REMARKS ON THE DOSAGE OF CHLOROFORM.

BEING THE SUBSTANCE OF A COMMUNICATION TO THE SOCIETY OF ANÆSTHETISTS.

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THE considerations upon which I am about to enter form part of those which were exposed at considerable length at Montreal a few months ago, and published in the *BRITISH MEDICAL JOURNAL* for November 20th, 1897. But whereas on that occasion I very deliberately laid principal stress upon the great power of chloroform and upon the absolute certainty of a considerable percentage of avoidable and therefore unjustifiable deaths if chloroform is administered without adequate recognition of this fact—and by adequate recognition I mean recognition in numerical values—on the present occasion, in presence of an expert audience, I am about to urge the importance of a complementary principle in the practice of anaesthesia by chloroform—namely, upon the paramount necessity for dosage in its administration. Many practical anaesthetists, I know, admit this principle; others, I believe, do not, or at least hold it to be, if theoretically desirable, practically impossible. My argument to-day is that the evidence in point shows that it is necessary and within reasonable limits of error practicable, and I should like at once to characterise and earmark that argument by the statement that successful chloroform anaesthesia requires the regular respiration of air in which the chloroform vapour is maintained between the limits of 1 and 2 per 100.

This conclusion, the arithmetical data of which I am about to submit to you, is indeed the second and final step in an argument to which I have been impelled, primarily by laboratory measurements, secondarily by the published records of anaesthetists, among whom I may name as having most influenced my mind, Snow, Clover, Bert, and Dubois.

Before actually embarking on details bearing upon the question of chloroform dosage, allow me to say that that question was fully present to my mind at Montreal when I formulated the two alternatives of the "chloroform dilemma," and seemed thereby to the heedless reader to be proscribing its right and proper administration. Lest now, in addressing myself to the dosage of chloroform, I should give rise to an opposite misreading, and be hastily put down as pleading for chloroform, let me reaffirm and further define the issue under consideration, which is the natural conclusion of my argument at Montreal, and the natural commencement of my argument here.

The dangers of chloroform are universally admitted. Whether chloroform be (1) dangerous under all circumstances, or (2) dangerous only when carelessly or unskillfully administered, death by chloroform employed for purposes of minor surgery is *prima facie* an unjustifiable event, which should be subject to judicial investigation.

As regards this elementary matter there is, I think, little room for doubt. Death by chloroform, employed for extraction of a tooth or evulsion of a toenail, can hardly be regarded as a justifiable accident. But as regards the further question, whether death by chloroform employed for the purposes of major surgery is a risk that must be simply accepted, or a risk that may be greatly reduced by a proper method of administration, it is of the utmost importance to consider what are the best possible methods, and what are the probabilities of overdose by methods other than the best possible.

Anticipating somewhat upon the main conclusion of the present communication, to the effect that the best possible method requires a uniform administration of chloroform vapour at between 1 and 2 per cent. of the inspired air, let me at once state my belief that it is possible to administer chloroform with far less danger than is at present customary. Whether the attainable decrease of risk may be of such

extent as some day to justify the employment of chloroform for minor purposes, I do not venture even to think of. For the moment it is better to limit oneself to the simple fact that, as matters stand, chloroform is a powerful and dangerous anaesthetic, not to be employed as a routine drug in all kinds of cases merely by reason of its superior convenience. With that principle distinctly stated, we may, without risk of confusion, proceed to consider the problem of "least danger" as regards chloroform administered justifiably, that is, on serious grounds.

Fig. 1.—Number of published deaths from anaesthetics in England (not Scotland or Ireland) during each year from 1887 to 1897, and for January and February of 1898.

The uniform result of the experiments upon which I have been occupied for the last few years has been to drive into my mind the conviction that quantity is the all-important factor in anaesthesia by chloroform and in death by chloroform.

Anaesthetise a nerve by mixtures of chloroform vapour and air at strengths of 1, 2, 3, 4, etc., per 100, and you find that the effect increases with the cause (Fig. 3). Consider chloroform at 1 per cent., chloroform at 2 per cent., chloroform at 3 per cent., chloroform at 4 per cent., applied to the nerve by means of the very simple apparatus shown in Fig. 2.

Fig. 2.—Plan of apparatus to test the effect upon a nerve of chloroform mixtures at different percentages.

