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HYDRATE OF CHLORAL, WITH CASES ILLUSTRATING ITS ACTION.

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CHLORAL was discovered by Liebig in 1832. Its chemical properties were more fully investigated by Dumas in 1834. It was afterwards studied by MM. Regnault, Kopp and Wurtz. It was known, however, chiefly or only to chemists, and regarded by them more as a curiosity than an article of value, till M. Liebreich, of Berlin, introduced it in the form of hydrate of chloral into therapeutics. Since then its physiological and therapeutical action has been investigated by MM. Bouchut, Bricheateau and Demarquay of France, Dr. B. W. Richardson, J. B. Russell, of England, Dr. William A. Hammond of New York, DaCosta of Philadelphia, and others both in this country and Europe. It has been tried both in hospitals and in private practice. On the whole, the verdict of the profession is in its favor. Its probable value as a therapeutic agent is such that clinical observations with regard to its action in disease are interesting and important. It is moreover interesting as an admirable illustration of the close alliance between the chemical constitution, the physiological action and the therapeutical use of drugs. This alliance is becoming every day more apparent, and the time is not far distant when it will be generally recognized by the practising physician, and constantly guide him in the art of prescribing.

Chloral, from which the hydrate is made by the addition of water, is described by Dr. Benj. W. Richardson, the distinguished London physician and physiologist, as "an oily liquid, colorless, and of pungent odor. It is an irritant to the skin. Its specific gravity is 1500 as compared with water at 60°; its vapor density is 74 compared with hydrogen as unity; and its boiling point is

99° Cent.—210° Fahr."* It is made by treating anhydrous alcohol with chlorine.

The hydrate of chloral is made by combining chemically water and chloral. This is described by Dr. Richardson, in the article just quoted, as a "white, crystalline substance. The crystals are rhombic. In the formation of the hydrate, about eight parts of chloral combine with one part of water, forming nine parts of the crystalline substance. Hydrate of chloral, therefore, contains 90 per cent. of chloral. The hydrate, although a solid, volatilizes like camphor without decomposition. It dissolves in water so freely that a saturated solution contains 50 per cent. It dissolves also in alcohol and ether." We learn from the same authority that when it is acted upon by an alkali, as potassa, soda or ammonia, it is decomposed into a formate and chloroform. If any quantity of potassa is added to a solution of hydrate of chloral, a corresponding amount of chloroform is evolved. The presence of the latter agent may not only be detected by the milkiness of the fluid, but by the characteristic odor of chloroform. This fact of the evolution of chloroform from the hydrate of chloral, when the latter is put in contact with alkalis, is an important practical one to the physician. It not only indicates the impropriety of uniting an alkali with the hydrate of chloral in prescriptions, but it points to the most probable explanation of its physiological action. Some account of this action will form an appropriate introduction to the clinical observations that follow.

Physiologists have experimented with hydrate of chloral upon all classes of animals. Its action has been studied on fishes, frogs, rabbits, cats, mice, dogs, pigeons, and I know not how many other living creatures as well as man. Upon all of them it exerts a certain similarity of action, though with some curious differences. When

* London Medical Times and Gazette for Oct. and Nov., 1870.

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fishes are put into water sufficiently charged with it, they absorb it by inhalation, grow sluggish and presently fall asleep. Frogs fall asleep by the subcutaneous injection of half a grain; they are apt to be killed by three-quarters of a grain, and are sure to be killed by more than the latter dose. A quarter of a grain will put a mouse into a sound sleep. Rabbits come easily under its influence, whether given by the stomach or subcutaneously, and may be put into a gentle sleep, or narcotized or killed by it, at the will of the experimenter. Pigeons, that according to Weir Mitchell,* tolerate enormous doses of opium with impunity, are easily narcotized by hydrate of chloral. Cats come readily under its influence, and when subjected to it they are said to purr with obvious comfort as they go to sleep.

We learn from the admirable researches of Dr. Richardson,† that the sleep induced in all sorts of animals by hydrate of chloral resembles natural sleep. Recovery from this sleep is unattended with any apparent derangement of the system. The drug may be administered in doses just large enough to produce this sort of natural sleep, or in doses large enough to produce a dangerous degree of narcotism, or in doses that shall rapidly prove fatal. In other words, the hydrate of chloral is to animals a pleasant and harmless anodyne, or a dangerous narcotic, or a rapid and fatal poison, according to the dose in which it is given. In this respect its action on animals resembles its action on man. When death is produced, the heart seems to be the ultimum moriens. The circulation may be seen going on in the web of a frog's foot, when the animal is so profoundly under the influence of the drug as to appear dead.

