

ELECTROENCEPHALOGRAPHIC AND CIRCULATORY EFFECTS OF CHLOROFORM ANESTHESIA IN DOGS

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SIMILARITIES of electroencephalographic changes occurring during diethyl ether and cyclopropane anesthesia are evident from studies (1-7) of these agents. Electroencephalograms recorded during nitrous oxide (8-10), xenon (11-12) and thiopental (13-16) anesthesia indicate different sequential changes from those produced by ether and cyclopropane. It was our purpose to determine characteristic changes produced in the electroencephalogram of the dog during chloroform anesthesia. To complement the electroencephalographic recordings, observations were made of blood pressure, pulse rate and electrocardiogram. Animal experimentation allowed these studies during very profound anesthesia.

In 1890, von Marxow reported (18) that galvanometric deflections could be recorded from the cortex of animals before and after chloroform and ether anesthesia, and noted that the postanesthetic deflections were not changed from the preanesthetic. In 1931, Berger (19) recorded the electroencephalogram of two persons anesthetized with chloroform. One was anesthetized to surgical levels while the other reached only the excitement stage. During excitement, high voltage, 11 to 14 cycle per second activity was recorded. In light narcosis the tracing approached a straight line. With deepening of the anesthesia the tracing approached even closer to a straight line. With the exception of these reports, no observations on the electroencephalogram during administration of chloroform were found.

METHOD

Mongrel dogs were given subcutaneously 0.1 mg./kg. atropine sulfate, and then curarized by injection intravenously of 1 mg./kg. of *d*-tubocurarine chloride. They were then intubated orotracheally and ventilated with oxygen while electrodes were placed on the scalp 2 cm. from the midline on either side of the vertex. Other electrodes were placed on the forelimbs for recording lead I of the electrocardiogram.

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With local procaine anesthesia, a mercury manometer was connected to one femoral artery, and the other femoral artery cannulated for withdrawal of blood samples for chloroform determinations. Continuous electroencephalographic and electrocardiographic recordings were made on a Grass 2-channel electroencephalograph, and blood pressure was noted and recorded at intervals.

Blood samples for chloroform determinations were drawn at intervals into heparinized syringes, sealed, and analyzed chemically within four hours of the conclusion of the experiment. The method of determination used was that described by Morris, Frederickson and Orth (20), except that a Bausch & Lomb photoelectric colorimeter was substituted for the Evelyn colorimeter.

The animals were anesthetized with chloroform in oxygen delivered by a Foregger Copper Kettle apparatus. Controlled ventilation by manual compression of the rebreathing bag was used to insure adequate ventilation. The delivered chloroform was diluted by 2,500 cc. per minute of oxygen not passed through the kettle vaporizer. The anesthesia system used was a semiclosed circle with soda lime carbon dioxide absorber. The concentration of chloroform was progressively increased by small increments with about ten minutes allowed to elapse between each increment. Recordings were obtained during the anesthetization of 6 animals.

RESULTS

A reproducible sequence of changes was seen in the electroencephalogram with progressive increases in blood chloroform concentration. This sequence could be divided, on the basis of changes in frequency, voltage, and pattern, into 6 levels. Representative portions of the electroencephalogram of one animal are presented in figure 1. The segments shown were selected to illustrate the characteristics of each of the 6 levels.

Control.—The initial tracing is a portion of the electroencephalogram for the awake, alert animal. This record is characterized by low voltage, fast activity.

Level I.—Shortly after the onset of chloroform administration there appeared a period of electrical activity characterized by slower frequencies and higher voltages than were present in the control. Fast background activity persisted.

Level II.—The electroencephalogram at this level was characterized by a return of low voltage, fast activity. This type of change may be considered an "alerting response."

Level III.—Frequencies in the beta range suddenly appeared giving a characteristic form to this level. The activity generally ranged from 20 to 30 cycles per second. The sudden appearance of this beta activity is in contrast to the more gradual transitions between other levels.

