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James B. Russell.**

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CLINICAL OBSERVATIONS

ON

HYDRATE OF CHLORAL

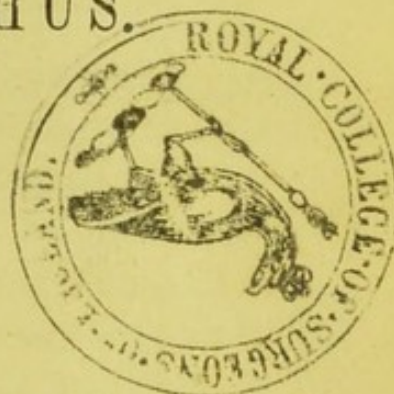
AS A

HYPNOTIC IN TYPHUS.

BY

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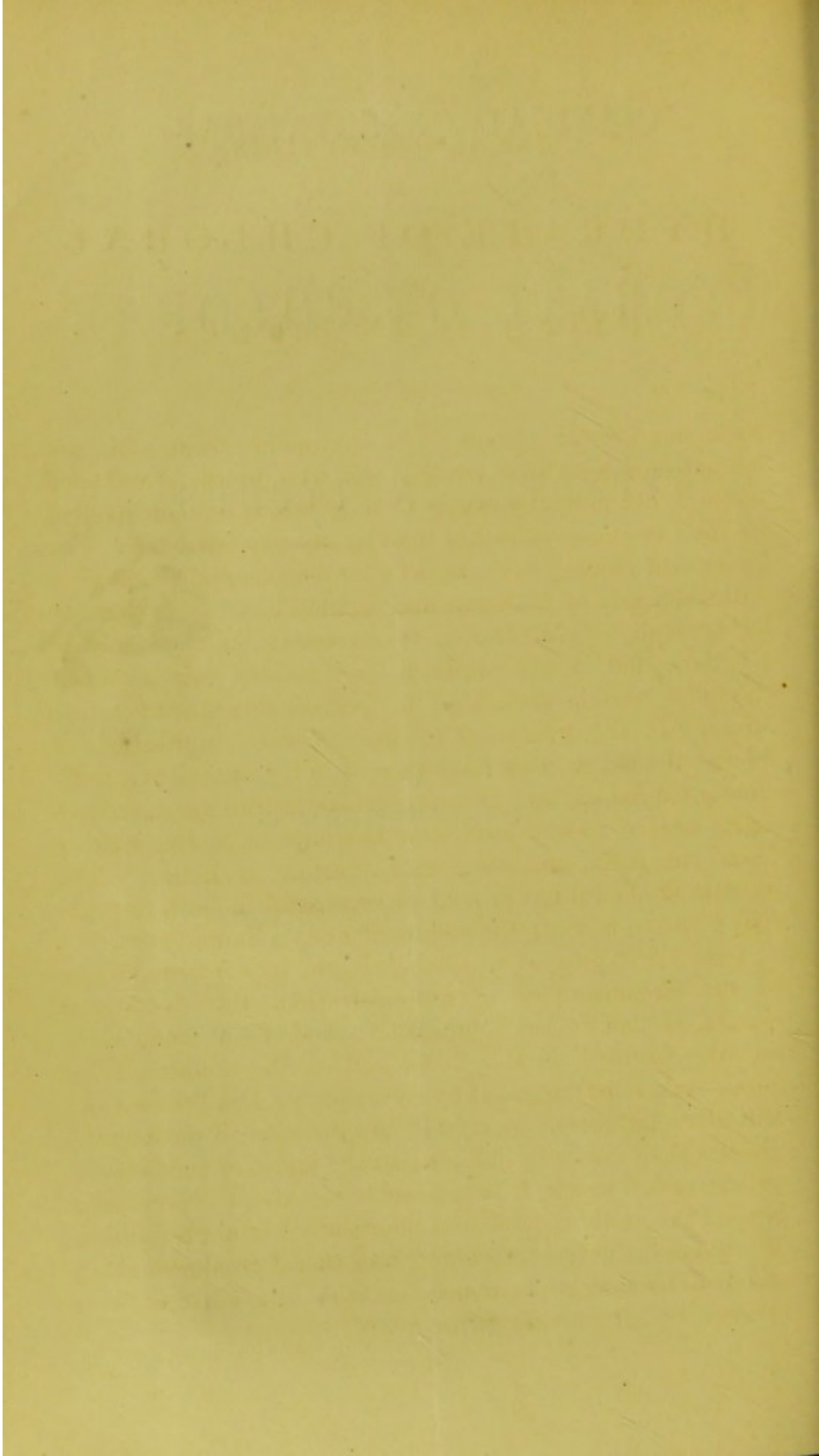


