

TRIONAL AND TETRONAL.

CLINICAL OBSERVATIONS ON THEIR ACTION AS HYPNOTICS AND SEDATIVES FOR THE INSANE.

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So far as known to the writer, no American observer has as yet recorded his experience with trional and tetronal, which are the latest claimants for recognition as hypnotics and sedatives for the insane.

The disulphones, to which these two new remedies belong, are said to depend for their physiological activity upon the ethyl groups and their hypnotic action is increased with the number of such groups. Trional (diethyl-sulfonmethylethylmethane) has three, and tetronal (diethyl-sulfondiethylmethane) four ethyl groups. They both have a slightly bitter taste and do not dissolve well in water at an ordinary temperature, although they are soluble in boiling water and, to a certain extent, in alcohol and ether. By reason of this partial insolubility they have generally been administered, finely powdered, in hot gruel, hot milk or beef tea. They have been reported favorably by Boettiger, Schultze, Schaefer, Ramoni, Barth and Rumpel and Garnier, and are said by these observers to be more active than sulfonal (which also belongs to the disulphones and contains two ethyl groups) as shown by the fact that the patient is affected more promptly, awakens readily and does not exhibit many unpleasant after effects. It is claimed that they have besides a hypnotic effect, a decidedly sedative action, and it has been found possible to keep quiet during the daytime many noisy, excitable and destructive patients. Tetronal is said to have a more decided sedative action than trional, while the latter acts better in the sleeplessness of neurasthenia and organic brain affections. Hypnosis lasts from six to eight hours and is not accompanied by dreams. Trional costs but little more than sulfonal, whilst tetronal is twice as expensive.

In the observations made it was found that the insolubility of these remedies prevented in two instances their satisfactory administration and so these cases are not recorded. They were

patients who were fully controlled by delusions of persecution, and were suspicious of all about them, and in giving the hypnotics mixed with food the slightly bitter taste imparted to it gave rise to ideas of poisoning.

TRIONAL.—The hypnotic action of trional was noted in the following cases:

Case 1. Female, age 65, form of insanity, acute melancholia. On February 19th thirty grains (grammes 2) were administered, and in half an hour the patient went to sleep and slept for nine hours. On the following night fifteen grains (gramme 1) were given, and the sleep which began in an hour continued eight hours. This patient formerly did not sleep well, but has rested quietly every night, since the second administration of the remedy, without the use of any medicine.

Case 2. Female, age 75, form of insanity, acute melancholia. On February 18th she was given thirty grains (grammes 2) and went to sleep in two hours. After resting an hour she awoke for a short time and then went to sleep again for five hours. The following morning she complained of feeling dizzy. February 19th, twenty grains (grammes 1.33) were given which was followed in two hours by sleep which lasted six and one-half hours. On February 20th trional was not employed and the effect of the dose given the night before was carried over and the patient slept six hours. February 21st, again the remedy was not given, but on this occasion the patient was awake and restless several times during the night. February 22d fifteen grains (gramme 1) were given, and the sleep, which resulted in an hour and a half, continued seven hours. With the exception of the first morning, no unpleasant after effects were noted.

Case 3. Female, age 34, form of insanity, sub-acute mania. On February 18th thirty grains (grammes 2) were administered and in an hour and a half the patient was asleep and remained so nine hours. On the following night the same quantity was given, after which patient went to sleep in an hour and slept for nine hours. On February 20th, patient slept well without its use. On February 21st, again it was omitted, but the patient did not rest well. On February 22d sleep was produced in an hour with fifteen grains (gramme 1), but she was restless during the night. February 24th twenty grains (grammes 1.33) were given and sleep, which resulted in an hour, continued for eight hours.

Case 4. Female, age 59, form of insanity, chronic mania. This patient received on four occasions doses of thirty grains (grammes 2) each, and the sleep which resulted in each instance began in half an hour and continued eight hours. Following the last dose she complained of slight nausea. Another effect noted was that the patient instead of being noisy and restless during the daytime, as was her custom, became quiet and orderly.

