SNOW’S WORK ON CHLOROFORM.

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On the 10th November 1847, Dr. J. Y. Simpson, as he then was, communicated to the Medico-Chirurgical Society of Edinburgh his paper entitled "Notice of a New Anaesthetic Agent as a Substitute for Sulphuric Ether in Surgery and Midwifery." It was dedicated to M. J. Dumas, the eminent French chemist, and sets forth in a concise manner Simpson’s first experiences with chloroform. In a private letter sent by him to Dr. Prothero Smith, to whom he had sent a proof copy of the pamphlet, he writes: "Here [i.e. in Scotland] we are all wild on the subject." The wording of the paper, however, is free from exaggeration and contains little information about the great discovery. It states that chloroform is exempt from the disadvantages of ether as then administered; that no inhaling apparatus is required, and that in tooth extraction and minor surgery, as well as in a few cases of midwifery, this agent had been employed, and found to be conspicuously successful. A few words borrowed from manuals on chemistry are added, which describe the pharmacological aspect of "perchloride of Formyle," and that is all. The plan of administering the drug suggested is to pour "a little of the liquid diffused upon the interior of a hollow-shaped sponge or a pocket-handkerchief or a piece of linen or paper and held over the mouth and nostrils." This method Simpson adhered to in his later papers. He used half a drachm, and, puckering the handkerchief into the shape of a cup, he at first held it half an inch from the face,
later applying it close to the mouth. In none of the succeeding papers do we find any attempt to explain the physiological action of this narcotic, or to trace the best method of preventing overdosage. Indeed, it would seem that although Simpson definitely stated that danger and even death may follow its employment, yet such contingencies were, in his view, highly improbable, and were due to lack of knowledge on the part of the administrators. When several deaths were recorded Simpson wrote explaining them away and in many cases asserting that the fatalities were due to causes other than the action of chloroform. It is remarkable that in the history of anaesthesia we find that those who were enthusiastic about certain agents or certain methods have been prone to gloss over the accidents which to the plain man appear to be the direct result of the agents or the methods of their employment.

Thus was initiated the unscientific system of the use of chloroform, "unmeasured chloroform, but plenty of air," a system which the reputation of Simpson and the vigorous advocacy of Syme and those who followed him rendered almost a cult. It must be remembered that fatalities were at first few, while of these many were attributed to any cause other than an overdosage by chloroform. This state of things could only have arisen through neglect of the study of the action of the drug upon the animal organism. The surgeons of those days, with whom the use of chloroform rested, it is true, were giants, but they were not physiologists.

Snow, as we have seen, was a thinker, and one who preferred to seek truth by experiment rather than to be led away by enthusiasm. As soon as Simpson's historic pronouncement on chloroform was made common knowledge, Snow commenced his exhaustive research on "Narcotism by the Inhalation of Vapours." This was published in the London Medical Gazette in 1848, and took cognizance of ether, chloroform, Dutch liquid, bromoform, bisulphide of carbon and many other bodies. Of these we need only pursue the work which dealt with chloroform.

Snow, in his experiments upon lower animals, set himself to discover what was the effect of different percentage strengths of the drug. First the phenomena of tenuous vapours, then the strength requisite to induce complete insensibility without
interference with the essential vital processes, and, lastly, the
happenings, including death, which arose when the strength of
the vapour inhaled was gradually or suddenly increased to
greater strength. He wrote: “The great point to be observed
in causing insensibility by any narcotic vapour is to present
to the patient such a mixture of vapour and air as will produce
its effects gradually and enable the medical man to stop at the
right moment. Insensibility is not caused so much by giving
a dose as by performing a process.” He insisted that the
vapour tension in the mixture must vary as the temperature
rises, so that what would produce a safely respirable mixture
at one temperature would give a dangerously high percentage
at another.

The experiments convinced Snow that definite quantities
of chloroform vaporised in air did in all cases produce the
phenomena which he grouped as the five degrees of narcotism.
He insisted that it is more scientific to speak of “degrees”
rather than of “stages,” since the phenomena of recovery
from chloroform narcosis are similar to those of induction, and
so to refer to a stage of excitement, for example, is to open
the door to misconception since excitement reveals itself
in the second degree of narcotism, and again during
recovery. The conclusions to which he arrived are that a
2 per cent. vapour of chloroform in air produces uncon-
sciousness and a condition of true surgical anaesthesia.
Further, that when this strength of vapour is exceeded the
respiration becomes embarrassed, and if the inhalation is
continued the breathing ultimately ceases. In the case of the
lower animals removal from the atmosphere of chloroform
will lead to recovery when the vapour breathed has been not
greatly above 2 per cent., but if the percentage is above 4 or
5 per cent., and is breathed continuously, death will ensue.

