Observations

ON

RESUSCITATION FROM ASPHYXIA AND PREVENTION AND TREATMENT OF SECONDARY PNEUMONIA BY INHALATION OF CO₂*

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The modern art of resuscitation takes its origin from the introduction, about twenty-five years ago, of the prone-pressure method of artificial respiration devised by Sir Edward Sharpey-Schafer. In America, where it was early adopted, the number of persons trained to administer it is estimated at fourteen millions. In the saving of life its efficiency far surpasses that of any other procedure or apparatus. It has almost entirely replaced in America the quite ineffective, and sometimes harmful, subcutaneous and intracardiac injections of adrenaline and other drugs by physicians ignorant of sound methods of resuscitation. Yet unfortunately the depression of vitality following many accidents, immersion, asphyxia, and anaesthesia still causes subsequent deaths among those temporarily revived.

It is not enough to resuscitate a man from drowning or from asphyxia, or other accident, if he is to die a few days later from a secondary pneumonia. The pneumonia should also be prevented; and this is now possible by the method which I shall describe.

The subject to be discussed in this paper includes, therefore, not only resuscitation from carbon monoxide asphyxia and from many kinds of gas poisoning, resuscitation from drowning, and the resuscitation of babies that do not breathe of themselves at birth, but also other, even more important, applications of the physiology of respiration, such as the elimination of the anaesthetic and the restoration of vitality in patients who, without this treatment after major surgical operations, may lie for hours in a state of functional depression. But most important of all is the recent discovery that in a wide variety of conditions inhalation of carbon dioxide is a highly effective preventive—indeed, it is essentially the specific preventive of the condition in the lungs from which it is probable that all secondary pneumonias develop.

Twenty-five years ago Haldane, Priestley, and Douglas in England began their epoch-making work on the part that carbon dioxide plays in respiration. Simultaneously in America I developed some other aspects of the regulation of vital functions by the carbon dioxide produced in the body. These observations led me to realize the possibility of using inhalation of carbon dioxide in the prevention and treatment of functional depressions after surgical operations and in acute disease.

The results have verified the almost inspired dictum of the Swiss physiologist Miescher, who, forty years ago, in a celebrated review of all previous investigations on respiration, remarked: "Over the oxygen supply of the body carbon dioxide spreads its protecting wings."

Eminent surgeons and physicians in public addresses sometimes complain that physiologists devote themselves too exclusively to theoretical problems and do not contribute as largely as they might to the practical matters of curing disease and saving life. In reply, it may be said that clinicians in all branches of medicine are extremely

slow to accept and apply the discoveries made by physiologists. In this complaint both sides have the same good excuse. For even after a new physiological principle has been discovered and its practical importance recognized, it is often an extremely difficult problem, requiring time, money, and patience, to work out its effective clinical application. The practical problem of administering carbon dioxide is not simple, for the various conditions to which it is applied require various special techniques, with or without rebreathing, with oxygen or merely air, with a mask or a tent, for the fire brigade, the surgical operating room, or the bedside.† As Sir Michael Foster once said, it is rarely possible to carry a physiological discovery "bleeding from the laboratory to the bedside."

On this account it was only ten years ago that Haggard and I were able to introduce inhalation of carbon dioxide in two distinct practical fields of resuscitation. One of these fields was that of the city fire brigade and the rescue crew in accidents in coal mines. The other was the surgical operating room. These two enterprises have developed separately, although along parallel and now converging lines. I will therefore tell the two stories separately.

RESUSCITATION FROM ASPHYXIA

In America city gas generally contains about 30 per cent. of carbon monoxide. Nearly every family has a motor car, and the exhaust gas contains about 7 per cent. carbon monoxide. In all American cities deaths from carbon monoxide asphyxia, often suicidal, are common. In New York City there are about five hundred a year.

