ELECTRO-ENCEPHALOGRAPHIC PATTERNS PRODUCED BY THIOPENTAL SODIUM DURING SURGICAL OPERATIONS: DESCRIPTION AND CLASSIFICATION

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It is known from studies on animals (Bickford, 1950) that thiopental (Pentothal) sodium anaesthesia produces characteristic changes in the brain-wave pattern in relation to the depth of anaesthesia. In man, Brazier has demonstrated that a similar relationship holds for the early stages of anaesthesia. The object of our investigation was to study the brain-wave patterns under the practical conditions of the operating room and at a depth beyond that which was achieved under experimental conditions by Brazier. An attempt has been made to classify the electro-encephalographic (EEG) changes in relation to deepening thiopental anaesthesia in a manner analogous to that of Courtin, Bickford and Faulconer (1950) for ether so as to produce a scale of anaesthetic depth that might be of practical value to the clinical anaesthetist.

The need for such a guide to depth is actually greater than in the case of ether anaesthesia because (1) clinical signs of depth in barbiturate anaesthesia are indefinite and (2) when barbiturate anaesthesia is used in combination with curare the most reliable sign, respiratory activity, is invalidated. The subjects, who agreed to have this study made, were patients undergoing surgical treatment for varicose veins of the legs.
Preliminary investigations of different areas of the cortex revealed that the characteristic rhythms produced by thiopental were present in all parts of the cortex. It was therefore decided to confine this study to the observations of changes in one area only.

**APPARATUS**

A two-channel ink-writing oscillograph was used and recording was made on one channel only. The high and low frequency filters were set to give approximately 50 per cent cut off at 0.75 cycle and at 45 cycles, while the response fell by 90 per cent at 0.4 cycle and 80 cycles respectively.

The second channel was not used for this study. Respiratory minute volume was registered by means of a volume-displacement gas meter connected in series in the breathing circuit and designed to operate an electro-mechanical ink-writing signal by opening and closing a dry battery circuit during the passage of each 500 ml. through the meter.

The electro-encephalographic electrodes were of the needle variety and provided with screened leads. Frontal and occipital leads were used. The frontal lead was placed over the frontal prominence about 1 inch from the midline and the occipital lead was placed directly behind, about 1/4 inches anterior to the occipital protuberance. A ground lead was attached over the mastoid process. In the early stages of the investigation troublesome interference from diathermy and other electrical apparatus was encountered. In an attempt to overcome this difficulty the technic suggested by Prast (1948) of introducing 50,000 ohm resistors in the grid leads of the input tubes of the amplifier was used successfully.
MATERIAL AND PROCEDURE

A total of 65 records was made on 24 and 41 female subjects whose ages ranged from 14 to 74 years (average 47). Recordings were, in all cases, taken from the immediate pre-anesthesia period and continued in most instances until the completion of the operation. In 3 cases recordings were continued into the recovery period. Patients were given $ grain (11 mg.) of morphine sulphate and 1/150 grain (0.43 mg.) of atrophine sulphate one or two minutes before induction of anaesthesia by the intravenous route.

The operation performed was the same in all cases and was a stripping procedure applied to the greater saphenous veins in one or both legs. Multiple incisions of the skin made during the operation provided adequate opportunities of studying the effects produced in the patient by this intense peripheral stimulation.

The actual procedure of stripping a vein requires a deep level of thiopental anaesthesia as the operation has been known to initiate laryngeal spasm when performed if the patient is carried at light levels. During the early part of this investigation one case of laryngeal spasm of short duration was encountered; its occurrence was attributed to inexperience in the use of the method. An oropharyngeal airway was used in all cases.

Anaesthesia was induced and maintained with 2.5 per cent solution of thiopental sodium. A continuous supply of oxygen was maintained throughout.

DESCRIPTION OF EEG CHANGES

Statements regarding frequencies are based on studies made with the Grey Walter frequency analyser. The first noticeable effect of thiopental sodium on the EEG is a break up of the resting rhythm into a fast spiky pattern of
greatly increased voltage. The predominant frequencies of this pattern lie between 20 and 30 cycles per second. This effect is seen very early in the administration; it may be expected to appear within one minute of injecting as little as 50 mg. of the drug and corresponds to the changes reported by Brazier and Finesinger (1945). Increasing dosage increases the overall amplitude of the pattern without altering the frequency during this phase. In the early stages the subject is awake but feels drowsy and euphoric. The exact moment at which he loses contact with the environment varies from patient to patient, and up to a point seems to depend on the strength of his effort to maintain consciousness. It is not constantly characterized by any special change in the pattern and may occur before the appearance of the slower wave forms to be described next.

