AUTOMATIC ELECTRO-ENCEPHALOGRAPHIC CONTROL OF THIOPENTAL ANESTHESIA *

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IT has been recognized for many years that anesthetic agents produce noticeable changes in the electric potentials recorded from the brain or the scalp of both animals and humans. That such changes in humans might prove of practical value in anesthesiology is suggested by the report of Courtin and two of us (Bickford and Faulconer) (1). Working with an electro-encephalographic apparatus especially designed and constructed for use in the operating room, these authors studied electro-encephalograms of patients undergoing operations who were anesthetized with ether. They made a classification of the electro-encephalographic changes observed during different depths of anesthesia and provided an estimate of the reliability of such a scale of changes as an index of the depth of anesthesia. In this way, visual monitoring of the electro-encephalogram during operation became accepted by them as of practical value to anesthesiologists.

During these observations, they noted that the summation of the output of energy of the brain as indicated by electro-encephalographic tracings showed characteristic changes when the dose of the anesthetic agent was increased. The significant changes were an initial rapid increase in output of energy, representing a stimulatory effect of the anesthetic agent, followed by gradual and progressive decrease in output until final extinction of recordable activity occurred in extremely deep stages of anesthesia. The fact that the useful clinical range of anesthesia varied between the peak of this curve and its base suggested that this measure of energy might be used as a direct index of the depth of anesthesia and might furthermore be harnessed to control automatically the amount of anesthetic drug reaching the patient.

The practical aspects of this problem were explored by one of us

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(Bickford) (2), who designed and built a machine for the automatic delivery of anesthetic agents by means of which it was possible to keep animals in a state of anesthesia for several days without the necessity for adjustment of the apparatus. This was achieved through the use of an electronic integrating circuit that rectified the amplified cerebral potentials recorded from the scalp of the anesthetized animal and converted them into mechanical energy which in turn was used to operate a pump designed to deliver the anesthetic agent. Successful clinical application of this method to the automatic control of ether anesthesia

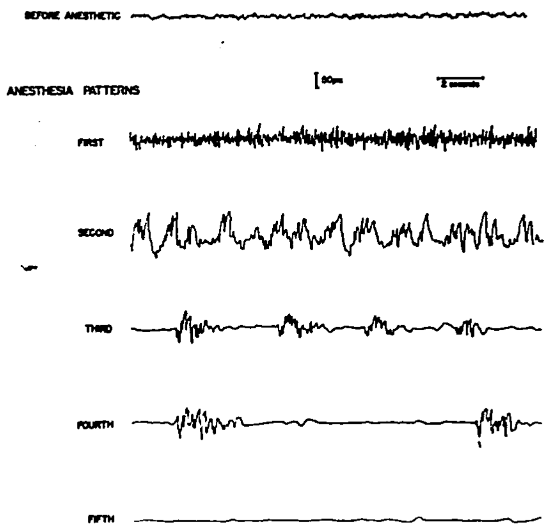

FIG. 1. Electro-encephalographic patterns during pentothal® sodium anesthesia. The first and second patterns are seen commonly during light and deep clinical levels of anesthesia respectively. The third, fourth and fifth patterns occur during excessively deep anesthesia.

in patients undergoing surgical operations was reported subsequently by Soltero and two of us (Faulconer and Bickford) (3).

The present study deals with the feasibility of automatic control of thiopental sodium (pentothal® sodium) anesthesia by use of a technique similar to that of Soltero and associates and the evaluation of the usefulness of such a system in the presence of nitrous oxide and the muscular relaxing agent *d*-tubocurarine chloride.

After investigation in the operating room, a classification analogous to that made by Courtin and associates for ether was made for pentothal sodium (4), in which electro-encephalographic changes corresponding to different depths of anesthesia with pentothal sodium were described (fig. 1). From this study and from observations made on animals, it was revealed that certain modifications in the integrator system used by Soltero and associates would be necessary for its satisfactory conversion to automatic control of anesthesia with pentothal sodium. These modifications were necessary because the signals obtained from the scalp are smaller and the frequency of their fluctuations

