WHAT IS THE SIGNIFICANCE OF HYPERCARBIA OR HYPOCARBIA IN THE ANESTHETIZED PATIENT?

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THE practicing anesthesiologist is constantly buffeted with data and opinions concerning the relationship of carbon dioxide and the anesthetized patient. He is informed that elevations in carbon dioxide tensions may lead to dire circulatory consequences and that prolonged reduction in carbon dioxide tensions may produce cerebral hypoxia. Some have implied that gradual shifts in carbon dioxide levels are harmless whereas precipitous changes are catastrophic. He is told of the respective virtues of big and little carbon dioxide absorbing canisters in closed rebreathing systems and of the pros and cons of nonrebreathing systems. He often finds it difficult to analyze these data and opinions and to chart his own course in managing his patients.

To assist the clinician, the Editor has posed questions to ten authorities in anesthesiology who have performed investigations in the field of carbon dioxide as it relates to anesthesia. Each authority was asked to be as concise and brief as possible in his answers. By a careful perusal of the replies, the reader can determine how the expert views the clinical application of the available data. No attempt has been made to summarize the opinions of the authorities; the reader must reach his own conclusions.

—EDITOR

THE QUESTIONS

(1) Is hypercarbia in the absence of hypoxia during anesthesia harmful? If so, what levels, or duration of maintenance of what levels? In association with what drugs? On what organs or organ systems?

(2) Is there a difference between the effects of hypercarbia produced artificially (e.g., by excluding carbon dioxide absorbing canister from a closed rebreathing system), and that occurring from respiratory depression (e.g., from narcotics or anesthetics)?

(3) Is hypocarbia during anesthesia (e.g., that produced by excessive pulmonary ventilation) harmful? If so, what levels, or duration of maintenance of what levels? In association with what drugs? On what organs or organ systems?

(4) How difficult is it to maintain a reasonably normal alveolar P_{CO_2} without monitoring equipment?

CHARLES R. ALLEN, M.D., *Chairman, Department of Anesthesiology, The University of Texas—Medical Branch, Galveston*

(1) Hypercarbia in the absence of hypoxia during anesthesia may be harmful. The carbon dioxide level and the duration of maintenance of this level necessary to give clinical evidence of harm varies according to the physical status of the patient, including such factors as autonomic tone, endocrine responsiveness and electrolyte balance. In general, the more harmful situation seems to develop over a period of one or more hours during which hypercarbia is allowed to exist. Under these condi-

tions an uncompensated respiratory acidosis develops which gradually tends to become compensated with the mobilization of base into the plasma. If at this time, adequate ventilation with rapid carbon dioxide removal is instituted, an uncompensated alkalosis will result. The more spectacular distress is evidenced by the cardiovascular system.

(2) The physiological response to hypercarbia would be more marked in the absence of the depressant effects of narcotics and anesthetics.

(3) Hypocarbia itself during anesthesia is probably not of much clinical significance. The physical effects of excessive pulmonary ventilation may prove harmful if the technique employed maintains positive pressure to the extent that it interferes with pulmonary blood flow.

(4) The difficulty in the maintenance of a reasonably normal alveolar P_{CO_2} without monitoring equipment varies with the premedication, anesthetic agents, technique, educational background (awareness) and professional caliber of the anesthetist. For example, with light premedication, a nitrous oxide-ether-oxygen anesthetic mixture, an adequate open airway and a hand that has been trained to continually follow the excursions of the breathing bag, the problem should not be difficult. The importance of the size of the carbon dioxide canister has probably been overdone. There are too many over-narcotized and over-curarized patients being hypoventilated through king-size canisters.