Muscular relaxation, complete anæsthesia, absence of reflex movements and reduction of animal temperature, in varying degrees, dependent upon the doses given, accompany the narcotism of hydrate of chloral. An apparent hyperæsthesia has sometimes been noticed, especially by M. Demarquay, but it is an occasional and exceptional phenomenon.

A knowledge of the physiological action of the hydrate of chloral on man is an indispensable guide to its use in disease. We do not yet comprehend this action completely, but we know enough of it to aid us materially in its clinical administration. The points of greatest importance to the practitioner are its absorption, its elimi-

nation, the changes which it undergoes in its progress through the system, and its action on the system from the period of absorption to that of complete elimination.

1st. *Absorption*.—Hydrate of chloral is readily absorbed by the mucous surfaces of the stomach and rectum, and also by the cellular tissue. For absorption by the latter tissue it should be administered by subcutaneous injection. This procedure, on account of the local irritation which it induces, is not one to be recommended. The ordinary method of giving it by the stomach is the best. If concentrated when thus given, it produces local irritation and nausea, and is apt to be thrown off. It is easily and quickly absorbed from the stomach if largely diluted. I have usually found that a solution stronger than a grain of the hydrate to a drachm of water will produce gastric uneasiness. When diluted to this or to a greater extent, it is well tolerated by the stomach. If a moderate dose is given, viz. one of thirty grains or less, it is probable that the whole of it is absorbed in a few minutes. In the first of the following cases, the hypnotic effect was produced in ten minutes after the administration of the drug. As the dose of it in that case was only fifteen grains, it is fair to infer that the whole, or nearly the whole, of the quantity given passed from the stomach into the blood within that space of time. The stomach appears to be capable of passing into the blood any quantity of hydrate of chloral that may be put into it, provided that the article is pure and sufficiently diluted. Hence any quantity of it may be given at a dose, so far as the stomach is concerned, that it is wise to administer. The presence of food in the stomach would be likely to delay its absorption. Any irritation of the stomach, like gastritis, would probably render that organ intolerant of it, though I have never proved this by experiment. The absorption of the hydrate of chloral by the stomach, then, is easily and quickly induced when it is given largely diluted upon an empty stomach whose mucous membrane is in a normal condition.

2d. *Progress through the System*.—The hydrate of chloral goes from the stomach into the blood unchanged. In the blood it meets with an alkali. The experiments of Dr. Richardson and others show that the hydrate of chloral in contact with an alkali is decomposed and chloroform evolved. Indeed, chloroform has been obtained from the vapor arising from a mixture of freshly drawn blood and hydrate of chloral.

* Am. Jour. Med. Science, Jan., 1870.

† London Med. Times and Gazette, Oct. and Nov., 1870.

We have the authority of Liebreich for stating that when the hydrate meets with an alkali in the blood, it behaves as it does when it meets with alkalies out of the system. That is, as soon as hydrate of chloral reaches the blood by any avenue, it commences to yield chloroform. The amount of chloroform thus given to the blood is proportionate to the quantity of chloral absorbed and also to the alkalinity of the blood. The total quantity of chloral absorbed is not immediately decomposed into chloroform. The drug mixes with the blood, passes with the blood to every part of the organism, and, as it circulates, continues to yield chloroform until it is exhausted. In cases of fever of a low type, such as typhus and typhoid fever, when the blood is highly charged with ammonia, that fluid is in a state to extract chloroform from chloral more rapidly than when it is less alkaline. Under such circumstances a given dose of hydrate of chloral should produce its physiological action more rapidly and powerfully than it ordinarily does. Since writing these words I have met with the clinical experiments of Dr. J. B. Russell* with the hydrate in typhus fever, at the Glasgow Fever Hospital, and these indicate that such is the case. Doubtless other substitution compounds than chloroform result from the decomposition of hydrate of chloral in the blood, and exert more or less influence on the organism till they are eliminated from it. What these compounds are, and what their physiological action is, cannot yet be stated. It is probable that some of the physiological actions of the drug we are considering are due to these compounds. Until they are discovered and their effects known, a complete solution of the problem of the physiological action of hydrate of chloral is impossible.