With reference to the lethal dose, he writes: “I have not
yet been able to determine satisfactorily the exact proportion of
chloroform which requires to be absorbed to arrest the respira-
tion of animals of warm blood. I believe there is a definite
proportion which has this effect, but there are two reasons why
it is not so easy to ascertain it as to ascertain the proportion
which causes minor degrees of narcotism. In the first place,
the breathing often becomes very feeble before it ceases, so
that the animal inhales and absorbs but little chloroform, and remains on the brink of dying for some time. In the next place, the temperature of the body falls in a deep state of narcotism, especially in small animals; and as the temperature falls the amount of chloroform which the blood can dissolve from any given mixture of air and vapour increases.*

From this and other passages it would appear that Snow clearly grasped the fact, now well established, that, so far as respiration is concerned chloroform acts, firstly, as a result of the strength of the vapour inhaled, and, secondly, as the result of the cumulative effect of the chloroform which becomes stored in the tissues of the animal body. It does not appear that Snow or the physiologists of his day appreciated that chloroform is not only a narcotic but is also a protoplasm poison.

Two important points must be noted at this stage of our study of Snow's teaching; the one is that he is dealing for the nonce solely with the effects of the drug upon the respiration, while any interference with the circulation and other vital processes are dealt with only as the result of respiratory embarrassment or failure. The other point is that at the time of his experiments an interrupted rather than a continuous system of inhalation was practised. The patient was made anaesthetic and then the inhalation was withheld until the administrator judged that the narcosis was becoming too shallow for the needs of the operator, when a renewal of the inhalation was allowed. The types of operations then in vogue permitted such a method; there were practically no deep dissections and no abdominal surgery, so that a surgeon would complete his labours in a much shorter time than obtains to-day.

Snow and others attempted to estimate the total quantity of blood in the circulation, and aimed at supplying so much chloroform as would produce various degrees of partial saturation. He calculates that certain percentages of vapour in air would necessarily cause a definite degree of saturation, and this would cause the definite phenomena of a progressive narcotism to emerge. In fact, he pioneered one of the lines

* "On Chloroform and other Anaesthetics," p. 69, et passim.
of the work of the Special Chloroform Committee of the British Medical Association published in 1911, and it is remarkable that with the scanty physiological knowledge existent in his day and the complete absence of accurate apparatus, that his results tally closely with those obtained by those engaged in the later research.

To return. Snow ultimately came to the conclusion, so far as respiration is concerned, that double the strength of vapour which induced anaesthesia would, if continuously inhaled cause death. Thus he taught that 2 per cent. led to anaesthesia; 4 per cent. was the lethal dose. As we shall see in the sequel, Snow nominally employed a 4 per cent. and even 5 per cent. mixture, and met with few fatalities. How can these apparent contradictions be reconciled? The discrepancy is more apparent than real, for Snow opposed any method of giving chloroform which was not sufficiently under the control of the administrator to allow him to restrict the strength of the vapour to his estimate of the requirements of the patient. To do this effectually he designed an inhaler which, although graded to supply a percentage up to 5 per cent., yet had valves under control of the anaesthetist which permitted a gradually increasing strength of vapour. The possible 4 per cent. or 5 per cent. seems seldom, if ever, to have been reached, at least wittingly. Further, as mentioned above, at no time was the use of a high percentage persistently adopted, nor was it used at the commencement of the inhalation.

A further result of his investigations brought Snow into direct antagonism with Simpson and those who followed what grew to be called "the Scotch" method of chloroformisation. He wrote calmly but vigorously anent the dangers of "unstinted chloroform," which, even in the hands of experienced surgeons such as those of Simpson himself were, Snow averred, fraught with danger. It would certainly appear that so convinced of its safety were the early advocates of the use of chloroform that their methods were crude if not casual. Snow quotes Professor Miller, who, in his "Surgical Experiences of Chloroform," describes the plans adopted in the Royal Infirmary of Edinburgh. "Anything that will admit of chloroform in vapour being brought fully in contact with the mouth and nostrils: a handkerchief, a
towel, a piece of lint, a worsted glove, a nightcap, a sponge," was used; the glove or nightcap being especially in vogue during cold weather. Professor Miller adds: "The object is to produce insensibility as completely and as soon as we can... whether it is done with fifty drops or five hundred is unimportant."