ROBERT D. DRIPPS, M.D., *Professor of Anesthesiology and Chairman of the Department of Anesthesiology, Schools of Medicine, University of Pennsylvania*

(1) Elevations in blood carbon dioxide tensions have been shown to cause certain bodily changes including a decrease in myocardial contractility, the production of ventricular arrythmias and an interference with certain enzyme activities. However, with the degrees of hypercarbia ordinarily found in man during general anesthesia (arterial P_{CO_2} up to 65 mm.), few harmful effects are noted. This is due to the fact that the homeostatic responses to carbon dioxide are usually effective. Indeed, in order to demonstrate certain actions of carbon dioxide, the body's compensatory responses to hypercarbia must be removed. For example, depression of myocardial contractility follows moderate degrees of respiratory acidosis only if mobilization of catecholamines is prevented. Nevertheless, despite the apparently benign aspects of this type of respiratory acidosis observed in anesthetized individuals, one can presume that if homeostatic reactions were blocked by disease, hypercarbia might become more of a threat.

(2) I do not know if there is any difference between the effects of intrinsic and extrinsic hypercarbia.

(3) As arterial P_{CO_2} declines to 20 mm. or less, cerebral vasoconstriction in conscious man is sufficient to cause symptoms attributed to cerebral hypoxia. Whether hypocarbia produces a similar effect during general anesthesia in man is unknown. If general anesthesia reduces cerebral metabolism and/or interferes with the ability of brain blood vessels to constrict, a P_{CO_2} level as low as 20 mm. may not cause cerebral hypoxia to a degree that is important. Studies are underway to determine this.

(4) Most patients during general anesthesia will be found to have arterial P_{CO_2} values in the range of 30 to 50 mm. It is impossible to maintain an arterial P_{CO_2} of 40 mm. without monitoring equipment; in fact it is difficult to keep the concentration within the range of 35 to 45 mm. of mercury. Patients with tracheal tubes in place, with minimal preanesthetic medication, and those whose efforts are controlled or assisted will, in general, have values of 35 mm. of mercury or below. Those breathing spontaneously without assistance and through a mask will usually have an arterial P_{CO_2} above 45 mm. of mercury. For the individual under general anesthesia, there may be, therefore, a wide range of P_{CO_2} which can be considered normal.

JAMES O. ELAM, M.D., *Director, Department of Anesthesiology, Roswell Park Memorial Institute, Buffalo*

(1) I have no controlled studies relating carbon dioxide levels with complications. My opinion is that hypercarbia without hypoxia

well tolerated by healthy patients but contributes to cardiac, circulatory, and gastrointestinal complications in the poor-risk patient. Abrupt hypercarbia can provoke interference with smooth anesthetic induction, maintenance, and emergence, *i.e.*, coughing or retching on the tracheal tube, excursions in blood pressure and pulse, and postoperative nausea and emesis.

(2) If the complications of hypoxia are excluded, the only important difference between the effects of hypercarbia produced artificially and from the respiratory depressants may be in the rate of rise in carbon dioxide and attending responses, but both extrinsic and intrinsic hypercarbia can progress slowly or rapidly. Slow accumulations of carbon dioxide may occur without clinically observable changes in circulation and respiration.

(3) One might occasionally blame postoperative hypoventilation upon sustained hypocarbia during anesthesia sufficient to deplete the body carbon dioxide stores. Aside from this unproved complication, my impression is that hypocarbia during anesthesia is harmless.

(4) We have demonstrated to our satisfaction that it is not difficult to maintain reasonably normal P_{CO_2} in the alveolar air and the arterial blood of most anesthetized patients. We routinely augment the patient's spontaneous ventilation either by conventional manual bag compression or by a ventilator. The amount of ventilation is regulated so that the patient's respiratory activity repeatedly approaches and reaches apnea. When he breathes spontaneously, we increase ventilation by increasing rate or tidal volume. Then when apnea is produced, we decrease ventilation slightly until spontaneous effort reappears. Since apnea recurs every few minutes, the slight hyperventilation counteracts the slight hypoventilation and produces excursions in alveolar carbon dioxide of the order of no more than one per cent (or 7 mm. P_{CO_2}), often of only 0.5 per cent. Anesthesia suitable for major surgery need not alter the apneic threshold by more than 0.07 *p*H unit below the preinduction value; this decrease in *p*H is often only 0.04 units. Deep planes short of respiratory arrest can alter the threshold by as much as 0.2 *p*H unit. This method of managing ventilation by hovering about the apneic threshold is compatible with the use of curare or succinylcholine. The observation of the patient's inspiratory effort is lost for only a few minutes following intermittent doses of relaxant drug or not at all with continuous intravenous dosage.

