# VARIATIONS IN THE SIGNS OF ACUTE OXYGEN-WANT DURING ANESTHESIA * †

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The clinical signs of acute hypoxia or of asphyxia may be easily recognized in the average patient who is not under the influence of depressant drugs. It is the purpose of this report to call attention to the fact that in the anesthetized patient hypoxia or asphyxia may result in irreversible tissue damage or even death without the intervention of the warning signs of distress such as pressure variations or the "slow bounding pulse of oxygen want."

The general signs and symptoms of hypoxia, such as mental and sensory dullness, muscular weakness, headache and excitement, are eliminated by general anesthesia and rendered obscure by the heavy premedication which often accompanies spinal anesthesia. If such manifestations are present after the patient recovers from the effects of the anesthetic, they may confirm the fact that oxygen-want was present during the period of anesthesia. The signs that remain for the clinical anesthetist to consider are cyanosis, marked dilatation of the pupils, and variations in pulse rate, blood pressure and respiration.

Cyanosis indicates the presence of 5 Gm. or more of reduced hemoglobin per 100 cc. of blood. If a diffuse, dusky or bluish color of the skin develops, the blood of the patient is not getting sufficient oxygen. One cannot overemphasize the fact that in the presence of a low hemoglobin level owing to acute loss of blood or anemia the patient may die of asphyxia without ever presenting this discoloration. Furthermore, the color changes of cyanosis may be masked by the presence of argyria, icterus, or heavy skin pigmentation.

Marked dilatation of the pupils suggests hypoxia particularly if the depth of anesthesia is in the upper planes of the surgical stage, if the premedication was not a midriatic alone and if other signs agree. The fact that the drapes about the surgical field often cover the eyes is a further impedient to the use of this sign.

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In the teaching of clinical anesthesia, the tendency is to stress the respiratory and circulatory variations that occur in the presence of hypoxia and asphyxia. The anesthetist should be familiar with these variations as they would occur in the unnarcotized individual. He should also be able to evaluate the effects produced by each volatile and nonvolatile agent that he may employ in order to realize that certain of the signs of hypoxia or asphyxia are masked.

The respiratory and circulatory effects of hypoxia and asphyxia were studied in dogs which were under the influence of various anesthetic drugs.

## PROCEDURE AND RESULTS

Seventy-five dogs were used. The effects of acute oxygen-want were produced by having the dog breathe pure nitrogen or by allowing the animal to rebreathe air from a 1 liter rubber bag connected to the endotracheal tube through a carbon dioxide absorber. Asphyxia was produced by clamping the trachea or by rebreathing a 1 liter air sample without a carbon dioxide canister in the line.

Blood oxygen and carbon dioxide combining power determinations were made (1) to make certain that the dogs were well oxygenated when the experiment was started. Blood oxygen values were satisfactory for all except the nitrous oxide-oxygen experiments. These dogs had been subjected to an 80:20 nitrous oxide-oxygen mixture for thirty minutes and were mildly hypoxic at the start of the experimental period.

Arterial blood pressure was recorded in each instance by means of a mercury manometer connected to a cannula in the femoral artery. Venous pressure was measured by a cannula in the innominate vein or in the superior vena cava. Respiratory changes were recorded by a pneumograph around the chest or by pressure changes through a side arm of the endotracheal tube. Electrocardiograms and stethocardiograms were recorded simultaneously to determine the heart rates. The heart sounds disappeared when the blood pressure reached zero but the electrocardiographic tracings sometimes continued for five to fifteen minutes longer. In some such instances direct observation of the heart revealed no myocardial contractions coincident with the electrocardiographic deflections. The heart rate was considered to be at zero at the point of the disappearance of the heart sounds.

