HYPOVENTILATION: ITS DANGERS IN GENERAL ANAESTHESIA

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Hypoventilation is the clinical state which results from a diminution in the rate of exchange of the respiratory gases between the blood and the alveolar air. The oxygen content of the blood and consequently of the tissues is reduced. This is conveniently referred to as *hypoxia*. The CO_2 content of the blood is increased, and this is known as *hypercapnia*.

While these two hazards are almost always associated in hypoventilation occurring during anaesthesia, the effects of each can be studied in the absence of the other under experimental conditions. Hypoxia has been studied clinically as the cause of mountain or altitude sickness. As a result of oxygen lack, the respiratory centre is reflexly stimulated *via* the chemoceptors. Unconsciousness ensues if the lack of oxygen supply to the brain is gross enough. The effects of hypercapnia can be observed in the absence of hypoxia by asking a subject to breathe in and out of a re-breathing bag to which an adequate amount of oxygen is delivered, but without soda lime in the circuit to absorb the CO_2. The respiratory centre is stimulated in this case by an overdose of its normal stimulant. Unconsciousness occurs from the anaesthetic property of CO_2 when its proportion in the inspired gases is 10% (Clements[1]).

During quiet breathing in adult subjects the amount of air inspired or expired measures 350-500 c.c.; this is the *tidal volume. It ensures an adequate oxygen intake and CO_2 output*, because this volume of air expands the lung alveoli and thereby provides an area of pulmonary epithelium sufficient to enable the necessary diffusion of the respiratory gases. If this area of epithelium is reduced beyond a certain minimum, by a reduced tidal volume, it becomes inadequate for efficient respiration; in other words, the oxygen intake will be reduced below what the body requires, and the CO_2 output will be restricted. Thus hypoventilation leads inevitably to hypoxia and hypercapnia.

General anaesthesia is an abnormal condition, a temporary disease produced by the anaesthetist in the process of abolishing the perception of painful stimuli by means of narcotics (known as anaesthetic agents). *Its pathological severity can be estimated by the degree of hypoventilation which is allowed to occur.*

'The anaesthetist ordinarily over-estimates the extent of ventilation. In a number of observations with the carbon dioxide analyser, *tremendous retention* of CO_2 was demonstrated in patients to whom the anaesthetist felt he was providing adequate ventilation' (Cullen[2]).

CAUSES OF HYPOVENTILATION

The causes of hypoventilation may be classified as (1) local, (2) central and (3) general.

1. *Local causes* include diseases of the lungs, e.g. emphysema, atelectasis, fibrosis. Other local causes are obstruction of the airway, excessively narrow intratracheal tubes, abnormal positioning, e.g. the extreme Trendelenburg or the jack-knife position, and faulty apparatus such as inefficient expiratory and to-and-fro valves or badly fitting face-masks. An assistant leaning on the patient's trunk is another possibility, as is excessive retraction of the costal margin.

2. *Central causes* are those producing paralysis of the respiratory centre. They include the anaesthetic agents, with or without premedicating drugs.

3. *General causes* are drugs producing muscular relaxation, and hence paralysis of the muscles of respiration.

HISTORY OF ANAESTHETIC METHODS

In the days of the rag-and-bottle method of anaesthesia, most of the CO_2, including the concentration necessary to stimulate the respiratory centre, was lost. It went unhindered into the surrounding atmosphere. Without this stimulus, it was difficult to ensure a depth of respiration which would convey enough of the anaesthetic agent to the blood stream, especially when the agent was only mildly potent. Hence the open method gave way to the semi-open—the face mask was covered with towels, so that the concentration of the agent in the inspired air would be increased, when of course CO_2 began to build up simultaneously.

The introduction of the re-breathing bag followed logically. By the semi-closed technique the stage of induction could be shortened and anaesthesia could be more easily maintained. Oxygen administration was also facilitated. Finally, the closed circuit method was evolved in an endeavour to control the amount and proportion of the gases respired. The soda-lime canister became an important part of the apparatus, as the danger of CO_2 accumulation was at once apparent.