Snow's inhaler was a distinct advance. In principle it consisted of a metal inhaler warmed with hot water, the chloroform was not "spilt" as Professor Miller advised, but dropped in measured quantity upon coils of bibulous paper. The arrangement of these formed an important part of Snow's technique. The vapour was allowed to pass through a long mohair tube to Sibson's valved facepiece, which last covered the mouth and nostrils and was guarded by inspiratory and expiratory valves. The inhaler was supposed to supply a 4 per cent, or even a 5 per cent. vapour, and this was diluted at the discretion of the administrator by opening or closing the inspiration valve. It is clear that so large a dead space and valve permitting the free entrance of air would materially lower the initial strength of the vapour. A low percentage strength was used at first, and this was gradually increased as time went on until anaesthesia being attained the inhaler was removed and reapplied as the exigencies of the case required. That this plan, although a great advance upon the crude methods advocated by professor Miller, fell short of ideals is shown by the fact that several deaths occurred during its use, and even in the practice of so skilled and philosophic an administrator as Snow.

Experimenting upon himself, Snow filled bags with known percentages of vapour, and arrived at results identical with those obtained in his research experiments. He admits such a procedure was the safest, but contends that some risk falling short of perfection might be allowed in order to simplify the procedure.

No doubt Clover's chloroform bag owed its origin to Snow's suggestion, and replaced in the former's practice the dangerous plan he initiated of applying to the patient's face lint wetted with the reagent and covering this with a towel. It is interesting to note that Clover met with no
deaths while using the lint and towel system, although others were less fortunate.

Up to this point we have dealt with Snow's views of chloroform so far as respiration is concerned, but that astute observer soon found that another and greater danger arose when the strength of the vapour inhaled was greater than those which induced death gradually by paralyzing respiration. He reasoned that chloroform given continuously in vapours of 4 per cent. or over produced effects upon the central nervous system, and did so when the blood had absorbed its optimum of safe saturation, but if a strong vapour was suddenly presented to the patient it passed, so Snow taught, through the coronary circulation to the heart and caused cessation of the general circulation even before the anaesthetising effect upon the brain had been produced. The cessation of breathing was immediate, the poisoning of the heart was fatal. It is of interest to note that in some of the animals killed by high percentages of chloroform the autopsy showed inchoate twitching of isolated bundles of muscular fibres in the myocardium, a phenomenon which has been studied by Professor MacWilliam and called by him delirium cordis. Snow also appears to have recognized that it was not the mass amount of chloroform which passed through the heart but the strength of the vapour which caused death.

Snow made some important experiments upon the analgesic effects of chloroform, confirming his views from the stores of his wide clinical experience. He differentiates sharply the central nervous- or brain-induced anaesthesia from the lessening or loss of common sensibility. This last, he points out, "does not keep pace with the degree of narcotism of the brain as shown by the presence or absence of consciousness and volition." This must depend upon the chloroform acting upon the peripheral distribution of the nerves. The fact has of late years been, in a measure, lost sight of that general anaesthetics do as a matter of fact not only annul perception of pain but protect the brain from the hypothetical "bombardment" of the nervous tissue by noxious centre seeking stimuli. He also made the pertinent observation that in order to obtain peripheral analgesia an evenly distributed partial blood saturation by the anaesthetic is requisite. Thus a slowly but
evenly induced narcosis is essential to this end. Waller's classical work on the effects of anaesthetics upon detached nerves has now bridged the gap in our knowledge, and has taught us that the analgesic effect arises from, first, a retardation and then an annulling of the conductivity of the nerve cylinders. Further, Snow points out that both the brain anaesthesia and the loss of common sensation vary in their time of onset in different types of individuals. In stout persons the time is short, in intellectuals it is the longest, while in heavy drinkers, although the tardily arrived at brain anaesthesia may be profound yet the lower reflexes would appear to persist, as such persons move their limbs and execute what appear to be protective reflexes even in deep narcosis, in much the same manner as in the case of the brainless frog. Snow does not deal with reflexes, but he arrives at conclusions given above; nor did he know of the avidity which lipoids possess for chloroform and ether.