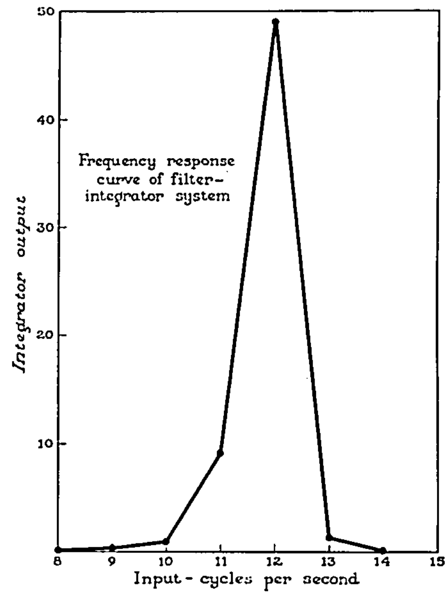

FIG. 2. Exaggerated response of the filter-integrator system to components of the total cerebral waves having frequencies centered about 12 cycles per second.

in potential is greater with pentothal sodium than with ether. Thus, the greater degree of amplification and the higher frequency response required from the apparatus rendered it more susceptible to disturbance by extraneous electric fields. Similar difficulties were encountered by one of us (Bickford) (5) in perfecting an automatic control system for use in animals and were overcome by restriction of the frequency band of cerebral potentials used for control purposes to a region lying outside the common range of interference. It was decided to adopt this technique to improve the reliability of the apparatus used in these clinical trials.

DESCRIPTION OF INSTRUMENT

Studies with the Walter harmonic analyzer revealed that from among the complex of electric potentials recorded from the scalp during pentothal sodium anesthesia a frequency component which was close to 12 cycles per second varied sufficiently in amplitude from light to deep anesthesia to reflect these changes in depth. It was thought that if the narrow band of frequencies in this range was selected for automatic control of anesthesia, the delivery of the anesthetic agent would not be influenced by extraneous interference. This selective

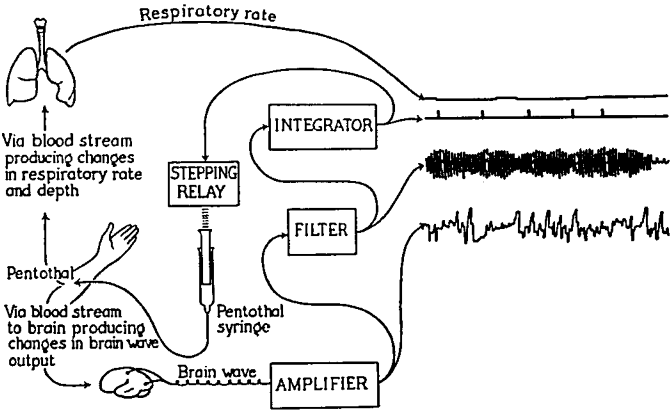

FIG. 3. Sketch showing mode of action of the automatic pentothal® sodium administrator.

process was achieved by use of a filter circuit that had a sharp peak at 12 cycles per second (fig. 2).

The general arrangement of the apparatus used in this study is shown in figure 3. Electric potentials from the brain are picked up through needle electrodes attached to the scalp and are carried by screened leads to an electro-encephalographic amplifier. The output from the amplifier, which represents the total range of frequencies of the cerebral potentials under the conditions of recording at the time, is fed into the filter circuit, which accepts only the previously mentioned narrow band of frequencies close to 12 cycles per second for transmission to the integrator. The latter is an electronic device capable of converting the summated amplitude of received waves into a series of electric pulses by means of charging and discharging a condenser. When fully charged, by the continually received signal, the condenser discharges automatically, sending out an electric pulse. The rate at which this takes place depends on the amplitude of the signals reaching the integrator circuit; if the amplitude is great, charging and discharging occur at rapid intervals, whereas if it is small, the cycle is proportionately slower.

The electric pulses from the integrator are transmitted to a stepping relay that responds to each pulse by a slight rotation of a threaded shaft, which in turn advances the plunger of a syringe containing pentothal sodium, thus delivering the anesthetic drug to the patient. As the anesthetic agent reaches the brain, the electric activity of this organ is reduced and less energy becomes available for operation of the stepping relay; as a consequence, the rate of delivery of the agent is slowed. The system soon establishes a state of equilibrium. On the extreme right of the diagram in figure 3 are shown the various tracings that monitor the operation of the machine and provide a continuous electroencephalogram and recording of the ventilation rate. The outputs of the amplifier, the filter and the integrator, together with the ventilation rate, are each represented by a separate pen writer. In adapting the stepping relay to the purpose described, a 100 cc. Luer-Lok syringe was employed, together with a 6 foot (183-cm.) length of narrow-bore rubber tubing. With this syringe, it was found that 1 cc. of pentothal sodium was injected for each 13 pulses of the stepping relay. The amplifier was of conventional design. A 5 stage push-pull condenser-coupled ink-writing oscillograph was used. The frequency response of this instrument was linear between 1 and 30 cycles per second. High-frequency filters were incorporated to eliminate electric transients.

