ELECTROGRAPHIC REFLECTIONS OF CEREBRAL HYPOXIA*

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ANAESTHETISTS ARE one of the few groups of strictly human physiologists left in the world of science today. The World War II emphasis on the investigation of pressing human problems by addressing oneself to human subjects, instead of toads, frogs, clams, and cats, has been lost, unfortunately. It is to anaesthetists and to human cardiopulmonary laboratories that we look today for a continuance of that most vital of all disciplines in medicine, "Clinical Science," as pioneered by Sir Thomas Lewis.

This is particularly true with reference to electroencephalography, where the very complexity and phylogenetic development of the human brain makes generalization from cat and dog observations not merely hazardous, but often meaningless. This presentation will discuss some clinical investigation carried out during the past year in association with Professor Henri Gastaut and his colleagues at the Laboratory of Neurobiology at Marseille. The detailed reports of this work are published elsewhere.[1,2,3,4] This review will dwell on the principles involved in the investigations and on findings having particular application in the field of anaesthesia.

We have been concerned with neuronal changes, studied electrographically, in the cortex and subcortex of the human brain as hypoxia becomes complete anoxia. The work has proceeded in the following sequence: (1) A study of cerebral anemia following reflex cardiac slowing or temporary arrest, induced by ocular compression; (2) EEG changes following Valsalva's manoeuvre; (3) Hemispheral and bilateral cerebral anaemia induced by carotid sinus and artery compression; (4) Cerebral hypoxia from hyperventilation, or anoxia from the breathing of pure nitrogen.

(1) Forceful, sustained digital compression of both eyeballs simultaneously has been a parlour trick and laboratory diversion for many generations. It is likely to become, however, in an age of electrical recording from the brain, a most useful tool in differentiating syncopal cases from epileptics. The work at Marseille in this field was financed by the United States Air Force in an attempt to find simple methods of clinical investigation applicable to aircrew candidates in their second decade of life.

As can be seen from Figure 1, 10 sec. of forceful bilateral ocular compression have arrested the heart for approximately 12 sec., as shown by the electrocardiographic tracing (channel 7). Respiration is unaffected in this, as in most, cases. However, the arrested heart fails to pump freshly oxygenated blood to the brain, with the result that the EEG shows bilaterally abnormal electrical

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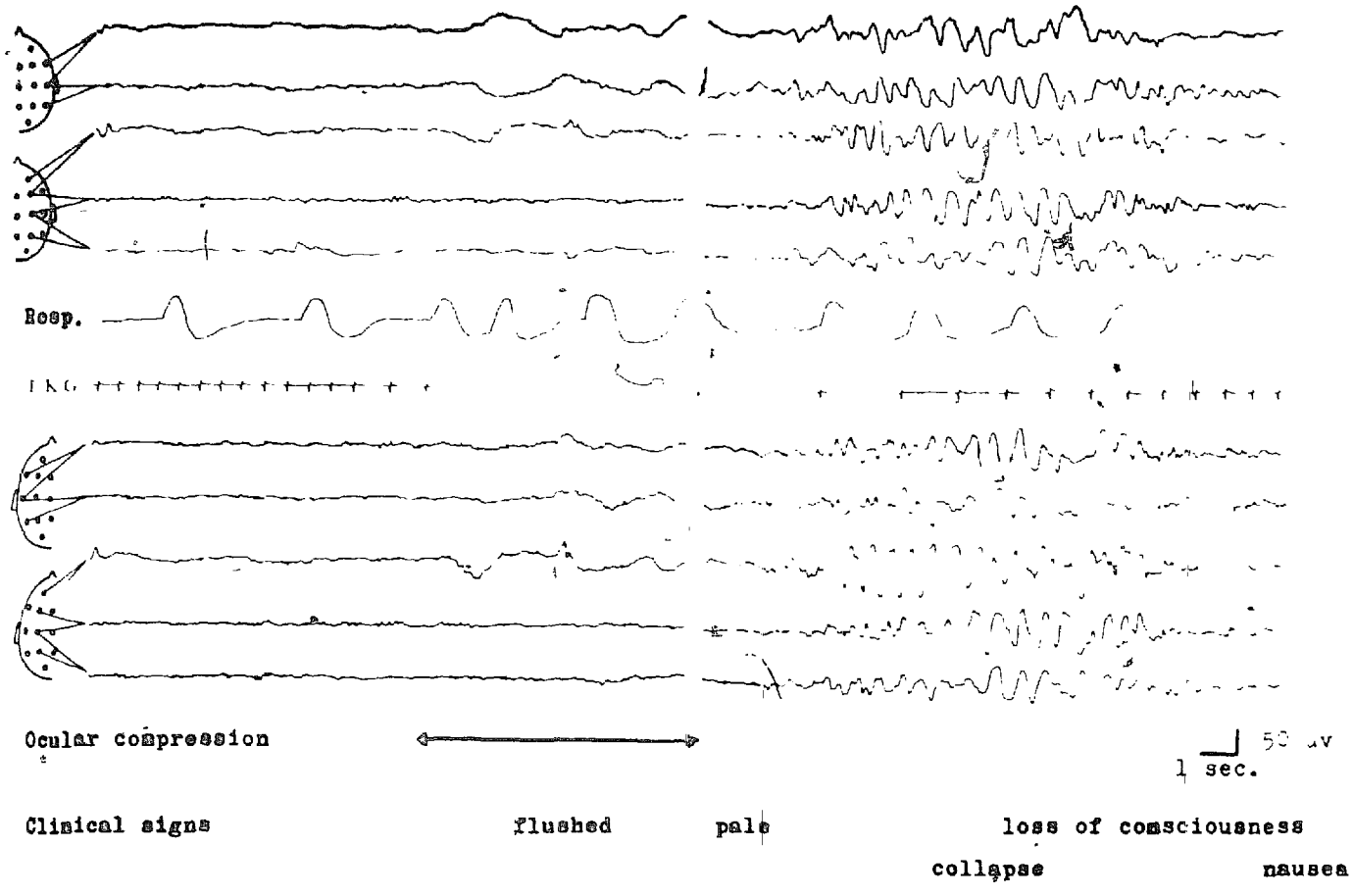


FIGURE 1. Ocular compression for 10 sec. (black bar) producing cardiac arrest (12 sec. approx.) with resultant slow waves bilaterally in EEG, and associated loss of consciousness.

activity. Another 10 sec. elapse before the re-established heart contractions can return the EEG to normal. During this period, collapse and loss of consciousness are seen to supervene briefly. Usually the blood pressure becomes so low as to be unmeasurable by the ordinary manometric method. A very high correlation was found between a positive oculocardiac reflex effect and a history of fainting in childhood or adolescence.[2] The lower the age group the higher was the incidence of reflexly induced cardiac arrest. Patients over the age of 45 years were not nearly as susceptible to this test, but, as we shall see later, they are increasingly susceptible to carotid sinus compression.

