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Acid-base balance in anesthesiology

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INTRODUCTION

Acid-base metabolism has been studied and evaluated since it was first recognized as being physiologically important. It has continued to gain importance as it becomes even better understood. Today there are easier, faster, and more accurate methods of measuring the desired parameters than ever before. These tests are frequently noted to be ordered almost routinely on many patients. In spite of this and its importance both academically and clinically, acid-base balance is probably one of the least understood subjects. This is partly as the result of poorly defined and confusing terminology which seems to vary, depending on one's location.

Equally intriguing and seemingly mysterious to anyone but an Anesthesiologist, is the field of Anesthesiology. In the past decade, research and advancement has led this field away from the primary use of a single agent, notably ether, to the use of many different agents depending upon the type anesthesia needed. This has brought added responsibility for better understanding of the body's physiological processes, including that of acid-base balance. This is especially important because of the ever increasing numbers of operations on elderly patients who often have physiological imbalances, and because of more difficult operations, e.g. Cardiac Surgery.

This paper was undertaken with the idea of reviewing the literature for recent studies showing the effect which each of the following have on acid-base balance: (1) Premedication, (2) Spinal Block, (4) Inhalation Agents, and (5) Hypothermia. To do this necessitates a brief review of terminology, physiology, and methods available for measuring the necessary parameters. Additionally there are a number of variables which are often associated with operations at the time of anesthesia and these warrent comment. These include the operation itself, age of the patient, shock, blood transfusions, and extra cellular fluid volume.

ACID-BASE REVIEW

1. Terms and Definitions

A synposium on acid-base measurements was held November 1964 under the auspices of the New York Academy of Sciences. The results of this was reported by Winters(1965)[31] and in Lancet (1965)[25]. This meeting resulted in agreement on many topics and some clarification in areas of disagreement. The current trend in acid-base terminology is towards the use of the Bronsted - Lowry system and to exclude the older terminology. This defines acids as proton donors and bases are hydrogen ion (proton) acceptors. Strong acids dissociate completely while weak acids ionize incompletely since hydrogen ion is bound tightly to a strong conjugate base. Carbonic acid, H_2CO_3, is a weak acid, ionizing only partially to H^+ and the conjugate base bicarbonate (HCO_3^-).

There was general agreement by those present that for clinical purposes Pco_2 is the only adequate measure of the respiratory component. Agreement was also unanimous for using pH to express hydrogen ion concentration. There have been some recent discussions, Whitehead (1965)[25], by those who feel the measurement of hydrogen ion in pH units should be abandoned in favor of nano equivalents. These units give a more accurate picture of the true H^+ ion concentration. For example, pH 7.4 equals 40nEqs. Removing enough H^+ ions to raise the pH to 7.7 will result in 20nEq of H^+ ions. If H^+ions are now added to the solution so the pH falls from pH 7.4 to 7.1 we find there are then 80nEq of H^+ ions present. This is more easily grasped if one observes the following chart.

CHART #1

difference in pH	pH -log (H)	nano equivalents	micro equivalents	difference in nEq
	7.90	12	.012	
	7.70	20	.020	
0.3				20
	7.42	38	.038	
	7.40	40	.040	
	7.35	44	.044	
0.3				40
	7.10	80	.080	
	6.90	126	.126	

This shows the relationship between hydrogen ion concentration expressed in nano equivalents in one column and pH in the other. The figures between the dotted lines express the normal physiological limits. Note that a 0.3 change in pH from 7.4 either doubles or halves the H^+ ion concentration in nEq. (Payne; 1962)[23]

This makes it readily apparent that it takes twice the H^+ ions to make a 0.3 pH change from 7.4 to 7.1 as compared to pH change from 7.7 to 7.4.

The conferees disagreed most on how best to determine and describe the metabolic component of acid-base balance. One group held that it is most precisely characterized by Base Excess which expresses the number of milliequivalents of acid or base lost or gained by 1 liter of whole blood. This value is obtained by titration in vitro. However, even those in favor of this admitted the Base Excess titration curve in vitro is not exactly the same as that in vivo. Another group at the conference were in favor of continuing with the traditional method of using the CO_2- Bicarbonate buffer system. They felt that since the metabolic component is not independent of Pco_2 in either a physiochemical or physiological sense that plasma bicarbonate (CO_2 Content) should continue to be used and that clinically Base Excess did not offer any advantages. It might be added that there has recently been considerable debate over use of Standard Bicarbonate Concentration as defined originally by Jorgensen (1957)[17]. While the Europeans apparently favor its use the clinicians in this country point out that it, like Base Excess, is different in vivo then the results obtained in vitro, and likewise does not offer any advantages over CO_2 Content.