The Muscle Relaxants. Before the advent of the muscle relaxants, muscular resistance added considerable difficulty to abdominal surgery. Forcible retraction of the abdominal muscles and peritoneum was often responsible for post-operative collapse. If deep anaesthesia was maintained for a lengthy period, the ill-effects of hypoventilation were superadded, caused by depression of the respiratory centre. Nowadays, muscular resistance is abolished as if by magic by the injection of a muscle relaxant, but post-operative collapse may still occur, especially after or even during long operations. The reason is that the relaxants paralyse the respiratory muscles peripherally. *They are probably the most potent, and also the most dangerous, cause of hypoventilation.*

The use of muscle relaxants has been accompanied by an increase in morbidity and mortality, just as occurred with the introduction of the intravenous anaesthetics. The increased dangers are due to lack of appreciation

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of the hazards of hypoventilation produced by these potent drugs.

The wounded animal shot with the curarized arrow of the South American Indian dies immediately from the effect of a massive dose of curare[3] on the heart muscle. However, when the dose is smaller, the unfortunate animal often dies a lingering death from paralysis of the respiratory muscles, i.e., from hypoventilation. Consider the exquisite torture which must be experienced by a conscious animal when the healthy respiratory centre is not able to invoke a response to the most powerful analeptic in existence—carbon dioxide. A similar situation is created by the inept anaesthetist who curarizes his patient and then permits him to hypoventilate, except that the narcotized patient is spared the sufferings of the conscious animal.

The full significance of the distress produced by hypoventilation cannot be appreciated by a healthy person. One may get some idea however by voluntarily hypoventilating or by being strapped into a very tight corset for 1-2 minutes.

CO_2 ACCUMULATION—HYPERCAPNIA

When a patient is deeply anaesthetized and allowed to hypoventilate for a long period, one has observed that he will remain unconscious for a considerable time after the effect of the anaesthetic agent has worn off. This is due to the narcotic property of the accumulated CO_2. This effect was known long before the discovery of modern anaesthetics. Italian surgeons used to put their patients into small grottos before operation. The small opening in the vault was insufficient for satisfactory ventilation, and after many hours the patient became stupefied by his own CO_2. Breathing in and out of a rubber bag (a re-breathing bag) will reproduce a similar situation in a few minutes.

In small amounts CO_2 stimulates the respiratory centre. In strong concentrations, however, it is a very powerful cardiac poison. Prolonged exposure to even moderate amounts can cause myocardial damage, often of a serious nature. The pulse is usually full and bounding in commencing hypercapnia. Twitchings and convulsions may occur, but these are often masked by the anaesthetic and the relaxants.

OXYGEN LACK—HYPOXIA

Following anaesthesia in which hypoxia is permitted to be the predominating extraneous factor, the patient on recovering may display some of the manifestations of mountain sickness—restlessness, garrulity, shivering and various degrees of cyanosis. He may complain of severe headache or abdominal pain. The pulse is often rapid and of poor volume. On the other hand, should the hypoxia have been complicated by hypercapnia—which is usually the case, but at a later stage—these signs and symptoms will be masked if the resulting circulatory collapse is gross enough.

The open and semi-open methods do not include the use of the re-breathing bag, and are therefore not complicated by the use of the muscle relaxants, but collapse can occur if the anaesthesia is excessively profound or prolonged. Hypoventilation results from depression of the respiratory centre. If a relaxant *is* used, a bag is essential, for it provides the only effective means of administering oxygen under pressure for combating acute hypoxia. The semi-closed and closed circuit methods permit the use of the muscle relaxants and thereby become correspondingly more dangerous in the presence of uncontrolled anaesthesia (no attention to the tidal volume).

Circulatory collapse ascribed to hypoventilation is therefore obviously due to the degree and duration of the hypoxia and hypercapnia produced, and is aggravated by (1) the type of anaesthetic agent (the effects will be more rapidly manifested with those that have a powerful depressing effect on the respiratory centre, such as thiopentone, cyclopropane and chloroform) and (2) the type of circuit used. The closed method is potentially more dangerous, because the re-breathing bag tends to allow accumulation of CO_2, *and its progressive displacement of oxygen.* Furthermore, gases are used in small amounts in this method—c.c. as compared with the litres used in the semi-closed method, and any leakage has thus a proportionately greater effect. Such leakage, occurring during expiration, implies that the bag does not receive the full tidal volume. Inspiration is consequently defrauded by the amount lost and hypoventilation commences. The soda-lime canister will take longer to warm up and the unwary anaesthetist is apt to interpret this as an indication of its high potency. The truth of the matter is that the soda-lime is actually doing less work, since it is not dealing with the full tidal volume. Its continued coolness should warn the alert administrator to check up on his apparatus immediately.