Case 5. Female, age 52, form of insanity, sub-acute melancholia. This woman generally slept well, but for two or three nights previous to the administration of trional, her sleep had been restless and broken. On February 8th she was given fifteen grains (gramme 1), went to sleep in fifty minutes and slept for six hours. Next morning she complained of still being sleepy. On February 19th, after taking ten grains (grammes .66), she went to sleep in thirty minutes and continued so for six and one-half hours. Medicine was then discontinued and she has rested well ever since.

Case 6. Female, age 29, form of insanity, acute mania. February 19th was given fifteen grains (gramme 1), the effects of which were produced in one hour and a half and continued for six hours. February 20th, after a dose of the same size, she went to sleep in forty-five minutes, and slept for seven hours. February 21st, with a similar quantity, sleep did not result for two hours and a half, but it continued eight hours. February 22d, twenty grains (grammes 1.33) were again given and the sleep which came in an hour and a half continued for seven hours. The drug, which was given for its hypnotic effect, also resulted in keeping this patient comparatively quiet during the daytime.

Case 7. Female, age 43, form of insanity, dementia. On February 18th, patient took fifteen grains (gramme 1), went to sleep in an hour and continued to rest for eight hours. February 19th, was again given fifteen grains (gramme 1), and the sleep which resulted in half an hour lasted nine hours. This patient was previously extremely noisy at night.

Case 8. Female, age 53, form of insanity, sub-acute melancholia. February 18th, was given thirty grains (grammes 2), went to sleep in fifty minutes and did not awaken until seven and one-half hours had passed. February 19th, after a similar dose, was asleep in thirty minutes and continued so for eight and a half hours. February 20th, was given fifteen grains (gramme 1), and the sleep which resulted in forty minutes continued for seven hours. Feb-

ruary 21st, was again given fifteen grains (gramme 1), went to sleep in forty minutes and slept for seven hours and a half. On the two following nights no hypnotic was given and she rested well the first night, but the second was restless and uneasy. This patient for several months had been unable to sleep without the use of either chloral or sulfonal.

Case 9. Female, age 37, form of insanity, acute mania. Fifteen grains (gramme 1) were given on the night of February 21st, after which the patient went to sleep in fifteen minutes and slept eight hours and a half. The same results were noted on the three following nights with the same dosage.

Case 10. Male, age 47, form of insanity, sub-acute melancholia. Trional was administered on one occasion in a dose of thirty grains (grammes 2), and the sleep which resulted inside of an hour continued for eight hours. On five nights, it was given in doses of fifteen grains (gramme 1) and produced each time eight hours of natural sleep, which commenced in forty-five minutes from the time of its administration. This patient had for a long time depended upon the use of sleep-producing remedies, and, after using trional, said that the sleep which the powders gave him seemed more natural than that produced by anything else he had ever taken.

SUMMARY.—In doses of ten grains (grammes .66) trional was given on two occasions; the sleep produced averaged seven hours, and the average time required to bring about sleep was thirty-five minutes. In fifteen grain (gramme 1) doses, it was given twenty-one times, required an average of fifty-eight minutes to produce sleep, and the average length of the hypnosis was seven and one-half hours. The shortest time which it took to produce sleep with this dosage was fifteen minutes, and the longest was two hours and a half. The shortest duration of sleep was six hours, and the longest nine hours. One dose of twenty grains (grammes 1.33) produced sleep in an hour which lasted eight hours. Thirty grains (grammes 2) were given eleven times, which produced sleep in an average of an hour, and continued for an average of eight hours. The shortest time which it took to produce its effects was thirty minutes, and the longest two hours. The shortest duration was five hours and the longest nine hours. It was given in all on thirty-five occasions and produced an average sleep of nearly eight hours in an average time of fifty-eight minutes.

Besides its hypnotic effect on these patients it produced a quieting effect the next day on two cases. In addition, in three patients its action seemed to be carried over until the following night and caused these cases to sleep well without any hypnotic. The quality of sleep produced was, save in one or two instances, quiet and restful, and, with the following exceptions, was not followed by unpleasant after effects. One patient was sleepy the following day, one complained of nausea, and another appeared dizzy.