Twelve dogs were used for unanesthetized controls. In the preparation of 10 of these animals the only drug to which they were subjected was procaine, 0.25 per cent, to facilitate the connection of the femoral artery with the blood pressure apparatus. The other two dogs were intubated after three minutes of cyclopropane anesthesia and then allowed to recover from the anesthetic for thirty minutes before proceeding with the asphyxia experiment. Figure 1(a) presents the usual changes of asphyxia in the unanesthetized dog. The pulse in Dog 81

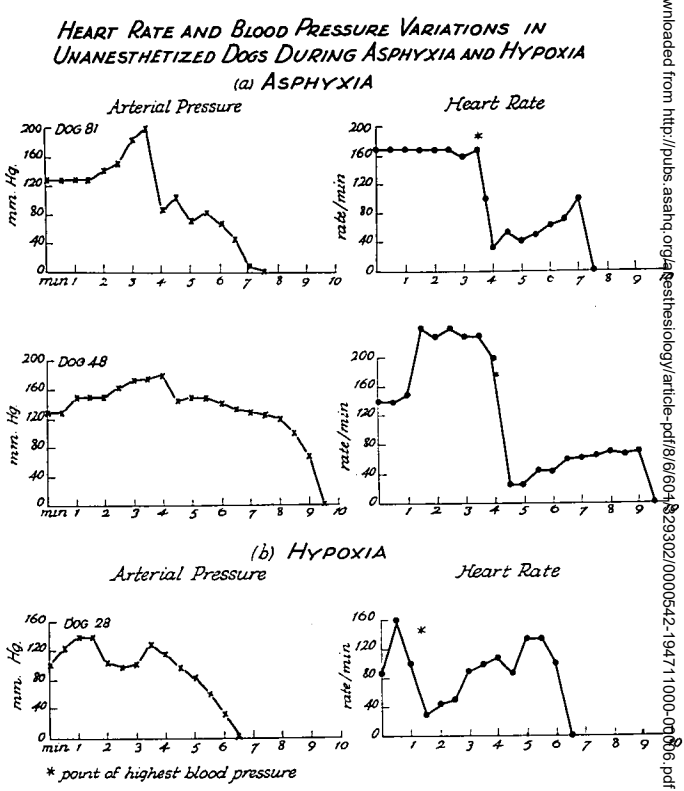


FIGURE 1

remained regular at 164 beats per minute for three and a half minutes with the animal rebreathing 1 liter of air. Then bradycardia of 32 developed abruptly and the rate stayed below 60 for two minutes. The rate gradually increased to 100 and then began to slow. The arterial pressure remained steady at 130 mm. of mercury for two minutes and then rose to 200 mm. of mercury at the three and a half minute point. The sudden bradycardia was coincident with a sharp fall in pressure to 82 mm. of mercury. This pressure then gradually fell to zero during the next three minutes. Breathing failed after four and a half minutes

but during the following two minutes there were 15 strong asphyxial gasps.

Figure 1(b) presents typical responses to hypoxia. Dog 28 showed a sudden bradycardia of 33 beats per minute after breathing pure nitrogen for ninety seconds. The heart rate then gradually accelerated to a rate of 136 at the five and one half minute period and then began

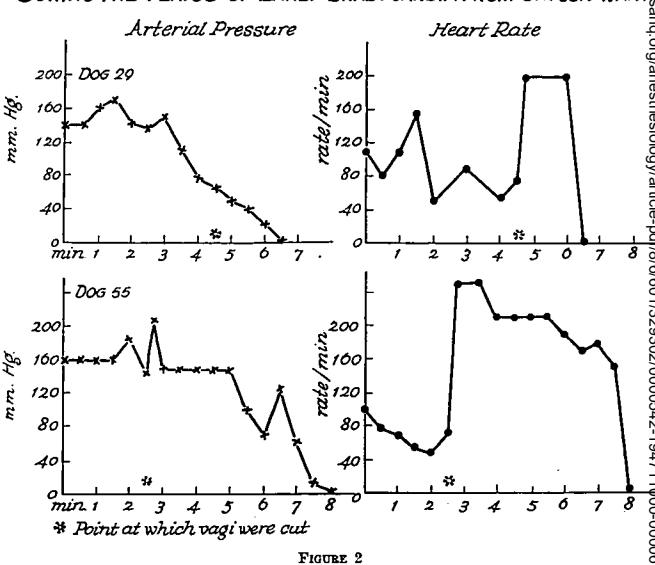


FIGURE 2

to slow as the blood pressure approached zero. The arterial pressure showed an early rise followed by a gradual fall to zero at the end of six and one half minutes. Breathing ceased at the four minute mark.