Alternating periods of hyper- and hypoventilation which produce intermittent apnea take into account the hidden factors which reduce the efficiency of an otherwise adequate ventilation, *i.e.*, leaks in the breathing circuit, poor carbon dioxide absorption, changes in the ventilation-perfusion of the lung, and increases in the metabolic rate of carbon dioxide production. We have used the apneic principle to manage ventilation in several hundred patients given common premedicants and anesthetic agents, using manually assisted and controlled ventilation as well as mechanical ventilators (Bennett, Bird, Emerson, and Jefferson). I prefer this technique of ventilatory management utilizing the patient's apneic threshold to avoid gross hyper- and hypocarbia, to preserve frequent indications of respiratory activity, and to minimize the possibility of drug overdose.

ALBERT FAULCONER, M.D., *Chief, Section of Anesthesiology, Mayo Clinic, Rochester, Minnesota*

Until the advent of the widespread—almost universal—use of muscle relaxants in the practice of anesthesiology, I had great faith in the adaptability of the anesthetized human to very wide variations in his usual respiratory environment—both internal and external. This faith was justified on the basis of many measured observations of marked deviations from the assumed norm, without apparent unpleasant sequelae. I spent the early years of my professional life observing the large scale survival of patients during and after exposure to the atmosphere of anesthesia machines whose bags were untouched by human hands. I remain unconvinced that there has been any great change in these survival rates as the result of the use of our more modern drugs and methods including almost routine and continuous application of "educated hands."

These comments are made with the firm belief that there is virtue in the maintenance of

the physiologic economy of the body as nearly "normal" as may be allowed by the surgical problem to be solved. I also believe in motherhood. However, just as motherhood is achieved at occasionally exorbitant cost, so may it be occasionally that the price paid for the attempt to maintain a "normal" elimination of carbon dioxide will require a heavy tax elsewhere.

Artificial ventilation may be effective in maintaining "normal" CO_2 levels only at the expense of circulatory impairment. The cost can be too great for a damaged cardiovascular system.

Moderate degrees of hypercapnia may, under some circumstances, be useful. Consider the effects on the efficiency of O_2 transport and the cerebral circulation. The corollary to this thought is that hypocapnia may at times be hazardous.

The respiratory center may be the source of continuing information of value as it reveals its activity through the patient's breathing. Usurping this motor function, the anesthesiologist denies himself an important source of information. He also assumes the heavy obligation to perform better the functions of this divinely conceived instrument—the respiratory center.

Do not judge these brief and undeveloped thoughts to be in condemnation of assisted or controlled ventilation, or to be in support of throwing the full burden of CO_2 disposal on a drug-depressed respiratory center and a paralyzed thorax. You will find a vast array of valid information in the preceding pages to show that such conclusions are unjustified. My plea is for the exercise of prudence in the clinical application of new and isolated bits of information issuing from the laboratory. Search well for hidden costs before buying new techniques.

M. Jack Frumin, M.D., *Professor of Anesthesiology, Jefferson Medical College, Philadelphia*

Carbon dioxide is very much like the weather. Everybody talks about it but very few do anything rational about it. For clinically it is rarely measured—and then often improperly. Broadly speaking, clinical judgments about CO_2 are usually based on extrapolations from someone else's experimental results rather than objective, reliable or quantitative information on the particular patient in question. Furthermore, the criteria "good" or "bad" are personal judgments which cannot be subjected to precise evaluation. For these reasons you should not expect these answers to be as definite as the earlier, experimentally based articles of this symposium.

