3. *Therapeutic Retrospect.*

By HARRINGTON SAINSBURY, M.D.

Trional and Tetronal in Mental Affections. ("Therap. Monatsh.," October, 1891.)

In the above journal Dr. Ernst Schultze reports the results of his trials with these two substances. His object is to compare their action with that of the allied compound sulphonal. All these three are built up on the same type—they are all methanes. They differ, however, in the number of ethyl groupings in their respective molecules; thus there are two ethyl groupings in sulphonal, three in trional, and four in tetronal, and for those interested in the relationship between chemical structure and pharmacological action there is much interest in the comparison of these bodies. Kast and Baumann had asserted that the soporific action of sulphonal belonged to the ethyl groups, and that accordingly trional and tetronal would be found more active than sulphonal because richer in these groups. Their assertions were based on experiments on animals. Barth and Rumpel next examined trional and tetronal clinically, and though they found them excellent hypnotics, they were not able to sustain Kast and Baumann's contention of a distinct superiority over sulphonal.

The trional and tetronal employed by Schultze were obtained from the firm F. Bayer and Co., Eberfeld. Trional occurs in the form of glistening tabular crystals melting at 76° C., soluble in 320 parts of water at the ordinary temperature, freely soluble in alcohol and ether. The watery solution has a distinctly bitter taste. Tetronal crystallizes out in similar form; the melting point of the crystals is 85° C. It dissolves in 450 parts of cold water, freely in alcohol, moderately freely in ether. It has a camphoraceous and bitter taste.

In all 15,500 grains of trional and 10,850 grains of tetronal were used in doses varying from 15-60 grains. These doses were administered as powders, either in a large quantity of warm water, or at times in soup, and about half-an-hour before bedtime. Seventy-six cases of mental affection were treated; these comprised 20 cases of mania, 15 of general paralysis, eight of paranoia, 16 of melancholia, and 17 of feeble-mindedness with excitement.

For simplicity's sake mania and general paralysis are taken together, since the indications in these two affections were very similar. It was found that trional acted with certainty as a soporific in a mild case of mania, and in two cases of general paralysis, but that in maniacal cases with great excitement it was exceptional to obtain sleep, though a considerable diminution

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of the unrest was effected. In those cases where sleep was obtained the dose was large, 45-60 grains, and trional was always more efficient than tetronal. Endeavour was also made to discover if any advantage resulted from a divided dose given at intervals, *e.g.*, 15 grains thrice daily, but none such was witnessed. Perhaps some advantage followed the dosage of 30 grains morning and evening; six patients were submitted to this method. Trional and tetronal, according to the results in mania and general paralysis, are not drugs which enforce sleep, but which induce or predispose to sleep, and their effect is the more striking the more feeble-minded the patient, or the less recent the excitement. In three cases of general paralysis and one of mania, sleep was never obtained by either drug, but in these cases sulphonal was equally ineffectual. Under the influence of the morning and evening dosage a troublesome patient became much more manageable.

In six out of eight cases of paranoia with marked hallucinations very decided benefit was obtained, especially with trional. In the cases of feeble-mindedness with excitement, good results, on the whole, were obtained. In two cases tetronal was more effectual than trional.

Lastly, in melancholia, with sleeplessness, trional and tetronal proved satisfactory, and gave, in general, from six to eight hours' sleep. One case, however, was wholly intractable, and another case, in which sulphonal in 30 grain dose caused, almost invariably, sleep, resisted both trional and tetronal.

Dr. Schultze further refers to four cases of sleeplessness from overwrought nerves in persons otherwise healthy. Doses of 15 grains of trional proved generally efficient in these cases.

The effects of suggestion in such of these cases as were possessed of sufficient intelligence to be open to suggestion were eliminated by controlling the results by occasional substitutions of an indifferent white powder in place of the hypnotic.

