Measurement of a Spinal Reflex Response (H-Reflex) During General Anesthesia in Man

Association Between Reflex Depression and Muscular Relaxation

Rudolph H. de Jong, M.D., William N. Hershey, M.D.,† Irving H. Wagman, Ph.D.‡*

An electrically evoked monosynaptic reflex (the H-reflex) was studied during general anesthesia, in 25 surgical patients. Different levels of muscular relaxation were obtained by varying inspired anesthetic concentrations of halothane or methoxyflurane. At each level, the ratio of maximum reflex response during anesthesia to maximum response when awake (the H-ratio), was calculated.

Poor relaxation, during light anesthesia, was accompanied by a large reflex response and a high H-ratio. As relaxation improved, reflex amplitude fell, and H-ratio decreased. With profound relaxation of jaw and abdominal muscles, the H-ratio approached zero. The relation between H-ratio and muscular relaxation was statistically significant.

Thus, muscular relaxation during general anesthesia is associated with decreased reflex excitability of the spinal motoneuron pool. This presumably is the result of direct or indirect anesthetic action at the spinal synapse. With increasing anesthetic concentrations, synaptic transmission is depressed, the reflex decreases in amplitude and muscular relaxation becomes more profound.

ALTHOUGH certain general anesthetics directly affect muscular contraction *in vitro*, this effect is inadequate to account for the profound muscular relaxation observed clinically with potent general anesthetics. Evidence obtained *in vivo*[1, 2] (and unpublished observations) indicates that general anesthetics in clinically employed concentrations do not significantly depress conduction in large myelinated motor or sensory fibers. Thus the sites at which general anesthetics act to produce muscular relaxation are most likely the junctional regions of the nervous system, or the contractile mechanisms of muscle.

General anesthetics, even when producing profound muscular relaxation have little effect *in vivo* on either myoneural transmission or contractility of muscle[2]; cyclopropane, indeed, increases muscle twitch tension. Furthermore, excellent muscular relaxation is obtained by subarachnoid injection of a local anesthetic. The local anesthetic, which is anatomically restricted to the spinal cord and its nerve roots, clearly has no direct effect on either myoneural transmission or muscle contractility. Thus, muscular relaxation produced by general anesthetics is probably not a peripheral effect and must be attributed to an action at the spinal cord or at higher levels or to interaction at a combination of these sites.

Considerable experimental evidence indicates that general anesthetics, including pentobarbital, chloroform, halothane, cyclopropane, diethyl ether, trichlorethylene and methoxyflurane, profoundly depress spinal synapses and transmission of reflex impulses.[1, 3, 4]

In view of these considerations we proposed the following hypotheses: (1) Much of the muscular relaxation produced during general anesthesia is attributable to synaptic depression of spinal reflexes; and, (2) the degree of

* Associate Professor, Departments of Anesthesiology and Pharmacology, University of Washington, Seattle. Supported by Public Health Service Research Career Development Award 7-K3-GM-28.

† Research Trainee, Department of Anesthesia, University of California, San Francisco.

‡ Professor, Department of Animal Physiology and the National Center for Primate Biology, University of California, Davis.

Received from the Departments of Anesthesiology, University of Washington (Seattle) and University of California (San Francisco) and the Biomechanics Laboratory, University of California (San Francisco). Accepted for publication October 7, 1966.

muscular relaxation is related to the degree of reflex depression.

To test these hypotheses we used the "H-reflex" as a means of obtaining a quantitative index of spinal reflex activity during anesthesia. The H-reflex is a reproducible response for the study of reflex activity in man. Furthermore, a simultaneous assessment of the action of the anesthetic on myoneural transmission was obtained by measuring the amplitude of the direct muscle response.

Methods

The technique of Magladery[5] was used in which the H-reflex is elicited by electrically stimulating the tibial nerve in the popliteal fossa and recording the resulting action potentials from the calf muscles (figs. 1 and 2). The technique was adapted to the special requirements of the operating room by substituting perineural stimulating electrodes for the commonly used surface electrodes. Stimulating and recording electrodes could be conveniently placed in the conscious patient and stable experimental conditions were maintained for many hours.