The conference also attempted to reach some agreement on use of descriptions of clinical disturbances of acid-base equilibrium. Though no unanimous opinion was reached there was general agreement on the following. The terms Acidosis and Alkalosis should be used in a physiological sense, ie, to describe abnormal processes which would cause a deviation of pH if no secondary responses occurred. The compartment of the body fluids in which the changes are occurring should be specified, but when not it is assumed that the extracellular compartment is being referred to. The terms Acidosis and Alkalosis either alone or modified by general adjectives (respiratory, metabolic) or more specific adjectives (renal, diabetic, lactic, diarrheal) describe the over-all process without making such usage dependent upon deviation of pH per se (since it may be 7.4 if secondary physiologic adjustments have occurred). When a single etiological factor produces the disturbance this is a "simple" acid-base disturbance. If produced by two etiologic factors it is a "mixed" disturbance. The usual secondary physiologic responses to a simple disturbance are not designated as Acidosis and Alkalosis nor are the terms compensatory or secondary used except to describe a change in composition of the blood (Pco_2, HCO_3^-) or a process (ventilation, renal). For example, in metabolic acidosis the increased respirations are termed secondary hyperventilation, and not secondary (or compensatory) respiratory alkalosis.

2. Important Buffers

Buffers are mixtures of weak acids and their salts, or weak bases and their salts, which in solution resist the change in pH which might be expected upon the addition of acid or base to the solution. Buffers are particularly important in the preservation of acid-base homeostasis in the body. Though there are several buffer systems in the body the main one quantitatively is that of bicarbonate and carbonic acid. Carbonic acid (H_2CO_3) is weakly ionized into H^+ and HCO_3^- and exists almost completely as molecular non-ionized H_2CO_3. However, the salt sodium bicarbonate, is highly soluble and is completely ionized into Na^+ and HCO_3^-. Therefore, the main forms in solution are H_2CO_3, HCO_3^-, and Na^+.

$$H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

$$NaHCO_3 \longrightarrow Na^+ + HCO_3^-$$

Hence, if the total quantity of hydrogen is increased by addition of acid the excess H^+ is buffered by combining with HCO_3^- forming more molecular H_2CO_3. If alkali is added, removal of H^+ from the solution is buffered by production of H^+ from the dissociation of H_2CO_3.

3. Maintaining Homeostasis

The retention or elimination of volatile carbonic acid is controlled by the rate and depth of breathing. Carbonic acid is in equilibrium with physically dissolved CO_2 which is directly proportional to the partial pressure of CO_2 (Pco_2) in the plasma. Ordinarily the concentration of dissolved CO_2 is 1000 times the concentration of H_2CO_3.

$$CO_2 + HOH \rightleftharpoons H_2CO_3$$

Hyperventilation lowers the Pco_2 releasing carbonic acid and elevates the pH while hypoventilation elevates Pco_2, adds carbonic acid, and pH decreases. Low pH is the greatest stimulus to respiration according to Handler, et al (1964)[13]. By pH 7.20 ventilation is multiplied fourfold. On the contrary an alkaline pH may not be associated with a decrease in ventilation. CO_2 excess is itself much more of a stimulant to hyperventilation than is oxygen deficit (hypoxia).

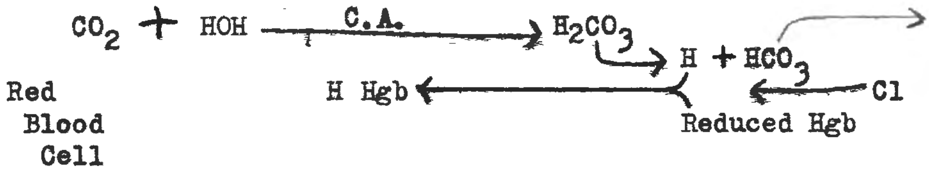
Plasma bicarbonate is affected primarily by (1) other anions, (2) hemoglobin, (3) a renal threshold, and (4) the Pco_2. Generally the bicarbonate concentration varies inversely as the concentration of chloride. This is also true between bicarbonate and the anions of organic acids. When an acid is neutralized by the bicarbonate the anion remains in solution while the H_2CO_3 formed decomposes to HOH and CO_2. The latter then escapes via the lungs.

$$H^+ + \text{anion} + Na^+ + HCO_3 \longrightarrow Na^+ + \text{anion} + H_2CO_3$$

$$\text{eliminated via lungs} \longleftarrow CO_2 + HOH$$

The buffering action of hemoglobin also plays an essential role. Of the large quantities of CO_2 produced in the body tissues and then diffused into venous blood a small amount dissolves in plasma.