Two of the most interesting and valuable sections in his book are those dealing respectively (1) with fatalities, real or assumed, and (2) with the symptoms of such fatalities. He dismisses the notion that there is an idiosyncrasy predisposing to chloroform accidents. He believes that fear, incomplete anaesthesia, that is, too light a grade of narcosis, are dangerous. The sudden deaths he imputes to high percentages stopping the heart and causing syncope. Wakley and the Emulation Society of Paris attempted to prove that the respiration always caused death, and the heart always failed subsequently; but Snow shrewdly points out that their experiments were faulty, as no attempt was made to paralyse the heart by overdosage by high percentages. This error was repeated in the more recent experiments of the Hyderabad Commission, a fact which the present writer pointed out at the time of the publication of the Report. Further, Snow discusses with great care and acumen the effect of chloroform when given to persons suffering from various diseases. His well-known dictum may be quoted, as it remains a guide to anaesthetists to-day. "If," he writes, "a patient's condition is such that he can be subjected to operative procedure, he can certainly be anaesthetised without undue risk." In this connexion we may recall his experience of hysterics and epileptics; the former he
found usually had a fit in the second, the latter in the third degree of narcosis. As regards epileptics, the present writer's experience goes to show that in the case of Jacksonian epilepsy the fit, which practically always occurs during induction, generally develops in the second degree, especially if the excitement is marked. Snow suggests that the administration of chloroform to malingerers who behave like an epileptic proves a useful test.

There is one important point in which the practice advocated and adopted by Snow differs from the view commonly held by modern-day anaesthetists. He could see no danger in the sitting posture, and he quotes over nine hundred cases in which he so placed his patients. But this was before the days of the radical operation of tonsillectomy and submucous resections. Whether Snow, had he our knowledge of the capillary circulation, and Leonard Hill's work on the "abdominal pool," would have adhered to the views he enunciates on this point in his book is, we think, at least doubtful.

It would be tedious, in a paper of this kind, to labour the matter further, but it will probably explain many of the discrepancies of Snow's dicta and the teaching of to-day if we quote his directions about administration, since they show in vivid contrast the method he adopted and the methods which the modern surgeon requires to be pursued by the modern anaesthetist. Snow writes: "The first application of chloroform often suffices for an operation, if it is of short duration, without repeating the inhalation. In a few cases the patient remains insensible to the knife for three minutes after the inhalation is left off, but this is an exception; and one cannot at all events make sure of this prolonged effect of chloroform, without producing a deeper state of narcotism than is desirable. More usually, if the operation lasts more than a minute or two it is necessary to repeat the inhalation; it is, indeed, generally desirable to let the patient have a few inspirations of air charged with chloroform vapour every half minute or so whilst the operation continues in order to keep up the insensibility." "In the greater number of operations, however, it is better to wait till there is some sign of sensibility, such as a slight cry or tendency to flinch, before the inhalation
is resumed; and then a few inspirations of well-diluted vapour made the patient quiet again."

In spite of the obvious difference between the exigencies of surgery in Snow's time and our own, the writer is convinced that Snow's work is still worth careful study and consideration. His analysis of fatal cases, his experiments undertaken to explain the mechanism of death under chloroform are admirable in their clarity and accuracy of reasoning. The fear of chloroform so prevalent to-day is largely due to our ignorance of its action and our neglect of the more accurate methods of employing it, and in this sense is deplorable. To study Snow's work and follow it by studying the more recent experimental research would, the writer believes, prove most helpful to those who, not being experts, have relegated chloroform to the limbo of bogeydom and so lost the aid of a most valuable asset to their anaesthetic armamentarium.

In keeping with the plans for the readjustment of the medical profession in America into regional groupings, it is the intention of the Reorganization Meeting of the Associated Anaesthetists of the United States and Canada to build up a strong parent organization, and thus realign the Regional Societies.

The Third Annual Congress will be held at Chicago, June 9-14, during the Medical Association Week, the Anaesthesia Session being a part of the Section of Miscellaneous Topics.

The five Regional Societies—Canadian, Eastern, Southern, Mid-Western and Pacific Coast—will be represented by delegates who will be empowered to form plans for the new organization which is to be known as the Associated Anaesthetists, and which is to be governed by a House of Delegates to consist of two or more delegates from each regional society, as well as officers and executive staff.

The Associated Anaesthetists will undertake the standardization of hospital anaesthesia service, will encourage graduate and postgraduate instruction, and, if thought advisable, develop a College of Anaesthesia.

If these plans are agreed to each anaesthetist member will be called upon to contribute a total of about four pounds annually in subscriptions, viz., to the Associated Anaesthetists, to his Regional Society, and to the Research Society.

If this arrangement is carried out it will place the specialty of anaesthesia in America on a solid basis. It will mean that on all matters of importance united action can be taken by an executive able and authorized to speak for the united membership of the United States and Canada.