Circulatory and Electroencephalographic Effects of Extreme Ether Anesthesia in Dogs

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Methods of monitoring circulation which are available to any anesthetist include palpation of the pulse, auscultation of the heart sounds, and sphygmomanometric determination of the blood pressure. Scientific publications as well as brochures from commercial manufacturers advocate the use of many electronic monitors. Some of these devices are triggered by the ventricular depolarization phase of the cardiac cycle, so are intimately connected with the electrocardiogram. Others show the electrocardiogram itself. Some depend on electronic sensing of the peripheral pulse.

Clinical experience indicates that these monitors do not respond simultaneously to give comparable information about the course of anesthesia. It was decided, therefore, to attempt to find which of the methods available might be most valuable in preventing administration of an overdose of anesthetic agent.

Methods

Healthy adult dogs were anesthetized with 25 mg/kg thiopental, intravenously. An endotracheal tube was inserted, a sphygmomanometer was applied to a hind leg, and a stethoscope was placed on the left chest. Frontal-occipital needle electroencephalographic electrodes were inserted into the scalp. Lead 1 of the electrocardiogram was monitored using needle electrodes. The EEG and ECG were recorded on a Grass Model III D electroencephalograph.

Pulses were palpated in the tongue to give information concerning a small artery, and in the femoral region to monitor a large artery. Sphygmomanometric blood pressures were determined every two or three minutes. Heart sounds were monitored continuously. The dogs were placed with the left side up so there would be no unusual pressure on mediastinal contents close to the chest wall.

When the equipment was in place and baseline recording had been made, ether was administered from a standard Heidbrink anesthetic machine using a circle absorption system. As anesthesia was deepened, spontaneous respirations tended to diminish, so respiration was assisted by manual compression of the reservoir bag to a degree of obvious hyperventilation. Ether was administered at such a rate that maximum depth was achieved in 30 to 45 minutes. The response of ten dogs was observed. In three cases the animal was allowed to recover and the experiment was repeated.

Results

As the animals were anesthetized progressively more deeply, the observed circulatory functions disappeared one by one and in fairly consistent, though not invariable, order. In all instances save one, the first noticeable change was related to character of the heart sounds. These became less distinct and assumed a distant or muffled character.

In all cases but two, the small artery pulse disappeared next as anesthetic depth was increased. In the two exceptional cases, the blood pressure became unobtainable shortly before the small artery pulse disappeared.

The blood pressure was depressed to less than 50 per cent of the original or disappeared entirely shortly after the small artery pulse became unobtainable, except for the two instances cited above. The pressure fluctuated during earlier stages of anesthesia, but these changes provided no consistent end point. An attempt was made to distinguish between the blood pressure measured by auscultation and by observation of the oscillation of the aneroid manometer needle. Neither one persisted predominantly beyond the other.
Changes were frequently apparent in the ECG complexes after the blood pressure had become severely depressed. In one instance, the ECG complex changed concomitantly with onset of muffling of the heart sounds. In other cases the ECG complexes were not materially altered until after the small artery pulse and the blood pressure were unobtainable. In all cases, the heart sounds were audible, though faint, so long as the femoral artery pulse was palpable. Electrocardiographic activity was apparent after loss of peripheral pulses in three fatal experiments. It was possible to resuscitate all animals by ventilation with oxygen and discontinuance of administration of ether so long as there was a palpable large artery pulse. In three cases in which the large artery pulse had disappeared, resuscitative efforts were futile. Table 1 summarizes the major circulatory changes observed.

In one non-fatal experiment, an electrical asystole of nine seconds occurred. A peripheral pulse which had been palpable with each electrical beat ceased simultaneously, showing the presence of mechanical as well as electrical asystole. Portions of the tracings from this experiment are presented in figure 1. Heart sounds were audible, and femoral pulses were palpable with each ECG complex. Ventilation with oxygen was followed by recovery.