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NEW therapeutic agents often disappoint those who are not satisfied with mere novelty, and who prefer old and tried methods of producing effects to those which are commended by their strangeness rather than by superior efficiency. The hydrate of chloral, as an anæsthetic, will scarcely rank even with protoxide of nitrogen and bichloride of methylene, in feeble rivalry of chloroform. As a narcotic, on the contrary, I believe that it will establish itself as not only new, but specially useful, preferable in certain circumstances to opium. In the treatment of the cerebral complications of febrile disease, opiates have proved in my experience, sufficiently capricious, and even precarious, to lead me eagerly to make trial of new sedatives, in the hope of finding among them one safer and even more certain in action. The hydrate of chloral has proved so successful in both respects that I hasten to state the results of even a limited trial.

I shall first present, in a tabular form, such information as to the circumstances of administration, the dose, and results, as can be so compressed; and then make some remarks founded on this table, and on the minute clinical notes—taken in some cases by my assistants, Drs Tennent and M'Kellar—but mostly by myself. At the outset I must apologize for their scientific defects. In the midst of an epidemic, with crowded wards, it is impossible to extend observations beyond the easily notable and practically useful phenomena. The hypnotic action of chloral was therefore almost solely watched for; such phenomena as the temperature being necessarily left over for future study.

TABLE OF RESULTS OF ADMINISTRATION OF CHLORAL IN TYPHUS.

No. of Case.	Circumstances preceding Administration.	Day of Fever.	Age.	Dose. Grs.	Slept.		Effect short of Sleep.	Condition Afterwards.	REMARKS.
					How soon. Mins.	How long. Hrs.			
I.,	14 hrs. A.D., ...	2nd week.	25	40	(20)	Prolonged and broken.	...	Unchanged.	Pulse irregular 3 hrs. afterwards.
—	(Same case) ...	Do.	...	30	*	...	Vomited at once.
—	Do. ...	Do.	...	40	10	3	Stimulated. Pulse not irregular.
II.,	5½ hrs. D. Ferox, ...	10th.	25	40	(30)	2
—	(Same case.) ...	12th.	...	40	†	D. recurred next day.	...
III.,	D.T. of Typhus, ...	19th.	20	40	(30)	5	...	Unchanged.	Pulse irregular 11 hrs. afterwards.
IV.,	D.T. of Typhus, ...	2nd week.	40	20	15	2	...	No recurrence.	Do.
V.,	Acute Mania,	30	20	5	3½	...	Unchanged.	...
VI.,	D.T. of Typhus, 22 hrs. without sleep, ...	14th.	19	20	30	4	...	No recurrence.	...
VII.,	Night of A.D., ...	?	3	3	20	Prolonged and broken.	...	Do.	...
VIII.,	D.T. of Typhus, 26 hrs. without sleep, ...	14th.	28	20	2 hrs.	4	...	Unchanged.	...
IX.,	Nearly 3 days sleepless, ...	?	3	3	8	2½, broken.	...	Do.	...
X.,	Sleepless night. ...	13th.	19	20	§	Do.	...
XI.,	Do. ...	11th?	30	20	10	4	...	Tranquillized.	...
—	(Same case.) ...	13th?	...	20	§
XII.,	D.T. of Typhus, ...	10th.	47	20	†	Unchanged.	...
—	(Same case.) ...	Do.	...	30	12	Short and broken.	...	Do.	...
—	Do. ...	12th.	...	20	...	Do.	...	Do.	...
XIII.,	36 hrs. A.D., ...	10th.	18	20	†	Do.	...
—	Sleepless night, ...	12th.	...	20	70?	Tranquillized.	...
—	D.T. of Typhus, ...	19th.	...	15	10	Prolonged and broken.	...	No recurrence.	...
XIV.,	A.D. all night, ...	9th.	9	10	7	Do.	...	Do.	...
XV.,	36 hrs. sleepless, ...	?	14	2	10	Short and broken.	...	Unchanged.	...
XVI.,	A.D. all night, ...	13th.	18	20	§
—	(Same case.) ...	Do.	...	20	At once	Prolonged and broken.	...	No recurrence.	2nd dose 9 hrs. after 1st.
XVII.,	A.D. for 36 hrs., ...	?	14	10	15	Do.	...	Do.	...
XVIII.,	D.T. of Typhus, ...	12th.	23	20	†
—	(Same case.) ...	14th.	...	20	15	3	...	Unchanged.	...
—	Do. ...	15th.	...	20	15	Prolonged and broken.	...	No recurrence.	...
XIX.,	D.T. of Typhus, ...	15th.	29	15	2 hrs.	3	...	Unchanged.	...
XX.,	D.T. of Typhus, ...	?	22	20	(30)	3½	...	No recurrence.	...
XXI.,	A.D. for 36 hrs., ...	10th.	12	15	(25)	Prolonged and broken.	...	Do.	...