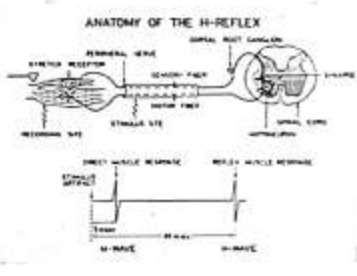

FIG. 1. Anatomy of the H-reflex. The monosynaptic reflex may be elicited by either mechanically stimulating tendon receptors or by electrically stimulating afferent fibers in the peripheral nerve. Impulses travel along afferent fibers to the spinal cord and are transmitted across a single synapse to fire corresponding motoneurons. Motor impulses travel down motor fibers of the peripheral nerve to excite corresponding motor units reflexly. Adequate electrical stimulation of the mixed nerve excites both motor and sensory fibers. An impulse is therefore also conducted in the motor nerve directly to the muscle motor unit. Note that the stretch receptor system is bypassed when the reflex is electrically induced. On the oscilloscope (lower drawing) the stimulus artefact is followed shortly by the action potential of the direct muscle response and, after a considerable delay, by the action potential of the reflex muscle response. Modified by permission from Eccles, J. C.: The Synapse, Sci. Amer. 212: 56, 1965.

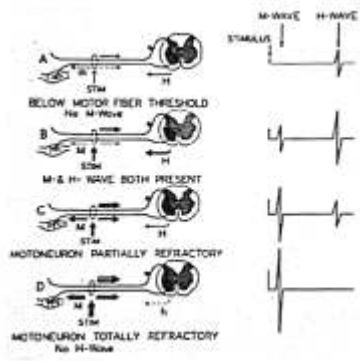

FIG. 2. Physiology of the H-reflex. Waxing, then waning of the H-wave with increasing stimulus strength is due to antidromically conducted impulses in the motor nerve which make the motoneuron or its axon increasingly refractory to synaptic transmission. *A*. The sensory fiber has a lower threshold than the motor fiber. At low stimulus strength only a sensory impulse is elicited. The record shows the synaptically transmitted H-wave and absence of M-wave. *B*. Both sensory and motor fibers are conducting impulses, but because of the lower threshold of the sensory fiber its impulse is greater than that of the motor fiber. The H-wave is maximal, the M-wave is still small. *C*. Greater stimulus strength excites more motor fibers; the M-wave grows taller. Antidromic impulse conduction in the motor fiber renders part of the motoneuron pool refractory to the synaptically conducted sensory input; the H-wave decreases in size. *D*. At maximal stimulus strength, the motoneuron pool is totally refractory at the time the sensory impulse reaches it. The H-wave has disappeared; the M-wave is maximal. Thickness of arrows represents magnitude of impulses in sensory and motor nerves. Dashed arrows and lower case letters (m, h) indicate absence of conducted or transmitted impulses. Amplitudes of stimulus artefact and M- and H-waves in right-hand column are relative only.

Stimulating electrodes were prepared by threading a length of 10 mil (0.25 mm. diameter) insulated stainless steel wire through a 1½ inches (3.8 cm.) long 22-gauge hypodermic needle (disposable needles are con-

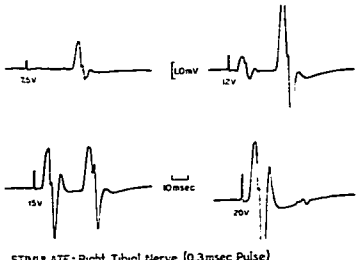

FIG. 3. Typical appearance of the M- and H-waves in the preanesthetic control record of a resting subject. Stimulus strength is indicated underneath the stimulus artifact. Note absence of M-wave in first tracing and nearly complete disappearance of H-wave in last tracing. The M-wave grows as stimulus strength is increased to maximal.

venient). The terminal 3 to 4 mm. of the wire was bared of insulation and formed into a hook. The wire was then pulled back until the hook caught the bevel of the needle. The electrode assembly was sterilized with ethylene oxide.

A subject was turned on his side and two skin wheals of local anesthetic were made in the popliteal fossa, about 2 cm. apart in the midline. The electrode was inserted perpendicularly through each wheal to a depth of 1.5 to 3.5 cm., depending upon the estimated depth of the tibial nerve. The needle was then withdrawn over the wire, leaving the terminus of the wire near the tibial nerve. The other end of the electrode wire was bared of insulation and connected to the stimulator. On completion of the investigation, the wires were removed and the tips examined for breakage.

