Title : A NEW METHOD FOR TESTING THE RESPONSE TO AN INHALATION AGENT

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Introduction. The unpredictablity of an individual's response to a given dose of an anesthetic is a significant problem for the anesthesiologist. One may give a "test dose" of an anesthetic and measure the response, but such a method is subject to errors. In addition, a test dose of an inhalation anesthetic, as conventionally understood, is not practical to administer. We present here a method for continously administering a "test dose" of halothane (H), the response to which can be mathematically described. The test is called a Pseudo-Random Binary Sequence (PRBS): Binary because the agent is either off or on at one level only; Random because the duration of off and on periods are randomized; and Pseudo because the randomized sequence is of finite duration and is repeated. This method allows the identification of the system's entire dynamic response. Such variables as time delays, as well as speed, duration and intensity of response can be derived exactly.

Methods. Mathematical Methods. A PRBS behaves like white noise. When the output of a linear system is crosscorrelated with its PRBS input (the delivered concentration of the agent), the result is as if the agent had been administered in an impulse -- a burst of very short duration and very high amplitude. This impulse is similar to administering an IV bolus of a drug and contains all of the information required to simply model the system. A PDP-11/34 was used to perform the analysis.

Animal Methods. We studied 7 dogs to test the feasibility of this technique for characterizing the response of mean arterial pressure (MAP) to rapid changes in concentrations of H. An Ohio DM-5000 anesthetic machine was modified to include a solenoid valve in the vaporizer oxygen supply line so that H could be turned on or off rapidly. The valve was controlled by a PRBS generator of our own design. The pulse duration (on or off) was in multiples (1-7) of twelve seconds (12-84 sec). The gas machine fed a Harvard ventilator through a Mapleson D circuit. The dogs were anesthetized by mask H in O2, intubated and ventilated. Respiratory rate was set at 10/min with a tidal volume sufficient to maintain E.T.CO2 at 4.5% and H at 1 MAC for a period of 20 min before instituting PRBS pulsing of the anesthetic supply between of 0-3.9 MAC. Rectal temperature and PACO2 were maintained within normal limits. We measured arterial pressure via a femoral artery. All physiological and PRBS signals were monitored on a strip chart recorder and recorded on an FM tape recorder.

Results. MAP was able to follow the rapid changes in delivered H concentration, although the response was considerably damped (Fig.). In all seven dogs the computed impulse response curves were similar. The response of MAP to an impulse of H was a decrease which was rapid in onset, and a gradual return to the baseline pressure suggesting first order kinetics. The mean drop in MAP was .80±.34 torr for a 6 MAC-Second delivered impulse. The mean time constant for the recovery phase of the response was 2.65±.89 min., and the mean time to return to baseline pressure was 8.17±3.2 min.

Discussion. The advantages of the technique which we have presented are several: 1)It permits the measurement of dynamic characteristics of a physiological system without necessarily disturbing its normal operation. 2)It is substantially more noise immune than step response testing and much faster to perform than multiple-frequency sine wave testing. 3)It does not require that the animal --or patient-- be in a steady state, an obvious impossibility during surgery. 4)Although the "On" concentration is high, the pulse duration is so short that little variation can be seen in the output, MAP in this case. But this variability is enough to be analyzed by the computer. 5)The pulses can be decreased in amplitude and superimposed on a steady-state level of anesthesia, for example, pulses of 0.25 MAC superimposed on 1.0 MAC. In this way the dynamic response of the system can be followed over time without interfering with the normal anesthetic administration. 6)Any variable that can be continously measured can be used as an output, for example, EEG, or cardiac output. 7)This technique can be used with other drugs, such as Nitroprusside.

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Reference. 1) W.D.T. Davies, System Identification for Self-adaptive Control. Wiley-Interscience, London, England. 1970.