Note. —A.D. = Acute Delirium. (—) Asleep then, but not observed how long. D.T. = Delirium Tremens. * Inert. † Partially soothing. § Decidedly soothing.

Physiological action of chloral.—Although the chloral was administered for therapeutic ends, the notes of these cases in some particulars illustrate the observations of Liebreich, Bouchut, Personne, and Richardson, as to its physiological effects. The full development of these effects depends, of course, upon the dose; and since, from the papers of these gentlemen, I was led to exhibit at first what proved to be an overdose, viz., 40 grains, the action of the drug went further than was necessary. I therefore give the notes of two such cases in full. At the close of the paper will be found some speculations as to the cause of this susceptibility.

CASE I.—Janet N——, aged 25, on 12th Dec., 1869, had been six days in hospital with very severe typhus of unknown duration, aggravated by debility from 15 months' lactation. On the forenoon of that day, although her pulse was falling and her bowels were free, *she had not slept for 14 hours*, but had sung and talked constantly, and was only held in bed by the canvas sheet.

12.50 p.m.—Pulse, 120; good. Temperature in rectum, 100.5°. Face flushed and whole aspect excited. *At this hour 40 grains chloral were given.*

1.10 p.m.—Pulse, 118; decidedly smaller and softer, and indeed seems to falter at times. Lies quietly half on back; eyes shut; respirations interrupted by a constant short cough. Eyelid lifted without awakening patient; *pupil almost pin-hole*. On pinching arm severely she awakes, looks up, and *pupils, at first small, become natural*. Coughs, and dislodges a quantity of mucus.

1.30 p.m.—Pulse, 124. Roused by nurse, contrary to orders, to take milk, and is, though not restless, noisy.

2.20 p.m.—Pulse, 112; soft. Quiet; saying "Awe! awe!" in a dreamy tone.

3 p.m.—Pulse, 110; soft. Still more absent and drowsy, but repeating "awe! awe!"

3.40 p.m.—Pulse, 84; small, feeble, irregular. As before; tranquil.

4.20 p.m.—Pulse, 82 to 86; improved in quality, but irregular. Same dreamy tranquil state. Evidently alive to what is being said. Passed urine in bed.

5 p.m.—Pulse, 92; improved in quality, and rather steadier. General condition unchanged.

5.40 p.m.—Pulse as before; asleep, but wakened by counting it. Has had no food or stimulant since draught. Give milk.

6.20 p.m.—Pulse, 112; quality good, and quite regular. Temperature in rectum, 102.5°. No more sleep; passive; talking to herself.

8.20 p.m.—Pulse, 120; good. Quiet, but talking, and waving hands in air. 30 grains chloral in half-an-ounce of water and syrup given, but vomited at once.

11 p.m.—Pulse, 120. Excited, and constantly chattering. Give 40 grains chloral again, in 3iss. water and syrup.

11.30 p.m.—Pulse, 116; much softer. Patient became quiet in about ten minutes after draught, and now sleeps calmly. Respiration is sometimes slow and full, sometimes hurried and short.

Dec. 13th.—Slept for three hours after last dose; then became wakeful and excited for about 6 hours, but again slept soundly. Patient never became restless again, but passed into convalescence.

CASE III.—Helen C——, aged 20, was in the 19th day of severe typhus, with general bronchitis and partial congestion of lungs; bowels free; delirium of nervous semi-hysterical type.

Dec. 16th, 12.30 p.m.—Pulse, 120; good. No sleep for some 48 hours. Got 40 grains chloral at this hour.

12.40 p.m.—Pulse, 120; still awake and chattering. Face blue; flushed.

1 p.m.—Pulse, 110; full and strong. Respirations 46; full and deep. Sleeping soundly; not disturbed by counting pulse.