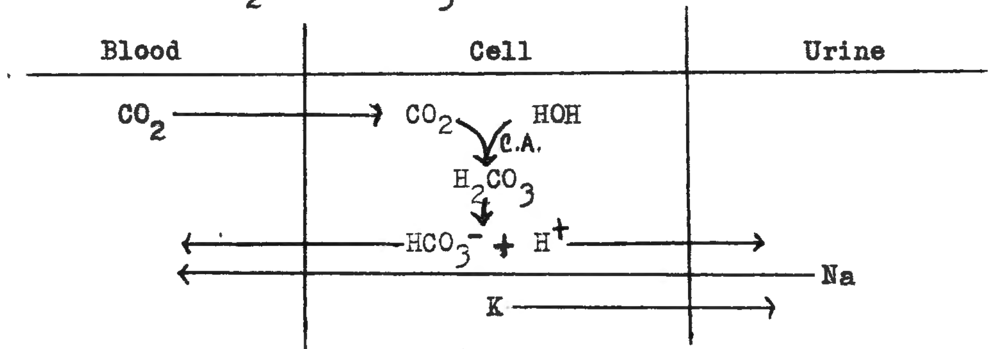
Most diffuses into the red cells and in the presence of HOH and Carbonic Anhydrase forms into Carbonic acid. This breaks down to hydrogen and bicarbonate. Reduced hemoglobin is a base and it accepts the proton. The bicarbonate then shifts out of the RBC and is replaced by chloride.



This isohydric shift allows 0.7 M of H^+ to be buffered for every 1 M of oxygen released from hemoglobin without changing the pH. Hence, the higher the hemoglobin concentration the greater the buffering effect. Note also that increasing the CO_2 will elevate the plasma HCO_3^-.

Plasma bicarbonate levels are usually between 25-27 mM/L. If greater (higher), excretion via the kidney then occurs. Bicarbonate excretion via the kidney also varies inversely with Pco_2 irregardless of the plasma levels. Elevated Pco_2 causes reabsorption of HCO_3^- even though the bicarbonate is already increasing because of the buffering action of hemoglobin. With a decreased Pco_2 the kidney excretes HCO_3^- even though the bicarbonate may already be lowered.

We have already reviewed how hydrogen is buffered by bicarbonate and hemoglobin. Other mechanisms are available in the kidney to neutralize the H^+ ion. The kidney removes 50 to 100 mEq of H^+ ion daily from the non-volatile acids formed in the body in order to maintain constant plasma pH. Additionally in the kidney tubular cells there is a hydrogen exchange mechanism. H^+ ion is excreted into the tubular urine in exchange for sodium. The mechanism is as follows: CO_2 diffuses from plasma into the tubular cell. Carbonic acid forms in these tubular cells from the CO_2 and HOH, and then dissociates into H^+ and HCO_3^-. Thus H^+ ions are supplied for the exchange mechanism and HCO_3^- is reabsorbed into the plasma. This also explains why an elevated Pco_2 causes HCO_3^- to be formed.



It should be noted that though H^+ must share this transport mechanism with K^+ that normally more hydrogen is exchanged than potassium. An exception to this is in hyperkalemia when K^+ exchange is greatest. Approximently 1/3 of the H^+ ion is excreted with phosphate and the rest with ammonia which is formed in the renal tubular cells. If blood pH is acidotic the urine pH will usually be acidotic, dihydrogen phosphate is excreted instead of monohydrogen phosphate, NH_4 formation increases, and Na^+ reabsorption is complete along with bicarbonate. The exception to this is in hyperkalemic acidosis when urine may be paradoxically alkaline. If blood pH is alkaline the urine pH will usually be alkaline and monohydrogen phosphate is excreted instead of dihydrogen phosphate so as to conserve H^+ ion. NH_4 formation stops, HCO_3^- excretion increases, and K^+ exchange is greater than that of H^+. Hypokalemic alkalosis is an exception and the urine may then be paradoxically acid.

4. Sources and Techniques of Measurements

The first practical means of quantitatively assessing an acid-base disorder was introduced by Van Slyke and Cullen in 1917 when they devised a method for determining plasma bicarbonate. Since then there have been a variety of methods and techniques put forward. The source of blood is either arterial or capillary blood collected anaerobically. With the proper equipment and technical skill there is apparently little difference which is used.