The vagi were cut in 4 hypoxic dogs after bradycardia began. The pulse rate at once became rapid and continued thus until a final slowing and asystole took place. Figure 2 shows the cardiac responses of Dogs 29 and 55 when the vagi were cut during the period of bradycardia.

In 2 dogs, the vagi were cut before the hypoxia was produced. During the entire course of increasing oxygen-want in these 2 dogs, no

significant changes occurred in the heart rate until the final slowing, owing to myocardial asphyxia, appeared.

There was always an increase in both respiratory rate and tidal volume. Breathing ceased about the time of the circulatory crisis. The period of apnea that followed was interrupted after about sixty seconds by a period of "asphyxial" gasping which usually persisted for two minutes or more. The rise in arterial pressure and the period of hyperpnea during the unanesthetized asphyxia controls were more

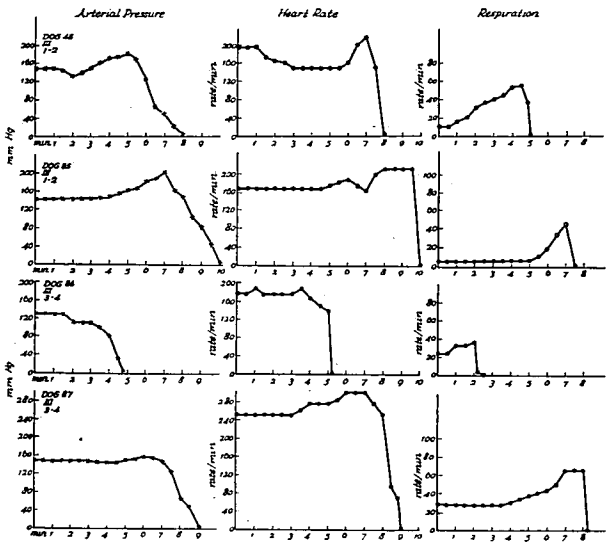


FIGURE 3

marked than during the hypoxia controls. Otherwise, there was no gross difference between the results of the two procedures so far as arterial pressure, heart rate, and respiratory changes were concerned. During the progress of these control experiments, there was a variation in the time of the appearance of the various heart rate and blood pressure changes, but the sequence of the occurrence of the signs was always the same.

Sixteen dogs were anesthetized with sodium pentothal and then asphyxiated. None of the dogs under pentothal anesthesia developed

bradycardia during the early stages of asphyxia. Cardiac slowing occurred only as a terminal event. In dogs in the lighter planes of surgical anesthesia a rise developed in arterial pressure which was highest at the time of maximum hyperpnea. Animals subjected to higher concentrations of sodium pentothal produced very little or no rise in pressure in response to carbon dioxide excess and oxygen lack. Blood pressure changes varied. In some of the animals the pressure gradually fell to zero without a significant change in heart rate. In others, the arterial pressure remained constant until the terminal stage and then fell to zero in two or three minutes. Figure 3 shows these circulatory variations. The dogs showed an increase in respiratory rate and tidal volume in response to asphyxia and to hypoxia. Deep anesthesia appeared to reduce the degree of response. The period of time between the cessation of breathing and the fall of arterial pressure to zero was shorter with sodium pentothal than with any of the other drugs except deep ether anesthesia. The period of asphyxial gasping occurred in only 2 of the 16 dogs.

