RECENT EXPERIMENTS DEFINING THE DANGERS OF ANESTHESIA

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(By Invitation)

The past five years have probably contributed more to precise knowledge of anesthetics, their practical use and the real nature of their dangers, than the preceding thirty. For many years there had been almost a condition of stagnation in this field. There were indeed investigations, for example those of the Hyderabad Commission on the dangers of chloroform—a commission which, by the way, overlooked the essential point and reached a wrong conclusion. But such investigations were to a great extent merely a rattling of dry bones. There was little that was new in technique of administration, and less that was suggestive for the opening of new fields of observation and experiment.

The conceptions of the dangers of anesthesia were simple and unquestioned. The expressions "failure of respiration" and "failure of the heart" summed up everything. Each was a single definite process, although a few particularly broad-minded persons recognized also a "vasomotor failure." In both, or in all three, of these supposed modes of death the cause of trouble was assumed to be nothing else than excessive anesthetic or some vaguely guessed-at weakness in the patient.

I cannot better express the renewed vitality of investi-

gation in the field of anesthetics than by illustrating it with some of the recent important contributions. I shall take first the work of A. Goodman Levy,[1] done in Professor Cushny's laboratory at University College, London. As you are aware, the Hyderabad Commission reached the conclusion that if the administration of chloroform be pushed it will happen "999,999 times out of 1,000,000, that respiration will fail before the heart." This amounted to saying that the fatalities under chloroform were mere carelessness on the part of the anesthetists. Naturally the practical anesthetists who had seen patients not only breathing at the moment the pulse disappeared, but even breathing vigorously for a minute or more thereafter, refused to accept such a statement.

The mistake lay in the assumption that fatalities under anesthesia must be due to excess of the anesthetic. This is an error which it seems extremely difficult to overcome in the minds of surgeons. They are prone to insist that "if that fool anesthestist had not poured on too much ether (or chloroform, as the case may be) we should not have had all that trouble." Anesthestists, on the contrary, are usually quite ready to recognize the fallacy, for they know as well as anyone can who has only a very inexact method of measuring dosage that trouble often comes when less rather than more has been given.

Levy's work has shown that primary heart failure under chloroform is a perfectly definite and easily induced result of very definite conditions. He quotes cases from the literature showing that one of the essential conditions of such fatalities is *light* chloroform anesthesia. Such mischances do not occur under deep chloroform anesthesia, for the heart is then merely depressed, and as respiration always fails first it is usually easy to effect resuscitation.

Most of the fatalities quoted by Levy occurred either

[1] Heart, 1913, iv, 319.

during the initiation or termination of anesthesia. They involved beside the light anesthesia another factor, namely, excitement, strong sensory stimulation, or an injection of adrenalin. A man was having the septum of his nose straightened. He was in excellent condition under very light anesthesia. Some adrenalin was injected and he promptly died. A girl had passed through an operation in excellent condition and the administration of chloroform had been discontinued. As she had a stiff knee the surgeon forcibly flexed it. She gave a little cry and died. A man was given an insufficient amount of chloroform, so that the stage of excitement was prolonged; finally enough was given to induce a moderate depth of anesthesia, and he suddenly became pale and pulseless. In nearly all of these and similar cases respiration continued and was even abnormally vigorous after the pulse disappeared.

These are types of cases which Levy has shown are easily reproducible on animals, particularly cats. I have myself seen many such fatalities unintentionally produced in animals by timid anesthetists. I have also repeated with entire success Levy's primary experiment in which adrenalin is administered to a cat lightly chloroformed, and have obtained exactly the same sudden heart failure and complete and irrecoverable fall of arterial pressure which Levy's experiments show.

What is it that occurs in these cases? Levy has shown by an almost excessive thoroughness of experimental demonstration that it is a condition of fibrillation of the ventricles—delirium cordis—a condition which, unlike mere cardiac inhibition or vagus or asphyxial standstill, is in as large an animal as man, in the majority of cases, practically irrecoverable.