1.30 p.m.—Pulse, 108; soft; asleep, but roused by counting pulse.

6.40 p.m.—Pulse, 136. Slept till 5.40; at times talking, but always falling over again. Is now in peevish delirious state once more.

11 p.m.—Pulse, 136; intermits three times in 15 seconds. Give teaspoonful of whisky every hour and Liebig.

17th.—Pulse, 124. Had a restless night, but afterwards, although irritable and hysterical, obtained abundant sleep, and recovered, although tediously.

In these cases, after a 40 grain dose, the toxic effect upon the heart was manifest. In one case only, the 4th, irregularity was developed by so small a dose as 20 grains, but lowered frequency was not uncommon. The large dose was given also twice to a bulky, robust man, but did not affect the heart, so far at least as to cause irregularity. The pulse seemed, but with exceptions, at first and that speedily to improve in quality, but in an hour it became soft and small, sometimes lowered in frequency, and finally the action of the heart became irregular. Although it is difficult to eliminate from the sedative effects of mere repose on the respiratory and circulatory organs of a delirious person, those which are due to the drug which induces the repose, there can be little question that the chloral acted directly and specially on the heart in these instances. In many of the cases also, from the aspect of the countenance, flushed and full, and from the improved colour of the rash, brightening when petechial,—the impression of stimulated action which we have said the pulse at the very first, and for a short time, conveys, receive further confirmation. The breathing also is quickened and short, but not laboured. These phenomena are, however, of the most transient description, and soon give place to those with which we are familiar in natural sleep. The state of the pupil is the same—contracted to the utmost, as in the “pin-hole pupil” of Graves;

but, differing from the contracted pupil of narcosis, it expands in the chloral sleep immediately the patient is awaked. The power of voluntary motion seemed never to be in abeyance, but always at command as in natural sleep; and no change in the susceptibility of sensation was present. The sedative effect on the brain and nervous system was sometimes visible in a few minutes, but seldom became developed into true sleep and unconsciousness until from 10 to 20 minutes. The transition from waking to sleeping was noted to be often very sudden. If disturbed by any external or internal irritation, as by counting the pulse, for instance, the patient often looked up, with natural pupils, then turned on one side, seemed to sleep *at once*, and on lifting eyelid, no movement was caused, and the pupil was found to be almost abolished. According to Richardson, thorough narcosis from chloral is accompanied, in the rabbit at least, by dilated pupil. In Case I., it will be observed that the pupil remained for a perceptible period contracted, as in opiate narcosis, after the patient had been roused by pinching. Dilatation was never observed from the doses employed in my cases.

Therapeutic action of chloral.—The therapeutic action desired was sedative and hypnotic, and as such the table shows that it was successful in almost every form of cerebral excitement incident to febrile disease, with remarkable uniformity and rapidity. Case II. illustrates its efficiency in a well-marked instance of *delirium ferox*.

CASE II.—Archibald B——, aged 25, on the 10th day of well-marked typhus, without previous warning, after a good night's sleep, suddenly jumped out of bed, and smashed a window in his endeavours to escape through it. Was forced into bed against violent resistance, and retained there by jacket and sheet. Bowels quite free.

Dec. 15th, 2.30 p.m.—After a pertinacious resistance, 40 grains chloral was administered.

3 p.m.—Pulse, 96. Apparently sleeping quietly.

4 p.m.—Evidently sleeping soundly.

7 p.m.—Pulse, 96; soft. Slept about 2 hours altogether. Is now awake, but quiet and rational.

17th, 2.30 p.m.—Pulse, 132. Has been sleepless since last note, and is now as violent as ever. 40 grains chloral again given.

3 p.m.—Pulse, 128; fuller. No sleep. Nurse thinks him quieter; but no effect further than this followed this dose.

Patient died on 15th day.

Chloral seems to have a more immediate and permanent curative action on such cases of acute delirium, at the acme of typhus, than in the *delirium tremens* of the second and third weeks, when the blood is loaded with the products of the fever, and there are general tremors and subsultus.

In the former class of cases, its action was sometimes quite magical, as in Case XIV., for example, where, in 7 minutes, the patient was calmed from a state of fiery excitement.

CASE XIV.—Ellen T——, aged 9. Well-marked typhus.

Jan. 8th, (9th day) 12.58 p.m.—Pulse, 140. After *sleepless night*, spent in shouting and getting out of bed, got 10 grains chloral at this hour. Bowels free. Pupils slightly dilated.