Figure 4(a) presents the arterial pressure and pulse changes that occurred in Dog 28 when he was asphyxiated to a zero pressure level without anesthesia. Figure 4(b) shows the response of the same animal on another day when the asphyxial procedure was repeated during pentothal anesthesia.

Dogs asphyxiated during light surgical anesthesia with ether and without any premedication gave cardiac, blood pressure, and respiratory responses which were similar to those presented in the control group of unanesthetized dogs. The period of bradycardia of oxygen-want, however, was delayed in appearance and, therefore, these animals were more hypoxic when this sign first appeared than were the dogs in the control experiments. Deep ether anesthesia prevented the development of the "slow bounding pulse of oxygen-want" and prevented or markedly reduced the pressure rise. The period of hyperpnea was reduced in duration and intensity. Asphyxial gasps were usually eliminated. Thus, it is seen that deep ether masks most of the signs of hypoxia. Figure 5(a) shows the responses to asphyxia of Dogs 75 and 76 during light ether anesthesia. Figure 5(b) shows the responses of Dogs 74 and 77 which were more profoundly anesthetized.

Divinyl ether was used on 3 dogs. The responses were too similar to those obtained with diethyl ether to warrant a longer series.

Cyclopropane was administered to 12 dogs. The fact that this agent is believed by some investigators to be a parasympathomimetic drug in its relation to the heart (2, 3, 4) gave added interest to the study of its effects on the signs of oxygen-want. These dogs were maintained in a constant plane of surgical anesthesia for thirty minutes and then asphyxiated. The response in planes 1, 2, and 3 was similar to those responses in similar experiments in which light ether anesthesia was employed. Profound cyclopropane anesthesia decreased the degree of

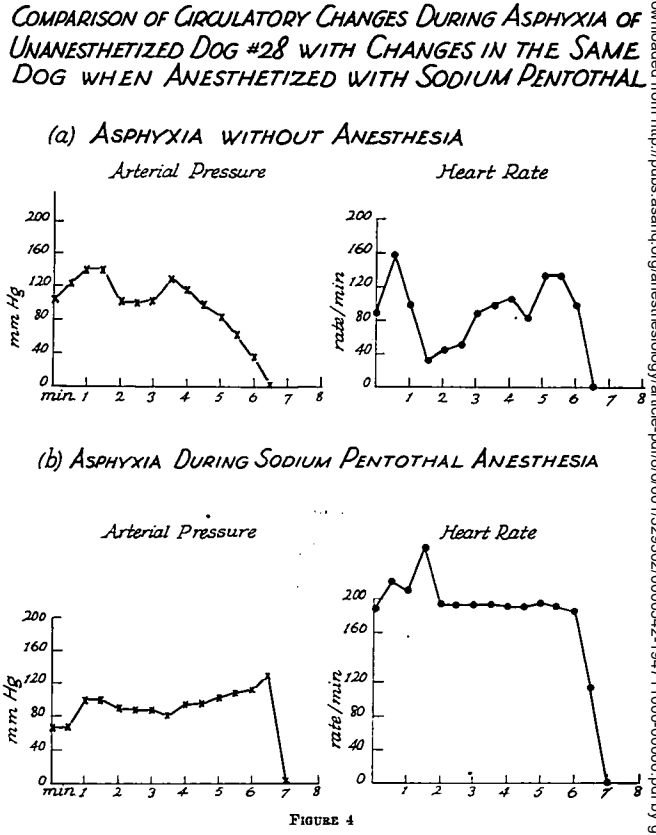


FIGURE 4

respiratory and circulatory response. Figure 6 shows the typical responses to asphyxia during cyclopropane anesthesia.