POST-ANAESTHETIC COLLAPSE FOLLOWING HYPOVENTILATION

A typical case history of this grave complication of hypoventilation is as follows: The patient is in good health, except for the complaint which requires a surgical procedure of long duration. Hypoventilation is allowed to occur, and hypoxia and hypercapnia develop insidiously. The colour remains deceptively pink—deceptive because it is the result not of adequate oxygen content of the blood, but of the excessive dissociation of oxygen from the blood to the tissues on account of the high CO_2 content. 'Too many anaesthetists for too long have been satisfied with having the patient "pink." One should not be lulled into complacency about the patient's ventilatory sufficiency on the basis of the oxygen supply alone' (Cullen[5]).

The blood itself becomes dusky, as may be apparent to the watchful surgeon if there is free bleeding. The blood pressure rises, and the pulse may become full and bounding. If the surgeon enquires after the patient's condition, he may be informed by the unsuspecting anaesthetist that everything is going well. The latter has been 'lulled into complacency' by the pink colour and the strong pulse. In marked hypoventilation, cardiac arrhythmia may occur.

Towards the end of the operation, collapse may set in, but is often delayed until the patient has been taken back to the ward. Here the sister observes that he lies limply

in bed, as if concussed. His colour is sickly pale and the breathing very shallow. The eyelids are slightly open, displaying dilated pupils. The pulse is rapid and thready and the blood pressure has fallen alarmingly. All reflexes may be absent.

The operating team is hastily summoned, and is often nonplussed by the suddenness of the collapse. '*But he was so well when he left the theatre, Sister! Was the jaw supported on the way down?*'

Very little blood may have been lost during the operation, and very little trauma may have been inflicted, nevertheless a pint of blood, or even 2 pints, is immediately ordered, and cardiac stimulants injected. *Neither the blood nor the stimulants exert any beneficial effect and the blood especially may well be harmful to the failing circulation in a severe case.* It is as illogical to transfuse a case of post-anaesthetic collapse as it would be to transfuse one of hyperglycaemic or hypoglycaemic coma.

CO_2 is sometimes administered, but it is absolutely contra-indicated, for the patient is already suffering from CO_2 intoxication and, furthermore, the paralysed respiratory centre is no longer able to respond.

Prevention

This implies prevention of the hypoventilation:

1. *Effective Apparatus.* Anaesthetists must in the first instance ensure that the more obvious causes, such as obstruction of the airway or leakages, are absent. An intratracheal tube minimizes the margin of error presented by the dead space, and also the additional hazard of obstruction.

2. *Maintenance of the Tidal Volume.* One must be able to estimate the tidal volume by the excursions of the thoracic cage and the abdomen, and of the re-breathing bag. This is not easy, but the required ability can soon be attained by practising assessment of one's own tidal volume with a re-breathing bag and a spirometer. If a decrease in the patient's tidal volume is noticed, it should be corrected immediately. Unless this is done, a lesser volume of gases is inspired (including less oxygen), and a lesser volume is expired (including less CO_2). Hence CO_2 must accumulate in the blood. Some administrators do not perceive the inexorable logic of this train of events. They do not comprehend how CO_2 accumulates in the blood when all the expired gases are released freely to the surrounding atmosphere. Nor do they appreciate how hypoxia can develop when the inspired gas is pure oxygen—forgetting that its volume is now insufficient to fill all the alveoli. However desperately the body requires more oxygen, it cannot absorb its requirements from the super-saturation of the volume of blood flowing to a limited area of lung tissue.

As soon as a diminution in the tidal volume is observed, mechanical or manual compression of the bag must be instituted. I consider the manual method easier and safer, provided one has learned to estimate the degree of compression required to raise the tidal volume to its correct level.