I have tried experiments to see whether similar deaths could be produced in cats by means of adrenalin or sensory stimulation or prolonged excitement under light ether

anesthesia. A certain degree of the cardiac irregularity, which is a condition precedent to delirium cordis, is thus producible, but I have never obtained a complete and fatal fibrillation of the heart by this means.

Another of the modes of fatality which is now under analysis is one occurring under ether. Cathcart and Clark[1] find that under light etherization the heart in rabbits is markedly depressed by a degree of asphyxiation which is quite harmless under full anesthesia. Exactly what this effect consists in, and how far it applies to human cases, we must await further investigations to learn. I have mentioned the observation here because, like the work of Levy, it bears out a point which was particularly emphasized in the report of the Committee on Anesthesia[2] of the American Medical Association a couple of years ago—a committee of which I was chairman—in which the point was specially emphasized that few anesthetic fatalities are due merely or mainly to excess of anesthetic. As a rule they result more or less directly from incomplete anesthesia and the stage of excitement. I may here repeat also another point made in that report, namely, that in view of what we now know of the dangers of postoperative chloroform poisoning and of the not infrequent toxic effects on mother and child when chloroform is used in labor, it is about time that the use of chloroform should be given up altogether.

I wish to return now to the subject of partial asphyxia under light ether anesthesia. Not very long ago I had occasion to observe a difficult subject under ether. For the most part it was administered by what is called an "open" method—although why the term "open" should be applied to the type of mask employed I am unable to see, for the patient became at times markedly cyanosed. Part of the time a frankly rebreathing method of mask and Rovsing

[1] Journal of Physiology, 1913, xlvii, 393.
[2] Jour. Amer. Med. Assoc., 1912, lx, 1908.

bag was used, and when too closely applied some degree of cyanosis was observed. From the Rovsing bag I obtained gas samples which were afterward analyzed for ether, CO_2, and oxygen. The figures obtained are shortly to be published by Dr. John Bryant, for whom I made the analyses. I may mention here, however, that throughout the series of analyses the oxygen content of the air in the bag and the patient's color showed the closest correspondence. Low oxygen in the inspired air occurred with cyanosis, and a fair amount of oxygen with a good pink color. It seems to me altogether probable that if analyses had been made of air from the open mask the same correspondence would have been proved. If so, this mask was really far from open, for when the patient became rigid not only was ether poured on in a steady stream, but the mask was also pressed down on the face until marked cyanosis occurred. The Rovsing mask and bag seemed to keep the patient a better color, in spite of the difficulties of the case, as well as to afford a better control of conditions, than did the open drop method with which it was alternated.

From such observations I have become very skeptical regarding the distinction between open and closed methods. The so-called open method is often far from open. There is in the cone a very considerable dead space from which the patient rebreathes, and at times there appears to be (and this is much worse) a considerable mechanical obstruction to the movements of air. The "open" method as applied to ether is a very crude and unscientific procedure. In the first place, more than half of the ether is volatilized during expiration and blown off into the room. That is one of the reasons why, when a refractory patient develops stormy breathing, the anesthetist is compelled to pour on such a volume. Boothby[1] has recently demonstrated that

[1] Journal of Pharmacology and Experimental Therapeutics, 1914, v. 379.

the amount of ether in the inspired air necessary to produce and maintain anesthesia is exactly the same in all subjects no matter whether refractory or otherwise. It is time that we recognized that although ether is for the anesthetist a liquid, it is for the patient just as distinctly a gas as is nitrous oxide. The time is close at hand, in my opinion, when in every well-ordered and scientific operating room, where ether is used at all, instead of its being poured as a liquid over the patient's face and into his mouth, there will be a device—and it can be a very simple device—on a stand at the anesthetist's elbow, or over in the corner, or possibly even down in the basement, in which the ether will be volatilized and from which it will be conducted to the patient's nose and mouth, as if it were merely an unusually strong variety of nitrous oxide. That this idea is rapidly gaining recognition and acceptance is evidenced by the insufflation method of Meltzer, the simple and accurate device of my colleague, Dr. J. M. Flint, and most recently by the anesthetometer of Connell.