During lighter stages of anesthesia, the EEG showed the same changes as described for man by Courtin, Bickford and Faulconer. The electroencephalographic depth of anesthesia, however, could not be correlated with the extent of the circulatory depression. In
some cases severe circulatory depression was observed while the EEG indicated only level 3 (only moderate depth). In other cases, the EEG was severely depressed and circulation remained adequate.

The electroencephalogram during extremely deep anesthesia deviated beyond the scheme presented by Courtin, and associates. As anesthesia was deepened, the progression of the EEG through burst-suppression to an essentially flat tracing was seen. After this flat (seventh level) electroencephalogram had developed, activity returned. This reactivation appeared initially as low voltage fast frequency activity, not unlike the ‘file’ activity previously described. With further administration of ether, activity of 2–4 cycles per second appeared, and in some cases spike discharges developed. This activity in the delta range was replaced by alpha frequencies of 10–12 cycles per second, at 20–30 microvolts. This tracing exhibited progressively lower voltage until, with circulatory failure, the record became isoelectric (flat) again. There were transitional periods between these reactivation patterns during which either (1) activity of two types appeared together, or (2) the tracings became disorganized and revealed the presence of multiple frequencies. These transitional periods were likened to the transitions seen between the various levels described by Courtin. Figure 2 shows representative segments illustrating these changes. The patterns are labelled level 8, 9, 10 and 11, following the scheme established by Courtin, et al. The activity of these levels may be thus summarized:

**Level 8:** Low voltage fast frequency (file) activity appearing in the electroencephalogram which had been depressed to a flat line by ether anesthesia.

**Level 9:** 2–4 cycles per second delta activity developing, either associated with or replacing, the file activity of level 8.

**Table 1.** Order of Circulatory Changes Observed During Progressively Deepening Ether Anesthesia

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<th>First changes:</th>
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<td>1. Heart sounds become muffled or distant.</td>
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<td>2. Pulse in small peripheral arteries is lost.</td>
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<td>Intermediate changes:</td>
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<td>3. Blood pressure is unobtainable.</td>
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<td>4. ECG complexes deteriorate.</td>
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<td>Fatal changes:</td>
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<td>5. Heart sounds disappear.</td>
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<td>6. Pulse in large arteries is lost.</td>
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<td>7. ECG activity is lost.</td>
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**Fig. 2.** EEG pattern at deeper levels of ether anesthesia. Levels 6 and 7 are those described by Courtin, et al.
Level 10: Faster frequencies, in the alpha range, usually 10–12 c.p.s., replacing the delta activity in level 9.

Level 11: Complete loss of electrical activity.

Figure 2 also illustrates the difference between level 7 and level 11. Some baseline motion is present in level 7, while 11 is completely devoid of movement.

Reactivation to levels 8, 9, and 10 occurred only after severe circulatory depression. When the EEG showed reactivation, the pulse in the lingual artery and the blood pressure were either faint or not obtainable. The only mechanical evidences of circulation were pulse in the femoral artery and faintly audible heart sounds. Levels 10 and 11 were seen only preterminally, when the large artery pulsations were almost imperceptible.

Discussion

All the circulatory changes studied, except the change in heart tones, represent late results of excessive depth of anesthesia. Many other signs (respiratory, pupillary, muscle tone) can give better estimation of anesthetic depth in the clinical range. However, it is believed that, even though these results were obtained with dogs, circulatory monitoring has definite worth in clinical anesthetic practice. The information obtained from this type of monitoring is especially important in (1) poor risk patients, whose depth of anesthesia with a small amount of agent is expected to be greater than average; (2) patients having head and neck surgical procedures where usual signs of depth of anesthesia are not available to the anesthetist, and (3) patients in the prone position. The worth of circulatory monitoring can be increased by better understanding the responses of the circulation. These experiments point out such values.