3. CO_2 *Absorption.* Soda-lime plays a most important part in closed-circuit anaesthesia. It is the only means of eliminating the excess CO_2. However, it is unwise to rely implicitly on the claims of the manufacturers concerning the life of the soda-lime. During lengthy procedures it is wise to use as many as 3 canisters, changing from one to the next as soon as it gets warm, not excessively hot—say, every 15-20 minutes. By so doing the accumulation of CO_2 from exhaustion of the soda-lime is prevented. The earliest detectable sign of hypercapnia is often a slight rise in the blood pressure, and this should be measured with regular frequency. Occasionally, the CO_2 content of the re-breathing bag should be measured with a CO_2 analyser as a confirmatory check.

4. *The re-breathing bag* is a potential reservoir of CO_2. It should not be very large. The bigger the bag, the greater the risk of CO_2 accumulation in it, and the greater the delay and difficulty in filling it with oxygen, when pressure is urgently required. A capacity of about 2 litres is quite adequate. Those who are not familiar with the size of tidal volumes can easily learn it by grasping a portion of the re-breathing bag so as to produce an hour-glass effect. The gas should now be made to flow into the upper compartment at the rate of the required volume in exactly 1 minute. Thus after 1 minute at the rate of say 500 c.c. per minute the compartment will either be over-distended or incompletely filled, and after a little practice the correct position of the hour-glass constriction will be found.

Once again it must be stressed that it is not sufficient to treat a hypoventilating patient by disconnecting him from the re-breathing bag and allowing the expired gases to pass unhampered into the ambient atmosphere. With a diminished tidal volume, less CO_2 will be excreted and more will be retained in the blood. Oxygen intake will also be lessened. The only logical method available is to retain the bag and compress it to maintain the tidal volume while absorbing the CO_2 by soda-lime.

5. *The muscle relaxants.* Long-acting relaxants are responsible for longer periods of hypoventilation and are therefore potentially more dangerous than the short-acting group. For this reason, mainly, I prefer Scoline. Some of my colleagues refuse to use it because there is no antidote. They say they feel safer with the longer-acting relaxants because an antidote is available—prostigmine. I consider this to be faulty reasoning. Sensitivity to Scoline is extremely rare—I have encountered 2 cases in over 3,000. Apnoea lasted 15 and 20 minutes respectively. In such cases, a sure antidote is in fact available—oxygen under pressure, and this was given with good effect. This type of apnoea must not be confused with that resulting from excessive loss of CO_2 or with a peculiar delay in the respiration probably due to irritation by the intratracheal tube. Secondly, I feel that the anaesthetized patient should be maintained as far as possible in his normal physiological state. The use of prostigmine (which must be accompanied with atropine) seems to be an example of treating an abnormal condition with an abnormal drug. Surely the administration of an antidote for an excessively-acting drug should not become an established routine. One may have to seek an antidote to the antidote! In any case, Scoline offers no such difficulty. The last fractionated dose is given to facilitate closure of the peritoneum, and has worn off long before the skin wound is closed.

Treatment

1. *Moderate collapse.* Provided that the patient was reasonably healthy before the anaesthetic ordeal, all that is necessary is to administer oxygen at the rate of 2-3 litres per minute through a clear airway, but with no bag. The foot of the bed should be raised and the patient kept warm. No narcotics should be given for the relief of questionable pain. Methedrine, 0·75–1 c.c. intramuscularly administered, at quarter hour intervals, may be of benefit.

2. *Severe collapse.* Severe cases must be treated on heroic lines. When the blood pressure has dropped alarmingly, the immediate danger is the circulatory failure and the consequent hypoxia of the vital parenchymatous organs. The aim of treatment is two-fold, viz. (*a*) restoration of circulation, and (*b*) effective administration of oxygen and elimination of the accumulated CO_2.

(*a*) *Restoration of circulation.* Add 4 c.c. of Levophed to a 1,000-c.c. vacolitre of fluid (5% glucose in water). To avoid the danger of tissue-sloughing, which may occur at the site of injection, insert a needle (or a cannula through a cutdown) into a vein, and connect up to the vacolitre. Raising of the limb to above the level of the heart may also help in the prevention of tissue-gangrene. The backward seepage of nor-adrenaline will also be minimized. Start the drip at about 40 drops per minute and regulate it according to frequent blood-pressure measurements. Usually, after 2-3 minutes, a rate of about 20 drops per minute will suffice to maintain the blood pressure at a safe level (which will obviously vary with the pre-operative level).