(1) It is entirely moot whether the many known changes of hypercarbia are harmful. For example, moderate hypercarbia does not seem to interfere clinically with intracranial operations despite the well-established changes in cerebrospinal fluid pressure and in cerebral blood flow. Short term severe hypercarbia (up to 160 mm. of mercury for 30 minutes) in healthy lightly anesthetized patients seems to be tolerated remarkably well with only minor transient sequelae. Clinically, the increased "tone" in both respiratory and non-respiratory muscle groups during hypercarbia may be troublesome, but this is readily corrected by relaxants. However the higher doses of relaxants needed to maintain apnea during hypercarbia are definitely undesirable, since they can lead to a higher incidence of postoperative respiratory depression.

(2) In general the effects of these two types of hypercarbia are similar. If rebreathing occurred in a spontaneously breathing patient, then the increased respiratory activity might seriously interfere at times with intra-abdominal or intracranial operations.

(3) Regarding hypocarbia, one might expect, from good experimental evidence, that the decreased cerebral blood flow and O_2 uptake would lead to significant cerebral anoxia, but clinically it seems to be unimportant. Two or more hours at a P_{CO_2} of 20 mm. produces no important mental sequelae. However, there is one serious clinical danger of hypocarbia. Many cases of "prolonged apnea due to relaxants" are really "hypocarbic apnea of overventilation." Hyperventilation is begun during apnea produced initially by the relaxant, and this hypocarbia maintains the apnea after the muscle paralysis has disappeared. Further, during prolonged hypocarbia, there appears to be a "resetting" to a lower value of the operating level of the medullary respiratory center servo. This contributes to the difficulties of differential diagnosis, and the failure to dis-

inguish between the different causes of apnea eads to incorrect treatment and at times to a :alse condemnation of the relaxants.

(4) What is a "reasonably normal" P_{CO_2} :evel? 30–50 mm. of mercury? Under certain special conditions Elam would use the pa-ient's own respiratory drive as a guide. But I believe it is better to measure—and hence to know—than to proceed by inference. And as measuring equipment continues to become simpler and more practical, today's question may soon have only historical significance.

LUCIEN E. MORRIS, M.D., *Professor of Anesthesiology, University of Washington School of Medicine, Seattle*

Despite a growing chorus of voices proclaiming the need for close attention to pulmonary ventilation during anesthesia, many patients are seen daily in every hospital, including our teaching centers, who are subjected to varying degrees of respiratory acidosis, or, less frequently to respiratory alkalosis. The nub of the difficulty appears to be the lack of a uniform concept as to what represents "adequate ventilation" in any given patient. Inadequate criteria have been offered to guide either the neophyte or the experienced physician in his attempts to help anesthetized patients compensate for the added mechanical dead-space of anesthetic apparatus, the respiratory depression of anesthetic drugs, and encroachments upon respiratory activity caused by muscle relaxants, high spinal anesthesia, an abdominal tumor, adverse operative position, or a tired surgical assistant.

Monitors now available for continuous measurement of respiratory tidal volume are helpful in providing a self-teaching aid in the moment to moment estimation of the amount of ventilation spontaneously accomplished by the patient or moved by the anesthetist's hand. Unfortunately, however, these in no way guarantee "adequate ventilation," nor does the arbitrarily set mechanical ventilator. Oximeters, carbon dioxide analyzers and *p*H meters are expensive and so complex in standardization and maintenance requirements as to make their routine availability in the management of every patient a virtual impossibility. Usually also, their use provides only hindsight information of intermittent variety rather than on the spot dynamic recording.