A square wave stimulus of one volt, lasting about 0.3 msec. and isolated from ground, was delivered at a frequency of one per second. The stimulus voltage was gradually increased until a weak muscular contraction was noted in the calf. With good placement a threshold of from 5 to 25 v. could be expected. If muscle contraction was not seen, one or both wires were relocated closer to the tibial nerve.

Recording electrodes were standard surface electromyographic (EMG) discs of 7 mm. diameter. One EMG electrode was placed over the lateral gastrocnemius muscle in an area of strong contraction, another over the Achilles tendon. Electrodes were taped in place and connected to a conventional preamplifier input. Muscle action potentials were displayed on an oscilloscope and photographed on 35 mm. film. Peak-to-peak amplitudes of the maximum H- and M-waves, expressed in millivolts, and latency of the onset of the H-wave, in milliseconds, were measured from the calibrated film, magnified 15-fold.

The recording technique consisted of finding thresholds for the reflex and for the direct muscle responses, gradually increasing stimulus strength to determine the maximum reflex response (H-wave) and further increasing it until the maximum direct muscle response (M-wave) was obtained. The higher stimulus strengths were associated with a vigorous jerk of the leg, usually well tolerated by the unanesthetized patient.

Twenty-five patients (11 female, 14 male) requiring elective operations on the jaw, face or upper extremities were studied. Patients were in ASA class I (17) or class II (8); the age range was between 19 and 66 years (mean: 40.6 years). Informed patient consent was obtained the day before operation. Anesthetics investigated were halothane (15 cases), methoxyflurane (4 cases), cyclopropane (2 cases), ether (1 case), fluroxene (1 case) and thiopental (2 cases). Patients were lightly premedicated with pentobarbital and scopolamine. Control records on conscious subjects were obtained in an anesthesia induction room (fig. 3). Induction was with inhalation agents only (nitrous oxide or cyclopropane). Endotracheal intubation was performed where required. When a muscle relaxant (succinylcholine; 12 cases) was used to facilitate intubation, the neuromuscular blocking action was followed electromyographically until recovery of muscle action potential was complete, prior to resumption of recording. Muscular relaxation, when subsequently needed, was provided by increasing the depth of anesthesia.

Maximum H- and M-waves were recorded intermittently at different levels of muscular

relaxation by altering the inspired anesthetic concentration. In several instances profound relaxation could not be achieved with halothane because the systolic pressure fell dangerously. Profound muscular relaxation was not produced during thiopental-nitrous oxide anesthesia. Where feasible the investigation was continued into the anesthetic recovery period to document return of the H-reflex to control values. The total period of observation was from 1½ hours to 8½ hours.

Relaxation of jaw and abdominal muscles was estimated grossly by ourselves in nondental cases. In procedures involving the oral cavity, relaxation of the jaw was estimated by the oral surgeon. Muscle tone was classed as "very tight" when rigidity of the abdominal wall, coughing or bucking, or spontaneous movement to surgical stimulation was seen (MAC < 1; Minimum Anesthetic Concentration, see Eger *et al.*).[6] Inability to open the mouth, firm abdominal muscle tone, and resistance to movement of the extremities in the absence of movement to surgical stimulation (MAC = 1) were classified as "tight." In "fair" relaxation, the jaw muscles did not resist opening of the mouth, abdominal muscle tone had decreased, but resistance to deep palpation was still present (MAC > 1). Relaxation was judged as "good" when the jaw could be widely opened, abdominal wall tone was almost completely absent, the abdomen assumed a scaphoid appearance and deep palpation was possible.

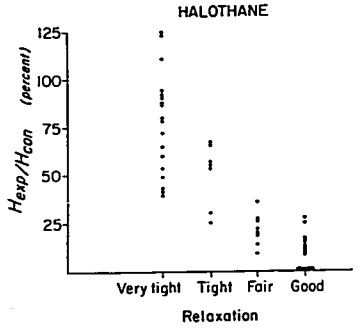

FIG. 4. Scattergram of percentile ratio of experimental to control H-reflex amplitudes plotted against estimated relaxation of jaw and abdominal muscles. Fifteen cases at varying levels of halothane anesthesia.

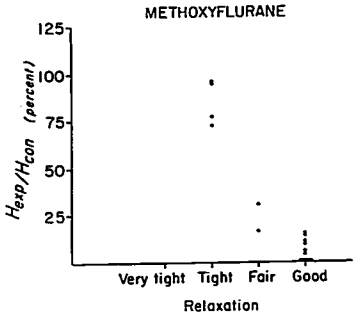

FIG. 5. Scattergram of percentile ratio of experimental to control H-reflex amplitudes plotted against estimated relaxation of jaw and abdominal muscles. Four cases at varying levels of methoxyflurane anesthesia.