Level IV.—Entrance of delta activity determined the beginning of this level. The beta frequency of level III continued, while the delta frequency became progressively better organized and more prominent. The delta activity showed a slow but progressive increase in voltage throughout this level.

Level V.—As abruptly as it entered, the beta activity ceased, thus initiating level V. The slow delta activity was left as the dominant frequency. During this period, there was a variable and irregular amount of activity in the faster theta range.

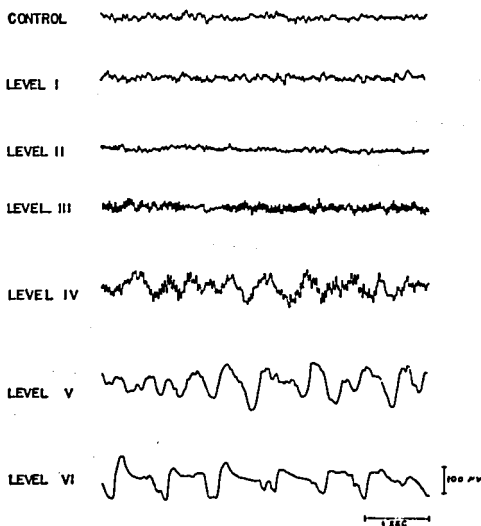


FIG. 1. Characteristic electroencephalographic changes during increasing concentrations of chloroform in blood.

Level VI.—A progressive decrease in the amplitude of delta waves characterized this level. Fewer theta waves were present than were seen in level V.

With further increase in the blood chloroform concentration, the electroencephalogram became essentially flat and if allowed to continue at this level, the animal could not be revived.

The progression of changes described apply to the electroencephalograms of all the animals. The degree of change in frequency and voltage in levels I and II, however, varied appreciably for the different animals. The described frequency and voltage characteristics of levels

III, IV, and V were similar in all cases. In the tracings of half of the animals studied, there was also noted in level VI a tendency toward an increase in the slope of the ascending portion of the delta waves as their amplitudes decreased.

Progressive reduction of the blood chloroform concentration likewise produced a constant sequence of electroencephalographic changes. The patterns seen during increasing concentrations appeared in reverse order as the chloroform was removed from the animal by ventilation with oxygen. From an electroencephalographic tracing characteristic of level VI, lightening of anesthesia brought return of the delta activity of level V, after which the beta frequencies of level IV were superimposed. The delta waves disappeared completely leaving only the fast beta waves of level III. Finally, the beta waves were replaced by the mixed frequencies seen in levels I and II.

TABLE 1

BLOOD CHLOROFORM CONCENTRATIONS AT APPEARANCE OF ELECTROENCEPHALOGRAPHIC LEVEL IV IN EACH EXPERIMENT

Animal	Milligrams Per Cent Chloroform
A	12-15
B	8
C	34-42
D	52
E	20-25
F	19-26

While the electroencephalographic levels appeared in each experiment as blood chloroform concentration was increased, the absolute concentration of blood chloroform at which an electroencephalographic level was attained varied considerably in different animals. Table 1 illustrates the ranges in blood chloroform concentration at which electroencephalographic level IV first appeared in each experiment. A similar variation in blood chloroform concentration was found associated with the other electroencephalographic levels in the different experiments. However, for a given animal, the relationship between blood chloroform concentration and electroencephalographic level was consistent. To establish this, anesthesia was progressively deepened, lightened, and deepened again. Electroencephalographic levels were seen to appear with comparable blood chloroform concentrations regardless of how this concentration of chloroform was reached. This is illustrated in figures 2 and 3 by comparing electroencephalographic level with the blood chloroform concentration.