The appearance of the slower waves was not found to coincide with loss of consciousness in all cases as was previously stated by Finesinger and co-workers (1947) and Tucci and co-workers (1949). Conditions of recording may explain this difference. After consciousness is lost, as evidenced by either cessation of counting or failure to respond to the spoken command, the eyelash reflex and eyelid tone remain active and a brisk withdrawal reaction is evinced in response to painful stimulation of the skin. As reflex activity becomes more sluggish and consciousness is lost or greatly dulled, the pattern begins to take on a different appearance due to the admixture of slower frequency components and often a further increase in amplitude over the preceding pattern. The slower waves vary greatly in frequency from 1 per second to 5 to 7 per second and show a correspondingly varied amplitude. As anaesthesia progresses so does the tendency to slowing of the waves. Superimposed on and intermingled with the slow
waves is a well-marked faster activity that approximates 10 cycles per second. This stage gives way to the next which is marked by a significant change consisting of an inhibition of electrical activity for periods which are short at first but later come to dominate the record, so that short complexes may appear isolated by many seconds of relative cortical inactivity. As administration of the drug is continued the periods of inactivity become longer and the amplitude of the isolated complexes smaller.

CLASSIFICATION OF EEG PATTERNS

First Pattern (Fast). This pattern is characterized by high-amplitude, fast spiky activity of mixed frequencies varying between 10 and 30 cycles per second with the predominant frequency near 20 cycles per second. The amplitude varies greatly; short runs of two, three, or more waves with an amplitude between 75 and 80 microvolts are characteristically preceded and followed by similar runs of lower amplitude; single elements of either of these groups are interspersed in a random manner at frequent intervals. This pattern is demonstrated in the tracing marked “first” in figure 1.

Second Pattern (Complex). This pattern is a complex of many frequencies but differs from the preceding because of the presence of predominantly slower wave forms of very irregular contour and random occurrence. The range of their frequency variation is wide as can be seen in the tracing marked “second” in figure 1, where the slowest waves occupy a time interval of nearly two seconds. There is also much variation in voltage, the larger and predominating waves representing close to 150 microvolts. Superimposed on these slower waves and occupying the intervals between them is a much faster activity rather
First Pattern. This is characterized by a high-voltage spike. The amplitude is comparable to that seen in the first pattern.

Third Pattern. This is characterized by a progressive suppression of cortical activity taking the form of short periods of relative quiescence that separate groups or bursts of waves. These bursts are frequently made up of two distinct elements. The first appears abruptly and consists of a short series of high-voltage waves of a frequency usually found to be near 10 cycles per second and continuing for about one second; the second element follows immediately after the first.
in the form of two or more slow waves at a frequency of near 2 per second and tailing off into the next suppression phase. In other instances the burst may have no slow-wave component or the fast element is superimposed on the slow waves. The complexes in the tracing marked “third” in figure 1 all show a slow-wave component. The whole complex occupies a time interval of two or more seconds. As there is a tendency to regular discharge, further classification is made on the basis of the duration of the periods of inactivity. This pattern is defined as one in which the intervals are recognizable but do not exceed three seconds in length.

**Fourth Pattern.** The difference between this and the preceding pattern is in the duration of the periods of cortical inactivity which are defined as lasting between three and ten seconds. The amplitude of the waves in the periods of activity may be slightly less than in the previous level but the frequency characteristics remain unaltered.

**Fifth Pattern.** In this pattern periods of inactivity do not appear more frequently than once every ten seconds and there is further reduction in the amplitude of the components which may, for all components, fall below 25 microvolts. The frequency of the waves is the same as that found in the active phases of the preceding pattern.

During the transition from one pattern to another there is usually a mixture of the characteristic frequencies of both patterns. This is especially noticeable in the persistence of fast waves in the second pattern, and in fact an activity of 10 cycles per second or faster can be followed through into the fifth pattern where it makes up part of the active elements.

Many of our patients were carried at a level of anaesthesia that was too light to bring up the full range of
patterns described; yet in all our records the sequence in which the changes occurred as anaesthesia became deeper or lighter was observed to be the same.