The above theory of the decomposition of hydrate of chloral in the blood into chloroform, not all at once, but with comparative slowness, particle by particle, just as fast as a particle of chloral meets with a sufficient quantity of an alkali, is that of Liebreich. It is a beautiful and ingenious theory, and one that seems to me justified by physiological experiment and clinical observation. The chloroform, yielded by the chloral to the blood, of course behaves in that fluid just as the same amount of chloroform would do if it were passed into the blood at the same rate by any other process. Hence hydrate of chloral, accord-

ing to its dose, may be soporific, anæsthetic or dangerous because it yields chloroform. But it is not probable that in moderate doses it will ever prove dangerous, because in such doses the chloroform evolved will be eliminated too rapidly to be so.

The hydrate of chloral, then, passes rapidly from the stomach into the blood unchanged. In the blood it is decomposed into chloroform, and perhaps into other compounds also. These substitution compounds continue to circulate with the blood throughout the organism, until they are oxidized in it or eliminated from it.

3d. *Elimination.*—Most, if not all, of the hydrate of chloral is eliminated from the system in the form of chloroform, into which it has been changed. Dr. Richardson states that he has detected the odor of chloroform in the breath of animals sleeping under the influence of chloral. Messrs. Lallemand, Perrin and Duroy* have shown that chloroform is eliminated chiefly by the pulmonary mucous surface. They have also shown that when it is rapidly introduced into the organism it is more rapidly eliminated than when it is slowly introduced. When it is slowly introduced, at least an hour and a half is required after the introduction of the last dose; that is, after the last quantity of it has been inhaled, for its complete elimination from the blood. So far as we know at present, the elimination of the hydrate of chloral is the same as the elimination of chloroform slowly introduced into the blood. So much of the hydrate as has been changed into chloroform is eliminated by the pulmonary mucous surface in an hour and a half, or less, after its absorption. When, therefore, it is desirable to keep the blood charged with the hydrate of chloral continuously, it should be given at intervals of not more than two hours. If this is undesirable, a second dose should never be administered until sufficient time has elapsed for the elimination of the first. The practitioner should select one or the other of these modes of administration, in accordance with the therapeutic object he has in view. How any of the other substitution compounds of the hydrate of chloral are eliminated, we do not yet know. They are probably oxidized in the organism.

4th. *Action on the System.*—Hydrate of chloral, while in the system, affects especially the blood, the cerebro-spinal axis, the heart and arteries, the muscular system, and the temperature.

* Glasgow Medical Journal, Feb., 1870.

* Du Rôle de l'Alcool et des Anesthésiques dans l'Organisme, p. 350, etc.

When a single therapeutic dose of chloral is administered, it passes into and out of the blood without producing any chemical change in that fluid. If the dose, however, is so large as to be a toxicological one, the blood undergoes a change. It becomes, as we learn from Dr. Richardson's experiments, less coagulable, and its corpuscles become shrunken and crenate; it is in fact devitalized. In this respect, the action of chloral on the blood resembles that of large or long continued doses of ammonia or potash. If chloral were administered in therapeutic doses for a long time, and with such short intervals between each dose, that its complete elimination from the blood, for at least a portion of each twenty-four hours, were rendered impossible, a devitalization of the blood would doubtless result. That such is not the case, provided chloral is given so as to allow for its daily complete elimination, we learn from clinical observation. Cases II., V. and VI. that follow are illustrations in point, for the patients there described took hydrate of chloral daily for many weeks, without loss of flesh, color, strength, appetite, or other ill effects. I have said that in this respect the action of chloral on the blood resembles that of alkalies. Alcohol would have been a better illustration; for alcohol administered in therapeutic doses, for a long period, with such intervals between them, that the blood may be completely freed from it during a portion of each twenty-four hours, does not change the character of the blood; while it does change and devitalize the blood, if its daily and complete elimination is not provided for.

The physiological action of chloral on the cerebro-spinal system indicates its chief value in therapeutics. My own observation confirms the statement of M. Briche-teau* that this action "is manifested by a period of agitation, more or less pronounced, sometimes very short, and not of importance; by a period of progressive somnolence, in which consciousness is first dulled and then extinguished under a profound sleep, accompanied by a slight or a complete anæsthesia, according as the drug is pure and given in a sufficient dose; and in some individuals, by a sort of intoxication, resembling drunkenness at the moment of awakening." Sleep and a certain amount of anæsthesia are two marked effects of therapeutic doses of chloral. Profound sleep and complete anæsthesia are the result of toxic doses. The sleep of a

therapeutic dose is strikingly like natural sleep. The limbs lie in natural attitudes. The respiration is easy. The skin is normal, or a little cool. The pupils of the eyes are contracted, but easily dilate. A sufficient noise or disturbance arouses the sleeper, who asks what is the matter, and directly falls asleep again. The patient of Case II. was constantly anxious about an aged and invalid father, who slept in the chamber below her. Any unusual noise in that chamber at night always aroused her from her chloral sleep; she would leave her bed, go below for a moment, investigate the cause of the disturbance, return to her bed and at once fall asleep again. The duration of the sleep varies from two or three to six or eight hours, according to the dose and to the impressibility of the subject.