Anaesthetists are only too well aware of the extreme danger of cardiac arrest during ophthalmological operations, such as the correction of strabismus, in very young children. Kirsch *et al.*[5] have shown the facility with which traction on the internal rectus muscle will stop the heart. My attention was recently drawn to an unfortunate case of a young boy whose eye had been penetrated by a barbed arrow. Only after much difficulty and manipulation was the arrow removed, by which time the child had suffered a prolonged cardiac arrest. As a result, cerebration is almost lacking in this patient today.

The trigeminovagal reflex arrest of cardiac function is but one of a dozen examples which might be cited in a study of cerebral ischaemia of reflex origin. There are many vagovasal reflex patterns directly applicable to the anaesthetist's problems of bowel surgery (gall bladder interventions particularly), chest and tracheal manipulations. A discussion of preventive measures will follow the presentation of our data.

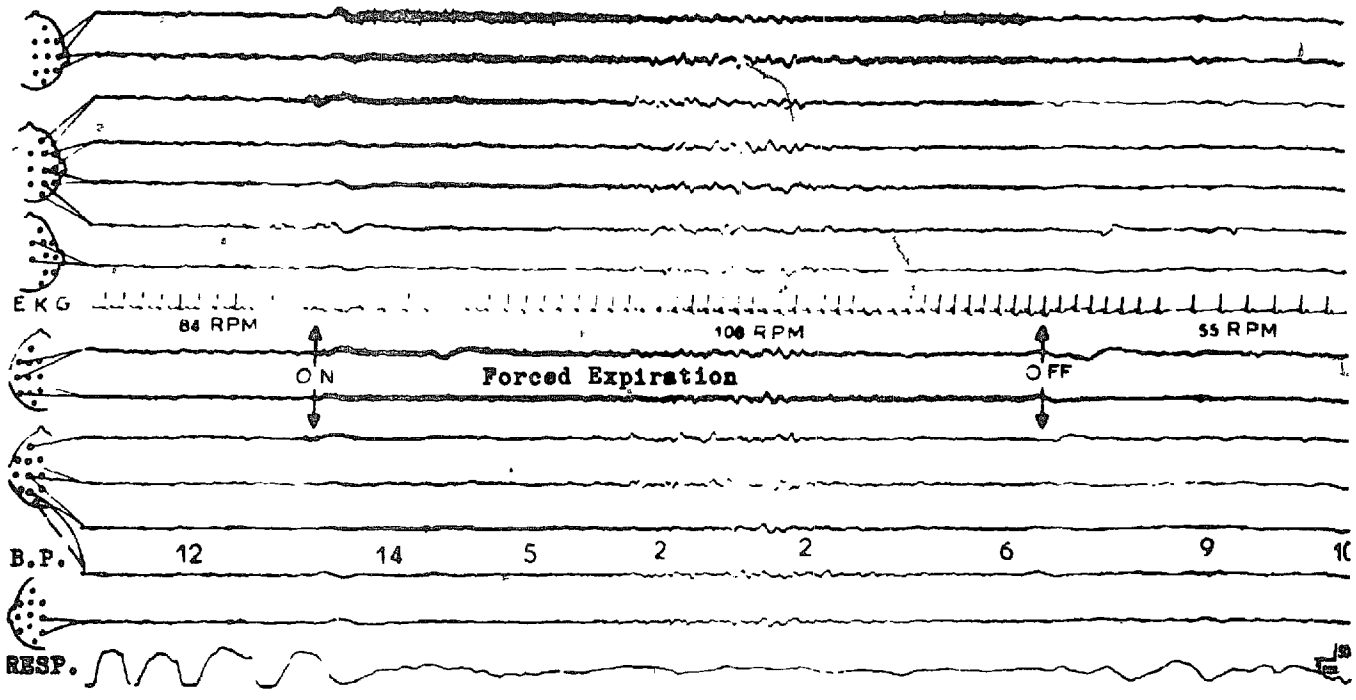


FIGURE 2. Forced expiration during which slowing is seen bilaterally in the EEG. Blood pressure drops from 120 mm. Hg, systolic, to an approximate level of 20 mm. Hg. Note acceleration of heart rate and cessation of respiration.

(2) Valsalva's forced expiration, such as that used in the 40 mm. Hg test during aircrew examinations in two wars, may have some remarkable effects on cerebral circulation. Figure 2 shows the bilateral slowing seen in the EEG in a patient being investigated for ptussive syncope. The lowest line of this figure shows the suspension of respiration, and the drop in blood pressure from 120 mm. Hg to a much lower figure, with an eventual rise to 60 mm. Hg as the expiration is terminated. The heart rate increased to 108 per min. While the causal mechanism is not generally agreed upon, the cerebral hypoxia, as shown in the EEG, is undoubted in these cases.