Figure 2 represents the reciprocal relationship between blood chloroform levels and blood pressure. The electroencephalographic levels as described for figure 1 are indicated numerically. The reciprocal relationship shown in this figure for one animal was observed during each experiment. Pulse rate is depicted to show the tendency noted in all

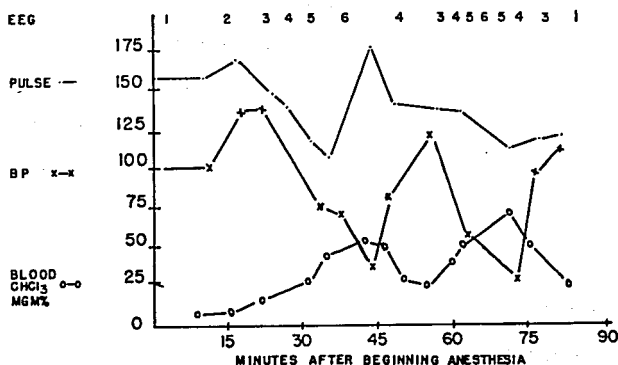


FIG. 2. Electroencephalographic, pulse and blood pressure changes with variations in the blood chloroform concentration.

animals toward initial tachycardia followed by a relative bradycardia as chloroform levels were increased.

Figure 3 shows typical electrocardiographic complexes recorded during the course of one experiment. Blood chloroform and electroencephalographic levels are shown for purposes of correlation with the electrocardiographic changes. Inversion of the T wave was seen in one animal, and ST-segment depression was present in 4. One animal showed an increase in T-wave depression with sharpening of the wave. P-wave changes were consistent in all animals. With increasing blood chloroform concentrations, the P wave became progressively higher in voltage. The voltage of the P wave in one instance approached that of the R wave. There was, however, no appreciable or consistent change in the PR interval.

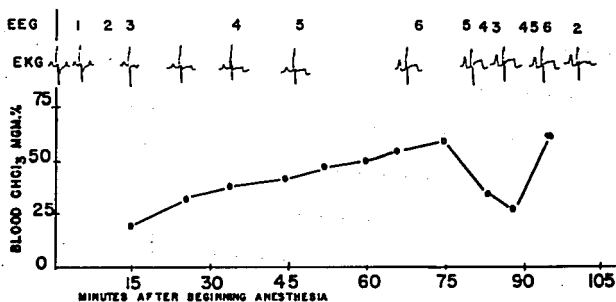


FIG. 3. Electrocardiographic changes during chloroform anesthesia.

The origin of the cardiac impulse remained at the sinoauricular node in all cases until the animal became terminal. There was no evidence of shift of the pacemaker to a lower point. Extrasystoles of either ventricular or auricular origin were seen in only 2 cases. In one, irregular complexes appeared when the animal was given a noxious stimulus in light anesthesia. In another, occasional ventricular extrasystoles were dispersed sporadically throughout the tracing, both before and during chloroform anesthesia. These did not become more frequent with increased blood chloroform concentrations, nor did their form change.

The QRS complexes remained quite stable, both in configuration and voltage, until the animal became terminal. QRS changes were seen in one animal and consisted only of diminished voltage of the Q wave. Thus, there was no evidence of disturbance of the ventricular electrical mechanism until extremely deep anesthesia.

The terminal electrocardiogram showed bizarre patterns which gradually decreased in total voltage until the tracing became flat. There was no peripheral blood pressure at the time the complexes deteriorated. Rate of impulse formation was reduced, and the last few complexes appeared at intervals of two or more seconds. Even at this level of chloroform depression, there was no evidence of cardiac fibrillation.

The various electrocardiographic changes mentioned were scattered at random through the several animals observed without predilection for any one.

The electrocardiogram improved but did not revert to normal with lowering of the blood chloroform level and return of the blood pressure to preanesthetic levels. The T wave in one instance remained inverted after anesthesia was lightened, and P-wave changes persisted in another animal. The trend toward recovery, however, was prominent.

DISCUSSION

Several considerations present themselves in reviewing the electroencephalographic records of these experiments. There would appear to be a consistent change in the cerebral electrical activity occasioned by exposure to chloroform, and this activity appears to have a consistent relationship, in a given animal, with the blood level of chloroform regardless of the direction of the change in that level. Thus, a pattern appearing during induction at one blood chloroform level reappeared at a similar blood chloroform level during emergence. This is contrary to the results reported with cyclopropane by Rubin and Freeman (6) where different sequences of electroencephalographic events occurred during induction and emergence. However, the electroencephalogram during emergence from ether was reported by Courtin, Bickford, and Faulconer (2) to mirror the electroencephalogram of induction.