It is at once a simpler, safer, and more scientific procedure to administer the gas which we call ether vapor than it is to handle liquid ether. In some observations on myself and others in my loboratory we merely put 5 c.c. of ether into a bottle and blow air through the bottle by means of a bellows or rotary air blower into a large bag of a capacity of 20 liters. This gives an air ether mixture of about 5.7 per cent. by volume, a little less than the amount needed, according to Boothby, to maintain surgical anesthesia. In our experiments after obtaining preliminary records, we administered this air-ether mixture to each other by means of a mask and pipe precisely as if it were nitrous oxide. We continued the administration several times to the point of unconsciousness. To all of the subjects of these experiments it was a surprise to find that ether taken in this way, provided it is the best quality of ether, is not appreciably

more unpleasant than nitrous oxide. And nitrous oxide is for me rather enjoyable.

The particular object of these experiments was to determine whether there is in reality such a difference in different samples of ether as some practical anesthetists believe. It has long seemed to me that if there is such a difference it must consist very largely in different degrees of intensity in exciting respiration. Some years ago I showed that in dogs one can administer ether so badly as to maintain for twenty or thirty minutes at a time a very excessive respiration, and that thereafter they were prone to a failure of the breathing, which without measures of resuscitation frequently proved fatal. Recently Meyer[1] working with Dr. J. S. Haldane, has confirmed on man my claims regarding the effects of pain and of ether in exciting hyperpnea. I may perhaps remind you that one of the great advances in physiology during the past few years, especially as the result of the experiments of Haldane and of those who have worked under his inspiration, has been the proof that ordinarily the breathing is controlled not by oxygen needs but by the CO_2 putput, that there is a large reserve of CO_2 stored in the body, and that if the breathing is abnormally excited and this store considerable reduced, there is certain to follow a compensatory period, a reaccumulation, during which respiration is subnormal to the point of cyanosis and partial asphyxia, or in which the breathing even fails altogether. Thus, in my experiments comparing different samples of ether, the points noted were both the degree of hyperpnea during a brief period of administration, and also the intensity and duration of the period of subnormal breathing which followed.

Briefly stated, it was found that with a grade of ether such as we buy for ordinary laboratory use in tanks of several gallons there was a marked augmentation of breath-

[1] Journal of Physiology, 1914, xlviii, 47.

ing in one subject and a fairly active hyperpnea in another. With the best grade of ether, such as comes in small sealed cans, the excitant effects were comparatively slight, while the same ether after being kept for two months, with the addition of a few cubic centimeters of water, a ready access of air through a loose cork, and standing in a place exposed to the sunlight, gave very marked hyperpnea in a sensitive subject and a considerable augmentation of breathing in insensitive subjects. Particular attention should be called to the fact that whenever hyperpnea was induced it was followed by exactly such a period of subnormal breathing, Cheyne-Stokes respiration, and apnea interrupted by deep gasps as is the well-recognized result of acapnia, that is, diminished CO_2, consequent on excessive respiration.

Such a condition of insufficient breathing is an extremely common consequence of etherization. It adds the evil influence of a more or less prolonged period of insufficient oxygen supply to the other conditions, lowering the patient's vitality. It is clear that the logical procedure to prevent this is some method of administering ether vapor such as Dr. Gatch showed to be so advantageous with nitrous oxide, and also some method of administering a sufficient amount of CO_2 in the air breathed after the anesthesia is ended to stimulate respiration to a more rapid elimination of the ether with which the body is saturated, and to prevent apnea or subnormal breathing, anoxemia, and cyanosis.