Three dogs were maintained in stage III, plane 2 to 3, anesthesia with chloroform for thirty minutes and then asphyxiated. The onset of the period of bradycardia of oxygen-want was delayed. The arterial pressure rose gradually and then fell gradually to the zero line. There was a marked increase in both rate and amplitude of respirations. One or two minutes after breathing ceased a period of asphyxial gasp-

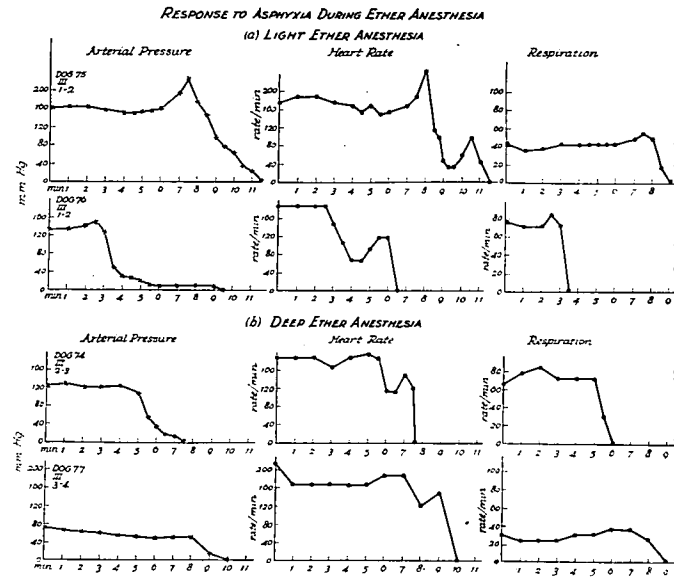


FIGURE 5

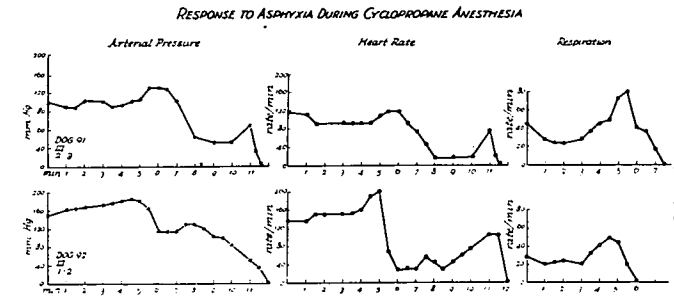


FIGURE 6

ing occurred. The circulatory and respiratory records were similar to those of the cyclopropane series. Myocardial depression was not more apparent with these dogs than it was when any of the other anesthetic agents was employed.

