This invention relates to an apparatus for the automatic administration of drugs at a rate that varies continuously in response to some bodily function which generates an electrical signal or is represented by an electrical signal. While the invention relates to drugs generally whose administration produces some bodily response, in this description it relates more particularly to the administration of anesthetic agents.

It has been known that the anesthetic agents such as cyclopropane, ether or the barbiturates produce characteristic changes in the electroencephalographic activity of the patient to which these drugs are administered. These changes vary in a definite manner with increasing arterial blood concentration of the anesthetic agent. For the anesthetic agents the change in electroencephalographic pattern may be employed in a servo system to control arterial blood concentration and therefore the depth of anesthesia automatically at a constant level. Other drugs that produce an effect on a bodily function which is represented as an electrical phenomenon (such as the electrical activity of the heart) or may be represented by an electrical signal which is proportional to the bodily response (such as blood pressure recorded by a strain gauge system) can also be administered automatically by the servo machine herein described.

It is the general objective of the invention to provide a method for controlling the functions of a patient which are alterable by drug action.

It is further the general objective of the invention to control the depth of anesthesia as measured by the electroencephalograph at a constant level by continuously controlling the rate of administration of the anesthetic agent so that it is proportional to the cortical activity.

In the past, anesthesia has been administered by an anesthesiologist who receives information through his special senses and in the light of previous experience forms an evaluation of the depth of anesthesia. He then compares this estimate with that depth of anesthesia required by the surgeon for the particular procedure performed. The administration of the anesthetic agent is then varied so that the estimated depth of anesthesia approaches that required by the surgeon. This is a gross method for administering anesthetic agents. The clinical signs of anesthesia are peripheral signs of central nervous activity and as such are often unreliable.

It has been possible to control the administration of anesthetic agents by integrating cortical activity and intermittently administering a fixed amount of anesthetic agent. These systems have not attained the finest control possible. I have been able to develop an automatic control for administration of drugs and particularly anesthetic agents. The control herein described utilizes a control voltage derived from the patient, himself, and which varies with the condition of the patient, for continuously regulating the rate of administration of the material in accordance with the requirements of the patient.

It will compensate for disturbance factors. These factors, such as elevated carbon dioxide, hypoxia, may produce electroencephalographic patterns similar to deeper levels of anesthesia. Other disturbance factors such as movement artifacts and artifacts from electrostatic interference fall outside the frequencies amplified and are therefore minimized.

It is further the general objective of the invention to indicate the depth of anesthesia as measured by monitoring certain frequencies of the electroencephalograph and displaying the rectified voltage on a suitable metering instrument.

It is a further general objective of the invention to provide an apparatus for administering an anesthetic agent in gas form to a patient continuously at a rate responsive to the potential output of certain selected frequencies of the cortex of the patient.

It is a further general objective of the invention to provide an apparatus for continuously administering an anesthetic agent in vapor form to a patient, at a rate responsive to the potential output of certain selected frequencies of the cortex of the patient.

Other objects and advantages will hereinafter appear. In the drawing Figure 1 is a schematic view showing chiefly the wiring diagram of practical and advantageous apparatus embodying the principle of the invention, certain related mechanical components being also indicated; and Figure 2 is a fragmentary diagram showing a variation of Figure 1 in which a pump is driven at a rate proportional to the rate of the output rotor shaft.

The illustrative apparatus is used in conjunction with an electroencephalographic recorder and an anesthesia machine which are not, per se, a part of this invention.

Figure 1 shows the components of the invention that receive their command input from the electroencephalograph and have an output that governs the motor means for controlling the gas flow of the anesthetic machine or the liquid flow of intravenous anesthetic agents.

The apparatus of the invention relates broadly to the automatic administration of drugs to a patient continuously in response to a signal function originating in or generated in consonance with a physical function of the patient. For simplicity in explanation but without limitation in scope, the use of this invention to control automatically gaseous inhalation and intravenous liquid anesthetics will be described.