Complete anæsthesia is not produced by hydrate of chloral on man, unless doses that approach or really are toxic ones are given. Therapeutical doses produce a moderate insensibility, and therefore may be used to allay a moderate amount of pain, but they will not replace opium in this respect. The order in which the nervous system is affected by therapeutic and toxic doses is stated by Dr. Richardson to be as follows. Therapeutic doses affect, 1st, The sympathetic ganglia. 2d, The cerebrum. 3d, The heart. In fatal cases, "the functions destroyed are, 1st, The cerebral. 2d, The voluntary muscular. 3d, The respiratory. 4th, The heart."

The action of the heart is often quickened soon after chloral is absorbed, but in a short time the quickened action gives place to a slower and weaker movement. It is the rule for therapeutic doses to decrease the frequency and force of the heart's beat. In nine observations made by DaCosta,* in one of which ten and in the rest fifteen grs. were injected hypodermically, the following result was obtained. In five cases the pulse fell in an hour from 90 to 78—104 to 86—96 to 82—96 to 44 and 100 to 96. In two cases the number of beats was unaltered; and in two it was increased from 60 to 64, and from 80 to 84. M. Bouchut, DaCosta and Dr. Anstie agree that the sphygmographic trace of the chloralized pulse is sinuous with a diminished rise and fall. Toxic doses render the pulse quick and small, and contract the arterioles, sometimes, says Dr. Anstie, "to the extent of strong spasmodic contraction."

The condition of the cerebral bloodvessels, while under the influence of hydrate of

* Bulletin de Therapeutique, Nov. 1869.

* Amer. Jour. Med. Sciences, April, 1870, p. 361.

chloral, varies with the dose and with the length of time after its administration. Dr. W. A. Hammond has demonstrated* by several ingenious and interesting experiments, that the primary effect of a full therapeutic dose is to cause congestion of these vessels; while the secondary effect is to induce the opposite condition. He has also shown that a small dose produces only congestion of the cerebral vessels. Such a dose is probably eliminated before there is time for secondary results to occur.

Animal temperature is lowered by chloral, if a sufficient dose is given. In all but one of DaCosta's cases just referred to, the temperature either fell slightly or was unaffected. In one case it rose from 99° to 100°·5. Bricheteau noticed the decrease of temperature. Dr. Richardson has confirmed it by fifty carefully conducted experiments. A comparison of the results arrived at on this point by these and other observers, however, points to decrease of temperature as the accompaniment of a toxic rather than of a therapeutic dose. An attempt to largely lower the animal temperature by chloral would be a dangerous experiment. I agree with M. Bricheteau that "the loss of one degree (centigrade) of temperature in an hour by the action of chloral would alarm me, if it occurred in one of my patients."

Under the influence of therapeutic doses of hydrate of chloral, the respiration is slowed as well as the action of the heart, but not to any great degree. Muscular relaxation also occurs.

Therapeutic Indications.—The therapeutic indications and contra-indications which these physiological phenomena point to, are obvious. Hydrate of chloral may be given so as to produce sleep, diminish sensibility, allay irritation, slow the heart, relax muscular tissue, lower animal temperature, devitalize the blood, cause anæsthesia and destroy life. Part of these phenomena have a therapeutic value, and part are toxic. They may be arranged in two groups, thus:—

Therapeutic Group.	Toxic Group.
Sleep.	Slow or irregular pulse.
Diminished sensibility.	Complete anæsthesia.
Diminished irritation.	Altered blood globules.
Muscular relaxation.	Great diminution of temperature.
Contraction of arterioles.	Great muscular relaxation.
	Death.

In the administration of chloral, the practitioner of course desires to obtain the therapeutic and avoid the toxic phenomena.