1.5 p.m. (7 minutes after)—*Quite quiet*, but opens eyes dreamily for a second as I look at her.

1.20 p.m.—Pulse, 128. Respirations, 48. *Sleeping soundly*. Aspect calm and perfectly natural. *Pin-hole pupils*.

11.30 p.m.—Pulse, 128. Has been *always tranquil, generally sleeping, throughout the day*.

No recurrence of delirium. Recovered.

Case XVII. is an equally good example, where two hours' unbroken sleep, followed by interrupted sleep during the entire day, was produced by 10 grains in a boy of 14. In both instances the patient became sensible and continued so. This permanently curative action was frequent, as the table shows, and more common in the active than in the adynamic form of delirium. Although this adynamic delirium, or the *delirium tremens* of typhus, as I call it, was less promptly amenable to chloral, as it is to all sedatives, Cases VI., XIII., and XVIII. show excellent results. Indeed there is no other sedative but chloral which I should have ventured to administer, still less to repeat, in the last two. Seeing that the delirium depends in such cases on the presence of impurities in the blood, the elimination of which is a process requiring time, all that we can expect from a sedative which does not act by hastening elimination, is to soothe from time to time, and to check vital exhaustion until the process is completed by the natural channels. In this aspect, the chloral appears in no case to better advantage. We shall quote Case XVIII. as an illustration of its beneficial action in one of the worst cases of such adynamic delirium I have ever seen. It will be observed that it even controlled the subsultus for a time.

CASE XVIII.—John M'D —, aged 23. Very severe case of typhus, with prominent cerebro-spinal symptoms from the 10th day.

Jan. 14th, (12th day) 2.30 p.m. Pulse, 128. Pupils natural. No sleep during night. *Delirium tremens of typhus*; ceaseless chattering, movement of hands in air, universal twitchings. Got 20 grains chloral at this hour.

7 p.m.—Pulse, 130; small and soft. Has been seen at intervals, and there has been *no sleep whatever*. Nurse thinks him on the whole quieter, but this is doubtful.

15th (13th day)—Pulse, 114. Nervous symptoms abated, but not a wink of sleep. No motion for two days. Give castor-oil.

16th (14th day)—Bowels were moved yesterday by the oil. Still, has had *no sleep since the 13th*. Nervous symptoms aggravated. Every muscle seems to twitch in turn. Rash petechial and copious.

11.30 a.m.—Pulse, 108; soft and small. Pupils natural. At this hour 20 grains chloral given.

11.50 a.m.—Pulse, 102; considerably improved. Has just fallen over. Aspect entirely that of a person in deep natural sleep. Snores. Hands are lying quietly on breast, and only a rare twitch is observed. Eyelid lifted, and pupil found to be pin-hole.

12.20 p.m.—Pulse, 104; good. Sleep continues, but is disturbed by slight muttering and subsultus.

12.50 p.m.—Pulse, 100. Quietly and soundly asleep, as at first. Passed urine copiously 5 minutes ago, having become very noisy and excited just before that, but falling quiet immediately after.

7.5 p.m.—Pulse, 100; pretty good. Sleep continued until about 2.30 p.m. unbroken. Has dosed and waked all afternoon.

17th (15th day) 2 p.m.—Pulse, 120. Has had *no sleep all night*. Nervous symptoms as bad as ever. At this hour, 20 grains chloral given.

2.20 p.m.—Pulse, 120. Respirations, 30. Sleeping soundly, and has done so for more than 5 minutes. No subsultus.

4.20 p.m.—Pulse, 124. Still sound asleep.

6.20 p.m.—Pulse, 124; but from subsultus difficult to count. Has slept and waked by turns during afternoon; but is now restless again.

Progressed favourably afterwards.—No recurrence.

In Case XIII., there was bronchitis and congestion of both lungs—a state of matters which forbids the use of opium—but chloral was given from time to time, producing sleep without promoting pulmonary stasis. In Case XV., the restlessness of tubercular meningitis supervening on typhus, in an infant aged 18 months, was temporarily calmed by a dose of 2 grains. The general statistics of results in all cases are as follows:—Chloral was administered 32 times in the treatment of 21 cases. Of these 32 doses, 24 were followed by sound and well-marked sleep, lasting without interruption from 1 to 5 hours, and nearly always prolonged by a succeeding period of broken sleep and general tranquillity, 3 doses had a decidedly, 4, a partially soothing effect, and 1 proved inert; but this last dose was immediately vomited,

and ought not therefore to be counted. Looking to the 21 individual cases, we find that *not one proved insensible to the chloral when repeated*. I never met with an equal number of consecutive cases of delirium, &c., in which any other sedative showed such uniformity of action, or even approximated to it.