The effect of anesthetics on spinal synaptic transmission was determined from the ratio of amplitudes of maximal experimental H-wave to control H-wave ($H_{exp}/H_{con} \times 100$ = percentage of synaptic transmission). The H_{exp}/H_{con} ratio (H-ratio) then was plotted against the estimated degree of muscular relaxation of abdominal and jaw muscles in a scatter diagram. Statistical analysis was done to test for association between the H-ratio and muscular relaxation.

Results

Data sufficient for analysis were obtained only for halothane and methoxyflurane. Inspection of figures 4 and 5 and tables 1 and 2 reveals an apparent correlation between depression of amplitude of the H-reflex and muscular relaxation. With poor relaxation ("very tight" or "tight") the H-ratio never fell below 25 per cent, while with adequate relaxation ("fair" or "good") it was always less than 50 per cent. With two exceptions, the H-ratio was always less than 25 per cent (28 of 30 observations) when relaxation was "good." In 14 of 30 observations the H-ratio

TABLE 1. H-Ratio and Relaxation—Halothane

Relaxation	$\frac{H_{exp}}{H_{con}}$ (per cent)				
	124–100	99–75	74–50	49–25	24–0
Very tight	3	8	5	4	0
Tight	0	0	5	2	0
Fair	0	0	0	4	5
Good	0	0	0	2	17

Observed percentile ratios of experimental to control H-reflex amplitude (H-ratio) grouped in 25 per cent intervals versus estimated muscular relaxation. Note how H-ratio decreases as relaxation improves (fig. 4); the association is significant at the $P < 0.001$ level. Fifteen cases at different levels of halothane anesthesia.

TABLE 3. H-Ratio and Relaxation—Halothane

Relaxation	$\frac{H_{exp}}{H_{con}}$ (per cent)			
	n	Range	Mean	95% C.I.
Very tight	20	124–40	77.7	89.6–65.7
Tight	7	67–53	50.7	65.9–35.5
Fair	7	36–18	24.9	30.3–19.4
Good	20	27–0	9.2	13.4–5.0

Range, mean and 95 per cent confidence intervals for n observations of percentile ratio of experimental to control H-reflex amplitude (H-ratio) during halothane administration (fig. 6). The trend to increasing proportion of depression of the H-ratio with increasing "depth" of muscular relaxation is significant at the $P < 0.001$ level.

was zero when relaxation was "good." When relaxation was less than "good" the H-ratio was always greater than zero. Mean, range and 95 per cent confidence intervals were calculated and plotted for halothane (table 3 and fig. 6). These same parameters were likewise calculated (but not plotted) for methoxyflurane (table 4).

A non-parmetric analysis of variance with the aid of the Kruskal-Wallis sum of ranks test [7] showed a significant association between H-ratio and muscular relaxation in the halothane and methoxyflurane series ($P < 0.001$ for halothane, and $P < 0.01$ for methoxyflurane). In addition, an analysis for trend in ranked proportions [8] showed a significantly increasing trend in the proportion of profound (24–0 per cent) H-ratio depression with increasing "depth" of relaxation for both halothane ($P < 0.001$; table 3, fig. 6) and methoxyflurane ($P < 0.01$; table 4).

Data so far obtained with cyclopropane (2 cases), ether (1 case), and fluroxene (1 case) were too few for analysis although a similar trend for association between H-ratio and muscular relaxation was apparent. Amplitude of the maximal evoked muscle action potential (M-wave) during anesthesia was compared with the control to evaluate the effect of anesthetics on myoneural transmission. The ratio

TABLE 2. H-Ratio and Relaxation—Methoxyflurane

Relaxation	$\frac{H_{exp}}{H_{con}}$ (per cent)				
	124–100	99–75	74–50	49–25	24–0
Very tight	0	0	0	0	0
Toght	0	3	1	0	0
Fair	0	0	0	1	1
Good	0	0	0	0	11

Observed percentile ratios of experimental to control H-reflex amplitude (H-ratio) grouped in 25 per cent intervals versus estimated muscular relaxation. Note how H-ratio decreases as relaxation improves (fig. 5); the association is significant at the $P < 0.01$ level. Four cases at different levels of methoxyflurane anesthesia.