According to Rossier, et al (1960)[26] the determination of CO_2 content manometrically is simpler than volumetrically, with the Van Slyke method generally regarded as the most reliable and most accurate technique.

These same authors point out that in the past CO_2 tension was usually calculated by Hasselbach-Henderson formula after determination of CO_2 content and pH. Recently, determination of CO_2 tension with an electrode simular to the pH electrode has gained popularity (Severinghans, Snell, Astrup).

Measurement of pH is possible by any of 3 methods. The colorimetric method is considered too crude to be satisfactory. The gasometric method is based on the fact that the pH of blood is represented by the ratio of total CO_2 to free CO_2 according to the Hasselbalch-Henderson formula. Since determination of free CO_2 is techniqually difficult and subjected to error this approach is not very satisfactory. The electrometric is the most accurate and universally used method today. In this method, a measuring electode and a reference electrode with known potential are connected as an electrical circuit. A potential difference will exist between the measuring electrode and the fluid to be measured. This difference in voltage is dependent upon the pH of the solution. There various electrodes with perhaps the most satisfactory one for physiological measurements of blood being the glass electrode. Measurements should be made at body temperature to eliminate errors caused by temperatures.

Jennett, et al (1964)[16] described the method of arterial blood sampling from the operative field for acid-base measurements by the micro-Astrup technique. He pointed out that an advantage with this technique is that estimations can be made on capillary blood which has been drawn from an extremity providing the latter is warm and pink. Results of studies where capillary blood from the finger and arterial blood from the operative site were drawn simultaneously show that their measurements consistently agree. Another advantage of the micro-Astrup was described by Ogilvie, et at (1965)[22] who showed that measurement of CO_2 tension was not invalidated by the presence of anesthetic gases and by nitrous oxide in particular. This is an improvement since the main error involved in estimating plasma CO_2 content in the presence of N_2O_2 using the Van Slyke volumetric apparatus without absorption of CO_2 by NaOH can be around 25%. This effect is not seen in the measurement of CO_2 content in the presence of halothane.

EFFECTS ON ACID-BASE

A. PREMEDICATION:

Preanesthetic medication has two main purposes: (1) to bring a rested, quiet patient to the operating room, and (2) to minimize as much as possible the hazards of anesthesia and surgery. There continues to be much discussion about what effects various drugs used in premedication have on bodily functious. Medrado, et al (1966)[18] studied the effects of atropine on arterial blood gases and pH. Samples were taken just prior to administration of 0.5mg IV and 0.25mg IM of atropine sulfate, and then at appropriate intervals therafter. A total of 47 patients without any cardiovasular or respiratory abnormalities were studied. 16 of these served as controls. Results showed no significant differences in pH or Pco_2 after the atropine was given. These results are in accordance with those of Gardiner, et al (1964)[11] who likewise studied the effects of atropine on arterial blood gases. In addition the latter clinician also studied the effects of papaveretum with scopotamine and found there were no significant changes of blood gases caused by these. Pierce, et al (1965)[24] studied the effects of preoperative medication on blood gases in two groups of patients. The first group of 16 patients received meperidine HCL, promthazine HCL, and pentobarbital while the second group of 16 patients received only pentobarbital. There were no significant changes in Pco_2 or pH with either group. Though Po_2 is not measured in acid-base and its discussion here is somewhat out of place, it is of interest that the first group who received meperidine did have a significant reduction in Po_2. Where as those who did not have meperidine did not have a reduction in Po_2.

B. SPINAL BLOCK

Epidural or Subarachnoid Anesthesia

The majority of the muscles of the abdominal and chest wall are innervated by the intercostal nerves which originate from the thoracic portion of the spinal cord. Thus, as the level of spinal block raises there will be an ever increasing number of muscles affected. Several authors point out that the upper thoracic level of motor paralysis during spinal block is from one to four myotomes lower than the corresponding dermatomal sensory level. This occurs as a result of the differential blocking effect of local anesthetics on nerve fibers of different diameter. Since the intercostal muscles are important muscles of respiration, there has been some discussion as to the advisability of administering a high spinal block, especially to patients with impaired pulmonary function.