The next series of cases recorded comprises those in which trional was used as a sedative:

Case 1. Female, age 37, form of insanity, chronic mania. On February 19th the patient was given three doses of fifteen grains (gramme 1) each, which resulted in keeping her quiet all day long, but made her drowsy and languid. February 20th she was given fifteen grains (gramme 1) in the morning, and fifteen grains (gramme 1) in the afternoon, and on this day was quiet and self-controlled, but did not appear to be drowsy. On the next three days she was given each morning fifteen grains (gramme 1) with the most happy results. In this case marked hallucinations of hearing existed in addition to motor restlessness and the patient was decidedly destructive to furniture. By the use of this remedy we were enabled to keep her quiet without stupefying her except in the single instance noted.

Case 2. Female, age 45, form of insanity, chronic mania. On February 19th three single doses of fifteen grains (gramme 1) each were given and the patient remained quiet all day. She was, however, drowsy and said that her head was "so dizzy" that she could not walk straight; she slept all of the following night. On the three following days she received fifteen grains (gramme 1) each morning and evening with the effect of keeping her quiet and self-controlled, whereas she had been formerly extremely noisy and given to scolding most of the time.

Case 3. Female, age 50, form of insanity, chronic melancholia, accompanied with great agitation. On February 19th three doses of fifteen grains (gramme 1) did not affect her in the least. The next morning she was given thirty grains (grammes 2), went to sleep in fifteen minutes, and continued so for half an hour. After awakening, her speech was thick and her gait staggering; she slept all of the following night. On February 21st fifteen grains (gramme 1) were given, and she soon became rather stupid and

remained so until the afternoon, when she again became restless and agitated. At night she received another dose of fifteen grains (gramme 1) and slept quietly until morning. On the two following days two doses daily of fifteen grains (gramme 1) were administered with the result of quieting, but not stupefying her.

Case 4. Female, age 50, form of insanity, periodic mania. In this case the outbreak of excitement began February 19th and for two days efforts were made to administer the drug, but, owing to the patient's strong resistance, she did not at any one time receive the full dose of fifteen grains (gramme 1), and the quantity she did receive produced no apparent effect. On February 22d she took at noon fifteen grains (gramme 1) without effect, but in the evening the same size dose resulted in her remaining quiet all night. On the three following days she was given morning, noon and night, fifteen grain (gramme 1) doses, and, with the exception of being noisy for two hours one afternoon, was quiet and well behaved. After the last administration the excitement subsided and she has been ever since quiet and self-controlled.

Case 5. Female, age 36, form of insanity, *folie circulaire*. On February 20th at the beginning of a period of exaltation fifteen grains (gramme 1) were given morning, noon and night, but the patient did not give any evidence of being under the influence of the sedative until the afternoon, when she became drowsy and continued so for an hour. She was talkative and noisy all the following night. On February 21st and 22d single doses of fifteen grains (gramme 1) were given in the morning and evening, the excitement subsided, and she has been quiet and self-controlled ever since. In this case the patient had usually been disturbed for ten days or two weeks at a time, and further observations should be taken to see if the period of excitement in this class of patients can be shortened by the use of this remedy.

Case 6. Female, age 67, form of insanity, chronic mania. In this case the patient was extremely restless and excitable and for a long time had been violent and destructive. In two days she received seventy-five grains (grammes 5) in divided doses of fifteen grains (gramme 1) each, but with no result. The following day she was given thirty grains (grammes 2) in the morning, followed in three hours by another dose of the same size; these doses also failed to quiet her. The next day a single dose of forty-five

grains (grammes 3) was administered and she became quiet for two hours, although during that time she made an attempt to break the glass in a picture frame, but apparently did not have strength enough to accomplish her purpose. No further trial was made.

Case 7. Female, age 48, form of insanity, dementia. This dement was generally restless and occasionally became extremely disturbed for two or three days at a time. During one of her disturbed spells she was given ten grains (grammes .66) and remained quiet all day. The following morning she again became disturbed and a dose of the same size produced a similar result.