This can easily be done by a proper attention to the purity of the article and to the mode of its administration. The indications to produce sleep, diminish sensibility and allay irritation, occur very often in the treatment of disease. Hence it is not surprising that chloral has been tried clinically in a great variety of diseases. Dr. James B. Russell has given, in the *Glasgow Medical Journal*, a table of 21 cases (of fever, previously referred to) in which he employed it. M. Bricheteau, in the *Bulletin de Thérapeutique* for November, 1869, has recorded the result of his experience of it in nephritic colic, extraction of teeth, chorea and tetanus. Dr. DaCosta, in an article in the *American Journal of the Medical Sciences*, quoted above, has presented a record of its use in lead colic, rheumatism, cerebral softening and abdominal tumor. Dr. F. Goolden tried it in paralysis; Dr. J. H. Barnes and Dr. Hammond in acute mania; Dr. S. Teller in puerperal mania; Dr. Hay (*Practitioner*, March, 1870) in puerperal convulsions; Dr. Hardy in neuralgia; Dr. H. Derby in iritis; and this article concludes with an account of its use in phthisis, insomnia, paralysis agitans, opium eating, hysteria, and cardiac disease.

The contra-indications to the use of the hydrate of chloral have not yet been fully ascertained. Its physiological action on the heart is such as to render one very cautious about administering it in cardiac affections. In Case VIII. of the following series, pain in the cardiac region and fluttering of the heart followed so directly after the taking of chloral that I could not doubt its action on that organ in that case—an action which no physician would care to push farther. The experiments of Dr. Hammond show that it is not safe to prescribe it in all forms of disease of the head. Organic disease of the heart, congestion of the brain, meningitis, and very probably cerebral anæmia, contra-indicate its use. An irregular pulse, and a cold skin, occurring soon after the exhibition of chloral, are signs of danger. Dr. J. R. Reynolds, in the *Practitioner* for March, 1870, records a case in which a dose of 45 or 50 grs. was followed in two hours "with cold extremities; an excessively rapid, weak, irregular and intermittent pulse; jactitation of limbs; an intolerable sense of sinking and oppression at the pit of the stomach; gasping breathing and confusion of thought." These symptoms disappeared as stimulants were given, and the patient rescued from imminent danger.

Dose and Mode of Administration.—In the

* New York Medical Journal, Feb. 1870.

first place, before giving hydrate of chloral at all, the physician should be assured of the purity of the article. I have experimented clinically with hydrate of chloral of English, German, French and American manufacture. In my hands the English has proved to be the best—the most agreeable to the taste of patients, accompanied with little or no nausea, and followed by no ill effects. The German and French article has caused some nausea and slight cerebral disturbance. I am sorry to add, that I have never given a dose of American chloral which has not produced a great degree of nausea, and been followed for twelve or twenty-four hours by headache and cerebral uneasiness. Chemists tell us that the hydrate of chloral is not pure unless, when added to a solution of caustic potash, it will disengage the odor of chloroform without coloring the solution. Coloring the solution indicates impurity.

The average dose for an adult is 30 grs. A decided hypnotic effect is produced in some impressible individuals by 15 grs. It is not safe to exceed the dose of 60 grs. in the course of ten or twelve hours. I have noticed that 30 grs., given in two doses of 15 grains each, half or quarter of an hour apart, will produce less gastric uneasiness and greater hypnotic action than when given in a single dose. Theoretically, in consequence of the rapid elimination of the chloroform evolved from the chloral in the blood, such should be the case. It may be administered by the stomach or by the rectum, and it is not necessary to give a larger dose by the latter than by the former method.

M. Claude Bernard has shown* that less chloroform is necessary to produce anæsthesia in an animal or a man previously narcotized by morphia, than in one to whom morphia has not been previously given. I have observed, clinically, that there is a similar mutual action between hydrate of chloral and morphia. Case VI., which follows, is an illustration of this fact. A fourth of a grain of one of the salts of morphia, followed in an hour by 15 or 20 grs. of hydrate of chloral, will produce a greater anæsthetic and hypnotic effect than a larger dose of either of them given alone. In many cases, where a certain dose of morphia is sufficient to allay pain, but not to produce sleep, it is better to follow the morphia by hydrate of chloral than to repeat the former.

In concluding this account of the physi-

ological and therapeutical action of chloral, I cannot express my opinion of it more clearly than to quote the words of Dr. DaCosta in the paper previously referred to, viz.: "that it is an important addition to our therapeutic means—chiefly, however, as a hypnotic. Its action as a destroyer of pain is limited; nor do I think it can compete with ether or chloroform to produce the insensibility requisite for surgical operations. Its chief value seems to be that of an auxiliary to opium, or to take its place when opium is not admissible." As a hypnotic, hydrate of chloral is better than opium. Chloral sleep is better than opium sleep.

The following cases illustrate most of the physiological actions of therapeutic doses of hydrate of chloral which have been pointed out.