Moir (1963)[20] first studied the effects of high epidural block in patients who were pain free and had not received any depressant drugs. Tidal volume, minute volume, vital capacity and peak expiratory flow rate were measured before and during the block using 1.5% lignocaine. Results indicated that only minimal changes occurred in these aspects of ventilation and that the ability to cough was unimpaired. In fact this investigator mentions that continuous epidural analgesia is probably the most effective method of relieving pain and improving respiratory function after surgery. Moir and Mone (1964)[19] then carried their investigation further in an effort to confirm the above findings by measuring of pH, Pco_2 and standard HCO_3^- values of capillary blood. These were measured in twenty unpremedicated patients before and after induction of epidural analgesia to the level of the T4 or higher. Twelve of these subjects had normal respiratory systems while eight had chronic bronchopulmonary disease. Results indicate that no patient developed any significant degree of respiratory acidosis and it was concluded that alveolar ventilation was unimpaired since alveolar hypoventilation causes CO_2 retention. It should be noted that these results were reached in patients with epidural analgsia who were not at that time undergoing an operation nor had they received any depressant drugs.

De Jong (1965)[7] investigated the effects of intercostal muscle paralysis on ventilation expressed as changes in arterial Pco_2 and Po_2. For our purposes of acid-base review we are interested here in the Pco_2. Of the 32 patients studied, 22 had subarachnoid anesthesia and 10 had epidural anesthesia. Cutaneous sensory levels varied from T10 to C5. 19 of the patients received additional sedation during the operation. The Pco_2 was measured after premedication but prior to induction of block, and then compared to values obtained during block. There was no singificant changes reported in the arterial Pco_2 before and after the spinal block.

C. INHALATION AGENTS

It has already been pointed out by Ogilvic and Howie (1965)[22] that there is a certain amount of error present when measuring Pco_2 and CO_2 content following the administration of volatile anesthetic agents. This depends upon the technique used in measuring these values. Beecher, et al (1950)[1] noted that until their review most standard pharmacological texts stated that ether anesthesia produced, or was regularly accompanied by acidosis. They even quoted the text of Goodman and Gillman which read "Most workers are agreed that general anesthetics tend to reduce the serum bicarbonate and pH of the blood. This occurs especially in prolonged anesthesia ...." Because this thinking prevailed there were many attempted explanations to show why. It was thought due to the fact that most of the previous work was done on dogs. Beecher, et al (1950)[1] felt that the response of dogs was very different from that of man. They therefore studied arterial pH and CO_2 content in twenty surgical patients. Half received ether by the open drop technique and half by closed circle system following nitrous oxide induction. They concluded that there was no evidence for clinical acidosis associated with either the open drop or the closed system. Though there was a slight, but definite tendency for fixed acid to rise using the closed method this rise was unimportant since in no individual case did it exceed the normal daily variation.

Since newer agents are available, what about their effects? Halothane is one of which considerable studies have been made. After publishing previous studies done with all the commonly employed anesthetic agents showing that, when adequate pulmonary ventilation was provided, it was usually possible to maintain acid-base homeostasis without difficulty, Dobkin (1959)[8] investigated the effect of Halothane. This was done with 90 patients together with nitrous oxide and oxygen in a non-rebreathing system. Artificial respiration was provided by a ventilator which was set to the requirements of the individual patient according to his size, age, posture, and condition of cardio-respiratory system. Results showed surgical anesthesia was accomplished with relatively small amounts of Halothane without evidence of fixed acid accumulation even during prolonged anesthesia. Graff, et al (1964)[12] noting that, though insufflation of oxygen and ether had been a highly satisfactory technic for maintaining anesthesia in cases of tonsillectomies through the first part of this century, it was being replaced by halothane because of the latter's lack of irritability, non explosiveness, and ease of deepening or lightening anesthesia. Since this halogenated compound will give rise to significant respiratory depression if no means are available to support respiration, these experimenters decided to study and compare the effects of this agent on acid-base balance if given by 1) insufflation, 2) endotracheal with Ayre's T Tube, and 3) via endotracheal with a circle-absorption system. Results indicate that there is little difference between technics 1) and 2), but the average fall in pH and rise in Pco_2 is statistically greater than by the circle absorption system. The investigators stated that any of these technics could be used without significant respiratory acidosis providing a suitable anesthetic level is maintained and attention is made to keeping a clear airway.

Dobkin and Song (1962)[9] studied effects of methoxyflurane (Penthrane) which is one of the newer agents. It is a combination of the desirable qualities of halothane and diethyl ether. Their study utilized 12 patients who were having major abdominal operations. Penthrane with nitrous oxide and oxygen administered through a calibrated vaporizer was used. Serial arterial blood samples were measured for pH, Pco_2, and CO_2 content. Pulmonary ventilation was augmented by a Takaoka respirator. Laboratory analysis showed a slight but definite trend towards metabolic acidosis with this agent. It is interesting to note that their experiments on dogs (not having operations) using this agent also showed the same results.