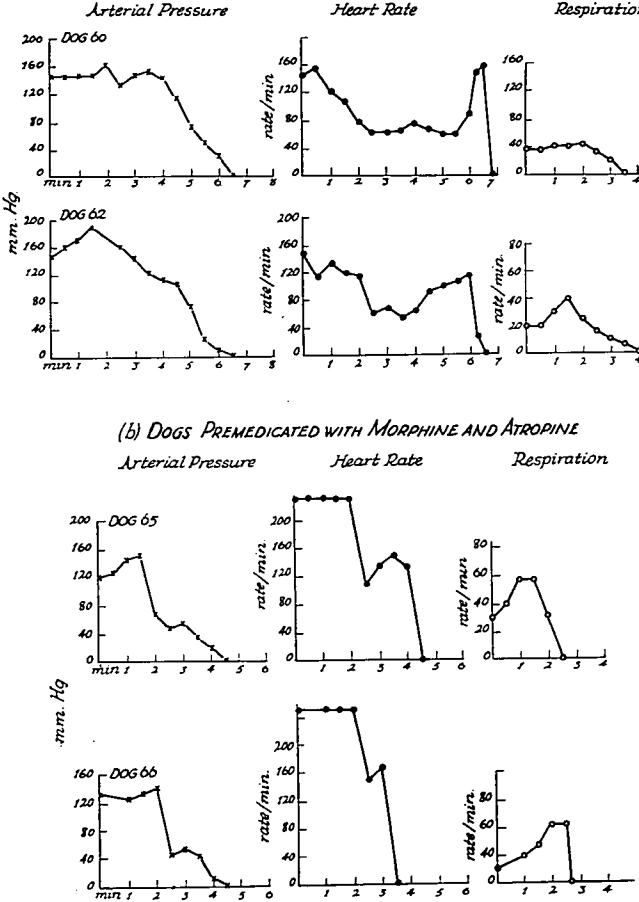


FIGURE 7

Ten dogs were anesthetized with a nitrous oxide-oxygen mixture in the ratio of 80:20. Four of the animals were unpremedicated. None of the signs of oxygen-want were masked in these dogs. Four dogs were given premedication with morphine 16 mg. and atropine 0.64 mg. ten minutes before induction of anesthesia and fifty minutes before the asphyxial period began. Sudden bradycardia did not develop in these dogs. The pressure response to low oxygen tensions and carbon dioxide excess was greatly reduced. Two dogs were given premedication with morphine 16 mg. and scopolamine 0.64 mg. one and a half hours before the period of asphyxia during nitrous oxide-oxygen anesthesia.

SUMMARY CHART ON THE EFFECTS OF ANESTHETIC AGENTS UPON THE SIGNS OF ACUTE OXYGEN-WANT IN DOGS

| Narcotic Condition of Dogs | Heart Rate | | | | | Arterial Blood Pressure | | | | | Respiration |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Initial Rate Per Minute | Bradycardia of Oxygen-Want | | | | Initial Pressure mm. Hg. | Elevation of Pressure With: | | Terminal Fall to Zero | | Period of Asphyxial Gasps After Breathing Ceased |
| | | Vagal Slowing | | | Terminal Slowing Only | | | | | | |
| | | Slowest Rate | Occurrence | | | | Asphyxia | Hypoxia | Abrupt | Gradual | |
| | | | Early | Late | | | | | | | |
| Unanesthetized | 110 | 36 | x | | | 132 | ++ | ++ | | +++ | +++ |
| Pentothal $III_{1-2}$ | 164 | No Brady. | | | x | 134 | ++ | ± | ++ | | 0 |
| Ether $III_{1-2}$ | 184 | 66 | | x | | 116 | ++ | ± | | ++ | ++ |
| Ether $III_{3-4}$ | 175 | No Brady. | | | x | 118 | ± | 0 | ++ | | ± |
| Cyclopropane $III_{2-3}$ | 136 | 35 | | x | | 128 | ++ | | | ++ | ++ |
| Nitrous Oxide $III_{1-2}$ (With Premedication) | 250 | No Brady. | | | x | 126 | ++ | | | ++ | + |
| Nitrous Oxide $III_1$ (Without Premedication) | 173 | 54 | x | | | 140 | ++ | | | ++ | ++ |
| Chloroform $III_{2-3}$ | 125 | 40 | | x | | 105 | ++ | | | ++ | ++ |

The interval between the cessation of breathing and the fall of the blood pressure to zero was diminished with Sodium Pentothal and with deep ether anesthesia. All dogs showed an increase in respiratory rate and tidal volume in response to asphyxia.

FIGURE 8

The responses of these dogs closely resembled those of the unpremedicated dogs. In Figure 7 the responses of unpremedicated Dogs 60 and 62 may be compared with the responses of Dogs 65 and 66 which had atropine and morphine premedication.

Figure 8 is a summary chart of the effects of anesthetic agents upon the circulatory and respiratory signs of oxygen-want in dogs.

## DISCUSSION

In the unanesthetized individual mild hypoxia results in an increase in respiratory volume exchange but there is no change in blood pressure (5). More severe degrees of hypoxia cause a rise in blood pres-

sure in addition to the respiratory increase. This excitation of the respiratory and vasomotor centers depends upon the chemoreceptors of the carotid and aortic bodies. If the nerves from these chemoreceptors to the medulla are sectioned or depressed, the administration of a gas mixture that is low in oxygen will cause a precipitous fall in blood pressure to shock levels and a rapid depression of respiration.