(3) Over the age of 45 years, cerebral ischaemia from carotid or vertebral arteriosclerosis is a problem of great significance to anaesthetists. Figure 3

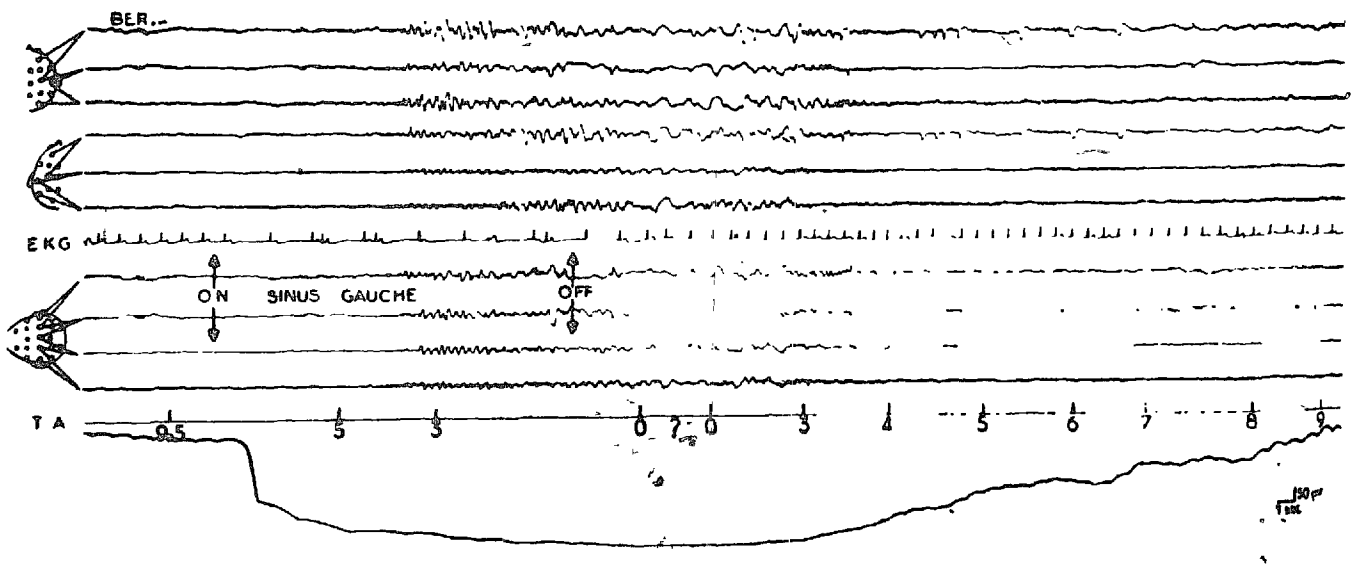


FIGURE 3. Effect of forceful pressure on left carotid sinus for 10 sec. with limited effect on heart rate but with marked effect on systolic blood pressure, and on EEG.

demonstrates slowing of cerebral electrical rhythms secondary to vascular collapse when the area of the carotid sinus is forcefully compressed. The effect on the heart rate is minimal, but on the blood pressure it is very serious. With re-establishment of the previous blood pressure all EEG abnormality is erased. Possibly because of changes in the adjacent tissue of the vessel wall, the carotid sinus itself becomes more sensitive with increasing age. However, sinus stimulation must be taken in conjunction with common carotid compression, if not temporary obstruction, in the tests here described. The EEG is one of the most sensitive and most easily recorded indicators of the function of (*a*) the carotid arteries, and (*b*) the collateral circulation available, through the Circle of Willis, from the opposite hemisphere.

(4) Forceful hyperventilation has for many years been a standard technique employed to "activate" the EEG. As Figure 4 shows, the blowing off of CO_2