Case 8. Female, age 50, form of insanity, dementia. A similar case to 7. Was given the same number of and the same size doses, and the results were likewise most satisfactory.

Case 9. Female, age 33, form of insanity, dementia. This woman received on the mornings of February 24th and 25th doses of fifteen grains (gramme 1) each, with the result that she was quiet all of the first but only four hours of the second day.

Case 10. Female, age 30, form of insanity, chronic mania. On February 24th and 25th single doses of fifteen grains (gramme 1) were administered three times a day without very satisfactory results, the patient being either noisy or restless or else stupefied with the drug. Doses of ten grains (grammes .66) did not have any effect.

Case 11. Female, age 44, form of insanity, dementia. Doses of fifteen grains (gramme 1) were given on four occasions, but the effect did not last more than an hour each time. She was then given thirty grains (grammes 2), but the result was likewise unsatisfactory.

Case 12. Female, age 44, form of insanity, chronic mania. On the morning of February 19th fifteen grains (gramme 1) were given. In half an hour patient became quiet, an hour later was drowsy and continued so for three hours, she then became noisy, when fifteen grains (gramme 1) were given, after which she was quiet for three hours without being drowsy. She slept all night, but the next morning was noisy and turbulent. After this, doses of the same size were given four times in the course of two days and the patient was quiet for two hours after the administration of each dose.

Doses of fifteen grains (gramme 1) three times a day were given for seven days. On three occasions this dosage kept the patient

quiet all day, and four times no effect was produced. Similar doses were given twice a day for fourteen days and kept the patient quiet all day on nine occasions, quiet for three hours once, for two hours twice and for one hour twice. On the three occasions it was given in fifteen grain (gramme 1) doses once a day, the results were satisfactory twice and once no effect was produced. Doses of ten grains (gramme .66) each were given once a day for six days and the result was in each instance good, although the excitement in these cases was not so great as in those in which larger doses were given. Similar doses given twice on one day were satisfactory. When given three times a day to very disturbed patients no effect was produced. Doses of thirty grains (grammes 2) once a day, were satisfactory in one instance and a failure in another. When given to one patient twice a day in the same quantity, it was likewise unsatisfactory. A dose of forty grains (grammes 3) caused the patient to remain quiet only an hour.

The attack of excitement in the case of circular insanity, Case 5, was shortened. The other effects noted were in five instances, a drowsy state, in one the patient was dizzy and staggered, and in another the speech became thick and the gait staggering.

TETRONAL.—The following cases are those in which this drug was used as a hypnotic:

Case 1. Female, age 53, form of insanity, acute melancholia. February 24th ten grains (gramme .66) were given, and the sleep which resulted in an hour and a half continued for seven hours. February 25th a similar dose gave the same length of sleep as that on the preceding night, but the effects were observed in an hour. On February 26th ten grains (gramme .66) were again given, and the sleep which resulted in fifty-five minutes continued for seven hours. On February 27th the amount was reduced one-half, but the sleep which resulted in two hours continued for only two hours and was restless in character. On February 28th ten grains (gramme .66) produced in an hour and a quarter sleep which lasted six and one-half hours. The two following nights the dose was on each occasion ten grains (gramme .66) and in both instances sleep resulted in half an hour and continued for seven hours.

Case 2. Female, age 33, form of insanity, *folie circulaire*,
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After having been in a comfortable mental condition for several months, this patient began to exhibit evidence of mental excitement, did not sleep well, became profane and was somewhat restless and noisy. On February 27th she was given ten grains (gramme .66), and in an hour went to sleep and slept for six and one-half hours. The following night ten grains (gramme .66) were given, but sleep did not occur for two hours and a half and lasted five and a quarter hours. On March 1st a similar dose produced sleep in an hour which continued seven hours.

Case 3. Female, age 44, form of insanity, dementia. February 25th five grains (gramme .33) were given, but the patient only obtained after an interval of four hours a restless sleep of three hours' duration. On the following night a dose of the same size produced exactly similar results. On February 27th and 28th she received nightly doses of ten grains (gramme .66), went to sleep in an hour and slept seven hours on each occasion.