CASE I. *Insomnia*.—An old gentleman of more than 80 years of age had an acute bronchitis in the summer of 1869. He got well, and in the following autumn had a second attack of the same disease, and recovered from this. During the winter of 1869–70, he suffered from an irritable bladder, which tormented him for two or three months and then got well. In consequence of these various attacks he became weak, and lost appetite and flesh. His nights were often restless, and he frequently required some form of opium in order to obtain sleep. It was not necessary to give him a large dose. Twenty drops of tinctura opii deodorata, or an eighth of a grain of the sulphate of morphia, were generally sufficient to enable him to get a requisite amount of sleep. Hyoscyamus, camphor, hops, &c., were tried without effect. Opium gave him sleep, but it also gave him a coated tongue and constipation of the bowels. It did not seem to diminish his appetite or disorder his stomach. I discontinued the opium and gave him fifteen grs. of chloral hydrate in three ounces of syrup tolu and water. This gave him several hours of quiet and apparently natural sleep. The same dose was repeated for a number of nights, with the same result. It was discontinued after a while, because he got well enough not to require any anodyne. This person came very quickly under the hypnotic influence of chloral. He fell asleep so soon after he swallowed it that I had the time measured, and found that, in one instance at least, he was asleep in less than ten minutes after he had taken it. He complained of no nausea, either at the time of taking it or on awaking. It did not seem to inconvenience him in any way. All the anodynes I tried him

* Bulletin de Thérapeutique, Septembre, 1869.

with, except opium and chloral hydrate, failed to induce sleep. Of these two, the latter served him much the best. The smallness of the dose in this case is worthy of remark. Perhaps at the age of 80 a smaller dose should be given than when a patient is 20 or 30 years younger.

CASE II. *Insomnia*.—A lady, between 50 and 60 years of age, received a blow on her head ten or twelve years ago, by which the skull was depressed. The surgeons who were called did not think it safe or necessary to trephine the skull. She got well without any surgical operation. Since the accident her head has frequently disturbed her in the way of headache, sense of cerebral oppression, vertigo and the like, though on the whole she has enjoyed a tolerable degree of health, and been able to attend to her usual household duties. The principal difficulty has been insomnia. She has not been able to sleep more than three or four hours at night. She reports her average sleep for the last ten years at three hours per night, and no sleep by day. After several nights of three or four hours sleep each, there would be a night of four or five hours sleep, and so on. All sorts of anodynes have been tried with her, such as hyoscyamus, opium, camphor, lupulin, ether, ardent spirits, Indian hemp, bromide of potash, &c. Of these, whiskey and Indian hemp produced the best results in the way of sleep. The bromide of potash did not cause sleep, and was followed by an intolerable sense of weight and discomfort in the head, and also by mental depression for many hours after it was taken. For the last few years none of these anodynes have been employed. The patient has got on with such sleep as came to her, unassisted. On the 13th of January last, I gave her twenty grains of chloral hydrate, which seemed to act favorably, but did not produce much increased sleep. The dose was increased each night till 50 grs. were taken. This was followed by five hours of quiet, easy and apparently natural sleep. From that date to this present writing, she has taken 50 grs. of chloral, in divided doses, every night, except a few nights, when it was discontinued to see what the result would be. When it was discontinued, she slept only three hours as before. On the other nights she has always slept five or six hours. She has complained of no sort of discomfort, either directly after taking the hydrate or at any other time. There is one exception to this statement. She took some hydrate of American manufacture a few times, which was invariably followed

by nausea for half an hour or more, directly after swallowing it, and by headache the next day.

CASE III. *Phthisis*.—Miss S., a young girl of 16, with the hectic, emaciation, cough and diarrhoea of advanced tuberculosis, during the past winter was especially troubled by her cough at night. It assumed an irritable and spasmodic character as soon as she lay down. Unfortunately, she did not tolerate opium well. I gave her ten grs. of chloral hydrate, and the dose was sometimes, not often, repeated once or twice during the night, so that she got (either 10 grs. or) from 10 to 30 grs. of chloral, in divided doses, during each night. The result was excellent for several weeks. The cough was quieted by each dose, and refreshing sleep followed, which generally continued about two hours. After a few weeks, the taking of the above amount of chloral was not followed by relief from coughing or by sleep. An increased dose produced nausea, and the drug was discontinued. In the case of this patient, the rapidity with which sleep was induced was as remarkable as in the first case.