Perhaps the results of Boyan and Howland (1965)[2] who decided to study the effects of all common inhalation agents on acid-base during operations, since no previous systematic comparison had ever been done, best express the over all effects of these agents. They found that operation and anesthesia with diethyl ether, halothane, and methylflurane for 1-4 hours, or cyclopropane for 1-3 hours, produce comparable metabolic acidosis in well ventilated and oxygenated adult patients. These are within the normal range of daily human variations and therefore cannot be considered of clinical significance.

D. HYPOTHERMIA

In spite of much careful research into the metabolic changes of the hypothermic state many problems remain unsolved. Brewin (1964)[3] and Nisbet (1964)[21] have written excellent reviews on the Physiology of Hypothermia and Acid-Base Disturbance in Hypothermia respectively. The rate at which chemical reactions proceed is dependent on temperature. Since reaction rate is decreased by falling temperature, so the metabolic rate of the cells of the living organism is reduced as temperature falls. This is the principle responsible for the majority of the physiological changes in hypothermia. Body temperature closely depends upon balance between heat production and heat loss. During exposure to a cold environment the hypothalamic centers bring into action mechanisms to 1) increase heat production, and 2) decrease heat loss. Heat production is increased by the increased secretion of epinephrine and thyroid hormone, and by increased muscular tone and shivering. Of these, shivering is the most important. Heat loss is minimized by cutaneous vasoconstriction. Shivering is by far the most prominent factor in attempting to maintain body heat. Suffice it to say that anesthetic management to induce hypothermia would include use of a myoneural blocking agent, and probably also the use of a vasodilator drug.

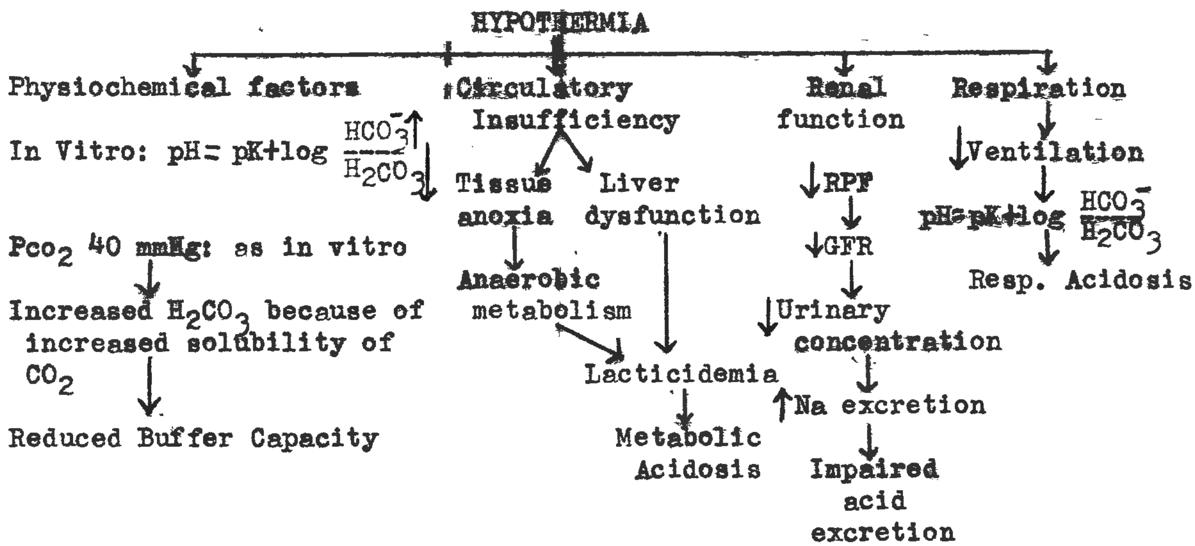
Respiration, like other functions, is depressed by hypothermia. According to Brewin (1964)[3] the degree of depression is similar to that in other systems so that respiratory exchange is more or less adequate to keep pace with oxygen intake and CO_2 excretion. However, under the influence of drugs such as barbiturates there would be severe respiratory depression.