Surely an ideally managed anesthesia provides adequate surgical conditions, while concurrently subjecting the patient to the least possible deviation from normal during the procedure. The currently popular minimal anesthetic techniques are an attempt to avoid serious depression of the vital centers by drugs themselves. However, inadequate spontaneous respiratory effort plus the side effects of mechanical dead space in anesthetic equipment, incompetent valves, or misguided efforts to "take over" respiration either manually or with mechanical ventilators lead to improper and unphysiologic ventilation more frequently than is realized. It is fallacious to assume that one can predict or second guess "adequate ventilation" for every patient. Full elimination of all the carbon dioxide being produced must be accomplished or acidosis is inevitable. All too often when respiration is "taken over" by anesthetists the patient remains or becomes acidotic. A patient's spontaneous respiratory effort can be abolished by drug overdosage (*e.g.*, muscle relaxant apnea), thus necessitating manual or mechanical ventilation; or it can be circumvented even in the presence of an elevated P_{CO_2} by eliciting the Hering-Breuer inhibitory reflex through rapid rhythmic pulmonary distention. In either instance ventilation may be quite inadequate.

There is what appears to me to be a current dangerous tendency to routinely take away a patient's ability to respire spontaneously. It is mistaken to assume that either the "educated hand" or the pre-set automatic ventilator can maintain adequately homeostasis without constant adjustment to changing needs of the patient. Some anesthetists believe that they routinely overventilate patients, but unless their results are confirmed by blood studies it may be a false assumption. If patients *are* successfully hyperventilated into a state of alkalosis there are measurable sequelae as determined by changes in flicker fusion frequency which may reflect some degree of central hypoxia. (Allen, G., and Morris, L. E., unpublished data.)

The presence or absence of spontaneous respiration can and should be a useful guide to determine the adequacy of ventilation dur-

ing anesthesia. This requires avoidance of apnea as produced by overdosage with any drug. If ventilation is then assisted by appreciably increasing the tidal volume of each spontaneous inspiratory effort the ensuing hyperventilation and increase in alveolar turnover rate will reduce P_{CO_2} to the point of apnea. This removal of stimulus to the respiratory center is the approach to "controlled respiration" which Waters originally described (Waters, R. M., Proc. Royal Soc. Med. 30: 11, 1937), and which appears generally to have been poorly understood. "Controlled respiration" is not to be confused with artificial ventilation in an overdosed apneic patient, nor with the "taking over" of respiration through rapid shallow inflation inhibiting respiratory effort by the stretch receptors of the Hering-Breuer reflex. The latter does not provide adequate ventilation so the patient rapidly becomes acidotic, while in the former either acidosis or alkalosis may occur frequently, since unfortunately the judgment behind the educated hand or the presetting of the ventilator does not include continuous *p*H and P_{CO_2} information.

Changes in *pH* in either direction from the normal may modify the expected action of drugs or the apparent need for them to an extent which will present a picture of overdosage when later attempts are made to awake the patient. Sometimes the cause is simply carbon dioxide narcosis. These consequences can be avoided if the current concept of anesthetic management is modified toward intermittent controlled respiration throughout anesthesia whereby apnea of 30 to 60 seconds duration is produced by lowering the P_{CO_2} through hyperventilation, and at intervals of no more than ten minutes the patient is allowed to demonstrate ability to make spontaneous respiratory effort. The former assures avoidance of acidosis, the latter avoidance of alkalosis. If drugs are added only during spontaneous respiration, unsuspected overdosage cannot occur.

EDGAR A. PASK, M.D., *Department of Anaesthetics, The Medical School, University of Durham, England.*

(1) Hypercarbia in the absence of hypoxia during anesthesia may be harmful. We have observed patients who (a) had been underventilated with oxygen-enriched atmospheres during relaxant anaesthesia; (b) failed to breathe sufficiently and failed to recover consciousness after operation; (c) were shown to have high carbon dioxide tensions in their blood (admittedly the means of estimation were indirect); (d) recovered consciousness and adequate spontaneous respiration following a period of plentiful artificial respiration as the only deliberate therapy. Hypercarbia without anoxia seems to me the most probable explanation and I accept it provisionally. Since mechanical ventilators became common in our Hospital, we have rarely seen such cases.