(*b*) *Effective administration of oxygen and elimination of the accumulated CO_2.* At the same time, administer oxygen at 0·75–1 litre per minute by means of a face-piece, with the expiratory valve almost completely closed. The CO_2 is absorbed by fresh soda-lime in a canister interposed between the patient and the re-breathing bag, which is vigorously and regularly compressed. The tidal volume should be raised to, say, 650 to 700 c.c. so as to hasten the excretion of CO_2. The apparatus at the same time should be checked for any leakage. It will be observed that the canister becomes abnormally hot in a matter of minutes and must therefore be changed frequently.

The pumping-in of 8-10 litres of oxygen per minute is not an effective method. The expiratory valve has to be kept far too open and, as a result, the full tidal volume cannot be attained with any degree of accuracy.

The Oxford Vaporiser is an apparatus which can be used effectively if no soda-lime is available. There is a 2-way valve which allows oxygen to be forced into the lungs but prevents any of the expired gases from re-entering the bag. This is a very useful apparatus and can be effectively used for maintaining the tidal volume.

DISCUSSION

It should be remembered that the anaesthetic agents were discovered and used by those who must have been well aware of their potency in the presence of normal ventilation. The abolition of pain was always the prime purpose. When these agents are abused, especially for the purpose of acquiring relaxation, extraneous factors such as hypoxia and hypercapnia frequently intrude. *The aim of general anaesthesia* should be to render a patient insensitive to painful stimuli with a minimal disturbance of his physiology. Muscle relaxants should be added when it is necessary to abolish muscular rigidity, including laryngeal spasm, and local anaesthetics when pain perception cannot be prevented by moderate amounts of anaesthetic agents.

The danger of anaesthesia should be measured in terms of the degree of hypoventilation, i.e. of hypoxia and hypercapnia. The anaesthetist must watch constantly and carefully for the signs of hypoventilation. These include a rising blood pressure and pulse rate, occasionally cardiac arrhythmia, and muscular rigidity.[6] They do *not* include alterations in the pupillary and other reflexes, which are an indication of the extent of overdosage with the anaesthetic agent.

In this connection, one must not confuse the effects of an anaesthetic agent with the effects of any associated hypoventilation, as is still commonly done in some of our text-books. Recent advances in anaesthesia have been revolutionary, and it might be advisable to re-assess findings published as long ago as 1911. In that year, for instance, Goodman Levy[7] stated that when cats under light chloroform anaesthesia were stimulated, they developed ventricular fibrillation. Surely one of the first rules of experimental human physiology is not to accept the evidence of animal experiments as being applicable to man! Levy omitted to describe exactly how his cats were anaesthetized. It would appear that they were not premedicated, and they may have been somewhat excited and uncooperative! They may even have hyperventilated! With the removal of the normal stimulus to breathing, they may then have taken in less oxygen. It is also possible that the ventricular fibrillation may have been due to factors only remotely related to the specific anaesthetic agent employed.

Even modern writers seem prone to make unwarrantable assumptions. Clements[8] believes that cardiac irregularities may occur with cyclopropane. In this he is supported by several other modern writers,[9] but it is the author's firm conviction *that the agent is being made the scapegoat for undetected hypoventilation.*

CONCLUSIONS

An appreciation of the nature and amount of the gases in the re-breathing bag is essential for the efficient administration of a general anaesthetic. It must be remembered that in an individual at rest any diminution of the tidal volume will reflect on the amount of oxygen absorbed and CO_2 expired.

Hypoventilation due to tampering with the tidal volume, whether this is effected with narcotics that depress the respiratory centre or the relaxants that so grossly interfere with the normal excursion of the thoracic wall, is a sure method of producing hypoxia and hypercapnia.

Many of the weird, worrying and so-called inexplicable

phenomena associated with general anaesthesia, including arrhythmia of the heart, and post-anaesthetic collapse, can be attributed to the extraneous factors—hypoxia and hypercapnia. In collapse from this cause blood transfusions are contra-indicated.

The anaesthetist should be constantly on the alert for the prevention of hypoventilation—not only during anaesthesia, but also when the patient has been returned to the ward.

No matter what method is adopted, hypoventilation may occur immediately the patient becomes anaesthetized. *The administrator should therefore strive at all times to maintain the tidal volume, which is the all-important factor in general anaesthesia.*

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