The invention can be understood most easily by reference to the drawing. The servo control consists essentially of a frequency discriminator, a detector, a balanced modulator, a push-pull power amplifier, and a servomotor having a rotary output shaft. The zones of these principal parts are substantially marked off by broken vertical lines and appropriate legends are applied.

The amplified brain potential signal from the electroencephalograph is coupled between a point 100 and a point 109 of grounded line conductor L1, and the signal is therefore impressed upon resistor R1.

The signal impressed upon R1 is tapped off by a variable terminal 101.

Tube VI, a high gain pentode (6AG5) has a heated cathode 99, a control grid 98, a first screen grid 102, a second screen grid 103 together with an anode 104, and serves to amplify a selected band of frequencies of the brain potential command signal. The cathode 99 is heated by a filament (not illustrated) and is connected through junction 108 to a variable resistor R3, which is in turn connected to junction 110 on L1. The control grid 98 is connected to R2 which is in turn connected to ad-
justable terminal 101 on resistor R1. The terminal 101 may be moved along the resistor R1 to vary the input. Grid 102 is connected to a 150 volt regulated voltage supply. A second screen grid 103 is connected to the cathode circuit at junction 108. A circuit extends from junction 118 through resistor R5 to junction 106. From the anode 104 a circuit extends through junction 105 and thence through R4 to junction 106, which connects to a 250 volt regulated voltage supply. A network is made up of condensers C1, C2, C3, and resistors R6, R7, R8, R9, and R10. Condenser C1 is connected to junction 105 and through junction 118 connects to condenser C2 which, in turn, connects through junction 117 to condenser C3. Resistor R6 connects to junction 116 between condensers C1 and C2 and through junction 115 to resistor R7 which connects with L1 at junction 111. Resistor R8 connects to junction 117 between condenser C2 and condenser C3 and at junction 112 connects to line L1. Resistor R9 connects to condenser C3 through junction 191, and through junction 114 connects to resistor R10, which connects to line L1 at junction 113. This network feeds back from junction 114 to the control grid 98 of tube V1 so that the desired pass frequencies may occur in phase with those on the control grid 98 of tube V1. Tube V1 amplifies these frequencies to a greater extent than frequencies lying outside the selected band. The output from this stage is coupled from junction 115 through condenser C4 and thence through junction 192 and is impressed across resistor R11 which connects with line L1 at junction 120. A tube V2, of the same type as tube V1, has a heated cathode 125, a control grid 124, a first screen grid 121, and a second screen grid 122, together with an anode 123, and serves to amplify and rectify the band of frequencies from the stage containing tube V1. The cathode 125 is heated by a filament (not illustrated) and is connected to a variable resistor R14. Resistor R14 is connected, in turn, to resistor R11 to vary the input to the stage. Grid 121 is connected to the 150 volt regulated voltage supply. The second screen grid 122 is connected through junction 127 to the cathode circuit. A circuit also extends from junction 127 through resistor R13 and thence to junction 129. From the anode 123 a circuit extends to junction 128 and thence through resistor R12 to the 250 volt regulated power supply. A circuit also extends from anode 123 through junction 128 to junction 130 and thence through resistor R13 and junction 135 which is common with junction 136. There is a connection of condensers C5 at junction 130 and also at junction 131 on line L1 and also a connection of condenser C6 at junction 135 and at junction 133 on line L1. Condensers C5 and C6 tend to minimize fluctuations in signal that appear across resistor R15. Voltmeter M is connected between junction 136 and junction 134 which is on line L1. This meter measures the rectified or command signal of the selected frequencies of the amplified brain potential signal and in operation may be used as an indicator of depth of anesthesia, light anesthesia being represented by a larger potential than deep anesthesia. The balanced modulator comprises tubes V5, tube V5, coupling transformer T1 and transformer T2 together with the associated resistors and capacitors. Tube V5 is of the same type as tubes V1 and V2. It has a heated cathode 