In Fig. 4 we have another group of records showing the effects on nerve of chloroform at 5 per cent., of chloroform at 5.6 per cent., of chloroform at over 10 per cent. And then finally (Fig. 5) is a series of four successive experiments with chloroform at 5 per cent., to anticipate a possible criticism as regards comparison between two successive experiments, showing you as it does that there is not any very marked

difference in the effects of four successive experiments on the same nerve.

Fig. 3.—Effect upon a nerve of chloroform vapour and air at 1, 2, 3, and 4 per 100. The shaded bar indicates in each case the time during which the anæsthetic was passed. The successive responses occur at intervals of one minute. The effect of chloroform at 1 per cent. is excitant; at 2, 3, and 4 per cent. the anæsthetic effect is more and more pronounced.

Effect upon a nerve of chloroform vapour and air at 5 per cent. Well-marked anæsthetic effect and not quite perfect recovery.

Effect of chloroform vapour and air at 5.6 per cent. Very slight and imperfect recovery.

Fig. 4.—Effect of chloroform vapour and air at about 10 per cent. No recovery.

Fig. 5.—Four successive doses of the same nerve by chloroform and air at 5 per cent. to show the approximately uniform and regular anæsthetic effects of a given dose repeated more than once.

The method and its measured results are, as will be seen, unexceptionable—so much so, indeed, that a critic, who finds they do not fit with his theories, is obliged to criticise, not the experiments themselves, which are tacitly admitted, but the inferences which I am said to draw—and which I expressly refused to draw—concerning doctrinal points *re* the chloroformisation of man.

Now, I need hardly say that I infer nothing about the important debate as to whether a man's death by chloroform is by syncope or by asphyxia. When I witnessed and demonstrated my first experiments three years ago,¹ I said: "One is rather inclined to diminish the stress that such documents must produce on the mind by saying: 'But this is only a frog's nerve; its current of action is a recondite phenomenon, not necessarily coextensive with physiological action; a nerve fibre is not a nerve cell. But, all possible discount made, the fact remains that here in the nutshell of a laboratory experiment lies sharp and concentrated evidence, similar in character to the diffuse and therefore less pointed evidence, of clinical experience.'"

From the point of view we are now at, in consideration of the question of quantity, I wish to comment further upon Fig. 4. At 5 per cent., the nerve is properly anæsthetised; at 5.6 per cent., it is all but killed. And from a considerable mass of experiments I was led to adopt 5 per cent. as the usual limit of strength beyond which a nerve could not be safely anæsthetised. I came to look upon 4 per 100 as "safe," 6 per 100 as "dangerous." Now it so happens that 5 per 100 is the limit that was named by Snow forty years ago as regards anæsthesia of the human subject by chloroform vapour and air. The coincidence struck me as being remarkable, but I did not regard it as other than a coincidence. I did not regard living matter in the shape of a frog's nerve as being identical with living matter in the shape of a man's brain; all that I assumed was that the scale of action of various anæsthetics on a man's brain might be indicated by the scale of action on frog's nerve. However, the coincidence was there, and it led me to the closer examination of Snow's data concerning the percentages of chloroform vapour required in the air and in the fluids of the body for anæsthesia of various degrees.

SNOW'S CHLOROFORM DATA.

1. To produce narcotism of the second degree 12 minims of chloroform are required in the blood.
2. To induce narcotism of the third degree (surgical anæsthesia) requires about 18 minims.

3. To induce the deep state of insensibility which I have termed the fourth degree of narcotism would require 24 minims.

4. To arrest the function of respiration would require that about 36 minims should be absorbed.

Fig. 6.—Snow's table, giving the percentages of chloroform vapour in air (saturated) at different temperatures.

These are Snow's main conclusions. I do not think that the amounts must be regarded as being absolutely correct, but I think that they are wonderfully near the mark, and undoubtedly based on correct principles of determination. And I think further that if only anaesthetists had been more universally alive to the quantitative principle underlying Snow's practice—I do not say to the absolute quantities that he laid down—the waste of life that has been the price paid for chloroform in the past forty years (and yet to be paid, it is to be feared, for many years to come) might have been, if not altogether avoided, at least largely curtailed.

It is not the discussion whether or no chloroform promotes primary syncope, and whether chloroform kills by the heart or by the respiratory centre, that has as yet fulfilled the declared object of the Hyderabad Commission—to save human life. This end is, in my view, more likely to be attained by attending to the arithmetic of chloroform vapour.