CASE IV. *Hysteria*.—Miss T., æt. 47, has been subject for several years to neuralgia in various parts of the body, and to chronic inflammation of the ovaries. She has also had frequent hysterical symptoms and general nervous derangement. One of her most prominent difficulties has been, for the past few years, sleeplessness. When troubled in this way, the bromide of potassium formerly produced quiet sleep. During the past year, however, I have abstained from giving it to her, partly because it did not quiet her as much as formerly, and partly because it seemed to be wise for her to take as few drugs as possible. During last January she slept so little that it became necessary to interfere. I accordingly gave her chloral hydrate. She took sometimes thirty and sometimes forty-five grs. in solution on going to bed. The immediate effect was generally to produce a slight amount of nausea. This lasted rarely more than fifteen minutes, after which she went to sleep, and slept quietly for several hours. For nearly three months, from the last week in January till the first of May, she took chloral more than two-thirds of the time at night. There were a few occasions when the largest dose above mentioned failed to cause sleep, and I did not wish to increase the quantity. These occasions were times of unusual excitement. Excepting these, she always got a suffi-

ciently good night from the drug. Besides the temporary nausea just referred to, it produced no ill effects. There was no headache, indigestion or discomfort during the day. She did not go to sleep so soon after taking chloral as I have usually seen persons do. Sometimes more than an hour elapsed after taking it, before sleep was induced.

CASE V. *Paralysis Agitans*.—A man between fifty and sixty years of age, had the first symptoms of paralysis agitans more than ten years ago. The disease has steadily progressed, exhibiting the tremors, paralysis, forward stoop and accelerating walk that are so characteristic of it. During the past year, it has evidently been approaching its final stage. The jactitations have not been entirely suspended by day, at any time lately, and have often aroused him at night. He has suffered from intense pain and weariness, and been unable to feed himself, or read or help himself at all. On lying down at night, the jactitations have been violent enough to shake the whole bed perceptibly. He was often one or two hours shaking in this way on his bed, before he fell asleep. If he awoke during the night, which not unfrequently happened, he had to go through another long process of shaking before sleep calmed him again. He awoke early each morning, and directly upon awaking the tremors began again, to stop only when another night's sleep brought him a little respite from them. Considerable relief was obtained from morphia, after conium, valerianate of zinc, cannabis Indica, &c., had either been tried and failed to do any good, or had ceased to afford relief. The relief which morphia yielded was partial, and it was necessary to increase the doses steadily in order to get much benefit from it. On Feb. 9th I gave him 20 grs. of chloral hydrate, with directions to repeat it if necessary. The effect of the first dose was most fortunate. In about ten minutes after it was swallowed, the jactitation ceased. Presently he fell asleep. In a few hours he awoke and got a second dose, with an equally good result. From that night to this present writing, a period of more than three months, he has taken every night from 40 to 60 grs. of chloral in divided doses, and has usually slept an average of eight hours, peacefully, after the taking of it. Two or three times, he has tried an article of American manufacture, and then has suffered from nausea, directly after swallowing it, and from a disturbed head on the following day. Excepting these occasions, it has produced no apparent

ill effects. I cannot see that it has checked the progress of the disease, or done other good than the unspeakable one of giving him rest from jactitation and pain, one-third of each twenty-four hours. His own estimate of the value to himself of the relief thus obtained may be gathered from the fact, that when, not long ago, there happened to be a short supply of foreign chloral in Boston, he bought up all there was in the city, lest he should be deprived of it for a time.

CASE VI. *Opium Eating*.—An octogenarian lady took morphia by the advice of her physician thirteen or fourteen years ago. She continued to take it of her own accord afterwards, and has persisted in the habit thus acquired. She now takes about two grains of sulphate of morphia every night. In consequence of an attempt to discontinue its use, awhile ago, she became restless, excited, nervous and sleepless, with symptoms not unlike those of delirium tremens. After two or three days and nights had elapsed without sleep, I gave her 15 grs. of chloral hydrate. This quantity calmed her. A second dose of the same amount was followed by a sleep of several hours. Unfortunately, the habit of taking morphia could not be broken up, and she resumed her customary dose at night. This has quieted and comforted her, but has not always induced sleep. When it has not, 15 grs. of chloral have always been sufficient to put her to sleep in a short time. Less chloral was required to produce sleep when morphia had been previously administered, than when the latter article had not been given. There is a physiological explanation of this fact which has previously been referred to.