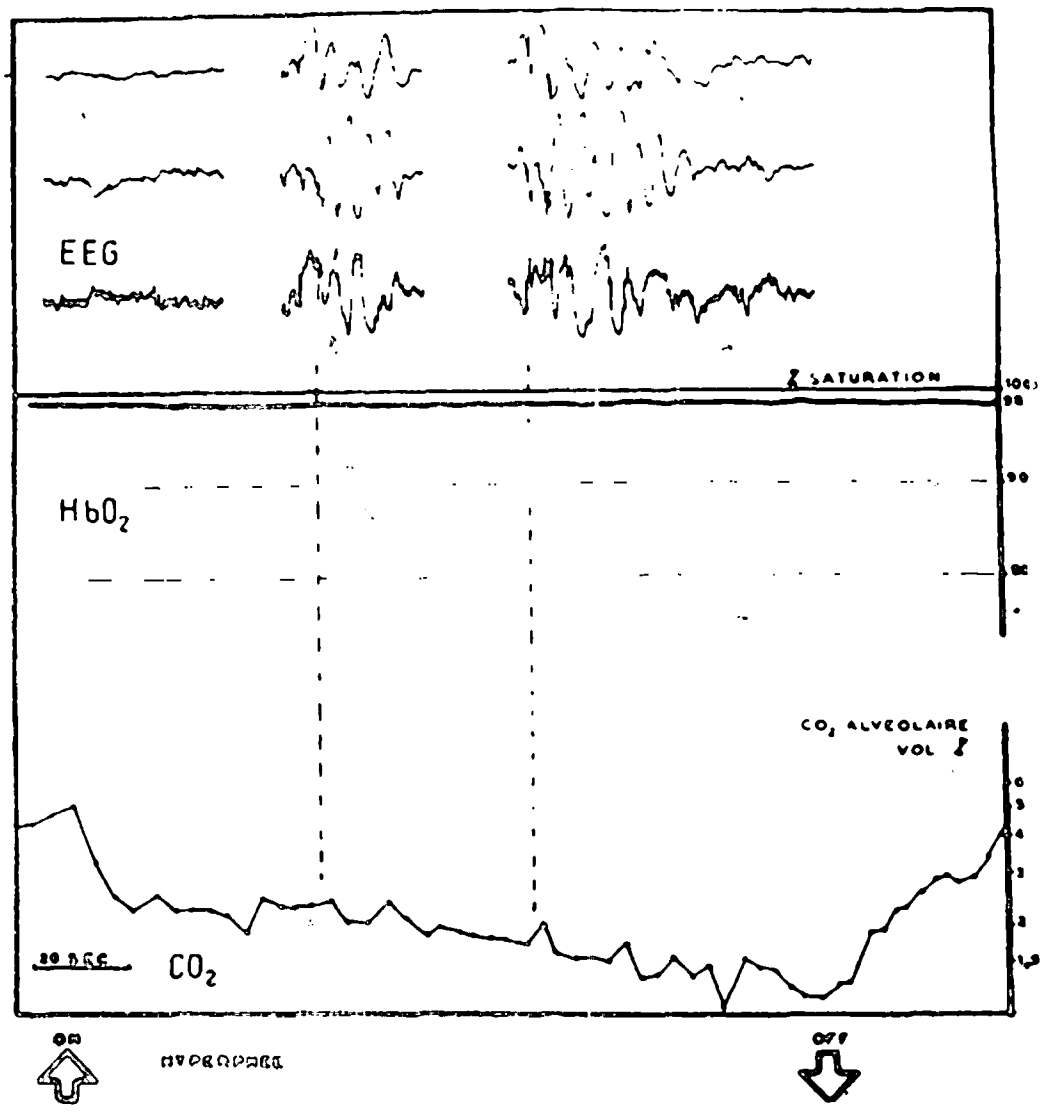


FIGURE 4 A marked loss of carbon dioxide, through hyperventilation, fails to affect the oxyhaemoglobin saturation, but leads to marked EEG changes.

leads to no decrease in oxyhaemoglobin saturation but to a marked change in the EEG. The appearance of the slowest cortical waves coincides with the lowest level of alveolar CO_2. As Figure 5 suggests, the inhalation of pure nitrogen ("a-zote" in French, meaning the gas which will not support life)

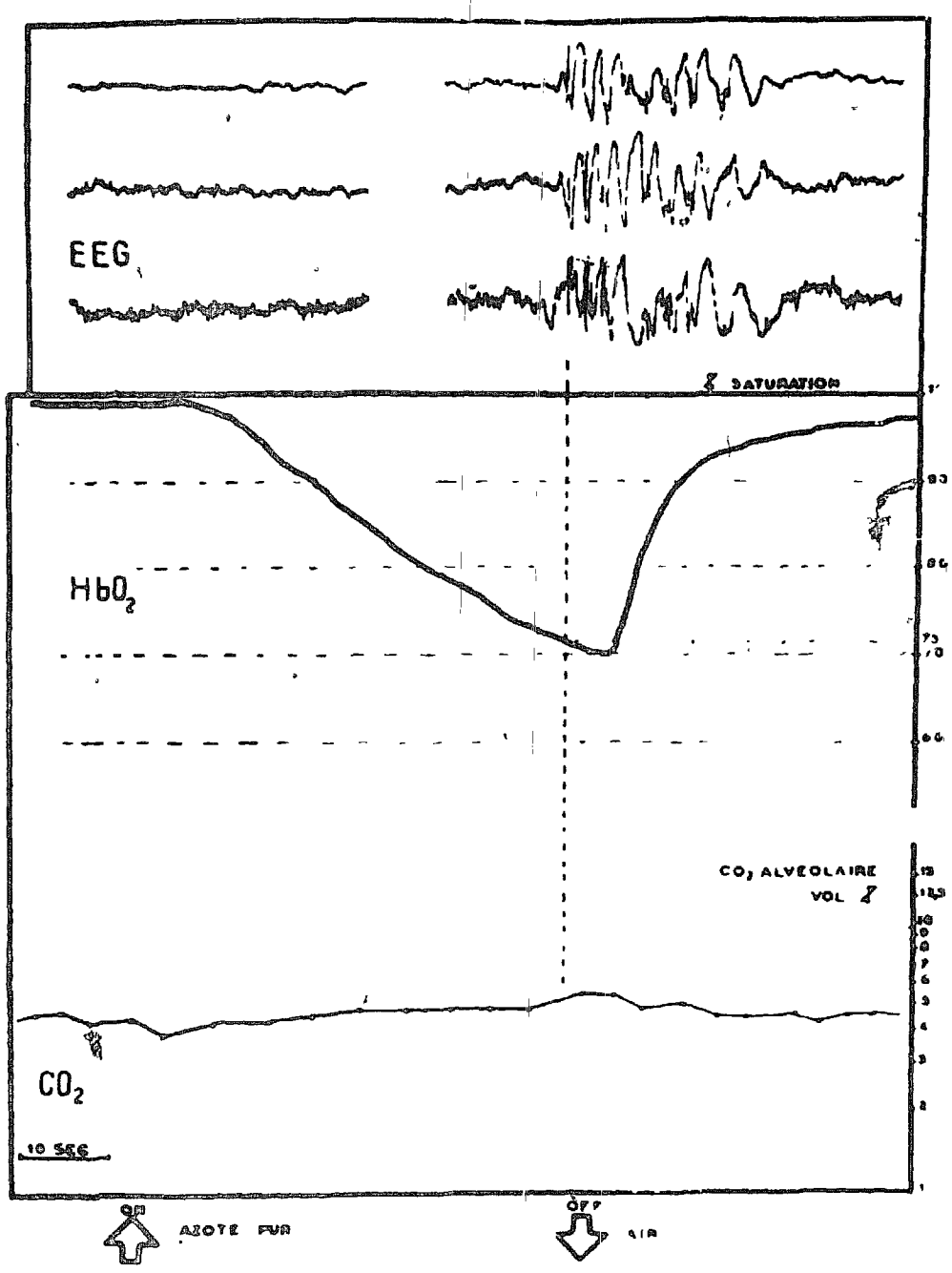


FIGURE 5. Pure nitrogen breathing fails to affect the alveolar carbon dioxide, but produces marked EEG effects when the oxyhaemoglobin reaches 70 per cent.

has no effect on the alveolar CO_2, but it has an effect on the EEG with that during hyperventilation (Fig. 4). This hypoxic effect is evic... the oxyhaemoglobin saturation approaches 70 per cent. We thus feel that hyperpnea and pure nitrogen inhalation produce their common hypoxic effect on the EEG by cortical capillary constriction and by hypoxaemia, respectively.