Material and Procedure

Recordings were made in 39 cases by means of this apparatus; anesthesia was administered automatically in 20 of these cases. The surgical operations in all cases consisted of stripping the greater or lesser saphenous vein of one or both legs. The average duration of the operations in this series was 1 hour and 28 minutes. A solution containing 25 mg. of pentothal sodium per cubic centimeter was used throughout. Induction of anesthesia was preceded by the intravenous administration of 1/150 grain (0.43 mg.) of atropine sulfate and 1/6 grain (10 mg.) of morphine sulfate. A continuous supply of oxygen was maintained and carbon dioxide was absorbed from the circuit.

During the time employed by the surgeon in preparing and draping the site of operation, two needle electrodes were placed in the superficial layers of the patient's scalp. An anterior electrode was placed well up on the frontal prominence or just behind the hair margin 1 inch (2.5 cm.) from the midline; a posterior electrode was placed 3 to

4 inches (7.6 to 10.2 cm.) directly behind this, on the same side of the head. A ground electrode was attached over the mastoid process and recording of the electro-encephalogram was then started.

The expected rate of delivery of pentothal sodium could be varied by adjustments made at one of several points in the apparatus. The gain control of the amplifier was variable, as was the sensitivity of response of the filter circuit. Changes in either of these influence the amplitude of the output from the filter. In order to obtain maximal

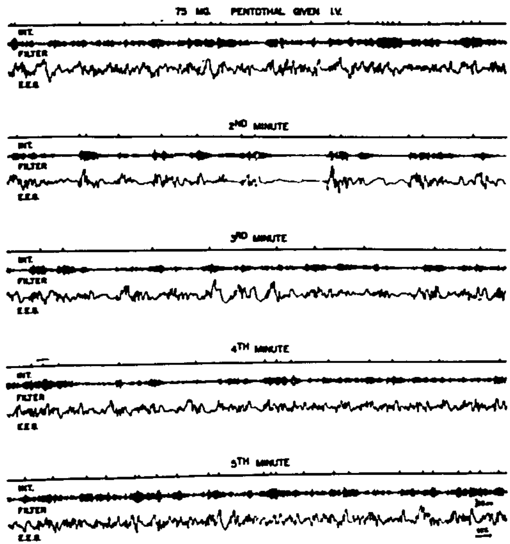

FIG. 4. Ability of the automatic pentothal® sodium administrator to compensate for outside interference. In this instance, 75 mg. of pentothal sodium was added to the amount normally injected by the instrument. The rate of administration governed by the cerebral waves (INT.) was slowed sufficiently during the next 4 minutes to allow restoration of the original rate of administration.

uniformity of conditions of recording and rates of administration of the anesthetic agent within this series, the only adjustments made in most instances were of the gain control of the amplifier. With experience this could be preset to approximate the required depth though subsequent adjustments might sometimes be required.

A 20 gauge hypodermic needle was introduced into a vein in the right hand or arm and the premedicant drugs were administered intravenously. A Y piece was attached between the hub of the needle and the tubing leading from the large syringe containing pentothal sodium, which was mounted on the machine. This allowed use of a second length of tubing fastened to a 20 cc. syringe from which the initial injection of pentothal sodium was made for induction. If desirable, administration of additional quantities of anesthetic agent during the remainder of the procedure could be done from this syringe. In order that each syringe might be used independently of the other and to prevent the communication of blood or pentothal sodium between them, a stopcock was provided for each length of tubing. For induction, the stopcock on the tubing from the main reservoir was closed and sufficient pentothal sodium was administered from the 20 cc. syringe

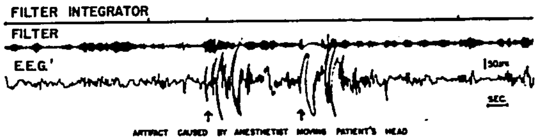

FIG. 5. Freedom of filter system from interference. Exaggerated activity in the unfiltered electro-encephalogram, introduced purposely by moving the patient's head, was virtually eliminated from the filtered output that drives the integrator. In this manner, such artifacts are prevented from significantly influencing the rate of administration of pentothal® sodium.

to establish the desired level of anesthesia. The accompanying electro-encephalographic activity was then usually sufficient to provide for continued automatic administration of the agent when the stopcock from the main reservoir of pentothal sodium was opened.