TABLE 4. H-Ratio and Relaxation—Methoxyflurane

Relaxation	$\frac{H_{exp}}{H_{con}}$ (per cent)			
	n	Range	Mean	95% C.I.
Very tight	0	—	—	—
Tight	4	96–72	85.8	—
Fair	2	31–17	24.0	—
Good	11	16–0	5.6	9.8–1.5

Range, mean and 95 per cent confidence intervals for n observations of percentile ratio of experimental to control H-reflex amplitude (H-ratio) during methoxyflurane administration. Confidence interval established only for $n > 5$. The trend to increasing proportion of depression of the H-ratio with increasing "depth" of muscular relaxation is significant at the $P < 0.01$ level. Relaxation of jaw and abdominal muscles estimated (see text).

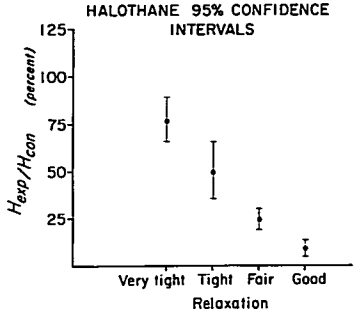

FIG. 6. Calculated mean and 95 per cent confidence intervals of H-ratio versus estimated relaxation (table 3). Fifteen cases at varying levels of halothane anesthesia.

of the experimental to control M-waves was little altered (less than ±10 per cent) by inhalation anesthetics even during profound abdominal muscular relaxation.

Recovery from halothane, especially in healthy young muscular males (7 cases) was frequently associated with complex neurologic symptoms resembling decerebrate rigidity. Extremities were rigidly extended and resisted flexion, the jaw was tightly clenched, the neck and vertebral column were hyperextended in opisthotonus, reflexes were hyperactive and muscle clonus was easily induced. Fasciculatory muscle movements, resembling shivering, were seen in extremity, trunk, and facial muscles although rectal temperatures were greater than 36.0° C. Spontaneous rigidity lasted from two to as long as ten minutes. The H-reflex could not be measured in this period owing to associated gross muscular movement resulting in displacement of the electrical baseline and also owing to spontaneous firing of motor units. With further recovery the H-reflex gradually approached control values.

Of interest, when contrasted with results obtained with potent inhalation agents, were 2 subjects anesthetized with nitrous oxide to whom incremental doses of thiopental were administered. In both, up to 500 mg. of thiopental greatly increased the amplitude of the H-reflex above the control level. One, after 300 mg. of thiopental, had a greater than two-fold increase in the H-ratio. An H-ratio greater than 100 per cent during thiopental-nitrous oxide anesthesia was associated with marked muscular rigidity, reaction to an oropharyngeal airway and movement upon minimal surgical stimulation; and the electromyogram of the calf muscles showed considerable spontaneous activity. Additional thiopental gradually lowered the H-ratio, reaching 74–50 per cent after 1,000 mg. of thiopental had been given. Relaxation at that time was either "tight" or "fair." It appears that thiopental initially increases excitability of the motoneuron pool and that large doses are required to reduce excitability sufficiently to permit surgical procedures.

Discussion

Our findings clearly indicate a strong association between degree of clinically observed muscular relaxation and amplitude of the reflex response. Both the H-reflex[9] and its equivalent in animals, the myotatic reflex,[10] have been shown to be monosynaptic reflexes. Therefore, changes in reflex amplitude, without accompanying changes in the direct muscle response, reflect modification of transmission at the spinal synapse. Since no interneuncial neurons are involved, the amplitude of the H-wave provides a direct measure of motoneuron excitability under a variety of conditions.[11] Reduction in amplitude of the H-wave observed here indicates, then, that inhalation anesthetics act, either directly or indirectly, to reduce reflex excitability of the motoneuron pool. In other words, anesthetics decrease synaptic transmission either owing to direct action on synaptic components or to effects on higher level brain structures (indirect action) which normally influence spinal cord mechanisms.