The reflections aroused by these and other of Snow's data are as follows: 18 minims of chloroform = a little over 1 c.cm. of chloroform (1.06 c.cm.). 1 c.cm. of fluid chloroform gives at ordinary temperature (15° to 20°) 294 to 300 c.cm. of chloroform vapour.

Taking the fluids of the body as 30 pounds, or 15 litres, Snow's anaesthetic dose of 18 minims gives the proportion of chloroform vapour in the lymph and blood as 300 in 15,000, or 2 per 100; Snow's lethal dose of 36 minims gives the proportion as 600 in 15,000, or 4 per 100. Water at body temperature will absorb its own volume of chloroform vapour, namely, 100 per 100. The degree of saturation S of blood holding 2 and 4 per 100 is therefore between S 0.02 and S 0.04.

Air at body temperature will hold 40 per cent., or nearly half its own volume of chloroform vapour; the degree of saturation S of pulmonary air holding 1 and 2 per 100 will therefore be S 0.025 to S 0.05, and will produce an equal degree of saturation of the blood, namely, S 0.025 to S 0.05. At body temperature the vapour tension of 1 per cent. CHCl₃ in air, and of 2.5 per cent. CHCl₃ in blood will be equal. There are no doubt elements of uncertainty in these calculations; nevertheless, all possible discount made, they remain valuable as affording a quantitative image of what should be the percentage and saturation of the lymph bath surrounding the

cerebro-spinal tissues, and of the air in contact with the pulmonary sheet of blood. And towards a recognition of the important point that the degree of saturation and vapour tension must be equalised very promptly in pulmonary air and pulmonary blood, it is worth while calling to mind that the blood in the lungs is an immense thin sheet 150 metres in area, and only $\frac{1}{100}$ th of a millimetre thick.

We may, then, draw up the following summary estimate exhibiting the quantities and percentages at which chloroform vapour is to be maintained in the surgical anaesthesia of a normal subject:—

Chloroform (1 c.cm. of Fluid = 300 c.cm. of Vapour).

	Anæsthesia.	Death.
Absolute volume of vapour in the blood and lymph	300 c.cm.	600 c.cm.
Percentage of vapour in the blood and lymph	2.00 per cent.	4.00 per cent.
Degree of saturation of vapour in the blood and lymph	0.02	0.04
Degree of saturation of vapour necessary in inspired air	0.02	0.04
Percentage of vapour in inspired air corresponding with these degrees of saturation	0.80	1.60
Quantity of vapour per respiration at 375 c.cm. required to produce these percentages	3 c.cm.	6 c.cm.]
Quantity of vapour per minute at 20 respirations, that is, in 7,500 c.cm.	60	120
Quantity of fluid per minute at 20 respirations, that is, in 7,500 c.cm.	0.2 c.cm. = 3.4 minims	0.4 c.cm. = 6.8 minims

In commenting upon this estimate, I may remark that:

1. The percentages are more important than the absolute volumes.

2. The important fact that the lethal quantity and percentage are double the anaesthetic quantity and percentage is fully confirmed by the independent measurements of Paul Bert.

3. The equality of saturation degree of chloroform vapour in air and blood implies the continuous respiration of the corresponding atmosphere.

With regard to this last remark several further reflections are aroused. I think Snow's limit of 5 per cent. is dangerously high, and altogether excessive for prolonged continuous respiration. Continuously applied to the pulmonary sheet of blood, such an atmosphere would necessarily effect a corresponding degree of saturation of the blood—namely, 0.125, implying 12.5 per cent. by volume of chloroform vapour in the blood; and as a matter of fact Snow names 5 per cent. as a high limit, and did not aim at its continuous exhibition. Moreover, in the numerous experiments on animals by which he very properly prefaced his trial of chloroform upon the human subject (beginning with himself), the percentage of chloroform and air, by continuous respiration of which anaesthesia was produced, comes out of its disguise of 2 grains to 7 cubic inches at the following percentages of chloroform vapour in air:

0.38, 0.59, 0.76, 0.76, 0.77, =not enough
0.96, 1.18, 1.35, 1.5, 1.5, 1.5, 1.5 =enough
1.7, 1.9, 2.1, 2.3, 2.8, 2.9 =too much.