Circulatory depression may occur if a patient is not kept on cardiopulmonary bypass. This is because of the slowing of the heart and increased viscosity of blood. This can certainly decrease the oxygen supply to peripheral tissues and cause development of metabolic acidosis as a result of incomplete carbohydrate metabolism in an anaerobic environment.

Hypothermia also brings about some basic alterations in gas transport: (1) Solubility of both O_2 and CO_2 is increased. (2) Oxyhemoglobin dissociation curve shifts to the left so that for a given partial pressure of O_2 in the tissues, less is unloaded from the hemoglobin. Rosenfeld (1963)[27] feels that because of the increased solubility of CO_2 there will be an increase in H_2CO_3. This leads to a reduction in buffer capacity.

Research has shown that hypothermia also decreases the ability of the liver to rapidly metabolize products of acidosis which develop. Likewise, the kidney normally responds to acidosis by increasing HCO_3^- reabsorption or increasing H^+ ion excretion. Hypothermia prevents this so that this regulatory mechanism is lost. Perhaps the following summary by Rosenfeld (1963)[27] gives the best concise overall picture of what occurs in hypothermia. "If the ventilation were normal, physiochemical factors would not affect the pH, but would seriously reduce the buffer capacity of the body so that any further disturbance in circulation, respiratory, or renal function will seriously affect acid-base homeostasis. Circulatory insufficiency, mainly at the capillary level, causes tissue anoxia. This stimulates anaerobic metabolism and excessive amounts of lactic acid are produced.

Hypothermia affects the capability of the liver to metabolize this excess, and metabolic acidosis develops. The reduced metabolism and need for oxygen do not stimulate the respiratory center any longer. This condition depresses the ventilatory rate, causes an accumulation of CO_2, and produces a respiratory acidosis. Normally the kidney responds to these changes by increasing the bicarbonate reabsorption in respiratory acidosis or by increasing the excretion of H^+ ions in metabolic acidosis. Hypothermia presumably blocks many of the enzymatic activities of the renal tubular cell, so that the regulatory effect of the kidney upon acid-base homeostasis is completely lost. However, assisted respirations and adequate circulation (as on cardiopulmonary bypass pump) minimize these acid-base disturbances and make hypothermia an important and useful addition to our therapeutical effects."



Reprinted from Amer. J. Cardiology, Nov. 1963, Acid-Base and Electrolyte Disturbances in Hypothermia.

E. OTHER FACTORS

There are many variables which can affect acid-base balance during anesthesia. Some of the more obvious ones include operative procedures, shock, circulating fluid volume, and blood transfusions.

Probably very little needs to be said about the operative procedure. It is quite obvious that any effects on acid-base resulting from an operation will be caused by acidosis. This will itself depend on the operative procedure, ie., whether it is a simple minor operation or an extensive prolonged traumatizing procedure. Regardless, the operation itself shouldn't have any significant effects if the patient is properly hydrated, ventilated, and within the proper plane of surgical anesthesia.

During anesthesia, as at any other time when shock develops, metabolic acidosis results. This metabolic acidosis results from altered tissue perfusion, with an accumulation of anaerobic products of metabolism. The acids that accumulate are lactic, pyruvic, and citric. This occurs as a result of the loss of whole blood, or plasma, or both. Howland and Schweizer (1962)[15] showed that hypovolemia resulting from loss of whole blood or plasma was the major etiologic factor in the production of metabolic acidosis during and immediately after operation (and thus anesthesia). It has been demonstrated that acidosis is a depressant to the myocardium and thus may be an important causative factor in the fatalities attributed to irreversible shock. According to Payne (1962)[23] acidosis and hypercarbia causes increased irritability of heart muscle and commonly results in ventricular extrasystoles and ventricular tachycardia. The treatment of this acidosis is not the use of buffering agents such as sodium bicarbonate, but rather the replacement of circulating fluid volume. Whether this replacement is to be blood or a balanced electrolyte solution will depend on what the patient needs. If there hasn't been sufficient blood loss to warrent transfusion, yet the patient is in a shock-like condition due to underhydration, then according to Fieber and Jones (1966)[10] infusion of large quantities of balanced electrolyte solution replaces the loss and maintains cardiovascular homeostasis. It is their belief that shock can be prevented (and hence any resulting acidosis) by proper preanesthesia preparation with balanced electrolyte solution so the patient has an adequate circulating fluid volume.