CASE VII. *Phthisis*.—Mr. E., æt. 28, died of phthisis not long since. The disease ran a rapid course. He was not troubled by a cough any more than most phthical patients are; perhaps not so much as the majority are. For the last two months of his life, he required some sort of anodyne every night to enable him to obtain a necessary amount of sleep. For this purpose I gave him 15 grs. of chloral hydrate in solution, with directions to repeat the dose according to circumstances. Sometimes one dose was enough to quiet him sufficiently for the night, and sometimes he took two or three doses before rest was procured. The anodyne action of the drug was so satisfactory, that it was undesirable to try any other. He took chloral nearly every night for the last two months of his life. No unpleasant effects were observed.

CASE VIII. *Organic Disease of the Heart.*

—Mr. S., æt. about 40, has suffered for many years past from valvular disease of the heart, the sequela of rheumatism. Last April he was attacked with an ulcerated sore throat and otitis of the right ear. The inflammation of the ear terminated in a central perforation of the membrana tympani of that ear. During convalescence from the acute attack of the throat and ear, he complained greatly of tinnitus aurium and a sense of unusual discomfort in his head. These disturbed him so much that his sleep was seriously interfered with. With the hope of relieving him, I gave him 15 grs. of chloral hydrate at night, with directions to repeat the dose in half an hour if necessary. He went to sleep shortly after taking the first dose. On the next morning, he asked me if chloral ever affected the heart. I replied by asking why he put the question. "Because," he answered, "in a minute or thereabouts after swallowing the drug, I felt pain in the region of the heart, together with palpitation. The pain and palpitation soon passed away, and I fell asleep." He did not know that chloral slows the action of the heart, or in any way affects that organ, so that his imagination did not prompt or excite the symptoms. He was moreover a man whose intelligence and temperament were such that he could be trusted to watch his own symptoms. I therefore advised him to repeat the chloral, and to ascertain if possible whether it did or did not act upon the heart as he supposed. He accordingly took it for three nights consecutively, in the dose of 15 grs. each night. Before taking it, he undressed and got into bed. Then laying his hand over his heart, he ascertained that the impulse and turbulence of the organ were not greater than what he was accustomed to. When these facts were determined, he swallowed the chloral. Directly, that is, in one or two minutes, as he reported to me, he felt a change in the character of the heart's action. The heart beat more irregularly—fluttered is the term he used—and with the fluttering came pain in the heart's region. The symptoms might be called anginiform. They continued less than a quarter of an hour, and then passed away. This experiment was repeated three times with the same result. I did not care to continue the experiment beyond this, or to increase the dose.

CASE IX. *Insomnia.*—Mrs P., æt. 48, has menstruated irregularly for the past year or two, and has suffered from many of

the symptoms incident to her age. Insomnia has perhaps been the most persistent and trying of all of them. I have not given her opium in any form. Indian hemp, hyoscyamus, &c., have not rendered her much service, but she has received great benefit from chloral hydrate. She has taken it in doses varying from fifteen to thirty grains. Sometimes one and sometimes two doses have been requisite to produce sleep. When she has required it, sleep has always followed, and there have been no unpleasant effects subsequently.

ACUPRESSURE AND SIR J. Y. SIMPSON.

MR. EDITOR,—Three years ago, while attending the visit of M. Gosselin at *la Pitié*, in Paris, the writer was introduced to Dr. Simpson. He was of medium height, somewhat inclined to corpulency and almost carelessly attired. In both dress and bearing his *confrère* in honors, Sir Wm. Ferguson, would have approached more nearly the ideal of a British baronet. But his kindly manner on greeting me, and the way in which his benevolent features brightened as he inquired after his transatlantic friends in Boston, naming each one, will never be forgotten.

Being accompanied by an English physician, who acted as an interpreter, he sought, during the remainder of the visit, to convince M. Gosselin, and the attentive *internes* and students, of the value of acupressure as a means of arresting hæmorrhage. He said that in the hospitals of Paris—in the very *Hôtel Dieu*—owing to the conservatism of French surgeons, the cautery and caustics were not superseded by the ligature till a century and a half after the introduction of the latter by Paré. This was assented to by M. Gosselin. In support of this new procedure, he cited the case of a child who had undergone a major amputation, and who recovered without hæmorrhage or suppuration, though twelve hours after the operation the house-surgeon found the little patient had drawn out the pins and was playing with them! He said, also, that he had known the pins to be withdrawn four hours after the patient had left the operating table, and with no untoward result. As he was to leave Paris on the following day, as enthusiastic as a young man, Dr. Simpson wished to have M. Gosselin try acupressure *then*; but as there were to be no operations on that day, he finally asked to go to the dead-house, where