The precordial stethoscope can give warning of circulatory impairment quite early, or it may be too late, depending on the attention of the listener. If the anesthetist has trained his ear to hear changes in the quality of the heart sounds, as first advocated by Rence, Cullen and Hamilton, the stethoscope can give early evidence of deepening anesthesia. If, however, he merely listens for the presence of sounds in an 'all or none' attitude, he loses much of the value of his monitor. When the heart sounds of the animals were gone, resuscitation without cardiac massage was impossible in most cases.

Palpation of the peripheral pulse has long been a part of routine anesthetic monitoring. These experiments indicate that palpation of a small vessel, such as the mandibular or temporal artery will alert the anesthetist to impending circulatory failure earlier than will palpation of larger vessels. In these experiments, when the femoral artery ceased to pulsate, the animal could not be resuscitated short of cardiac massage. In all cases, however, the lingual artery pulse became non-palpable while there was yet ample time for resuscitation by ventilation with oxygen.

The electrocardiogram proved to be of limited value in anticipating overdose of ether. Consistent change in the ECG complex occurred early in two cases, but appeared only as the animal approached death in the others. Absence of all electrical activity was a late occurrence. Monitoring devices triggered by the R-wave deflection, therefore, are of negligible value in warning of impending circulatory failure. Further, such devices may give a false sense of security by continuing to signal activity when in fact there is no circulation. Others have stressed this point.

Blood pressure was found to fall only in deep anesthesia, and when it fell, circulatory deficiency was far advanced. No justification is found, therefore, for using the blood pressure as a measure of depth of ether anesthesia.

It is interesting that 'file' activity has recently been reported following normothermic circulatory occlusion in the dog.

The inability to correlate EEG depth with circulatory depression comes as no surprise to clinicians who have employed the electroencephalograph. The EEG gives information concerning depression of activity of the central nervous system. The depression of other organ systems may not be of equal magnitude to central nervous system depression. In our experience, the several organ systems are usually not depressed to the same extent at any given time. The anesthetist must, therefore, give attention to each system separately, seldom relying on monitors of one system to give information about another system.
The reactivation of the electroencephalogram with extreme depth of anesthesia may be a phenomenon peculiar to dogs. It has not seemed desirable to attain such depth in man simply to test for this phenomenon. It is interesting that the "file" pattern seen during this reactivation is also seen in man after cardiac arrest, and after circulatory occlusion during hypothermia. Man is known to respond, under other extreme circumstances, with activity similar to that seen during reactivation in the dog. Since the earlier levels 3 through 7 were found to be similar in dog and man, it is reasonable to suppose that the reactivation would also occur in man.

Reference to the first tracing of figure 1 will reveal what little circulation is necessary for maintenance of the "reactivation" electroencephalogram. During four seconds of asystole, activity was maintained. Activity disappeared only during nine seconds of asystole, and return forty seconds after pulses returned.

In extremely deep anesthesia, failing circulation results in progressive cerebral ischemia, so it is suggested that this ischemia produced the reactivation the electrocortical changes which were observed. Further evidence implicating ischemia is the occurrence of spike potentials in some cases during reactivation. These spikes are probably electrical evidence of anoxic convulsions, the peripheral components of which were masked by the anesthesia.

Summary

Dogs were deeply anesthetized with ether and were artificially ventilated. Common clinical signs of circulation were observed. It was found consistently that qualitative changes in heart sounds were the first circulatory evidence of the presence of a profound depth of anesthesia. This may be of considerable clinical significance. With further depth, the pulsation of the lingual artery was lost, and shortly thereafter the blood pressure deteriorated. Pulses in the femoral artery, audible heart sounds, and electrocardiographic activity were late to disappear. When these three latter events were allowed to vanish, resuscitation without cardiac message was impossible.

A reactivation of the electroencephalogram was noted when circulation began to fail. This reactivation followed a fairly consistent pattern. It is hypothesized that this reactivation is the result of cerebral ischemia resulting from the failing circulation.

References