During periods of hemorrhagic shock treated with bank blood the body must combate excess hydrogen ion supplied by two sources. One from citrated blood and the other resulting from the inadequate tissue perfusion. The first line of defense, as has already been discussed, is the buffer mechanism of the blood, and the second is the respiratory system. Both these mechanisms will come into action in case of a patient in shock given transfusions of bank blood. If fluid replacement is adequate the additon of acid bank blood will not result in further acidity of the patient's blood. According to Howland, et al (1962)[15] this is because of the large amount of dissolved CO_2 in the plasma of bank blood which is responsible for its acidity. He feels that contrary to popular belief this acidity is not comparable to a metabolic acidosis but is analogous to the respiratory acidosis occurring in vivo. When ventilation is adequate the normal respiratory mechanisms will compensate for this acidity even if large amounts of bank blood are given.

Return to normal base balance after treatment of shock by the administration of large quantities of ACD preserved blood is explained by three main factors. First, normal perfusion of the tissues following replacement would diminish formation of excess lactate and also produce adequate removal by the liver. This eliminates one source of fixed acid and permits more effective buffering of the remaining citric acid. Second, the sodium citrate in bank blood is in itself an effective source of $NaHCO_3$. This is because each unit of bank blood contains 17 mEq of sodium (as sodium citrate). 10 units would yield 178 mEq of sodium which is the amount found in 4 ampuls of $NaHCO_3$. Third, elevation of blood citric levels during blood replacement is directly proportional to the rate of administration. Diminution in the speed of transfusion concomitant with improvement of the patient's condition, and the rapid metabolism of citric acid, could account for reduction of hydrogen ion concentration at the end of an operative procedure.

This discussion can perhaps be summarized by reviewing briefly one of the studies reported by Howland, et al (1962)[15]. A total group of 86 patients were divided into group #1 of 34 patients who did not show any acidosis, and group #2 consisting of 52 patients. This latter group showed metabolic acidosis in varying degrees during anesthesia for an operative procedure. The major variations between the two groups were found in the preoperative acid-base balance , and in the number and type of operative complications. 22 of the 52 had increased acid before their operation and were found to be suffering from conditions such as hemorrhage, ureteral obstruction, severe cachexia, marked anemia, uncontrolled diabetes mellitus, and plasma deficiency.

Results indicated that age, preoperative physical status, anesthetic agent, and volume and rate of blood replacement played little part in the development of fixed acid excess during operation (anesthesia) and the postoperative period. On the other hand evidence is strongly suggestive of the importance of hypovolemia as a major factor in the production of fixed acids during these periods.

SUMMARY

This has been an attempt to review the recent literature dealing with anesthetic agents and their effect on acid-base balance. In order to adequately do this it first required a review of acid-base itself. We reviewed primarily terms and definitions currently used, buffering mechanisms important in maintaining homeostasis, parameters used for accessing acid-base, and briefly mentioned methods available for measuring these parameters.

Our review of the most recent studies reveal that generally premedication, spinal block, inhalation agents, and hypothermia, as they are respectively used in anesthesia today, do not cause any notable effects on acid-base balance.

Certainly there are many variables which must be considered. Results of studies reviewed indicate that age, preoperative physical status, anesthetic agents, and volume and rate of blood replacement, has little effect on acid-base balance. The most frequent variable to have a significant effect is hypovolemic shock which causes the production of fixed acids, and results in a shift towards acidosis.

CONCLUSIONS

1. Premedication for anesthesia as it is usually done does not affect acid-base balance.

2. Spinal block, either epidural or subdural, as routinely used for anesthesia does not appreciably affect acid-base balance.

3. Inhalation anesthetic agents used in the typical individual does not cause acid-base disturbance providing ventilation and hydration are adequate.

    a. Uncomplicated ether anesthesia, contrary to early beliefs, does not produce any greater change in acid-base balance than any other agent.

4. Mild disturbances in acid-base balance, whether respiratory or metabolic in nature, during uncomplicated anesthesia and operation needs no special therapy.

5. Concentration of H^+ ion, HCO_3^-, and pCO_2 as measured by pH, Pco_2, and CO_2 Content (bicarbonate content) are the 3 best guides to acid-base balance.

6. A blood pH will differentiate between acidosis and alkalosis.

7. An abnormal Pco_2 will indicate respiratory involvement.

8. Deviation from the normal CO_2 Content will refect a disorder of metabolic origin.

9. In absence of shock large volumes of acidic bank blood does not affect the metabolic status of the patient during anesthesia.

10. Usually no acid-base change is noted as a result of age, physical status, anesthetic agent, type of operation, or transfusion.

11. Metabolic acidosis during anesthesia is usually associated with hypotension and low circulating blood volume.

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