Haldane early showed that the compound which carbon monoxide forms with haemoglobin is dissociable, and that haemoglobin is restored to normal condition under the mass action of oxygen. It was long supposed that the logical treatment for carbon monoxide asphyxia must be the administration of oxygen. But experience on the victims of asphyxia and on animals in my laboratory showed that in many cases the breathing becomes greatly depressed; a deeply asphyxiated man or animal does not draw the oxygen into the lungs in sufficient quantity, and the inhalation of oxygen alone does not quickly displace carbon monoxide from the blood. We found, however, that when carbon dioxide of 5 to 8 per cent. is administered to such cases respiration is greatly stimulated. When a mixture of oxygen and carbon dioxide is administered after a short but intense asphyxia the effects are truly extraordinary. A workman may be overcome in a trench over a leaking gas pipe, or at a blast furnace. He may be non-breathing and nearly pulseless. The inhalation of a mixture of oxygen and carbon dioxide is initiated under prone-pressure artificial respiration. As the carbon dioxide reaches the lungs natural breathing quickly returns, and, after half an hour of inhalation, the man is not only resuscitated, but feels well again, and goes back to work. The inhalation not only eliminates carbon monoxide, it also restores to the tissues of the body the normal content of carbon dioxide lost during the development of asphyxia. With the restoration of carbon dioxide the general tonus of the body returns.

After longer, although less intense, asphyxiations, resuscitation is not so rapid. But in these cases there is another effect of great importance; for the subsequent development of pneumonia is prevented. Before inhalational treatment was introduced, pneumonia was a very frequent sequel of asphyxia, and was often fatal. The first of several discoveries to which this treatment has led

† I have arranged with Messrs. Siebe, Gorman and Co., Ltd. (187, Westminster Bridge Road, London, S.E.1), to supply: (1) a CO₂ and oxygen inhalator for infants; (2) a CO₂ and oxygen inhalator for adults of the type used by American fire brigades for carbon monoxide asphyxia; and (3) a CO₂ and air inhalator for prevention of post-operative pneumonia, treatment of angina pectoris, and other medical and surgical purposes.

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is that the inhalation of carbon dioxide in oxygen not only relieves asphyxia, but also prevents post-asphyxial pneumonia. This is a fact big with promise.

There are now many thousand inhalators in active use in American cities. There are between three and four hundred in New York, and the number is rapidly increasing. In some cities physicians frequently ask for the help of the rescue crews of the fire brigade or the city gas company with their inhalator in cases of pneumonia. Even more often they call for the inhalator for newborn babies that fail to breathe effectively.

Out of this experience has come a clearer conception than we have had heretofore regarding the state of the asphyxiated respiratory centre both in the newborn child and in persons who have been immersed almost to drowning. It has always been supposed that there must be an overpowering excess of carbon dioxide in the blood in such cases. But our experience now demonstrates that it is not excess of carbon dioxide, but deficiency of oxygen, that induces the depression of the centre. No very great excess of carbon dioxide is, or can be, produced when the supply of oxygen is shut off. The asphyxiated centre is like one deeply morphinized. Its sensitivity is decreased; its threshold for carbon dioxide is abnormally elevated. But the inactive centre promptly becomes active again if the amount of carbon dioxide supplied to it is sufficient to stimulate. Accordingly, we find that when the normal 5 per cent. of carbon dioxide pressure is insufficient to stimulate, 7 per cent. carbon dioxide is often effective; or 10 per cent., or even higher pressures, may be needed. When sufficient carbon dioxide is administered to reach the elevated threshold and to overcome the decreased sensitivity, then spontaneous respiration begins. As the oxygen supply is renewed the threshold drops again to normal, the sensitivity of the centre is restored, natural breathing returns, and the asphyxiated newborn child or drowned person is resuscitated.

In American maternity hospitals, now, the old barbarous and often ineffective methods of resuscitating the newborn by swinging, spanking, and dipping in cold water are being replaced by inhalation of carbon dioxide. As much is used as may be necessary to start breathing, usually 7 per cent., mixed with oxygen. Many babies that cannot be resuscitated in any other way are thus saved. This improvement is also making its way in England, for among the first to adopt it was Dr. Louise McIlroy, at the Royal Free Hospital in London.

Recently another advance has been made. In addition to the four babies in every hundred births that are stillborn, some of whom can, however, be saved by inhalational treatment, there are four other babies that breathe for a few days but die in the first few weeks of life. Until recently no efforts have succeeded in reducing this huge mortality; for the decrease of infant mortality effected in recent years has been confined to the period after the first month. A large part of the neo-natal mortality is a consequence of continuing atelectasis. The lungs are not fully dilated by the first cry, or for many hours or even days, after birth. The ancient practice of making a child cry several times a day is often ineffective in overcoming atelectasis. It has now been shown by Cruikshank that the majority of neo-natal deaths are due to pneumonia developing in undilated areas of the lungs. Combining this fact with other evidence, I have proposed that the lungs of every newborn child should be fully dilated by inhalation of carbon dioxide in the first few days of life. In maternity hospitals where this measure has been adopted mortality from pneumonia has ceased.

