REMARKS ON DEATH DURING CHLOROFORM ANÆSTHESIA.

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IN giving a short description of the results of the Hyderabad Chloroform Commission I may remind you that the object of the research was essentially a practical one: it was to save people's lives, to use the words of his Highness the Nizam himself, to whose generous and enlightened liberality the Commission owed its existence. The Commission was originally suggested to the Nizam and his ministers by Surgeon-Major Lawrie, resident surgeon at the hospital of Hyderabad, and, like myself, an old pupil of Professor Syme.

The chief rule laid down by Professor Syme for administering chloroform was to attend carefully to the respiration, and take it as a guide for the continued administration or the suspension of the inhalation. This was the rule which had chiefly attracted Dr. Lawrie's attention, and upon it he founded his practice. Two other rules which Syme also laid down and which chiefly attracted my notice, were always to use the best chloroform and always to use plenty of it. Syme's utterance was brief and dogmatic, and he entered into no explanation of these latter rules, but I attempted to do so in a paper which appeared in the *BRITISH MEDICAL JOURNAL*, December 4th, 1875. I then attributed death during imperfect chloroform narcosis to the occurrence of shock, which was prevented by full anaesthesia.

In making their experiments the Commission had before them the questions how far death during the administration of anaesthetics was likely to be due to the action of the anaesthetic itself, and how far to the effect of shock from the operation. The question regarding the action of the anaesthetic also divided itself into two, namely, how far the lethal effect might be due to affection of the heart, how far to affection of the respiration, and how far to both. Before we attempt further to describe the experiments made by the Commission, I think it might be well to clear the way by mentioning that the time was too short to allow of the general action of chloroform or ether upon the tissues generally being investigated, and that we had to confine our attention to the methods in which death was likely to occur during surgical operations as usually performed. Previous researches had pretty well established that chloroform is a universal protoplasmic poison, and will destroy the contractile power of individual cells, of cilia and of muscular fibres, and, when injected into the artery of a limb, will produce rigor mortis in it, and make it stiff as a board. There was no question, therefore, of the power of chloroform to destroy any structure of the body if applied to it in sufficient concentration, nor do we attempt to deny that chloroform will destroy the contractility of the heart just as it would that of a voluntary muscle, provided always it reached the heart in sufficient concentration. But this was just the point at issue. If we drive chloroform into the trachea, or air very heavily loaded with chloroform vapour into the lungs by artificial respiration, it will be absorbed in sufficient quantities to paralyse the heart, but the question is an entirely different one if the chloroform be administered in the usual way, by inhalation. Our contention is that when chloroform is administered in this way it acts more readily upon the respiration than it does upon the heart, and from the respiration failing first, a sufficient quantity to paralyse the heart is never conveyed to it, and that therefore death from chloroform inhalation is respiratory death, death beginning with the respiration and not with the heart.

It will be convenient to take up, first, more fully the question of death from the anaesthetic, by which I mean death due to the action of the anaesthetic itself, and, later on, to

discuss the question of death during anaesthesia—that is, death from operation or other causes than the anaesthetic, sometimes in spite of its action, and at other times, perhaps, aided by its action.

The experiments made by the first Chloroform Commission showed that in dogs subjected to its action the respiration invariably failed before the circulation. Those made by the second Commission confirmed this, but they brought out a new point—namely, the rapidity with which the heart fails from the combined action of asphyxia and chloroform. This action is of two kinds: First, asphyxia during chloroform stops the heart's action through the vagus nerve. This is the action which was looked upon by the Glasgow Committee as so dangerous, but which, as Dr. Bonfort pointed out, is rather a safeguard, tending to prevent the too rapid conveyance of chloroform vapour from the lungs to the medulla. The second action of asphyxia and chloroform combined is a paralyzing one upon the heart itself. If an animal inhales pure chloroform vapour with free admixture of air its heart will go on for a long time—in fact, we might say, almost indefinitely. If an animal is asphyxiated, either by stoppage of the respiratory movements or by obstruction to the free entrance of air into the lungs, notwithstanding the continuance of respiration, the heart will go on for a certain time, but in the course of a few minutes will stop. This stoppage, however, occurs very much more quickly if chloroform be administered at the same time as an animal is asphyxiated, so that we may say that the great risk of death from the action of chloroform lies in the occurrence of asphyxia during its administration.