147, a control grid 146, a first screen grid 145, a second screen grid 144 together with anode 143 and serves to control the phase of the current in the balanced modulator. The cathode 147 is heated by a filament not illustrated and is connected through junction 148 to resistor R21 and thence to junction 149 on line L1. The control grid 146 is connected to junction 150, and thence through condenser C9 to junction 131 on line L1. A phase shifting network is made up of condensers C7 and C8 together with resistors R28, R30, and R29. The secondary of transformer T2 connects to junction 157 on line L1 while the other side connects with condenser C7 through conductor 158. A circuit extends from condenser C7 to junction 155, through condenser C8 and resistor R30 and thence through junction 152 to resistor R29 which connects to line L1 at junction 153. Resistor R28 is connected between junction 155 and junction 156 which is on line L1. The output of this network at junction 152 is connected through junction 150 to control grid 146 of tube V5. The resistors illustrated and resistor R30 and thence such that the phase of the signal applied to the control grid 146 of tube V5 is shifted 90° from that of the line current E1, which excites the primary of transformer T2 as well as the reference winding of the servomotor. Grid 145 is connected to the 150 volt regulated power supply. The screen grid 144 is connected to the cathode circuit at junction 148. From the anode 143 a circuit extends to junction 142 in the cathode circuit of tube V3 and tube V4. Tube V3 is a triode (6H51). It has a heated cathode 141, a control grid 139 and an anode 140, and serves to form part of the balanced modulator. The cathode 141 is heated by a filament not illustrated and is connected through junction 142 to the anode 140 of tube V5. The control grid 139 is connected through junction 138 to junction 137 and hence receives the output of the rectified selected frequencies of the brain potential signal. The anode 140 connects to one side of the primary of coupling transformer T1. Tube V4 is of the same type as tube V3. It has a heated cathode 165, a control grid 166 and an anode 167 and serves to form part of the balanced modulator. The cathode 165 is heated by a filament not illustrated and is connected through junction 142 to the anode 140 of tube V5. The control grid 166 is connected to junction 164 and thence through resistor R20 to the variable contact of Helipot resistor R17. A circuit extends from junction 163 through resistor R19 to junction 160 and thence through resistor R22 to junction 159 on line L1. The anode 167 connects to the opposite end of the primary of coupling transformer T1 from anode 140 of tube V3. The center tap of the primary of coupling transformer T1 connects to a 500 volt regulated voltage supply. A voltage divider network is made up of Helipot resistor R17, resistor R23 and resistor R22. A circuit extends from junction 174 which connects to a 250 volt regulated voltage supply, through resistor R17 and thence through resistor R23 and resistor R22 to junction 173 on line L1. A circuit extends from control grid 139 through junction 138 and thence through junction 137 and resistor R24 to the variable contact 161 of resistor R23. In operation the adjustable contact 161 on resistor R23 is used to set the reference level of the balanced modulator and thus the level of anesthesia. The variable contact 162 of Helipot resistor R17 is geared mechanically to the shaft of the control motor and automatically moves in such a direction so as to correct or overcome any unbalance of the balanced modulator caused by a variation in the rectified selected frequencies of the amplified brain potential signal impressed on control grid 139. A circuit extends from control grid 139 through diode D1 to switch S1 and thence to junction 172 and control grid 166. This circuit is employed only when the servo-regulator is used as a velocity servo for administration of intravenous fluids. In this application the control motor is mechanically disconnected from the variable contact 162 on Helipot R17 as well as the anode junction and then the control valve is connected to a suitable pump for the administration of intravenous fluids. The switch S1 is closed so that diode D1 will not permit control grid 139 to become negative in respect to control grid 166. In
this manner only one half of the primary of coupling transformer T1 can conduct more current than the other, and thus the control motor will turn in only one direction.