Case 4. Female, age 52, form of insanity, chronic mania. February 27th ten grains (gramme .66) produced sleep in an hour which continued for eight hours. February 28th a similar dose required two and one-half hours to produce sleep, which lasted five hours. March 1st and 2d fifteen grain (gramme 1) doses were given, and the sleep in each instance resulted in half an hour and continued for eight hours. The day following the administration of the last dose the patient was drowsy.

Case 5. Female, age 49, form of insanity, dementia. February 26th ten grains (gramme .66) were given, and the sleep which took place only after four and one-half hours had passed, continued for seven hours. The two following nights with doses of the same size the results were similar. On March 1st fifteen grains (gramme 1) brought in an hour sleep which lasted nine hours.

Case 6. Female, age 75, form of insanity, acute melancholia. February 27th five grains (gramme .33) gave after three hours a sleep which lasted five and one-half hours. February 28th ten grains (gramme .66) produced sleep in two hours and continued seven hours, but it was restless in character. March 1st with a dose of fifteen grains (gramme 1) sleep resulted in half an hour and continued for eight hours.

SUMMARY.--Tetronal was given as a hypnotic on twenty-five occasions and produced in an average of one hour an average sleep of a little more than six hours. With five grain (gramme .33) doses

it required an average of three and a quarter hours to produce sleep, and the duration of hypnosis averaged only about three and one-half hours. With ten grain (gramme .66) doses, effects were noted on an average in an hour and fifteen minutes and continued on an average six and one-half hours. With fifteen grain (gramme 1) doses the average time to procure sleep was thirty-seven minutes, and the average duration was eight and one-quarter hours. From a study of these cases this drug does not appear to be effective in doses of less than ten (gramme .66) or fifteen grains (gramme 1) and, considering the price, sulfonal or trional would produce better results. Case 2, *folie circulaire*, appeared to be benefited by the use of this remedy. The only unpleasant after effect noted was a drowsiness in one instance on the following day. The sleep produced was, with the smallest dosage, rather restless and unsatisfactory.

The last cases noted are those in which tetronal was used as a sedative:

Case 1. Female, age 44, form of insanity, chronic mania. On February 25th and the three following mornings patient received five grain (gramme .33) doses, but was only quiet for two or three hours each day. On March 1st five grains (gramme .33) were given in the morning and five in the evening, but the effect was no better. On the next two days doses of ten grains (gramme .66) given in the morning caused the patient to remain quiet all day, and this condition was unaccompanied by drowsiness.

Case 2. Female, age 37, form of insanity, chronic melancholia. February 27th ten grains (gramme .66) were given in the morning, patient became quiet in an hour, and remained so all day but was rather stupid. February 28th five grains (gramme .66) were given in the morning and resulted in keeping the patient quiet all day, but no stupefying effect was produced. On the four following days similar doses were administered, and with one exception, when the patient was agitated and restless for three or four hours, the results were similar to those produced on the last mentioned date.

Case 3. Female, age 46, form of insanity, melancholia with agitation. On February 25th patient received a dose of five grains (gramme .33) which caused her to become quiet in an hour and continue so for four hours. On February 26th a similar dose was given in the morning, but she remained quiet only two hours.

She was therefore given another dose at noon, with the result of causing her to remain quiet all the afternoon. On the five following days patient was given two doses daily of five grains (gramme .33) each, with the result of reducing very largely her agitation.

Case 4. Female, age 45, form of insanity, sub-acute mania. February 25th, five grains (gramme .33) given at eight o'clock in the morning caused the patient to become fairly quiet in an hour and to remain so all day. February 26th a dose of the same size produced similar results, although the patient complained of feeling heavy and dull. On the next three days doses of five grains (gramme .33) given once a day caused her to remain quiet for several hours, without any feeling of drowsiness.