EFFECT OF CURARE

To determine whether the intravenous administration of curare produced a change in the EEG pattern during thiopental anaesthesia the following procedure was carried out on 7 patients. When the intermittent dosage of thiopental required to maintain an even level of anaesthesia and a constant EEG pattern was determined for the patient, d-tubocurarine chloride was given in divided doses while the administration of thiopental was continued at the predetermined rate. When the patient was curarized to the extent of reducing his respiratory minute volume by 50 per cent or more the administration of curare was discontinued. In no case was any change in the EEG pattern produced in this manner. Figure 2 shows cuttings from the

Fig. 2.
Electro-encephalographic patterns during thiopental anaesthesia showing absence of any change in response to curarization.
record of such a case. The first tracing was recorded just before the administration of curare, at which time the respiratory minute volume was 9 litres. The second tracing was recorded during the period of curarization, the spontaneous respiratory minute volume having fallen to 2.5 litres. The third recording was made some eighteen minutes later when the respiratory minute volume had returned to 9 litres. If curarization is prolonged without compensation for respiratory depression being made by aiding respiration one would expect changes characteristic of hypercapnia and anoxia to appear in the EEG. This condition was avoided in the present investigation.

In patients followed to recovery of consciousness the changes seen were, as was observed by Brazier (Brazier et al., 1945), less clear-cut although they mirrored fairly closely those seen during induction as regards frequency and pattern form; less evidence of alteration in voltage was noticed and the initial great increase and subsequent fall from the late first pattern to the late second pattern was not seen when the changes were observed taking place during recovery.

RELATION OF EEG PATTERN TO CLINICAL SIGNS

It is not proposed to try to correlate rigidly the electro-encephalographic changes described with detailed observations of clinical signs of anaesthesia as it is known that these signs in themselves are inconstant; however, it has been possible to make some generalizations in this respect.

During the period of the first pattern, consciousness, though dulled, is retained in the early phases. The eyelash reflex or response of the eyelid to gentle stroking of the lashes is brisk; there is no loss of eyelid tone, and muscular
reaction to painful stimulation is quick and purposeful. As this stage advances and usually before the appearance of the slow waves characterizing the next stage, consciousness is lost, the patient if counting will cease to do so, or he will fail to respond to a spoken question or command. Occasionally he will continue to count for a short period of time, if prompted, even after the appearance of the second pattern.

The second pattern is accompanied by the loss of consciousness and reduced reflex activity; the withdrawal reaction to painful stimuli is abolished; the eyeballs become centred and immobile; eyelid tone and eyelash reflex are lost, the reflex disappearing before all eyelid tone is gone; and the pupil reaction to light remains brisk. This stage is usually accompanied by a slight fall in blood pressure and there may be some depression of respiration. When the pattern is well established the majority of patients will tolerate the placing of skin clips, incision of the skin, retraction of the edges of a wound and the introduction of the pharyngeal airway. Late in this stage, but before the onset of pattern 3, stripping of veins can be carried out without fear of initiating laryngeal spasm or any sign suggesting intolerance of this interference.

As the third pattern appears, reduction of respiratory minute volume becomes more marked. This respiratory depression increases progressively through the fourth and fifth patterns and during the latter it may be necessary to aid the respirations. The pupil has been found to retain its reaction to light throughout all stages observed; its size will have been influenced by the morphine administered before anaesthesia, which tends to produce myosis. Mydriasis was not recorded in any case at any period of anaesthesia. The type of operation performed did not permit the making of any observations on abdominal relaxation.
When operations requiring considerable muscular relaxation are performed under thiopental anaesthesia, recourse is made to the use of the curare-like drugs in order to obtain the desired relaxation. Such drugs have a potent depressive effect on respiratory movements and so render the observations of these movements unreliable as a guide to depth of thiopental anaesthesia; thus, as noted in the introduction to this paper, one is deprived of the most reliable sign. Under such circumstances reference to the EEG pattern should prove to be of real value since it allows the depth of anaesthesia to be assessed in the presence of curare.

In considering the value of clinical signs in thiopental anaesthesia Adams (1944) noted that a certain sign denoting adequate anaesthesia may be unreliable in one case and not in another. Although it is not claimed that in 100 per cent of cases EEG changes alone can tell whether a patient will tolerate an incision of the skin (which is usually the most acutely painful stimulus during any operation), observation and interpretation of such changes as an index of anaesthetic depth have proved of greater value than any other single sign we have observed.

SUMMARY

Electro-encephalographic recordings were made in the operating room on 65 patients undergoing thiopental (Pentothal) anaesthesia. The changes in frequency and amplitude that occurred during anaesthesia are described. They are classified into five distinct patterns representing progressively deepening levels of anaesthesia. An effort is made to correlate these patterns with commonly observed clinical signs denoting anaesthetic depth. Curare was found to produce no alterations in the electro-encephalographic pattern during thiopental anaesthesia. It is therefore felt
that when a combination of these agents is used, observation
and interpretation of the electro-encephalogram is a most
valuable index of anaesthetic depth.

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