Tubes V6 and V7 are components of a push-pull amplifier whose output controls the servo motor. Tube V6 is a beam power pentode (6V6). It has a heated cathode 177, a first grid 178, and a second grid 179 together with the anode 180. The cathode 176 is heated by a filament not illustrated and is connected through junction 182 to resistor R26 which is in turn connected to junction 183 on line L1. The control grid 177 is connected through resistor R25 and thence through junction 168 to the secondary of the coupling transformer T1. The first screen grid 178 connects to the first screen grid 186 of tube V7 and thence to the 250 volt regulated voltage supply. The second screen grid 179 connects through junction 181 to the cathode circuit at junction 182. The anode 180 connects to one side of the control winding of the control motor.

Tube V7 is of the same type as tube V6. It has a heated cathode 184, a control grid 185, a first screen grid 186, a second screen grid 187, and together with the anode 188 connects to one side of the phase of the output of the push-pull amplifier for driving the control motor. The cathode 184 is heated by a filament not illustrated and is connected through junction 182 to resistor R26 which is connected to junction 183 on line L1. The control grid 185 connects through resistor R27 to junction 171 and thence through junction 168 to the secondary of the coupling transformer T1 at the opposite end of the secondary from which control grid 177 of tube V6 connects.

The first screen grid 186 connects to the first screen grid 178 of tube V6 and thence to the 250 volt regulated voltage supply. The second screen grid 187 connects through junction 181 to the cathode circuit at junction 182. The anode 188 connects to one side of the control winding of the control motor.

The center tap of the secondary of coupling transformer T1 is connected by line 193 to a suitable ground point in common with line L1. One side of the secondary of coupling transformer T1 is connected to control grid 177 of tube V6 while the other side is connected to control grid 185 of tube V7 as described. Resistor R18 is provided across the secondary of control transformer T1 between junction 169 and junction 168. Condenser C10 is provided across the secondary of control transformer T1 between junction 170 and junction 171. Condenser C10 and resistor R18 are provided across the secondary of coupling transformer T1 in order to suppress parasitic oscillations.

The control motor which is geared mechanically to the adjustable contact of Helipot resistor R17 has a control winding and also a reference winding. The control motor is also geared mechanically by means not shown to the anesthetic gas control valve of the anesthesia machine. The control winding of the motor is excited by current from the anode 180 of tube V6 and anode 188 of tube V7. The center tap of the control winding of the motor is connected at junction 169 and thence to the regulated voltage supply. The reference winding of the control motor is excited by the alternating current of the line voltage E2, which current is supplied through terminals 189 and 190.

The operation is as follows:

When the servo control is used as a position servo to control the amount of opening of an anesthetic gas valve, a steady state condition will be achieved when the rectified selected frequencies of the brain potential impressed on the grid 139 of tube V3 will be equal to the voltage impressed on the control grid 166 of tube V4. Both the V3 and tube V4 will conduct equal amounts of current and there will be equal current in both halves of the primary of coupling transformer T1 so that there will be no output in the secondary of coupling transformer T1. This means that the secondary of coupling transformer T1 will have no output to control grid 177 of tube V6 and control grid 185 of tube V7, so that the push-pull amplifier will have no output to the control winding. When these conditions exist the motor rotor will stand still, Helipot resistor R17 variable contact 162 will not be moved, and the flow of anesthetic gas will be maintained at a constant rate.

When the rectified signal derived from the encephalographic input decreases in potential, the voltage impressed on control grid 139 of tube V3 will decrease. Under these conditions tube V3 will conduct less current than tube V4. This will cause the unbalance of the primary of coupling transformer T1 and therefore an output in the secondary of coupling transformer T1 to control grid 177 of tube V6 and control grid 185 of tube V7 in the push-pull amplifier. The push-pull amplifier will have an output of phase in relation to the polarity of unbalance between control grid 139 of tube V3 and control grid 166 of tube V4, and of a magnitude in proportion to the voltage unbalance between the control grid 139 of tube V3 and control grid 166 of tube V4. The servo motor will turn in a direction determined by the phase of the output of tube V6 and anode 188 of tube V7 to the control winding, and at a speed proportional to the amplitude of the output of tube V6 and tube V7.

The rotor of the control motor will then turn in a direction so that the anesthetic gas flow is decreased, and at the same time the variable contact 162 of Helipot resistor R17 will be moved so that the potential on control grid 166 of tube V4 is decreased until the system balances, i.e., until the voltage on control grid 166 equals the voltage on control grid 139 of tube V3. The rate of the response of the system is governed by the transfer functions of the components of the system and these are well known. In operation the system continuously varies the anesthetic gas flow in response to the rectified selected frequencies of the brain potential and continuously corrects the anesthetic gas flow so that the anesthetic level of the patient is maintained constant at a level determined prior to the administration of the anesthetic agent by the potential selected by variable contact 161 on resistor R23. Since the response of the system is very rapid and since it continuously corrects for error, the level of anesthesia is maintained within very narrow limits. There are no substantial fluctuations.

