseases. In criticizing these results we would point out—1. The desirability of having actual statements of the number of experiments performed, in particular of those on blood pressure, and pulse and respiration, and on metabolism. 2. That the recorded experiment on blood pressure does show a notable reduction of this with the large doses. 3. That the experiments on urea and phosphate excretion seem by no means conclusive, more especially those which show a reduction in the phosphates greater with the smaller dose; here, more particularly, a large number of experiments are necessary. The results obtained clinically agree with those already recorded by other observers, but again we should like to know the total number of cases in which chloralamide was employed; the nine cases given are "types of many cases," according to Dr. Gordon. The most important parts of the investigation are the blood

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pressure and metabolic experiments. These bear on the value of the statement that the introduction of the group NH_2 or a substitution derivative of NH_2, does actually remove or lessen the depressant action belonging to the chloral group. The examination of the more delicate action of a hypnotic drug can only be undertaken in hospital practice, and on a large scale, and in this investigation we shall do well to watch the influence of such drug on what may be called the tone of the nervous system, as measured by the brightness of the eye, the steadiness of the hand, the sense of refreshment experienced by the patient, etc., as already insisted on by Dr. Clouston.

Synthetical Hypnotics and Digestion.

Dr. Gordon communicates some further experiments on "The Action of some recent Hypnotics on Digestion" to the "Brit. Med. Journ." His method was that of Grützner, viz., he peptonized freshly-prepared and carefully-washed blood fibrine, which had subsequently been stained by an ammoniated solution of carmine. This carmine-stained fibrine, also carefully washed till the washing were colourless, was digested by pepsine in the presence of hydrochloric acid. The influence of the hypnotics was ascertained by adding varying quantities of each drug to the tube in which digestion was to take place. Each set of tubes was controlled by one tube containing no hypnotic. The rate and amount of digestion were determined by the liberation of the carmine stain and the diminished bulk of the fibrine. In this way it was found that weak solutions of chloralamide, urethane, and sulphonal were without appreciable influence on the peptonizing process. Strong solutions, however, did retard digestion, and in proportion to the amount of the hypnotic present. On the putrefactive process it was found that neither in weak nor in strong solution did the drugs interfere markedly. This latter result is somewhat surprising, seeing that chloral hydrate ranks as an antiseptic; if confirmed it would suggest that the amido group is the cause of the loss of antiseptic action, for we know that ammonia compounds are frequent products of putrefaction. A similar explanation may perhaps hold for the amido compound urethane. As to the sulphonal, it would be interesting to learn to what extent it was soluble in the acid peptic fluid. Paraldehyde was investigated in capped tubes, on account of its volatility, and in them it was found that a certain proportion of the drug favoured very decidedly the digestion; putrefaction, on the other hand, was prevented or delayed, according to the amount, large or small, of the paraldehyde. So far as these experiments go they are very interesting. They furnish another reason for favouring the use of paraldehyde.

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