Experience in cases of drowning is affording similar evidence. Inhalation of carbon dioxide and oxygen has

proved to be not only a valuable supplement to manual prone pressure artificial respiration, but also an effective preventive of the pneumonia which often causes the deaths of persons rescued from drowning.

PREVENTION OF POST-OPERATIVE PNEUMONIA

I turn now to the companion story of carbon dioxide inhalation in the surgical operating room. For many years I urged this inhalation; and it gradually came to be recognized as a procedure promoting the elimination of the anaesthetic, diminishing nausea, and restoring a vigorous heart action. It is also the most effective method of controlling an exhausting hiccup. Now another advantage has developed. Almost simultaneously three years ago in several clinics in America and also in Germany it was noted that patients who received this inhalation after operations and anaesthesia were free from the otherwise considerable risk of post-operative pneumonia. Even in the best practice the mortality from post-operative pneumonia has been four for every thousand major operations. The number that have had pneumonia and recovered has been many times greater; indeed, some degree of pulmonary involvement has occurred probably in as many as one in ten, or even one in five, of all cases after surgical operations, especially those in the abdomen. But now in clinics which have adopted as a routine procedure full dilatation of the lungs by inhalation of carbon dioxide, all pulmonary complications, such as in the past have led to post-operative pneumonia, have been eliminated. The reason for this result throws light on problems that have still to be solved.

Several observers in the last century, and particularly the English physician Pasteur early in this century, described a condition following bronchitis or diphtheria in which a part or the whole of one lung collapses and returns to a state like that before birth. But it is only since the use of the x ray and the bronchoscope became common that this condition in the lungs, from which post-operative pneumonia starts, has been generally recognized. This is the massive collapse of a lung or the atelectasis of a lobe or lobules. It is now only three years since the relation of atelectasis to pneumonia was first demonstrated experimentally by Coryllos. This demonstration goes far to explain why the victims of motor and other accidents, whose ribs are broken and whose chests are partially immobilized, rather often develop pneumonia.

Normally the lungs are kept constantly expanded and their airways open. Through these tubes they are the best-drained organs in the body. The force which keeps them open is the tonus of the diaphragm and the other muscles of the thorax. Whenever this tonus is lowered, as it is after asphyxia, anaesthesia, immersion, and in elderly and debilitated patients long confined to their beds, and in those who have suffered chest injuries, the vital capacity of the lungs is diminished. In the unaerated areas mucus accumulates until some of the airways are filled and closed. If there happens to be present also inhaled foreign material or catarrh from bacterial invasion, these conditions also contribute to the blocking of airways. As soon as any part of a lung is thus shut off, the air within it is absorbed into the blood; for the total pressure of all the gases in the venous blood is always forty to sixty millimetres less than the total pressure in the arterial blood, which is the same as in open areas of the lung, and in the outside air. The occluded lung or lobe or lobules are soon collapsed, and in such collapsed areas any bacteria that happen to be present find conditions favourable for their growth and activity. It is in this way probably that all secondary pneumonias develop.

This conception assigns to the tonus of the skeletal muscles of the body a place of prime importance in

respiration. It is this tonus that keeps the lungs expanded and prevents atelectasis. The movements of respiration do not consist merely in the alternate contraction and relaxation of the thoracic muscles. In reality, as W. R. Hess expresses it, these muscles pass at each breath from one tonus level to another and back again. When respiration is depressed the tonus level of the entire musculature of the body is depressed also. The capacity of the thorax is greatly decreased by the relaxed and elevated diaphragm and the flaccidity of the other respiratory muscles. In the partially deflated lungs atelectasis readily develops, and, if infection is present, pneumonia may follow.

When, on the contrary, respiration is stimulated, as it is in normal muscular activity by an increased production of carbon dioxide in the body, or as it is by inhalation of carbon dioxide, the tonus of all the muscles of the body, and particularly those involved in respiration, is increased. The lungs are expanded, occlusion of airways is prevented, and any airways that have already been occluded are reopened. The normal drainage from the lungs through the airways is maintained, or re-established, and the development of a secondary pneumonia is prevented.