I must here draw attention to what I believe to be a grave fallacy in some experiments of my friend Professor H. C. Wood, mentioned by him in his Address on Anaesthetics at the Berlin Congress. A tracing which he there showed seemed to indicate most clearly that the action of the heart failed long before the respiration. I here reproduce, as nearly as I can remember it, the general effect of this tracing. In it we seem to see clearly a stoppage of the beats of the heart while the blood pressure sinks, and yet the respiration goes on freely. Now I believe that the stoppage of the heart in this tracing is only apparent and not real, and that it is, in fact, due to a small clot of blood in the cannula which connects the artery of the animal with the kymograph. I have had many such tracings, and my experience has led me, whenever I got them, to disconnect the cannula and remove the clot. Had there been no clot, the stoppage of the heart would have caused the blood pressure to fall abruptly instead of gradually, as shown in the tracing exhibited by Professor Wood.

In comparing the action of ether and chloroform, we found that the great points of difference between them were, first, that ether was a less powerful anaesthetic than chloroform: and, secondly, that while neither of them paralyses the heart when giving plenty of air, the heart would continue to beat much longer during asphyxia when combined with ether than when combined with chloroform. Chloroform is thus a more powerful agent, and, as I have already said on a previous occasion, it is like a sharp knife in the hands of the surgeon as compared with a blunt one. It is more efficient for good if properly handled, it is more powerful for evil if misused.

Shortly before the Commission began its labours a most unfortunate case of death occurred in Edinburgh during anaesthesia from nitrous oxide—an anaesthetic which is usually supposed to be absolutely free from danger. The report of this case led the Hyderabad Commission to suppose that death in it was due, not to the anaesthetic, but to asphyxia from tight lacing, and accordingly they made some experiments to test the effect of compressure upon the chest and abdomen. These experiments caused a storm of indignation amongst the antivivisectionists, who falsely stigmatised them as horribly cruel, whereas, in truth, there was absolutely no cruelty about them. The only thing that was done was to imitate upon monkeys already under chloroform that compression of the chest and abdomen which is daily exercised at the bidding of fashion by thousands of women in this country without chloroform. The Commission found, as was to be expected, that tight lacing greatly increased the risk of death from chloroform on account of the imperfect respiration and consequent tendency to asphyxia to which it gave rise.

The second part of the labours of the Commission consisted in attempting to determine the effect of shock as a cause of death during chloroform inhalation. In a paper published in the *Practitioner* I have attempted to distinguish between shock and syncope, my idea being that syncope is due to temporary stoppage of the heart's action and may be rapidly recovered from, while shock is due to paralysis of the abdominal vessels and is a very grave and persistent condition. Many attempts were made to produce syncope in the animals experimented upon by raising the head, by attempting to stimulate the vagus reflexly or even by direct irritation, but all these experiments seemed to show that stoppage of the heart's action through the vagus was not a dangerous condition. We also attempted to produce shock by a blow upon the intestine or by such an operation as avulsion of the toe nail—an operation which has frequently been followed in man by fatal results. In these attempts, however, we were unsuccessful.

REMARKS ON THE EFFECT OF CHLOROFORM ON THE RESPIRATORY CENTRE, THE VASOMOTOR CENTRE, AND THE HEART.

Made in the Section of Therapeutics at the Annual Meeting of the British Medical Association, held in Bournemouth, July, 1891.

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DR. LEWIS SHORE, after remarking on some of the points raised by Dr. Brunton's address, gave an account of certain experiments made by Dr. Gaskell and himself on the action of chloroform on the respiratory centre, the vasomotor centre, and on the heart. In these experiments the application of chloroform directly to the exposed *fourth ventricle of the medulla* in the rabbit always caused a rapid cessation of respiration, by quickly diminishing the extent and depth of the breathing without markedly influencing the rate. This effect was sometimes preceded by evidence of excitation of both the respiratory centre and the vasomotor centre at the moment of application. One or two drops so applied were sufficient to kill the animal. With the failure of respiration the blood pressure gradually fell, but was still considerable when the respiration stopped.