During the progressive increase in the degree of oxygen-want, three stages may be defined (6, 7, 8, 9, 10, 11). The pre-crisis stage is evident when the inspired air contains about 12 volumes per cent oxygen. There is an increase in both rate and depth of respiration due to stimulation of the aortic and carotid bodies. The heart accelerates progressively, primarily because of a diminution of vagal tone and to a lesser degree because of an accelerator stimulation. The systolic pressure tends to increase and the diastolic pressure either remains unaltered or slightly decreases, thus tending to increase pulse pressure. During this stage of increased systolic discharge, an increased heart rate and a reduced peripheral resistance combine to increase the minute flow of blood through the body and thus help to supply the tissues with normal volumes of oxygen.

When the blood oxygen concentration is reduced to about 9 volumes per cent circulatory crisis occurs (11). This is the beginning of the second stage. The heart begins to dilate and the systolic pressure begins to fall when suddenly bradycardia occurs. There is an increase in diastolic volume and the output per beat increases (6). These changes produce the "slow full bounding pulse of oxygen-want." This sudden slowing of the heart rate is caused either by central hypoxia or by chemoreceptor reflexes (12) and is mediated by the cardio-inhibitory nerves. If the lungs are inflated with oxygen at this time the pulse will immediately return to its former rate or even a faster one. Soon after the beginning of the second stage dyspneic breathing ceases. The apnea which follows is interrupted during the next five minutes by a period of asphyxial gasps which should arouse any anesthetist to institute corrective maneuvers. There is a gradual fall of arterial pressure and a rise in venous pressure during this period. There is a gradual increase in the pulse rate in the latter part of the period as the cardio-inhibitory center loses its effect upon the heart because of central depression.

The third stage is the terminal one and occurs after the blood oxygen concentration has been reduced to 4 volumes per cent or less. There is a rapid fall of blood pressure and a terminal slowing of the pulse. The heart may stop immediately or it may continue to beat for a short period after the pressure becomes unobtainable. Some hearts go into ventricular fibrillation as a terminal event. The usual mode of cardiac exodus, however, is that of asystole. This stage may transpire in only thirty seconds. A heart that fails and stops because of direct

myocardial depression by hypoxia will not respond very satisfactorily to the usual attempts at resuscitation.

If the vagal tone has previously been reduced but is still effective, the heart rate may only gradually slow during stage II of hypoxia. If the vagi have been cut the rise in pulse rate and blood pressure of the first stage will be markedly reduced or not occur at all (13). In the second or crisis stage the heart rate will not slow. The heart rate will remain rapid until the third stage develops when the effects of oxygen-want upon the myocardium cause a final slowing and stoppage. Thus, good vagal tone and active chemoreceptors are essential for clear-cut circulatory signs of the first two stages of hypoxia.

In most instances in which hypoxia is present during clinical anesthesia there is an accompanying excess of carbon dioxide so the term asphyxia may be applied. The two components of asphyxia, oxygen lack and carbon dioxide excess, stimulate the vasomotor and respiratory centers through the chemoreceptors (5). In their direct action on the medullary centers, anoxia depresses whereas carbon dioxide excites. Therefore, anoxia produces a fall in blood pressure only when it acts directly on the vasomotor center. Early asphyxia results in a marked rise in blood pressure owing to the central action of the carbon dioxide and the weakened chemoreceptor reflexes. The signs of asphyxia and of hypoxia depend upon the response of the vagi, the cardio-accelerators, the vasoconstrictors, the carotid and aortic bodies, the carotid sinus and many other components including the hypothalamus and the adrenal glands.

The "slow bounding pulse of oxygen-want" did not occur in the experiments in which (a) sodium pentothal, (b) deep ether, or (c) nitrous oxide with premedication of morphine and atropine was used, so it seems apparent that these agents blocked the vagal response. When nitrous oxide and oxygen without premedication were used, the vagal slowing occurred early in the period of asphyxia and was similar to that occurring in unanesthetized controls. With light ether anesthesia and with surgical anesthesia in planes 2 and 3 of cyclopropane or chloroform anesthesia, marked periods of bradycardia occurred but the time of appearance was delayed. This delay may be evidence of some chemoreceptor depression. The vagal center itself probably is not depressed because its ability to slow the heart rates to 40 and lower during this period indicates a strong vagal tonus.