Comparative effects of chloral and other hypnotics.—In the treatment of fever one has necessarily an unusual opportunity of studying the effects of hypnotics and sedatives. Very few cases pass through the physician's hands without at some period demanding the use of some means of producing sleep artificially; and the question which to employ is neither unimportant nor easy of solution. I have a very decided opinion as to the danger attending the use of opiates in fever, no matter how guarded with eliminants, as antimony, grey powder, &c. Nothing astonishes me more, as being opposed to my whole experience of their disastrous results, than the free and unguarded way in which preparations of opium, either alone or combined, are recommended even in treatises on fever,* and employed by some practitioners. From the want of a better agent I have hitherto, after Graves, used Battley with tartar-emetic (5 drops to $\frac{1}{12}$ grain), but I never order such a draught without apprehension, and have repeatedly seen patients put into a dangerous state of narcosis even by *one* such minute dose, a state always requiring active and prompt measures to save the life, and not unfrequently ending in fatal coma, or pulmonary engorgement or congestion. As is well known, opium always cripples the eliminating functions, especially of the kidneys; and as antagonistic to this action, I always combine with it some diuretic. Even in health you cannot develop the narcotic action of opium without this effect on the excretions. The general action on the nervous and

* See *Reynolds' System of Medicine*, Vol. I. Article on "Typhus Fever," by Dr Buchanan; p. 534. Also, even *Murchison* gives this questionable special indication for opium, "delirium approaching to typhomania or *delirium tremens*." (p. 276.) The dangers of opiates in fever are given with great clearness and good sense by Hudson. "*Lectures on Fever*." (p. 376.)

muscular tissues is also paralyzing. The bronchial muscles and epithelium, and the external muscles of respiration, share in the narcotic paralysis. Hence the invariable tendency in opium poisoning to stasis of the blood in the pulmonary vessels, and of the bronchial secretion in the bronchi. Suppose now a case of typhus in the second week, in a state of sleepless delirium from the circulation of poisoned blood through the brain. The cerebro-spinal nervous system manifests the results of its impaired nutrition by violent excitement, or low muttering insomnia; the muscles also, voluntary and involuntary, suffer changes of structure, which can be seen under the microscope; the external muscles of respiration are partially paralyzed, and stasis, set agoing in the lungs by the altered relation of the impure blood to the capillaries, is promoted by the imperfect expansion of the chest wall. The external and internal pathological conditions act and react on each other. When therefore we give an opiate to a typhus patient, we combine two similar pathological tendencies, and may precipitate into narcosis functions which were previously on the brink, and by cautious management might have been preserved in some measure of vital activity. It is impossible to say what dose will *not* have this effect. As I have said, 5 drops of Battley and $\frac{1}{12}$ gr. of antim. tart. will do it. In rare cases I have seen even the slight lowering of vital action, which accompanies natural sleep (in this case, however, sleep coming without artificial aid to a blood-poisoned fever patient), develop in a case such as I have described, congestion of the lungs, general lividity, and partial coma. But as a rule, in natural sleep there are no such dangers, and it is the almost perfect analogy between natural sleep and the sleep induced by chloral, in properly adjusted doses, which commends that drug to my mind as the best hypnotic in febrile diseases. I am well aware that the clinical experiments here recorded are but limited, and that my conclusions must be subjected to prolonged trial and observation before they can be thoroughly established. Still I see in the chloral sleep something different from opium sleep, and both positive and negative