When, as shown in Figure 6, carbon dioxide is added to the nitrogen to be inhaled, it is found necessary to drive the oxyhaemoglobin down to a figure of 50 per cent in order to evoke marked slow wave activity in the cortical EEG.

In practice, the pure nitrogen was inhaled through an open circuit for an average of 40-50 sec., by which time hypersynchronous slow waves would usually appear in the EEG, as indicated in Figure 7. The onset, in the case of the petit mal epileptic there illustrated, was, as in most cases, very sudden

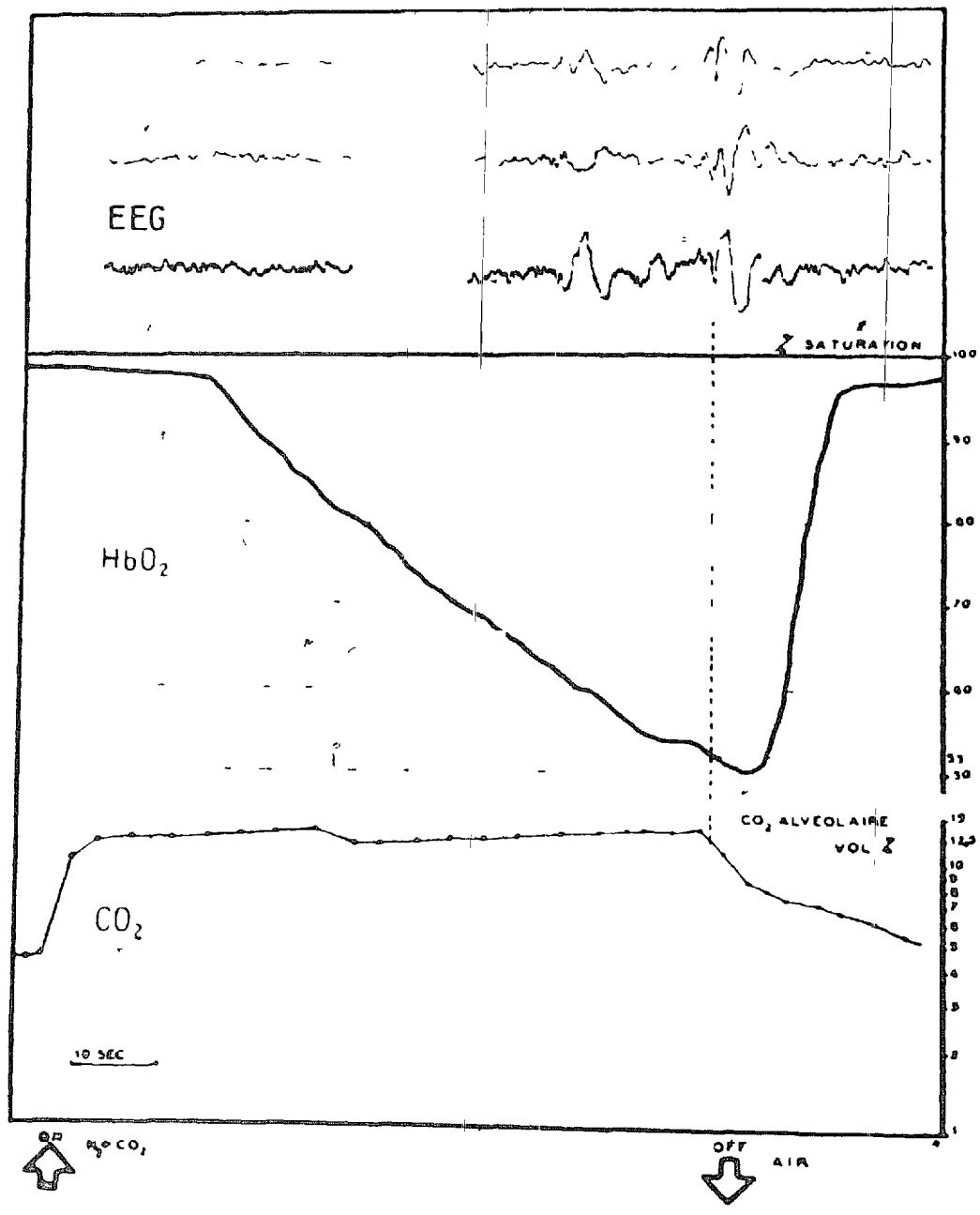


FIGURE 6. A mixture of carbon dioxide and nitrogen produces EEG effects only as the oxyhaemoglobin approaches 50 to 55 per cent.

and dramatic. An immediate switching over to pure oxygen, or 95 per cent oxygen-5 per cent carbon dioxide mixture was always practised. In many hundreds of tests, carried out with these precautions, no accidents occurred.

It should be mentioned that in children it was found useful to add a small amount of oxygen to the nitrogen inhaled to slow down the appearance of slow activity in the EEG in order that it could be studied adequately.

Nitrogen inhalation activated the EEG record in approximately 60 per cent of the generalized epileptics. The remaining 40 per cent were shown up electrographically by photic stimulation. The former group in no way overlapped the latter. Nitrogen proved to be better at activating generalized epileptic cases than hyperventilation.