Arterial pressure rose in response to the central action of carbon dioxide in all the asphyxial experiments except those in which profound anesthesia was used. In these latter cases, a slight fall in pressure was as common as a slight rise. The blood pressure response to hypoxia was markedly reduced by sodium pentothal and by light ether anesthesia. No rise occurred when deep ether anesthesia was used. These records suggest that sodium pentothal and light ether anesthesia depress the chemoreceptors but profound anesthesia abolishes their ac-

tivity. The terminal arterial pressure fall to zero was gradual and extended over a period of three or more minutes in the unanesthetized animals and in those in which the anesthesia was light ether, nitrous oxide-oxygen with or without premedication, cyclopropane, or chloroform. The terminal arterial pressure fall was abrupt when sodium pentothal or deep ether anesthesia was employed. The desirability of a gradual fall in pressure as a warning sign of distress is obvious.

All of the dogs showed an increase in respiratory rate and in tidal volume in response to asphyxia. This is primarily the response of the respiratory centers of the medulla to direct stimulation by the carbon dioxide, but in many instances there are additional stimuli from the response to oxygen-want by the chemoreceptors. When sodium pentothal or deep ether anesthesia was present, the interval between the cessation of breathing and the fall of the arterial pressure to zero was shorter than in the unanesthetized dogs or when the other anesthetic agents were administered. After breathing ceased in the unanesthetized dogs there was a period of apnea for one or two minutes followed by two or more minutes of asphyxial gasping. The period of asphyxial gasping did not appear in the sodium pentothal experiments and was markedly reduced when profound ether anesthesia or nitrous oxide-oxygen anesthesia with morphine and atropine premedication was used. Light ether, nitrous oxide-oxygen anesthesia without premedication, cyclopropane and chloroform anesthesias did not appear to reduce the period of asphyxial gasping. Both sodium pentothal and atropine tend to depress vagal tone more readily than do the other anesthetic agents. Most of the anesthetic agents commonly employed for profound anesthesia probably depress chemoreceptor response in the lighter planes of surgical anesthesia. When these agents are employed to produce plane 4 of surgical anesthesia or stage IV, the medullary centers are so depressed that it is unlikely that any blood pressure or pulse variations would appear coincident with severe oxygen-want.

The dangers of overpremedication in an effort to employ smaller concentrations of anesthetic agents should be stressed. A comparison of the responses of dogs anesthetized with mixtures of nitrous oxide and oxygen only and those that had received morphine and atropine as premedication to anesthesia with a similar anesthetic mixture make this point evident. If one will review the various reports (14, 15, 16) on deaths during nitrous oxide anesthesia, it will usually be noted that in those instances in which the premedication was listed the patients received heavy premedication with barbiturates, morphine, and atropine. The fact that most of these report are made by anesthetists with much experience in the use of nitrous oxide emphasizes the fact that deaths from asphyxia can occur under such circumstances without distress signals, such as a slow bounding pulse or a period of asphyxial gasping.

This report does not attempt to cover the various effects of all anesthetic agents on the signs of acute oxygen want. It is primarily

intended as a reminder that the warning signs of asphyxia and of hypoxia vary with the depth of anesthesia and with each drug employed.

## SUMMARY

The signs of asphyxia and of hypoxia which are ascertainable by the anesthesiologist are demonstrated in the unanesthetized dog and are discussed.

The effects of certain volatile and nonvolatile agents upon the occurrence of these signs of distress are demonstrated.

Attention is called to the fact that death from acute oxygen want may occur in the operating room without the patient evidencing such significant developments as a slow bounding pulse, a gradual arterial pressure fall, or a period of "asphyxial" gasping.

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