And in conclusion he expressly says that quantities of chloroform exceeding 2 grains to 100 cubic inches of air have a tendency to embarrass and arrest the function of respiration if the inhalation is continued.² Now 2 grains of chloroform per 100 cubic inches of air is a proportion of chloroform vapour by volume of 1.5 per 100. Could a more definite statement be desired? Is it not better worth while to try to make out whether it is anywhere near the mark than to pass by the glaring probability of death by overdose, and waste time and life in the quarrel as to how chloroform kills?

Paul Bert's experiments of 1881-3, on the same principle as those of Snow, but evidently conducted in ignorance of Snow's work, are confirmatory of Snow's results in a remarkable way when the scale in which Bert's statements are expressed is realised. He gives the lethal quantity of chloroform (and of several other anaesthetics) as being twice the anaesthetic quantity. He and his pupil Dubois state as regards chloroform that the continuous inhalation of chloroform "à 10 pour 100" produces anaesthesia in a few minutes,

and is fatal (to dogs) in two to three hours, while with chloroform "*à 8 pour 100*" insensibility is slowly produced, and death occurs after four hours. Bert finds that the continuous inhalation of chloroform "*à 4 pour 100*," and even "*à 6 pour 100*," will not anæsthetise dogs, and he quotes in one of his papers Clover's experiences with a mixture of 4.5 per 100, apparently under the impression that the two scales are identical. They are not identical. Bert's mixture "*à 10 pour 100*" signifies 10 grammes of fluid chloroform volatilised in 100 litres of air, and since 10 grammes of fluid chloroform give 2 litres of chloroform vapour, is in reality a 2 per 100 mixture. Percentages as given by Bert and Dubois have, therefore, to be divided by 5 to be expressed on our scale of percentages.

This point being clear, we are in a position to appreciate properly the statements of Dubois that the continuous inhalation of the chloroform and-air mixture "*à 10 pour cent.*," produces anæsthesia in 7 to 8 minutes, and that the anæsthesia once produced can be maintained by a mixture "*à 6 pour cent.*" Dubois's 10 per 100 is our 2 per 100. Dubois's 6 per 100 is our 1.2 per 100, and the correspondence thus recognised between careful dosage, experiments in England and in France is complete.

Such are the desiderata—the indications to be as far as possible fulfilled. If we are sufficiently convinced of this, the next step is to discover and adopt the best means of doing so.

I should like to preface this portion of my remarks by briefly quoting one most authoritative opinion behind which I am anxious to take shelter. For whereas at Montreal, in stating the chloroform dilemma I had not ventured to form any opinion as to whether deaths by chloroform are the result (1) of an agent dangerous under all circumstances, or (2) of an agent dangerous only when unskillfully administered, to-day I am prepared to limit the dilemma almost wholly to the second alternative, and to say that deaths by chloroform are in the overwhelming majority of cases the result of an agent potent under all circumstances, and most dangerous when unskillfully administered. I am in fact convinced that death is nearly always due to unskillful administration, and that unskillful administration is the administration of an overdose. Lord Lister, writing in Holmes's *System of Surgery*, says: "Death from chloroform is almost invariably due to faulty administration." Yes indeed, that is also my own independent and unreserved opinion, but inasmuch as I am not an administrator of anæsthetics, and am not therefore professionally entitled to any opinion in so weighty a matter, I prefer to be covered in this matter by the opinion of Lord Lister.

Let me, however, justify the further statement that faulty administration is the administration of an overdose. Referring to the table given above in estimate of quantity and percentage of chloroform in the body that may be considered as "anæsthetic" or as "lethal," you at once recognise the extreme danger of overdose by irregular administration, whether by what is usually termed the "open method," or by what is usually termed the "Junker method," and the extreme necessity of a regular administration of dilute vapour.

The administrator is, let us say, convinced that the open method is most efficacious and safe; he begins rather cautiously, but in all probability not uniformly, with, say, about a drachm (= 3.5 c.cm. fluid = 1050 c.cm. vapour). The patient goes under properly, and all is well. But perhaps he chokes, or holds his breath; perhaps the surgeon says, "push the chloroform," and in spite of choking or gasping the chloroform is pushed. What may that mean as to quantity? There is already some unknown quantity of chloroform in the body and in the lungs—say $\frac{1}{2}$ c.cm. or 150 c.cm. vapour. To this comes one inspiratory gasp of say 1,000 c.cm., taking from the towel or lint held close to the mouth and nose no less than 100 c.cm. of chloroform vapour. Then a second deep inspiration, and another 100 c.cm.; then a third, and a third 100 c.cm. How soon is the reservoir, which is the patient, likely to be overfilled, and to contain more than 600 c.cm. of the vapour?