(2) I do not think there is an essential difference between artificially produced hypercarbia and that from respiratory depressants, but the rate of increase in carbon dioxide tension in the blood is likely to be different in the two cases, and the degree of carbon dioxide storage is likely also to be different. Furthermore, an accumulation of carbon dioxide from respiratory depression is likely to be complicated either by deep chemical coma or partial paralysis, whereas in the case of hypercarbia produced by adding cylinder carbon dioxide, these effects may be absent. The brief use of a high concentration of carbon dioxide in the inspired air in a lightly anesthetized and unrelaxed patient, will produce a high carbon dioxide tension in the blood, but this will be transient and there will be little addition to the carbon dioxide stores. It may nevertheless be an effective respiratory stimulus.

(3) Hypocarbia during anesthesia may be harmful, but I do not think it is commonly so. I think there are two protective factors—(a) In practice, it is hard to produce very great ventilation artificially during anaesthesia. (b) Though alveolar carbon dioxide tension may fall very low, the net amount of carbon dioxide removed from the body may not be very excessive during a period of over-ventilation under anaesthesia. There are other barriers to the loss of carbon dioxide apart from the ventilatory barrier in the lungs. In fact, during a brief period of apnea or respiratory depression, the metabolic carbon dioxide production can make good the net excess loss of carbon dioxide which may have occurred dur-

ing quite prolonged over-ventilation. Hypocarbia can be dangerous, I think, in a patient whose circulation is poor and, of course, in certain special metabolic states.

(4) As for maintaining reasonably normal alveolar P_{CO_2} without monitoring equipment, it depends on what you mean by 'reasonably normal.' Apneic patients can, I think, generally be somewhat overventilated without significant risk. This 'normal-to-generous' ventilation can, I think, generally be assessed by physical signs. However, when the ventilatory function of the lungs is abnormal, I find this assessment extremely difficult by physical signs alone.

HENNING RUBEN, M.D., *Director of Anesthesiology, The Finsen Institute, Copenhagen*

When the respiration of a patient is not continuously monitored by analyzers, then with the techniques of anesthesia generally used today, a normal arterial P_{CO_2} is obtained by chance only. Using the patient's preoperative exchange as a guide for controlled (or assisted) respiration, or basing his respiration on the Radford nomogram, I have found, does *not* ensure a normal CO_2 level.

Although death rarely occurs from a very abnormal CO_2 level this does not mean that hypercarbia is always without harm. Especially, it is impossible to predict *when* physiologic disturbances of a patient make his tolerance to an even slight increase in CO_2 level more or less harmful to his circulatory, nervous or metabolic functions. But it is particularly the rate of change, rather than the absolute change in CO_2 level, which constitutes the acute (circulatory) danger. Presupposing that hypoxia is absent, (which may be difficult to ensure in every case of open chest, pulmonary disease, or circulatory disturbance), then a ventilation, maintaining a "near" normal *p*H, e.g. between 7.25 to 7.55, probably could be regarded safe in most cases, while a rapid change, even though it restores the *p*H from low to normal preoperative levels, may be fatal. On the other hand, after rather excessive hyperventilation resulting in higher *p*H than indicated (7.60 or more) maintained for hours, I have seen no clinical evidence of brain damage (hypoxic sequela) postoperatively. Also, I have not observed signs of seriously impaired circulation with such *p*H increase, which is produced by respiratory exchanges ordinarily used for deliberate hyperventilation.

Because it is impossible in every circumstance to predict when hypercapnia, or elimination of it, will prove dangerous, and considering, that ventilation calculated to maintain a P_{CO_2} can be produced with extreme uncertainty clinically, then, if monitoring equipment is not available, I respire every patient in such a way as to avoid hypercapnia. This results in hyperventilation in almost every case. I not only consider this a lesser evil than hypercapnia, but innocent enough to justify it in every case. A simple way to get quantitative information of the ventilation being accomplished is to use the nonrebreathing technique.