The injection of chloroform into the *internal carotid artery* of the rabbit caused a small long-maintained rise of blood pressure, due to a stimulation of the vasomotor centre. The respiration became slower and changed in character, the inspiratory phase being markedly increased. Two or three minims of chloroform were usually sufficient to produce these changes. Further injection of one or two minims brought about rapid failure of the respiration, usually, indeed, a sudden cessation, notwithstanding a very high blood pressure. Immediately the respiration stopped, the blood pressure began to fall. That this was associated with the maintenance of the respiratory act, and not due to a depression of the vasomotor centre by the direct action of the chloroform, is shown by the fact that it did not occur if artificial respiration was maintained. Chloroform readily acted on the respiratory centre, first slightly stimulating it, then paralysing it. It stimulated the vasomotor centre, successive injections driving the blood pressure higher and higher, but large doses ultimately paralysed it. The respiratory centre always completely failed long before any depression of the vasomotor centre occurred. Injection of chloroform into the *vertebral artery* gave similar results, a smaller amount being needed; even half a minim sometimes sufficed to stop the respiration. With the cessation of respiration the blood pressure at first fell, but that the vasomotor centre was not paralysed was proved by the fact that a rise of blood pressure occurred later on, due to the action on that centre of the asphyxial condition of the blood. In one case this asphyxial rise was as much as from 66 mm. of mercury to 102 mm.

Injection of chloroform into the *jugular vein* produced very

different effects. Its marked characteristic was a rapid fall of blood pressure with weakening heart beats; in one case, in a rabbit, 1 minim of chloroform injected into the jugular produced a fall of pressure from 104 mm. to 40 mm. in one minute, and another minim further reduced this to 26 mm. The respiration was at first not markedly changed, but after a few inspiratory gasps stopped rather suddenly one minute and fifteen seconds after the last injection; and although no pulse was evident in the carotid, the heart was found beating regularly but feebly three minutes later. The heart, although not absolutely arrested by the chloroform, was rendered inefficient to maintain an adequate circulation for the continuance of respiration. These experiments point to the conclusion that the fall of blood pressure produced by chloroform is due to failure of the heart's action rather than to paralysis of the vasomotor centre. It may, however, be questioned whether the action of chloroform, when injected into the vascular system, is the same as when it is inhaled in the ordinary way.

In order to decide this question the following experiment was devised: Two animals were taken, two dogs or two rabbits, and the arteries supplying the brain of one animal were gradually ligatured so that its brain was completely prevented from receiving blood from its own heart. The arteries, carotids or vertebrals, and in some cases both carotids and one vertebral, were then connected to the corresponding arteries of the other animal, and the brain thus supplied with blood, which returned by one pair of jugular veins cross-connected in a similar way. Care was taken that the brain was at no time without a supply of blood, the last artery being ligatured at the same moment as the cross circulation was established. Thus one animal, the *feeder*, was supplying its own brain by one carotid or one vertebral (and this always adequately sufficed) and also supplying the brain of the other animal, the *fed*. The blood pressures of both animals were taken from the femoral arteries. When chloroform was given in the ordinary way, by inhalation, to the feeder and the usual effects produced in that animal, namely, fall of blood pressure and slowing of respiration, chloroform-carrying blood was also being sent to the brain, and the brain only, of the fed animal, and there produced insensibility, a rise of blood pressure, and slowing of respiration. When the fed animal, on the other hand, inhaled chloroform, a marked fall of blood pressure was produced, and as the chloroform could not reach the brain, this could only be due to a direct action of chloroform on the heart. In the latter case the chloroform could be pushed till the blood pressure was nearly zero, and no heart beats were visible on the tracing, and the animal would continue for some time to breathe regularly, the respiratory centre, of course, deriving its blood supply from the other animal, the feeder. If the brain of the fed animal, on the other hand, was richly supplied with chloroform, by giving large doses to the feeder, the respiration could be brought into a very precarious condition without the slightest fall of blood pressure, the chloroform depressing the respiratory centre, but not the vasomotor. Complete stoppage of the respiration of the fed animal could not be produced before the feeder succumbed to the large quantity of chloroform given to it.

These experiments confirmed the results obtained by injection and showed that the fall of blood pressure observed in chloroform inhalation is due, primarily, to direct action on the heart, and not to a depression of the vasomotor centre.

A fall of blood pressure was not, however, inevitable; complete insensibility may be produced without any fall at all, and usually the fall is slight, and a dangerous depression is only produced when the chloroform is given after insensibility is produced. The respiration begins to fail before the fall of pressure is dangerous.

These experiments were in accordance with those of the Hyderabad Commission, inasmuch as they show that, when chloroform is administered without interfering with perfectly regular respiration, complete insensibility can be produced without obvious weakening of the heart's beat. Inefficiency of the heart is brought about by the rapid inhalation of chloroform in too concentrated a form. The experiments supported in two respects the practical teachings of the Hyderabad Commission, namely, that chloroform should be given gradually and with plenty of air, and that great care should be