In comparing together sulphonal and these other sulphones, Schultze remarks that in three cases sulphonal failed, whilst trional in the same dose, or in smaller dose, acted efficiently. Again, hallucinations were not infrequently complained of during the use of sulphonal, whilst, on the other hand, trional in 10 cases, with marked hallucinations, appeared to exert a lessening effect upon the hallucinations.

Lastly, delayed action, common enough with sulphonal, was not observed for either trional or tetronal, sleep setting in, if at all, during the first hour.

On the other side, the tastelessness of sulphonal must be placed against the bitter taste of trional and tetronal. This quality of the latter drugs did not cause much objection on the part of the patients, and in no case were they refused. Further, in two cases in which 45-60 grains of trional were taken over-night complaint

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was made next morning of ataxy of the limbs, especially of the legs. This symptom, however, passed off during the course of the day.

In five cases of tetronal use vomiting set in a few hours after the administration of the drug, or else the next morning; with this there was anorexia. Both symptoms, however, soon disappeared. For the rest no unpleasant effects on lungs, heart, or kidneys were at any time observed.

Schultze found trional, on the whole, more effective than tetronal. Roughly he values them numerically as 75-60. He thinks that trional can rank as equal to sulphonal, perhaps in some respects as its superior.

Subcutaneous "Infusion" of Salt Solution in Collapse from Abstinence in a Case of Acute Psychosis. ("Therap. Monatsh.," October, 1891.)

Dr. Mercklin, of Riga, refers to a most interesting case of collapse successfully treated by the hypodermic injection of salt solution. The record is as follows:—The patient, æt. 22, the wife of a publican, had been infected with syphilis since her marriage, and had undergone prolonged inunction treatment. On October 23rd, 1890, the first symptoms of mental excitement, sleeplessness, motor unrest, etc., appeared; food was taken in insufficient quantity. On admission, October 29th, great motor unrest was noticed; the attention could not be fixed. For two days all nourishment had been refused. Great mental confusion was next recorded. On November 1st patient looked very prostrate, and the œsophageal tube was employed, and continued for the next two days; sulphonal was also given for the unrest. November 4th—Patient vomited after each feeding with the tube; increased weakness. Two subcutaneous injections of ether. November 5th—Complete abstinence; increased prostration; skin cool, eyes dull. Food by the tube vomited; an enema of lukewarm water returned quickly. 10 a.m.—Facies hippocratica; pulse not palpable. A solution of common salt, 0·3 per cent., in distilled water, was now made, filtered, and boiled, and of this 500 c.c. (17½ fl. oz.) were introduced under the skin of the thigh. The apparatus had to be improvised. A needle of about 3 × the bore of an ordinary Pravaz syringe was fixed to the end of a long rubber tube, to the other end of which a glass funnel was attached. To prevent cooling of the solution several coils of the tube were placed in a vessel of warm water. The infusion of the solution was very slow, though the funnel was raised high. Careful massage expedited the absorption of the solution. Rapid improvement occurred. The radial pulse was soon felt, and the features of the patient became reanimated. At 2 p.m. the same quantity was injected into the other thigh. Patient distinctly stronger. 8 p.m.—Patient fed with the œso-

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phageal tube (milk), but vomiting followed directly. At 9 p.m. patient more lucid. Stated that she had held the food to be poisoned, and now asked for and began to take food. From November 6th the patient progressed satisfactorily. On November 28th she left the institution. The reviewer, Rabow, then refers to a similar case of his own, viz., great mental confusion, with motor unrest and collapse, in which surprising recovery followed similar treatment. In this case the patient had wasted to a skeleton. The subcutaneous infusion, to the extent of three times 17½ oz. of salt solution, took place on two separate days. By the time the patient had left the asylum she had gained 60 pounds in weight.

Dr. Mercklin's original paper is to be found in the "Sep. Abdruck des Cblatt f. Nervenheilk. u. Psychiatrie," March, 1891.