properties in the former drug, which mark it as safer than the latter. 1. The action of the pupil to which I have already alluded illustrates excellently the close approximation to a natural sleep which chloral bestows, and the difference between it and opium in physiological effect. In all forms of sleep the pupil is contracted to the utmost. But in natural sleep, the moment the sleeper is roused, and the eyes are opened, the pupil expands; while in an opium sleep the pupil remains contracted, it may be only for a few seconds, or for minutes, or hours. This illustrates in little the general condition of the nervous and muscular system in natural and chloral sleep, and in opium and other narcotic forms of sleep. As we have seen, the chloral sleeper may be roused at any time. He is at once in the full command of his functions, may take food, pass urine, cough with full strength, expectorate, &c.; and whenever the temporary excitation ceases, he may drop over again into unconsciousness. Indeed as a rule, the chloral sleep consists of a continuous initiatory stage, followed by a period which may extend over 6, 8, or more hours of sleep, interrupted by intervals in which food, &c., may be given without the necessity of waking the patient, or any risk of re-establishing the excitement. This was specially noted in some of our cases, as in Case VII, "8 p.m. Sleeping; had drinks at intervals, falling asleep at once afterwards." Not so with the patient after an opiate which will produce an equally sedative effect. His pupils are small; if his lungs are gorged with mucus, he has neither the intelligence to see the necessity, nor the muscular energy at command to cough and expectorate. 2. The excretions are not affected by chloral. They are by opium. The bowels are made costive, the urine scanty, the mouth parched, and the skin dry. 3. The administration of an opiate to a child is in any circumstances a procedure which the practitioner adopts with misgivings. Chloral may be given with perfect safety, and with perfect success. 4. Opiates, even as combined by Graves, with tartar emetic, are uncertain, very frequently quite futile. As already stated, I have met with no patient who resisted the action of chloral.

I have contrasted chloral with opium at much length, because opium is really the only hypnotic of sufficient value to be contrasted with it. Having in the course of practice gradually acquired the opinions regarding its dangers in fever, to which I have already given strong expression, it was natural that I should employ any drug or method which promised good results as a sedative. Space forbids any lengthened reference to this partly experimental practice. For some time, the bromide of potassium and cold-sponging have almost entirely displaced Graves' mixture, and Battley and ether, which, for a long time, were my only sedatives. The bromide formerly tried, but imperfectly, and thrown aside, was revived by Dr Tennent, at the request of the Professor of Materia Medica in the University, and has been extensively used. It is capricious, sometimes acting with excellent effect, but oftener proving useless in apparently similar circumstances. We give it in drachm doses, three times repeated, at intervals of an hour. It rarely acts, even when the best results ultimately follow, within forty-five minutes, or an hour. No dysphagia or other toxic effect has ever been observed, and its narcotic action manifests none of the dangerous tendencies of opium. Chloral, however, far excels the bromide in efficiency and certainty. In cases IV., VI., and VII., where chloral produced prolonged sleep, followed by no recurrence of delirium, it was appealed to after the bromide had failed. *Cold sponging* again, soothes by the abstraction of heat from the periphery, and is consequently useful only in the acute delirium and insomnia of the acme of fever, when the skin is pungently hot, and the condition such as I usually describe by the adjective "fiery." In these circumstances, sponging with iced water every 2 or 4 hours, has often a calmative effect. During the prolonged course of Case V., various sedatives were used. The following notes will show their comparative action. The effects of the bromide, though not so rapidly produced, were quite as good as those of the chloral in this case.

CASE V.—Elizabeth H———, aged 30. A case of severe typhus, with prominent cerebral symptoms throughout, which ultimately outlasted the

fever, and passed into *acute mania*; the second case of the kind I have seen after typhus. Both cases went on, unchecked by treatment, to a *fatal termination*. The following sedative agents were employed from time to time in the present case.

1. Tartar emetic, $\frac{1}{2}$ grain; Battley, 5 drops; once, no effect; and once, half hour's sleep.
 2. Tartar emetic, $\frac{1}{2}$ grain; tinct. digitalis, 5 drops; every 4 hours. No effect.
 3. Bromide of potassium, in drachm doses, repeated for three successive hours. Given on 4 occasions, with excellent effect on three, but no effect on one.
 4. Battley, 10 drops; chloric ether, 20 drops. No effect.
 5. Blister to scalp; twice. No effect.
- Dec. 21st.—Pulse, 124. Wild delirium for at least 24 hours. At 2.30 p.m., 20 grains of chloral given.
- 3 p.m.—Pulse, 116; soft. *Sleeping soundly and naturally; fell asleep in 5 minutes after administration.*
- 4 p.m.—Pulse, 108. Continues in same placid sleep.
- 5 p.m.—Pulse, 100; soft. *Sleeping soundly.*
- 6 p.m.—Pulse, 132; feeble. Just wakened, and as *maniacal as ever*.