There is considerable individual variation in the blood chloroform level at which the electroencephalographic levels appear. This is believed due to individual dose response relationships. A wide individual variation in blood ether concentrations was also reported by Faulconer (3) using nitrous oxide and ether.

There also appears a close correlation between the blood chloroform levels described by Morris, Frederickson, and Orth (20) as being representative of surgical anesthesia in the dog and the appearance of well organized beta activity of levels III and IV in the electroencephalogram.

Level II may represent the excitement stage of anesthesia. In these experiments, spontaneous motor activity was masked by curarization. One animal, however, was incompletely curarized and showed motor activity during this phase of the experiment. The muscle artefact from the motor activity so marred the electroencephalogram that it became necessary to paralyze the animal more completely with curare. This having been accomplished, the electroencephalogram progressed from level II to level III.

The electroencephalogram seen during deep anesthesia with chloroform was not like that reported with deep ether and cyclopropane anesthesia. There was no evidence of burst-suppression as reported in man by Courtin, Bickford, and Faulconer (2) and in the dog by Clowes and associates (17) for ether, and by Possati and associates (5) for cyclopropane in man. With chloroform, the predominant delta pattern continued without interruption. When, terminally, the tracing became essentially flat, there were no periods of activity to compare with the bursts recorded during ether and cyclopropane anesthesia.

The similarity of the prominent beta frequencies noted with chloroform to the fast activity of thiopental (13, 14, 15), and ether analgesia (4) in man was striking. The fast frequencies of both thiopental and ether appear before loss of consciousness and onset of surgical anesthesia. During chloroform anesthesia in dogs, however, the beta frequencies appeared with blood chloroform levels associated with loss of consciousness and surgical anesthesia (20). Species difference cannot be ruled out; and must be considered before final conclusions are made.

Cardiac irregularities were infrequently seen. This observation was consistent with the statements of Orth, Liebenow and Capps (21).

Blood pressure appeared to be inversely related to blood chloroform level and relatively unrelated to duration of anesthesia. Severe hypotension could be produced regularly by increasing the blood chloroform concentrations. Ventilation with oxygen could return the blood pressure to normal ranges. These effects could be produced either early or late in the course of the anesthesia.

The T-wave changes seen in the electrocardiogram were indicative of myocardial depression. One might speculate that cardiac ischemia produced by blood pressure fall, as well as the presence of chloroform

in the blood, contributed to these changes. The mechanism underlying the high voltage P waves is not understood. Similar P-wave changes were present in the electrocardiographic tracing used for illustration by Orth and associates (21), but apparently were not considered significant.

SUMMARY

Dogs were anesthetized with chloroform-oxygen, and continuous electroencephalographic, electrocardiographic, and blood pressure readings were obtained. Arterial blood samples were drawn periodically for the determination of chloroform levels.

Electroencephalographic patterns were classified into levels on the basis of frequency, voltage, and pattern. Correlations were made between these electroencephalographic levels and blood chloroform levels. In surgical anesthesia, as defined by blood chloroform concentration, the electroencephalographic pattern was characterized by 25-30 per second beta activity (which initially appeared abruptly and usually also disappeared in the same fashion) with gradually increasing 2-3 per second delta activity. Other electroencephalographic levels appeared to correlate well with blood concentrations of chloroform above and below the surgical level for a particular animal. At comparable blood concentrations during either increasing or decreasing blood concentrations of chloroform, the electroencephalographic patterns were quite similar.

Blood pressure fluctuated inversely with blood chloroform concentration. Electrocardiographic activity and pulse were less clearly correlated. Cardiac electrical activity was maintained rhythmically in deep anesthesia, even after cerebral electrical activity and blood pressure had disappeared.

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