In cases of focal epilepsy, nitrogen breathing promoted the appearance of localized discharges where none were seen in the resting record. It also had the effect of reinforcing any existing EEG focal abnormalities. While not quite as-

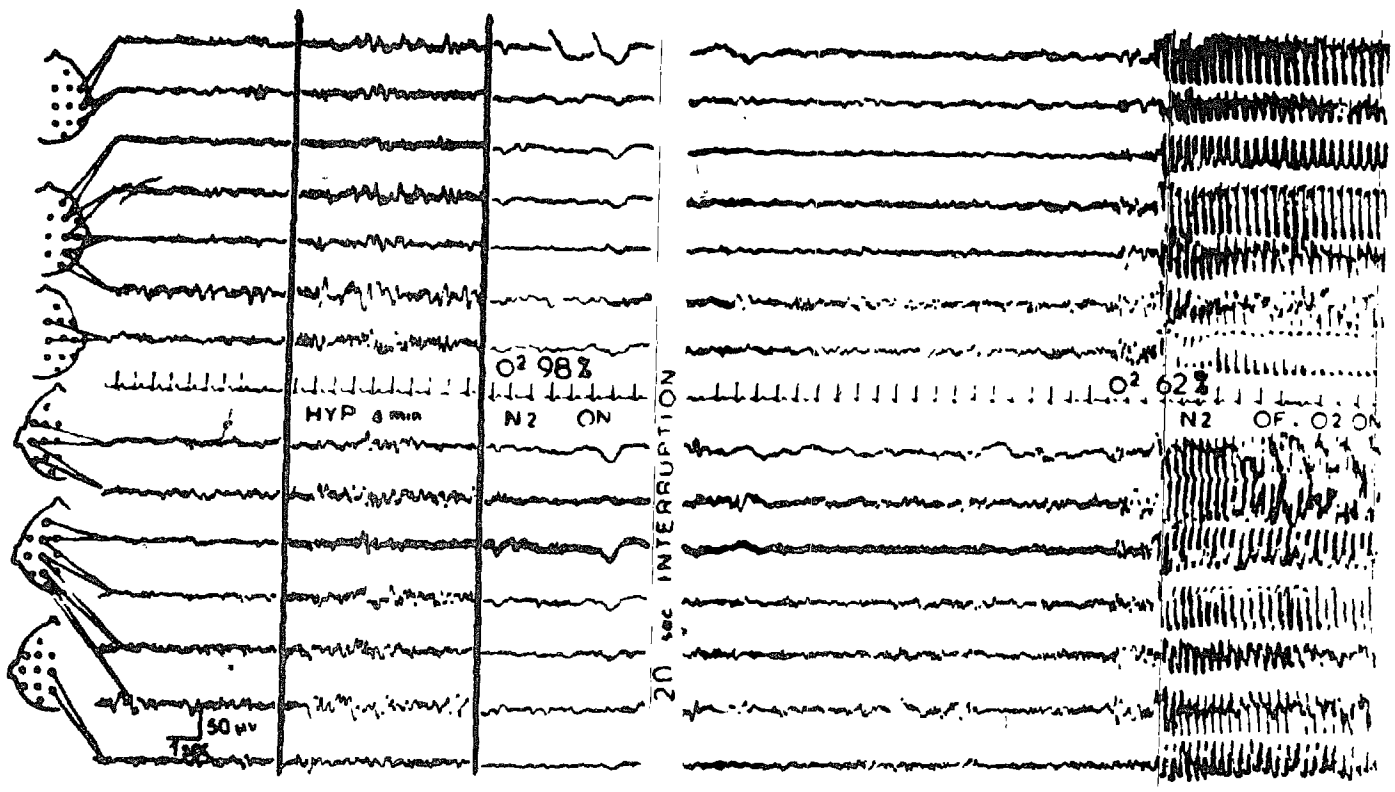


FIGURE 7. The petit mal case illustrated here showed little abnormality at rest or during hyperventilation. The breathing of pure nitrogen for approximately 50 sec. produced a spike and wave pattern bilaterally when the oxygen saturation reached 62 per cent.

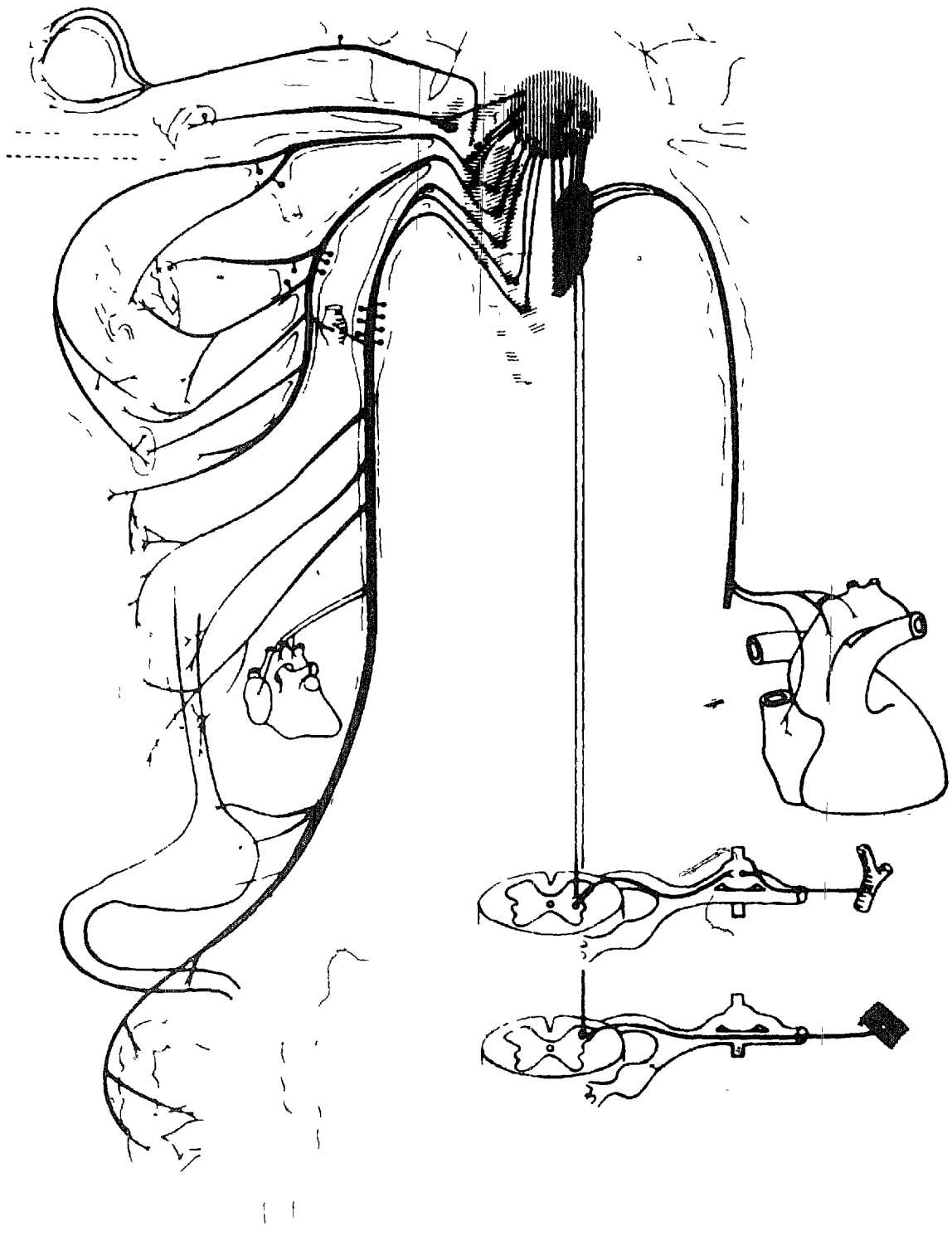
effective as metrazol in activating abnormal EEG's, nitrogen inhalation was nevertheless considered to be safer and easier to administer. Nitrogen caused no olfactory phenomena such as those attributed to metrazol by some workers. In senile cases in which explanations are of no avail, for example, as to the technique of hyperventilation, nitrogen inhalation presents no problem in administration.