Dose of chloral. Mode of administration. Dangers.—My first cases proved conclusively, that for the class of patients under my care, 40 grains is a toxic dose. It produced depression and irregularity of the heart's action. In my cases, all the benefits without the dangers of chloral were obtained with 20 grain doses for adults; 2 grains for an infant of 18 months; 3 grains for two of 3 years; 10 grains for children of 9 and 14 years. The drug was given in an ounce of water sweetened with half an ounce of syrup.* Children take the draught quite readily in this way, and like it. If not sufficiently diluted, the medicine is vomited, as in Case I., where 30 grains were dissolved in only half-an-ounce of water and syrup. When sufficiently diluted it may be borne by the most irritable stomach, as it was in Case X., in which nutrient enemata were required from obstinate vomiting, and yet the chloral was not rejected. The dangers of an over dose of chloral are manifest from the cases in which 40 grains were administered. The depressing action of chloral on the cardiac ganglia is then developed. For the sake of the purity of the experiment, in some of my cases, all stimulants, and to some extent even food, were prohibited. This is, however, un-

* This dilution is enough for the lessened sensibility of a fever patient, but, from personal trial, *not for ordinary use*.

necessary, especially in view of the readiness with which the chloral, like the natural sleep, may be broken and resumed. Indeed, the same rule applies here as to all the circumstances of a fever patient,—not to interrupt the regular administration of food for any cause, and remembering that we are dealing with a drug which has a special action on the heart, we should first be cautious in adapting the dose to the age and vigour of the patient; and then, having given it, should watch the pulse at intervals, more particularly during the next six hours.

The mode of action of chloral.—This theoretical question assumes some practical importance when we employ chloral in typhus. According to Liebreich, the ultimate physiological action is not that of chloral, but of chloroform produced by the decomposition of chloral by the alkalies of the blood. This theory is strongly supported by the fact that chloral mixed with fresh blood does evolve chloroform. M. Personne and Dr Richardson agree with Liebreich. Indeed M. Personne has gone further in the proof of the theory by demonstrating the presence of *chloroform in the blood* of dogs, to whom *chloral alone* had been administered.* Now it is well known that the tendency of the typhus process, as it advances, is to *increase the alkalinity* of the fluids of the body. Ammonia can be detected in all the excretions in an amount much greater than in health. The urine, at the close of a severe case, gives off free ammonia so copiously as to cause lachrymation, and to be sometimes quite unbearable by one auscultating the back, for example, of a patient passing it involuntarily. “There is good reason for believing,” says Murchison, “that the unnatural fluid state [of the blood] in typhus results from an abnormal amount of ammonia.” Whatever may be the precise pathological product, there is no doubt of the fact that typhus blood is more highly alkaline than the blood in health. Hence, if its action depends upon alkalinity at all, and M. Personne seems to have demonstrated that fact, then chloral must be *par excellence*, the hypnotic suited for typhus. Liebreich’s theory is in itself beautiful and attractive, and

* *Gaz. Hebdomadaire*, November 19th, 1869.

in the words of a recent reviewer, "it is impossible not to feel a genuine admiration for the stroke of genius which is indicated in the prediction, from purely chemical considerations, that chloral would yield up chloroform to the blood in precisely the form in which it might be expected to do the maximum of good and the minimum of mischief." The illustration of the theory furnished by the rapid and magical effects of chloral in typhus involves an idea even more attractive. We transform a pathological into a therapeutic process. The fever-products liberate the soothing agent, and so calm the excitement which they themselves have made.

The subject of special susceptibility in typhus patients to the influence of chloral, in reference to the theory of its action, is one which must be reserved for future investigation. But it is entirely confirmatory of my supposition to find that there is such a susceptibility. The chemical conditions on which, according to Liebreich, the physiological action of chloral depends, exist in typhus in excess. The physiological effects of chloral ought therefore to be developed in a typhus patient with smaller doses and with greater rapidity. My experiments are few, but they are all *positive in their result*. Liebreich states that *the nervous power of the heart is the last which suffers*. Richardson says—"In fatal cases the functions destroyed are: 1. The cerebral. 2. The voluntary muscular. 3. The respiratory. 4. *The heart*." In my observations on *physiological action*, it will be seen that a dose so small as 40 grains, in two out of three cases, proved toxic to the extent of developing the ultimate of the series of functional effects—that upon the heart; and that in one case even 20 grains seemed to produce this result, while the whole series of cases illustrates the striking facility with which small doses produce the primary effect on the brain and voluntary muscles, and sometimes lower the frequency of the pulsations.