Case 5. Female, age 32, form of insanity, dementia. February 26th five grains (gramme .33) in the morning resulted in the patient becoming quiet in an hour and remaining so all day. February 27th five grains (gramme .33) given at 8 A. M., produced a quiet condition in one hour and a half which lasted until noon, when she became noisy and destructive. At one P. M. she was given another dose of ten grains (gramme .66), but did not become quiet until four hours had passed and then remained quiet until bedtime. On the two following days single doses of five grains (gramme .33) in the morning, resulted in keeping the patient in a fairly comfortable condition for several hours each day.

Case 6. Female, age 48, form of insanity, dementia. This woman received on February 26th and the three following days five grains (gramme .33) each morning, she became quiet in each instance in the course of an hour, and remained so seven hours each day.

Case 7. Female, age 32, form of insanity, dementia. On February 27th patient was given at noon five grains (gramme .33), after which she became quiet in half an hour and remained so for five hours. On February 27th a similar dose produced no result. On February 28th ten grains (gramme .66) were given in the morning, the patient became quiet in an hour and remained so during the rest of that day. On March 1st like results were produced with a dose of the same size.

Case 8. Female, age 50, form of insanity, chronic mania. February 26th was given five grains (gramme .33) in the morning, became quiet in two hours and continued so all day. February

27th, a similar dose caused the patient to become quiet in an hour and remain so nine hours. On the two following days, with doses of the same size, the results were alike gratifying.

Case 9. Female, age 34, form of insanity, sub-acute mania. On February 25th patient was given five grains (gramme .33) in the morning, and five grains (gramme .33) at noon, but no quieting effect was manifested. On the three following days ten grain (gramme .66) doses were given each morning, which caused the patient to become quiet on each occasion in an hour and remain so for eight hours.

SUMMARY.—Five grain (gramme .33) doses were given once a day on twenty-seven occasions, and produced in five instances a quiet state which lasted two or three hours, in one instance it lasted four hours and in one five hours, on two occasions a fairly comfortable mental condition resulted, on one no effect was produced, and on nineteen the patients remained quiet all day. Five grain (gramme .33) doses were given twice a day in ten instances. On one occasion it quieted the patient for two or three hours, on two there was no effect produced, and on seven the patients remained quiet all day. Ten grains (gramme .66) were given once a day on four occasions and in each instance the patient became quiet. The same dosage was given twice a day to one patient with a like good result.

In one case with a dose of ten grains (gramme .66) patient was rather stupid, and in another with five grains (gramme .33) a dull and heavy feeling was produced.

CONCLUSIONS.—These new remedies both have a marked hypnotic and sedative action, but trional appears to be the more serviceable as a hypnotic for the insane. On the other hand, small doses of tetronal appear to give the best results as a sedative. As a rule, the hypnosis which is produced is calm and quieting and resembles very closely natural sleep. In a few instances unpleasant after effects were noted, but they did not continue long and were not at any time alarming. They do not depress the heart's action.

In the majority of cases fifteen grains (gramme 1) of trional given in hot milk at bedtime will produce sleep of from six to nine hours' duration which is not accompanied by dreams. The time it takes to produce this effect, is, in favorable cases, from fifteen to forty-five minutes, although it may be prolonged to over two

hours. With tetronal it was found that generally fifteen grains (gramme 1) were required to obtain the same results, and as this remedy is twice as expensive as trional the latter is to be preferred, as a rule. Both of these drugs have the effect with some patients of producing sleep for two nights after a single administration.

Their sedative action appeared to be most satisfactory, and with few exceptions did not produce a drowsy or stupid condition. The dose of trional as a hypnotic is from ten to thirty grains (grammes .66 to 2.) but it is advisable to begin with fifteen grains (gramme 1). As a sedative ten or fifteen grains (gramme .66 or 1.) at least are required, but in some patients even forty-five grains (grammes 3) will not produce any effect. The dose of tetronal as a hypnotic is from five to thirty grains (grammes .33 to 2.) but in the majority of patients fifteen grains (gramme 1) will be required to procure a satisfactory sleep. As a sedative five or ten grains (gramme .33 or .66) given once or twice a day will generally prove to be of benefit.