Even in the development of primary pneumonia low muscular tonus, partial deflation of the lungs, and the resulting atelectasis probably play an important part; for it is a well-recognized fact that lobar pneumonia may spread from patient to patient in the beds of a hospital, but that the physicians and nurses, who are moving about and keeping their lungs expanded, are relatively immune to the contagion.

If the length of this address permitted it could be shown that respiration exerts its chief effect upon the circulation also through its influence upon the tonus of the musculature of the body. This tonus is the chief factor in the veno-pressor mechanism—a mechanism largely distinct from the vasomotor system and scarcely less important. It is the tonus of the skeletal muscles which normally presses the blood out of the tissue capillaries into the veins and back to the right heart. Whenever respiration is stimulated, as it is by physical exercise, the increased tonus of all the contractile tissues increases the volume of the venous return, improves the heart action, and augments the circulation.

When, on the contrary, respiration and muscle tonus are depressed, the blood stagnates in the tissues, the venous return is diminished, the heart action is weakened, and the circulation is retarded. The extreme form of such depression is surgical shock. The inhalation of carbon dioxide after anaesthesia and operation, and in other conditions of lowered vitality, by restoring respiration and muscle tonus, counteracts both the depression of the circulation and the tendency to atelectasis and pneumonia.

Such in brief outline are the contributions which the physiology of respiration is making to the science and art of resuscitation. From the developments of the past few years it appears probable that in the near future all secondary pneumonias will be preventable.

CONCLUSIONS

In cases of drowning, asphyxiation, and other accidents, and after surgical anaesthesia, the prevention of secondary pneumonia is almost as important as the immediate resuscitation. Inhalation of carbon dioxide mixed with oxygen or with air is the most effective means of stimulating respiration. This inhalation has proved to be also a highly effective preventive—indeed, it is essentially the specific preventive—of the collapse of the lungs which leads to pneumonia. These two advantages have now been demonstrated by experience in large numbers of cases of carbon monoxide asphyxia, drowning, and other accidents. In the asphyxia of the newborn this inhalation is replacing

the old brutal and often ineffective methods of swinging, spanking, and dipping. In surgical clinics this treatment is used to counteract failure of breathing under anaesthesia, to restore a normal circulation, and especially to prevent post-operative pneumonia.

Respiration is closely associated with the tonus of the muscles, especially of the thorax. Depressed breathing and low tonus permit collapse of parts or the whole of a lung. From this collapse, if infection is present, pneumonia develops. If respiration and muscle tonus are stimulated by inhalation of carbon dioxide the lungs are kept open and the development of pneumonia is prevented.

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DIABETES INSIPIDUS FOLLOWING FRACTURED SKULL

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Diabetes insipidus, a comparatively rare condition, has been recognized since 1674, when Willis noted that in a certain number of cases which were classed as diabetes mellitus the condition of the urine was different, in that it did not have the same sweet taste. This suggested to him a basis of differentiation. It was not until one hundred years later that Simmons described two cases of this disorder, and these were published in detail by Fitz. Following this, Frank referred to diabetes insipidus as "a long-continued abnormally increased secretion of non-saccharine urine, which is not caused by a diseased condition of the kidneys."

Although this malady was definitely recognized by clinicians, nothing was known of its etiology except that it was not due to renal disease. The nineteenth century literature contains several articles dealing with experimentally produced diabetes insipidus. Claude Bernard, in his experimental puncture of the floor of the fourth ventricle, produced this syndrome, and believed that he had found a centre in the base of the brain which governed it. If diabetes insipidus is due to some disturbance of the pituitary, as we have every reason to believe, then the experimental work of Schäfer, Magnus, and Herring, and the deductions and observations of Cushing, are invaluable. Briefly, Schäfer, in 1902, proved that a polyuria in animals could be experimentally produced by the injection of pituitary extract. Other experimental work showed that the diuretic action of the pituitary extract was caused by the pars intermedia. At the same time, Cushing noted that in a certain number of his operation cases in which the pituitary body was subjected to manipulation a severe polyuria frequently resulted, which