In Figure 2 a variation is shown in which the two control is used as a velocity servo to control the rate of administration of an intravenous anesthetic agent, the rotor of the control motor is suitably mechanically connected to drive a pump P for the intravenous administration of fluids. The rotor of the motor is disconnected from the variable contact 162 of Helipot resistor R17. Switch S1 is set in the closed position.

Under these conditions, when the output of the rectified selected frequencies of the brain potential impressed on control grid 139 of tube V3 is positive in respect to the potential on control grid 166 of tube V4, there will be a modulated signal in the primary of the control transformer T1 and therefore an output from the secondary of coupling transformer T1 through the push-pull amplifier to the control winding of the control motor of such phase so as to cause the rotor of the control motor to turn in a direction to administer the intravenous agent by suitable mechanical means. The velocity of the rotor of the control motor will be proportional to the unbalance in potential between control grid 139 of tube V3 and control grid 166 of tube V4. When the potential on control grid 139 of tube V3 equals the potential on control grid 166 of tube V4 there will be a balanced signal in both halves of the primary of coupling transformer T1. There will be no output from the secondary of coupling transformer T1 and therefore no output from the push-
pull amplifier to the control winding. The rotor of the control motor will stand still and no intravenous agent will be administered.

2. Selected frequencies of the brain potential signal decreases so that the potential on control grid 139 of tube V3 tends to be less than the potential on control grid 166 of tube V4 the diode circuit through switch SI and diode DJ will keep the potential on control grid 139 of tube V3 from becoming less that on control grid 166 of tube V4. This will prevent an output from the secondary of coupling transformer T1 through the push-pull amplifier to the control winding, so that the motor will not be caused to turn in a reverse direction. Thus, in the velocity mode the servo mechanism will admit intravenous agents at a rate which varies with the potential of the rectified selected frequencies of the brain signal, but when this signal falls below a certain level the administration of the intravenous agent will be discontinued. In the velocity mode the depth of anesthesia is set by the variable contact 161 of resistor R23.

I have described what I believe to be the best embodiments of my invention. I do not wish, however, to be confined to the embodiments shown, but what I desire to cover by Letters Patent is set forth in the appended claims.

I claim:

1. An automatic apparatus for administering material to a patient comprising, in combination, means for deriving an electrical command voltage from a measurable condition of the patient which is susceptible of modification by the administered material, means providing a reference voltage of predetermined magnitude independently of the patient, means for comparing the command and reference voltages and deriving therefrom a control voltage, and means responsive to the control voltage for continuously administering the material at a variable rate, in accordance with the requirements of the patient.

2. An automatic apparatus for administering gaseous medication to a patient comprising, in combination, means for deriving an electrical command voltage from a variable condition of the patient which is susceptible of modification by the administered medication, means providing a reference voltage of predetermined magnitude independently of the patient, means for comparing the command and reference voltages and deriving therefrom a control voltage, means for continuously administering the medication at a variable rate comprising a container for holding a supply of the gaseous medication under pressure and a valve operable in one direction to increase the rate of administration and in the opposite direction to reduce the rate of administration, and rotary means responsive to the control voltage for continuously adjusting the valve in one direction or the other to conform the rate of medication to the patient's needs.

3. An automatic apparatus for administering medication to a patient by intravenous injection comprising, in combination, means for deriving an electrical command voltage from a measurable condition of the patient which is susceptible of modification by the administered medication, means providing a reference voltage of predetermined magnitude independently of the patient, means for comparing the command and reference voltages and deriving therefrom, a control voltage, means for continuously administering the medication at a variable rate, and means responsive to the control voltage for continuously regulating the rate in accordance with the requirements of the patient.