No doubt some chloroform escapes; no doubt some chloroform is exhaled; but how much or how little no one can tell. It is rather the recovery than the death of that patient that is surprising, if 600 c.cm. of vapour is anything like the lethal

dose, and I do not think that we need go to the length of such expressions as "drenched with chloroform" or "sodden with chloroform." Why, "drenched with chloroform" would mean saturated fluids and tissues, or, taking only 15 litres of fluid in the body, no less than 15,000 c.cm. of chloroform vapour. Or, taking percentages, "drenched with chloroform" would mean 100 per 100, the lethal percentage being 4 per 100. This point needs no further insistence, it is too fearfully obvious.

But a subsidiary point, which is sometimes urged in defence, is not so obvious. It is claimed (or rather admitted) that by an open method an unknown (smaller) quantity of chloroform gets into the patient, while an unknown (larger) quantity of chloroform is dissipated. It is further urged that the fact of the occurrence of accidents nearly as frequently with small quantities as with large is a token of the uncertainty of the agent and of the variability of patients. It is quite true that patients vary, and it is the business of the administrator to adjust his dose to his patient. But it is not true that chloroform is an uncertain agent, nor is the uncertainty of its effects to be laid to the charge of indeterminate impurities; the uncertainty is mainly if not wholly an uncertainty of quantity, and the so-called small quantities, "not more than 1 drachm," "not more than $\frac{1}{2}$ ounce," are at least as liable to overfill the patient as large quantities—2 ounces or more. In fact I am inclined to the opinion from published accounts of accidents (in so far as any opinion is possible from such accounts) that taking into account time of administration and quantity of chloroform used, overdosing has been at least as probable by "small" as by "large" quantities administered on the "open" method.

The open method is more or less open. The administrator by the drachm, who closely surrounds his patient's mouth and nose, may easily get more chloroform vapour into the blood than does the administrator by the ounce, who keeps his evaporative fabric at a greater distance from the face, or who merely drenches the patient's pillow. I think that "drachms" in a report may often signify a closer method of "open" administration than "ounces" in a report, and, if so, I should stand in even greater dread of the drachm-chloroformist than of the ounce-chloroformist. This impression may be right or wrong; in any case it is only an impression, for the data justify no more. But what is certainly not wrong, for it is a definite conclusion from definite data, is that drachms of chloroform, if they get into a patient's body quickly enough, will with certainty kill him—one drachm in one minute would more than suffice. (1 drachm = 3.5 c.cm. fluid = 1050 c.cm. chloroform vapour.)

By what means, then, may we best fulfil the indications set forth in the tabular estimate given above? My own precise experiments upon one particular animal tissue, the consideration of the experiments and of the clinical experience of Snow, of Paul Bert, and of Dubois, have convinced me:

1. That chloroform vapour is in itself a certain and uncapricious agent, producing effects more and less pronounced in gravity according as it acts in greater and smaller quantity.

2. That anæsthesia requires the continuous administration of a mixture of chloroform and air, at an average percentage of 1.5—not below 1 per cent. and not above 2 per cent.

This second indication has been more or less perfectly effected:

- (1) By Clover's gas-bag.
- (2) By Paul Bert's gasometer.
- (3) By Dubois's anæsthetic machine.
- (4) By Junker's inhaler.
- (5) By an "open method."

As regards the first two of these, they must, I fear, be regarded as inadmissible for general use. Clover's bag is cumbersome, the percentage is not susceptible of convenient and known alteration during administration, and the figure he adopted, 4.5 per cent., seems to have been too high for continuous administration. Bert's gasometers are still more cumbersome, and their use has, I believe, been completely abandoned; moreover, there would appear to be a danger that in a large volume of chloroform vapour (specific gravity 4.5) and air, even as diluted as 2 per cent., the percentage should not be uniform throughout, but below 2 per cent. in the upper strata, and above 2 per cent. in the lower strata.