In the supplementary volume of the "Zeitschr. f. Klin. Medicin," 1891, pp. 49-86, an elaborate article is contributed by Dr. Biernacki, of Warsaw, on the influence of hypodermic injections of large quantities of 0·7 per cent. solution of sodium chloride upon the blood and the secretion of urine. The author refers to the rise and progress of the intravenous injection of saline solutions (0·6-0·7 per cent.), and subsequently to the use of hypodermic injections of the same solutions in the same states, *e.g.*, after losses of blood, in the collapse of cholera, in other states of collapse. The author next proceeds to examine physiologically the effects of subcutaneous injections upon animals, seeking to establish the physiological basis upon which this treatment rests, he worked in the like manner that Ott investigated the *intravenous* method. All the animals experimented upon recovered sooner or later. The quantities injected varied from ¼ of the bulk of the blood in the animal (reckoned as $_{1}{}^{1}{}_{3}$th of the body weight) up to ½-¾ or even an equal volume. The salt solution was first warmed to about the body heat (37-39°C.), and then the injection was made by means of a syringe of 15 c.c. capacity under the skin of the thorax or of the flank. Massage was never employed to accelerate absorption. Complete absorption took place in from ¾-1 hour, sometimes rather longer. The blood pressure was tested, and the amount of hæmoglobin, the proportion of red cells, the specific gravity, etc., determined. The blood was also examined chemically as to its proportion of water and organic and inorganic constituents. The following results were obtained: —Following the massive injection of saline the red cells per unit of blood diminish in number, the hæmoglobin percentage falls, likewise the specific gravity and the proportion of solids; on the other hand, the number of white cells, the water percentage, and the inorganic blood constituents rise — in fact, but for the increase of white cells, we have the phenomena of simple

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blood dilation. After a period of 1-2 days a second period supervenes, in which the number of red cells, the hæmoglobin percentage, the sp. gr., and the quantity of organic solid constituents rise above the normal. The number of white cells, however, lessens. The inorganic salts remain in excess. After another day, rarely two days, the red cells fall greatly in number; the white cells show oscillations in their number, but gradually reach the normal standard. By about the fourth day from the injection the proportion of water and of red cells attain about the normal percentage. The proportion of salt and the sp. gr. are the last to return to the normal levels.

The phenomena of blood-dilution, first stage, do not reach the degree witnessed when the saline is injected directly into the veins. The fall in sp. gr. is more marked in the venous than the arterial blood. Blood pressure is not appreciably altered.

Strong diuretic action follows the injection, and this causes the appearance of the second stage, viz., condensation or thickening of the blood. During the diuresis the watery element of the injection is thrown out in greater proportion than the saline.

Marked chemical changes in the blood determine the appearance of the third stage. The red cells are destroyed in great numbers, and accordingly we witness for two or three days a hæmoglobinuria.

Toxic Effects of Cocaine and their Treatment. Andrew Fullerton, M.D., B.Ch. ("Lancet," September 19, 1891.)

Dr. Fullerton's results were obtained chiefly from the local application of cocaine to the mucous membrane of the nose and mouth in the treatment of local affections in these regions. He is of opinion that the stronger solutions are less readily absorbed than the weaker, and that, for example, two grains in one per cent. solution would be more liable to yield toxic symptoms than the same quantity in a 10 per cent. solution. He has experienced very unpleasant effects from the absorption of less than one grain. The symptoms produced may come on in a few minutes, and last 3-4 hours or more. With small doses there is exhilaration, the mental faculties being stimulated. With much increase of the dose a kind of affective insanity may result. It appears to consist of a kind of mild mania, "in which illusions, hallucinations, and delusions have not yet made their appearance." Insomnia is a troublesome symptom, but strangely it does not appear to be followed next day by as much fatigue as would have been expected.

The vascular system shows excitement except for large doses; with such there may be a rapid, weak, irregular pulse, with oppression at the chest, and some orthopnœa. The temperature

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