In cerebrovascular diseases, nitrogen breathing will often bring out quickly a focal EEG change or increase the voltage in a particular area of the cortex. If the patient is then switched on to pure oxygen such cases show an immediate replacement of the nitrogen-induced abnormality, and even of the pre-existing abnormality.

DISCUSSION

Cerebral hypoxia presents an anaesthetic problem second to none, whether it be due to true anoxia or to cerebral ischaemia. The latter is so intimately related to cardiac arrest that the anaesthetist of today must be a human physiologist alert to cardiac as well as to respiratory problems. Nor is the role of the anaesthetist to be a passive one in this field; otherwise the patient's brain may suffer, and the anaesthetist will be blamed for the subsequent poor recovery.

Preventive measures lie in the anaesthetist's province and he would be wise to use them unreservedly. If the choice lies between giving 1/50 of gr. of atropine intravenously just before an operation, or ripping a chest open after cardiac arrest has occurred, the former would seem preferable. Atropine will protect



RE 8. Reflex pathways (sensory on left, motor to heart on right) involved iac arrest.

the heart from the acetylcholine released by the vagus nerve endings, and it is here that the final step in the reflex arc can be interrupted (Fig. 8). True, good anaesthesia will reduce the likelihood of reflex arcs being completed, but it is important to realize that in the case of the trigeminal nerve, to take but one example, one can still slow or stop the heart by ocular compression.

The elementary fact which is too often overlooked is that atropine protects the heart in successful or unsuccessful anaesthesia. Cardiac arrest during intubation, during a bronchogram, or during gall bladder manipulation with its vagovasal reflex arc is too common an occurrence to be dismissed as mere

failure to achieve sufficient depth of anaesthesia. Atropine in something more than homeopathic doses is required to prevent such arrest.

Finally, cardiac arrest is often attributed to the anaesthetist, when, in fact, it may more fairly be laid at the door of extensive extraocular, tracheal, gut or genitourinary procedures performed on apprehensive patients. Syncope of reflex origin may sometimes be difficult to explain, but it is always easy to prevent if adequate atropine is employed. The perfunctory administration of 1/150 gr. one hour before operation is really not meeting the physiological problem. It is now well established that doses of 1/10 gr., once thought to be heroic, are well tolerated by humans.[6,7]

In summary, then, cerebral anoxia is amenable to study by electroencephalographic methods and such studies suggest the necessity of interrupting vagal reflex arcs by atropine.

RÉSUMÉ

Nous avons fait une description d'études électrographiques sur les modifications s'opérant dans les neurones de la région corticale et sous-corticale du cerveau humain au cours du passage de l'hypoxie à l'anoxie complète. Les conditions expérimentales employées ont consisté en une anémie cérébrale provoquée par la compression de l'artère et du sinus carotidiens ou à la suite d'un arrêt cardiaque temporaire provoqué par la compression des globes oculaires, par l'expiration forcée Valsalva, l'hypoxie par hyperventilation et l'anoxie par l'inhalation de 100% d'azote. Toutes ces épreuves peuvent produire des effets sérieux sur le cerveau surtout chez les personnes sensibles. Ces phénomènes soulèvent un problème sérieux pour les anesthésistes; nous suggérons des mesures préventives et, tout particulièrement, nous conseillons de couper les arcs réflexes vagaux avec de l'atropine.

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The end results of anoxia have been studied extensively by Courville[1] who has contributed much to our knowledge of this aspect of the subject. The standard concepts by Saklad[2] and by Dripps and Comroe[3] of different types of anoxia are common knowledge and serve to show how the state cannot be assessed by any single test, for example, the so-called physiological test.[4] That the oxygen saturation can be considerably reduced without the appearance of cyanosis has been established,[5] which indicates how the recognition by clinicians of this state may be difficult. A knowledge derived from pulmonary ventilation and other respiratory measurements may in future do much to help the anaesthetist avoid anoxia.

The anoxic hazard has altered with changes in anaesthetic procedure. The greater use of endotracheal anaesthesia, although it has contributed to anoxia at times, has, in general, reduced the hazard. The same may be said of the era of relaxant drugs. At first anoxia probably accounted for some of the deaths, but as anaesthetists became more accustomed to their use, so the hazard declined. The so-called circulatory deaths from relaxants[6] were in all probability primarily anoxic in origin.

The use of relaxant drugs during anaesthesia has made anaesthetists more conscious of the need to maintain an adequate pulmonary ventilation so as to interfere as little as possible with respiratory functions, either in terms of carbon dioxide elimination or of oxygen lack. As a result of this change, techniques developed in which artificial respiration replaced spontaneous respiration. This applied particularly to abdominal work. At first there was considerable opposition, for it was maintained that a functioning respiratory centre was preferable, especially as some patients developed persistent curarization post-operatively.[7] However, it seems that artificial respiration for abdominal operations has become almost a routine in some quarters. Further work by the Liverpool school under Professor Gray[8] has resulted in a technique with a sleep dose of thiopentone (sometimes the induction is with nitrous oxide and oxygen), nitrous oxide and oxygen, full curarization, and artificial respiration with *hyperventilation*.