And that this is no imaginary fault, but one that is brought to light by the method of investigation I have pursued—testing anæsthetics by means of nerves—may be incidentally illustrated by Fig. 7, where a nerve was anæsthetised from a so-called 5 per cent. chloroform-and-air mixture in a bottle that was allowed to stand so that the mixture was at less than

Fig. 7.—Anæsthesia of a nerve by chloroform nominally at 5 per cent., but really at considerably less than 5 per cent. for the first few minutes, and subsequently at considerably more than 5 per cent.

5 per cent. in the upper atmosphere which the nerve underwent first, and at more than 5 per cent. in the lower atmosphere which the nerve received last.

Dubois's machine, in which by means of a plunger dipping more or less deeply into a flask of chloroform more or less fluid is volatilised at each stroke of a piston which delivers a given volume of air, appears theoretically excellent, but I have no experience of it, nor any information as to the results of its regular use.

Our choice remains limited to the last two methods—Junker's method, or the open method—which last has been the main field of contention as regards right or wrong administration.

I think that in point of fact both these methods may, as regards quantity and percentage, be rightly or wrongly carried out.

In my view, the desideratum to aim at is a continuous proportion of chloroform vapour in pulmonary air of 1 per 100. This percentage will be got if with each 100 c.cm. of inspired air the patient inspires 1 c.cm. of chloroform vapour. Taking the inspiratory volume per minute at 6,000 c.cm. more or less, the requisite volume of chloroform vapour per minute is 60 c.cm. more or less.

Now this supply of chloroform vapour may be either secured or grossly exceeded by either method. If, as is done in the ordinary routine of laboratory anæsthesia, and in some hospitals, air is pumped into the lungs through a wash-bottle of chloroform without regard paid to rhythm of respiration, volume of stroke, and therefore volume of volatilised chloroform, then, unless the animal or patient is closely watched for signs of danger, and the pumping accelerated or retarded as seems at the moment desirable, the necessary supply of vapour will be grossly exceeded, and trial will then have to be made of one or other of the long list of remedial measures.

But ordinary skill and care may surely be expected of an administrator. If he takes, for instance, a particular Junker apparatus, learns upon it what volume of air carries off what volume of chloroform, learns to time his stroke so as to coincide with the act of inspiration; above all, if he just once follows by the watch the gradual development of anæsthesia on his own person, and measures the actual volumes of chloroform used, then assuredly he will never misuse the Junker on other people, and run the risk of grossly exceeding the margin between "enough" and "too much." "Enough" is something like 0.2 c.cm. of chloroform per minute. "Too much" anything above twice that amount per minute. And in making trial on himself of the Junker method he will not run the slightest risk of overfilling himself. He will necessarily stop pumping long before he gets "too much," more probably before he gets "enough," somewhere in the lighter stage of anæsthesia, such as is customarily safely used to dull the pains of parturition.

But whereas the Junker method is not likely to be wrongly applied, apart from gross ignorance, the open method is very likely to be wrongly applied in the absence of very considerable skill and experience. The problem is to hold an evaporative surface at such a distance from the patient's face that from the invisible cloud of chloroform vapour falling and diffusing in the air he shall inspire 1 part of chloroform

vapour in 100 parts of air. That is the form in which I express what Lawrie expressed when he says that "the essential factors in safe administration of chloroform are diluted chloroform and regular breathing."

The numerical ideal, by the open method, cannot possibly be knowingly maintained; nevertheless by extraordinary skill and by acting upon the full persuasion that the uniform inhalation of highly-diluted chloroform is the condition of safety, it is possible to avoid dangers that must be incurred on the common slap-dash plan.

I have already alluded to the drachm-chloroformist and the ounce-chloroformist proceeding on the open method. It is clear that in different hands the open method is more or less open and more or less safe. The whole of the discussion as to the relative safety of different methods of administration seems to me to have turned upon this one point; even the drop-chloroformist who tries to give one drop of chloroform at the beginning of each inspiration (one drop of chloroform weighs 0.066 g., measures 0.044 c.cm., and gives 13.3 c.cm. of vapour) follows an open method in so far as the safety of his patient demands that the greater part of this chloroform shall not be absorbed nor even inhaled. But leaving on one side the drop method, which is rather a lame compromise between dosage and no dosage, it seems very clear that by the open method the fluctuations of intake between "too little" and "too much" must be considerable in the most skilful hands, excessive and dangerous in the hands of an administrator who uses the drug as if it were rather more powerful than ether. The chloroformisation of his patient will assuredly not be uniform, but merely lucky or unlucky.