4. An automatic apparatus for administering an anesthetic agent to a patient comprising, in combination, means for deriving an electrical command voltage from a measurable condition reflecting the depth of anesthesia of the patient, means providing a reference voltage of predetermined magnitude independently of the patient, means for comparing the command and reference voltages and deriving therefrom a control voltage, means for continuously administering the anesthetic agent at a variable rate, and means responsive to the control voltage for holding the rate unchanged or for increasing or diminishing the rate, all as required for maintaining a prescribed depth of anesthesia.

5. An automatic apparatus as set forth in claim 1 in which the reference voltage is maintained constant and adjustable gain control means is provided for amplifying the control voltage linearly in any desired degree thereby to determine in advance the chosen condition of the patient which will be maintained.

6. An automatic apparatus as set forth in claim 1 in which adjustable gain control means is provided for amplifying the control voltage linearly in any desired degree whereby to determine in advance the chosen condition of the patient which will be maintained, and indicating means responsive to the amplified command voltage for controlling the operation of the apparatus.

7. An automatic apparatus for administering a gaseous anesthetic agent to a patient comprising, in combination, means for deriving an electrical command voltage from a measurable condition reflecting the depth of anesthesia of the patient, means providing a reference voltage of predetermined magnitude independently of the patient, means for comparing the command and reference voltages and deriving therefrom a control voltage, means for continuously administering the anesthetic agent at a variable rate comprising a valve settable to control the rate, a rotary member continuously responsive to the control voltage for holding the position of the valve unchanged or for increasing or diminishing the opening of the valve, in accordance with the deviation of the true state of anesthesia of the patient as compared with that for which the apparatus is set.

8. An automatic apparatus for administering material to a patient comprising, in combination, means for deriving an electrical command voltage from a measurable condition of the patient which is susceptible of modification by the administered material, means providing a reference voltage of predetermined magnitude independently of the patient, means for comparing the command and reference voltages and deriving therefrom a control voltage, a motor having a variable resistance in the circuit of the modulator adjustable to restore the balance of the modulator when the balance is disturbed by a variation of the control voltage, the output shaft of the motor being connected to adjust the variable resistance in a direction to restore balance whenever, and so long as, unbalance occurs, and concurrently to adjust the rate of administration of the material to the patient in a direction to produce the desired condition of the patient.

9. An automatic apparatus for administering liquid material intravenously to a patient, comprising, in combination, means for deriving an electrical command voltage from a measurable condition of the patient which is susceptible of modification by the administered material, means providing a reference voltage of predetermined magnitude independently of the patient, means for comparing the command and reference voltages and deriving therefrom a control voltage, a motor having a rotary output shaft which it drives continuously at a rate which varies with the magnitude of the control voltage, and
means responsive to said shaft for supplying the administered material continuously at a rate proportional to the rate of rotation of the shaft.

10. An automatic apparatus as set forth in claim 1 in which reference voltage control means is provided for adjusting the reference voltage and thereby determining in advance the chosen condition of the patient which will be maintained.

11. An automatic apparatus as set forth in claim 1 in which means is provided for adjusting the magnitude of at least one of said command and reference voltages independently of the other, thereby to determine in advance the chosen condition of the patient which will be maintained.

12. An automatic apparatus for administering material to a patient comprising, in combination, means for deriving a D.C. electrical command voltage from a measurable condition of the patient which is susceptible of modification by the administered material, means providing a reference voltage of predetermined magnitude independently of the patient, means for comparing the command and reference voltages and deriving therefrom a control voltage, a motor having a rotary output shaft for continuously regulating the rate of administration in accordance with the requirements of the patient, a balanced modulator to which the control voltage is applied, the motor being responsive to the modulator for driving its output shaft in one direction or the other in accordance with the direction of unbalance of the modulator, and a variable resistance in the circuit of the modulator adjustable to restore the balance of the modulator when the balance is disturbed by a variation of the control voltage, the output shaft of the motor being connected to adjust the variable resistance in a direction to restore balance whenever, and so long as, unbalance occurs, and concurrently to adjust the rate of administration of the material to the patient in a direction to produce the desired condition of the patient.

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