F. H. VAN BERGEN, M.D., *Professor and Head, Department of Anesthesiology, University of Minnesota Medical School, Minneapolis*

It is my hope that the Editor will allow me to approach the questions on hypocapnea and hypercapnea from a single perspective, that of the impact upon the enzyme systems. In the past two decades many investigators have worked to uncover the etiology of cardiac standstill and fibrillation. Numerous factors, singly and in combination, have been investigated.

Studies of the autonomic nervous system reactivity, hypoxia, acid-base alteration, electrolyte imbalance and various endocrine phenomena have proved to be significant and have contributed much to our present understanding of circulatory arrest. Even more important, but imperfectly understood, are the complex interdependent relationships of the above factors. Mindful of the intricacies, I am hesitant to introduce additional confusion; yet the importunate role of the enzyme systems merits scrutiny in the over-all consideration of this biochemical problem.

To illustrate, Campbell (Surg. Forum, pp. 283–287 (Sept.)1952) found that the response of the dog heart to vagal stimulation was related to blood *p*H. During states of acidosis (respiratory or metabolic) marked

cardio-inhibitory effects, manifested by prolonged asyotole and bradycardia, resulted when faradic stimulation was applied to the vagus nerve. When alkalosis (respiratory or metabolic) was present, the heart showed a markedly decreased response to the same degree of vagal stimulation.

Anesthesiologists have observed and correlated laryngeal responses with blood *p*H. Endotracheal intubation, under pentobarbital anesthesia, is accompanied by severe laryngobronchospasm and paroxysms of coughing; however, these responses may be greatly reduced or eliminated if the patient is made alkalotic by hyperventilation prior to tracheal intubation.

Why should there be such marked differences in physiologic responses under varied states of hydrogen ion concentration? The citation above proposes a plausible hypothesis, that of altered enzymatic function. Since cholinesterase activity is optimal in the *p*H range of 7.5–8.5, it stands to reason that the degradation of acetylcholine will proceed at faster rates during states of alkalosis. Conversely, acidosis may so inhibit cholinesterase activity that greater than normal concentrations of acetylcholine are permitted to act over longer periods of time thereby promoting a pathologic response of the affected organ.

To further illustrate my thesis, Campbell and his associates (Dis. Chest, 33: 18, 1958) studied cardiovascular responses to catechol amines in humans subjected to acidosis and alkalosis. They found that identical doses of epinephrine produced minimal changes during acidosis and maximal changes during alkalosis. Many of us have observed the same phenomenon in patients who have suffered circulatory arrest and, through such observations, have come to realize that intracardiac injections of epinephrine evoke stronger responses if preceded by an alkali such as molar sodium lactate. Assuming that the rate of degradation of the catechol amines is dependent upon some enzyme, it is quite possible that the activity of this enzyme also varies with the hydrogen ion concentration of blood and tissue fluids.

Doubtless there are many other illustrations of enzymatic activity in relation to acid-base balance and ionic equilibrium that could be cited. It is evident, in the light of our present ignorance, that we can be neither complacent nor dogmatic in our attitude toward hyper- and hypocapnea. I believe that every effort should be exerted to maintain that blood *p*H which mammals assumed eons ago.

RONALD WOOLMER, M.B., *Director, Research Department of Anaesthetics, Royal College of Surgeons, London*

(4) I think it is very difficult to maintain normal alveolar P_{CO_2} during anaesthesia without monitoring equipment. I know that it is difficult for the anesthetist under these circumstances to conform to a specified level of ventilation. I know this because I have measured it with an integrating minute volume recorder designed for the purpose. As long as he can see the level of ventilation being recorded (in terms of liters per minute) on the chart, the anesthetist can conform pretty well. As soon as the record is obscured from his view, the ventilation diverges from the specified level. The divergence is usually, but not always, in the direction of over-ventilation. It does not seem to be much less when the anesthetist is experienced than when he isn't. The comforting idea of "the educated hand of the skilled anesthetist" has no foundation in fact.