The difficulty of regularity by the open method has presented itself to me very forcibly in my own experiments on nerve. I can anæsthetise a nerve by the open method, but I cannot do so with absolute certainty as I can by a mixture of known percentage. I may altogether fail to affect it, or I may affect it too much; and although not very likely to fall into either of these two extremes, I am altogether unable to anæsthetise it with that gradation of intensity which, as you have seen, is possible by mixtures of known percentage (Fig. 3). Nerves vary and exhibit peculiarities as do patients. I cannot, however, attribute the varieties of effect produced on the open method to peculiar qualities of the nerves or of the chloroform; they are assuredly due to variations of the vapour tension of the chloroform cloud by which the nerve is surrounded.

One more point as regards the open method as compared with Junker's. The latter is well in one's hands, and may be safely tried on oneself. The former is not and may not be safely tried on oneself. I should not dream of advising a student to try what chloroform anæsthesia is like by the open method; for whereas with the Junker the powerlessness which early supervenes in the experiment is certain to cut short the supply of poison at an early stage, with the lint or towel it is altogether different; the powerlessness, when it did come, would have the diametrically opposite result, and cause, it may be, a sudden and dangerous flooding of the system by chloroform vapour.

The Junker method, as known to me through the apparatus of Messrs. Krohne and Sesemann, seems to me that best adapted practically to fulfil the indications as to quantity previously stated. It is adjusted to deliver 1 minim of fluid chloroform at each stroke of the piston. The large opening of the facepiece allows of almost perfect freedom of respiration, and is provided with a light feather which serves to indicate the commencement of inspiration which is the instant at a given stroke or half-stroke or quarter-stroke of the piston is to be made driving into the facepiece and in-rushing air the vapour of 1 minim or $\frac{1}{2}$ minim or $\frac{1}{4}$ minim of chloroform.

From preliminary trial of this apparatus with respect to the quantity of chloroform volatilised by a given volume of air, I found that at 18° (=65° F.) very nearly 1 c.cm. of chloroform = 300 c.cm. vapour, was carried off by 1,000 c.cm. of air (16 strokes of the pump). This was a percentage of chloroform and air of 300 in 1,300, or 23 per cent., rather higher than the saturation percentage as stated by Snow, which at the same temperature of 65° F. is only 19 (see Fig. 6). But with the pump the chloroform was agitated; Snow's 19 per 100 refers to still chloroform, so that the discrepancy is not serious.

I then went on to see whether by this apparatus I could deliver anything like a known percentage of chloroform vapour to the nerve, selecting for the purpose percentages that were known to me as ineffective and fully effective—namely, $\frac{1}{2}$ and 2 per 100; and as a matter of curiosity I tested upon myself the effects of these same two percentages. For the latter purpose I assumed my inspiratory quantum of air per minute to be 6,000 c.cm., and delivered to myself 30 c.cm. and 120 c.cm. of chloroform vapour per minute by, namely, 20 one-eighth strokes and 20 half-strokes respectively, keeping up the shorter strokes for five minutes, and the longer strokes for a minute and a quarter.

By the first dosage I was not perceptibly affected; by the second I was very markedly affected, almost to the point of unconsciousness. By the first dosage, using per minute 30 c.cm. of vapour—that is, in five minutes 150 c.cm. vapour or 0.5 c.cm. fluid, I felt nothing remarkable; by the second dosage, using per minute 120 c.cm. vapour—that is, in one minute and a quarter the same total amount—namely, 150 c.cm. vapour or 0.5 c.cm. fluid, I felt myself rapidly going under.

Now I have no doubt from even this slight experience that 2 per cent. is an inconveniently high percentage with which to begin the production of anæsthesia. I should prefer, when the necessity arose, to be started at about 0.5, and then sent up to 1, 1.5, 2, and if need be higher until the production of anæsthesia, and then let down again to between 1 and 1.5 for its maintenance.