Techniques with hyperventilation result in a low arterial tension of carbon dioxide and a high pH. This state causes a reduction of the blood flow through the brain. This may or may not result in cerebral hypoxia- a good deal will depend upon the demand for oxygen which will be reduced by anaesthesia—however, there is an additional effect which is that the high pH will shift the oxygen dissociation curve to the left so that the haemoglobin holds on to its oxygen more strongly, with the result that the tissues may suffer from oxygen lack although the blood is well oxygenated.

In contrast, the introduction of Fluothane has resulted in techniques which may influence anaesthetists in such a way as to encourage them to allow patients to breathe spontaneously during even upper abdominal operations. Fluothane is gaining in popularity because it is non-explosive and relaxes skeletal muscles. One particular advantage is that respiratory spasm is a good deal less than with the older agents such as diethyl ether. Respiratory records show when anaesthesia is too light for surgery how the respiration may increase in volume, instead of decreasing by inhibition (Fig. 1). More Fluothane may

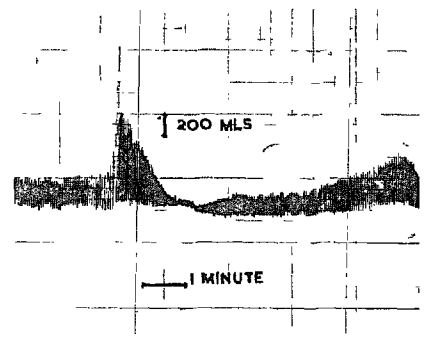

FIGURE 1 Effect of increasing the concentration of Fluothane on respiration of a patient being stimulated by surgery

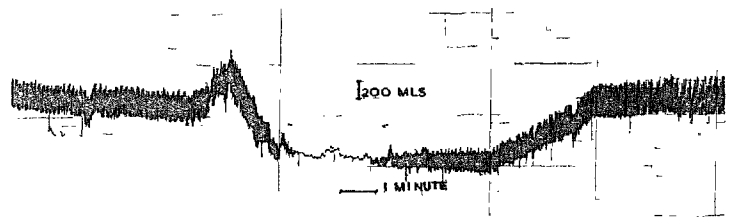

FIGURE 2 Respiratory depression to the point of apnoea with Fluothane on opening the peritoneal cavity

be added by inhalation and the depth increased rapidly Respiratory depression (Fig 2) depends to some extent upon several factors, but it is possible to conduct anaesthesia with Fluothane in the closed circuit (using the technique advocated by Marrett[9]) with a minimal amount of respiratory depression, and with only short periods of more profound reduction in ventilation for opening and closing the peritoneal cavity (Fig 3) The patient breathes a high concentration of oxygen and induction is with a sleep dose of thiopentone with atropine (to reduce the effect of Fluothane in slowing the heart) Suxamethonium is used before intubation, but thereafter no more relaxant is injected because sufficient relaxation results from the Fluothane Nitrous oxide is not used With this technique there is a high tension of oxygen, a high tension of carbon dioxide, and a low pH in arterial blood The oxygen dissociation curve will be shifted to the right and in consequence the haemoglobin's affinity for oxygen will be reduced so that its transport to the tissues is facilitated On the other hand, the high oxygen mixture respired may reduce cerebral blood flow so as to produce a tendency towards anoxia, this, however, may not be a feature of importance

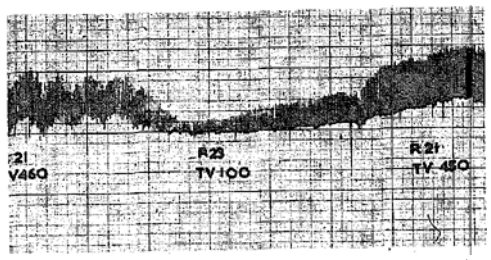

FIGURE 3. Minimal respiratory depression with Fluothane on opening the peritoneal cavity.

At present it is not possible to be dogmatic about the relative merits of these and similar techniques and further research is needed in relation to the problem of anoxia. One thing seems to be emerging, namely, that the dangers of high tensions of carbon dioxide appear to have been over-emphasized. This is not to be taken to mean that there is no danger or disadvantage in conducting anaesthesia with a technique allowing high tensions of carbon dioxide. Several workers[10,11] have given evidence of hypercarbia during anaesthesia, particularly with spontaneous respiration, but the writer has seen no evidence that harm has resulted within the ranges studied, for example, under 50 mm. Hg carbon dioxide tension; however, changing the state from one of hypercarbia to one of acapnia in a short period of time may be dangerous.[12]

Certain anaesthetic techniques predispose to anoxia: deep anaesthesia with any agent, and the hypotensive technique with ganglion blocking drugs, especially when this is combined with the anti-Trendelenburg position. This technique is not one for the novice and demands extra skill and care; with these hypoxia can be avoided. Techniques such as hypothermia or the extracorporeal circulation are specifically designed to reduce the hypoxic hazard.

The immediate postoperative period is one of potential danger for the patient. After a prolonged administration of nitrous oxide and oxygen the alveolar concentration of nitrous oxide may rise to produce "diffusion" anoxia; the administration of oxygen at this stage will prevent it. The provision of special accommodation and an adequate and competent staff with the necessary equipment is a responsibility which no hospital can ignore, because these measures will undoubtedly reduce hypoxic and many other hazards immediately following surgical operations.

The growth and recognition of the specialty of anaesthesia will eventually make it possible, because of better agents, better techniques, improved aids for measurement, and more organized facilities, to have effective training programmes for anaesthetists and also for all those who come into contact with unconscious patients. In such ways the hypoxic hazard should decline to the barest minimum.

Acknowledgment

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