RESULTS

The apparatus was found capable of maintaining a constant level of anesthesia and of possessing compensatory properties against outside interference. The latter property is illustrated in figure 4. Five consecutive minutes of automatically controlled anesthesia are represented; interference with the automatic control was occasioned by the manual injection of 75 mg. of pentothal sodium toward the end of the first minute. A change in the level of anesthesia was produced which was reflected by a change in the electro-encephalographic pattern, resulting in a slower rate of discharge of impulses from the integrator. In the third minute, this rate fell to less than half of its value in the first minute, but during the fifth minute it returned to approximately its original value; in consequence, the automatic delivery of pentothal sodium became re-established at the rate of delivery obtaining before the interference took place.

Gross electric disturbances reached the amplifier during the making of the record illustrated in figure 5; however, the integrator-filter sys-

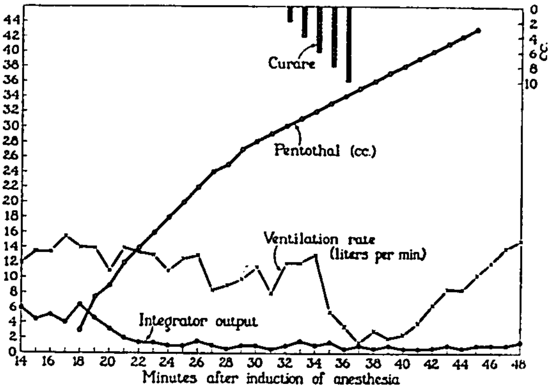

FIG. 6. Lack of effect of curare on the rate of administration of pentothal® sodium governed by the cerebral waves. An amount of curare sufficient to produce a great decrease in ventilation rate failed to produce a significant effect on the rate of administration of pentothal sodium.

tem maintained its stability and prevented the disturbance from causing an increase in the rate of injection of pentothal sodium.

The stability of the apparatus in operation was tested repeatedly in the case of patients who received *d*-tubocurarine chloride and was found to be undisturbed by use of this agent. Sufficient amounts of *d*-tubocurarine chloride were given to 1 patient to reduce the ventilation rate by more than 50 per cent (fig. 6). However, the integrator output remained steady.

COMMENT

The limitations in the earlier system of automatic anesthesia, which makes use only of the summated value of the cortical potentials, arise mainly from the fact that the amplifiers themselves are subject to disturbance from electric signals other than those arising from the brain. Low-frequency disturbances (from 0.5 to 3 cycles per second) arise from movements of the electrodes on the scalp or the movement of statically charged objects. High frequency interference (60 cycles per second) commonly is due to radiation from diathermy machines or other electrically operated devices used in the operating rooms or nearby. The method described in this report is less subject to disturbances from outside interference than is the original method.

The expense of the apparatus and the special knowledge and skill required for its maintenance and operation necessarily hamper acceptance of this technique for the administration of anesthetic agents. Nevertheless, it has been demonstrated that it is clinically feasible to employ electronic control of anesthesia. Further developments and refinements in instrumentation are being directed toward a reduction of the bulk of the apparatus and the time required for setting it up for operation. The most likely field of application of this method in clinical anesthesia is in regulation of the dose of anesthetic agents when used in the presence of relaxant drugs such as curare.

SUMMARY

A logical sequence to the development of automatically controlled anesthesia with ether is the extension of the clinical investigation to include pentothal sodium anesthesia.

An apparatus was designed and built that is suitable for the automatic administration of pentothal sodium during surgical procedures. It differs from the machine used in ether anesthesia chiefly in the fact that it contains a filter circuit which limits the cerebral potentials used for automatic control to a narrow band which is outside the range of electric disturbance. The advantages of this technique are demonstrated.

The behavior of the apparatus during use of *d*-tubocurarine chloride together with pentothal sodium was found to be the same as it was when pentothal sodium was used alone.

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