To test the same apparatus upon nerve at the same percentages was a little more troublesome, since it was necessary to have an air bellows of known capacity to imitate the action of the lungs, and to deliver simultaneously with the discharge of air a discharge from the chloroform flask of a given volume of chloroform vapour. This was effected as shown by the diagram (Fig. 8). The stroke of the bellows was

Fig. 8.—Plan of apparatus to test by means of a nerve the efficacy of the Junker method of chloroform dilution. At each stroke of the bellows 40 c.cm. of air driven through the chloroform bottle carries with it 12 c.cm. of vapour which, mixed with 560 c.cm.—or more exactly 548 c.cm.—of ordinary air driven on by the same stroke of the bellows, gives a 12 per 600, or 2 per 100, mixture.

adjusted by a stop to deliver 560 to 590 c.cm., and to its handle, as shown in the diagram, a bag was fixed of 40 c.cm. and of 10 c.cm. capacity. At the commencement of each stroke of the bellows, first the small bag was compressed, driving 10 or 40 c.cm. of chloroform-charged air into the reservoir bag; then by the continued stroke a further 590 or 560 c.cm. of air was sent on, giving thus an atmosphere of approximately 0.5 and 2.0 per 100. Fig. 9 gives the result of an experiment of this nature.

Fig. 9.—CHCl₃ and air at about 0.5 per cent.

CHCl₃ and air at about 2.0 per cent

It would be quite out of my province to pursue this matter into further details; these properly concern the practical administrator. The principles that I have desired to urge in the present communication may be summarised in a very few words:

1. Chloroform is not an uncertain drug.³
2. The notorious uncertainty and danger in chloroform administration is an uncertainty in the quantity administered.
3. The uncertainty of quantity administered can be most easily avoided by following the principle of Junker's method.
4. The great danger of the open method is an overdose.

Unless a man is fully and really (that is, numerically) cognisant of these four principles, then of necessity he is a dangerous administrator.

One last word with regard to the obvious objection that any practical man will feel and raise, and the unfortunately less obvious fallacy of that objection. He says, "I have given chloroform by the open method in 500 cases without special apparatus and without a death, and I do not feel inclined to encumber myself with apparatus." To this the answer is, "Well, perhaps you had better not change from a simple method with which you are familiar and that you have hitherto applied so successfully. An inferior method in skilful hands may give far better results than a superior method in unaccustomed hands." If, however, you consider not only your own experience, but the general sum of experience, you must recognise that chloroform anæsthesia by the open method is very appreciably risky—the chance of death is, I believe, 1 in 1,250; last year in England alone there were 96 published deaths, and no one can tell how many unpublished deaths. I do not ask you to change your plans, any more than you would ask a clever dispenser not to guess his powders with the point of a spatula; I only want you to admit that the guesswork or slapdash plan is not the best possible, and that the power of chloroform is such that on any large number of administrations, good, bad, and indifferent, there must be several unnecessary deaths by overdosing, just as there would be if many dispensers, good, bad, and indifferent, made up medicines without a balance. You may get on without dosing your chloroform, but your son will not, and even you yourself may some day come to grief. If so, and if a coroner's inquiry is necessary, your case will add one more to the series of customary verdicts, "Death by misadventure, and we find that all possible care was exercised by Dr. —, who has had an exceptionally large experience of anæsthetics, and has not previously met with a case of death under an anæsthetic."

No, indeed, and it is to be hoped not. The probability in the case of any one average administrator is 1 against 1,250, or, if you prefer other statistics, 1 against 1,500; in other words, the probability in one average man's practice is 2 to 1 against a death in his first 625 (or 750) cases, 1 to 1 against a death in his first 1,250 (or 1,500), 2 to 1 for a death in his first 2,500 (or 3,000), 4 to 1 for a death in his first 3,750 (or 4,500), etc.

I need lay no further stress upon this statistical probability question; it is clearly not the few hundred successful cases of one administrator of average, or of more than average, skill, that will settle the safety or danger of a method, but only the collective results of large numbers of administrators that are of any value; and in this particular I submit that the open method as practised on the average in England stands condemned, by its mortality statistics, by the existence of numerous chloroform commissions to inquire into the mode of death by chloroform, and by the private and individual knowledge that every medical man possesses of cases of death by chloroform that are never published.

And the remedy to this state of things is to be sought, not indeed by the wholesale rejection of chloroform as an anæsthetic, but in the right and proper valuation of its power and in its quantitative administration; not in the sudden adoption of any new-fangled modification by the old style and in such style experienced and skilful administrator, but in the rational education of our future administrators concerning the physiological arithmetic of chloroform, ether, and other anæsthetics.

NOTE AND REFERENCES.

¹ Brain, 1896, p. 64. ² Chloroform, p. 69. ³ This statement does not apply, of course, to obviously decomposed chloroform. Chlorine is intolerably irritant, so is carbonyl chloride.