The lack of significant changes in amplitude of the maximal direct muscle response, even during profound muscular relaxation, indicated that changes in amplitude of the reflex response cannot be attributed to alterations in neuromuscular transmission. In view of the association found between muscular relaxation and reflex depression—in the absence of significant effects on motor nerve or myoneural transmission—muscular relaxation during general anesthesia probably may be attributed to

anesthetic effects on spinal reflex transmission resulting in decreased excitability of the motoneuron pool. Furthermore, the relationship between increasing reflex depression and increasing "depth" of relaxation obtained with increasing inspired anesthetic concentrations, indicates that "depth" of muscular relaxation is governed by the extent to which synaptic transmission is blocked. Thus, measurement of the H-reflex provides a quantitative index to "depth" of relaxation. Although not measured here, it seems reasonable to expect that amplitude of the reflex response will also be found proportional to anesthetic concentration in the spinal cord.

Conversely, the increased H-reflex amplitude, observed during thiopental administration, was associated with increased muscular tone, clinically manifested as rigidity. The finding that thiopental increases neuronal excitability may have bearing on the interpretation of its "anti-analgesic" properties.[12] These properties may well be related to heightened reflex activity and not necessarily to alterations in the perception of pain alone.

Whether anesthetics act directly to alter motoneuron excitability is still not clear. It is known that, in adult man, certain supraspinal structures have considerable control over the spinal synapse.[11, 13, 14, 15] Feldman and Wagman found in cats, for example, that stimulation of hypothalamic areas facilitated the monosynaptic spinal reflex while stimulation of the reticular formation caused inhibition.[16] Administration of pentobarbital altered the balance of these factors, resulting in predominant reflex inhibition. The amplitude of the directly elicited reflex on the other hand was little altered by moderate doses of pentobarbital, so that the central actions of this agent are related, at least in part, to its supraspinal effects. With higher concentrations of pentobarbital however an increasing effect on synaptic transmission may be demonstrated; this has been attributed to stabilization of the postsynaptic membrane by Brooks.[17]

In contrast with the predominantly indirect effect of barbiturates on the monosynaptic reflex, ether (as well as other inhalation anesthetics) apparently has a more direct effect on the reflex. Light ether anesthesia (arterial ether content 50–70 mg./100 ml.) was shown to depress the monosynaptic spinal reflex of cats. Deep ether (arterial ether content 100 mg./100 ml.) profoundly depressed it, while at 140 mg./100 ml. the reflex was abolished. Transection of the spinal cord did not materially alter reflex responses during ether anesthesia; neither did ether affect conduction in dorsal or ventral roots.[18] Thus, the action of ether is primarily directed at the spinal synapse and not at descending pathways. More recent studies have localized the synaptic action of ether at the subsynaptic soma-dendritic membrane where it apparently produces a non-specific stabilization.[4, 19, 20]

Ngai and co-workers studied commonly used inhalation anesthetics in decerebrate cats and found that the polysynaptic spinal crossed extensor reflex was depressed during light anesthesia and nearly abolished during deep anesthesia. Comparison with cranial (jaw and corneal) reflexes indicated that, with the exception of methoxyflurane, cranial and spinal polysynaptic reflexes were about equally affected by anesthetics.[3] Their observation that neuromuscular transmission *in vivo* is not impaired by general anesthetics (except at high concentrations of ether) and their conclusion that loss of muscle tone during deeper levels of anesthesia is attributable to anesthetic depression of motoneurons and reflex motor pathways in the cat is consistent with conclusions reached from the present investigation in man.

Summary and Conclusions

A monosynaptic spinal reflex (the H-reflex) was elicited in 25 fit surgical subjects by electrically stimulating the tibial nerve in the popliteal fossa and recording the reflex muscle action potential from the calf muscles. Changes in reflex amplitude during anesthesia were expressed as percentage of change from awake. Relaxation of jaw and abdominal muscles obtained at varying levels of anesthesia was estimated against an arbitrary scale of muscular tone. The effect of general anesthetics on neuromuscular transmission, determined by changes in amplitude of the orthodromically elicited maximal electromyogram (M-wave) were slight (less than ±10 per cent).

A strong association ($P < 0.01$) between progressive depression of H-reflex amplitude and decreasing muscular tone was found for

increasing inspired concentrations of halothane and methoxyflurane. In the few cases studied during cyclopropane, diethyl ether, and fluroxene anesthesia a similar association appeared but was not statistically tested. Less than 500 mg. thiopental increased the amplitude of the H-reflex and produced muscular rigidity.

Muscular relaxation produced by inhalation anesthetics is attributable to decreased excitability of the spinal motoneuron pool, brought about either by direct effect on synaptic transmission or indirectly by affecting more rostral areas which influence synaptic mechanisms or both.

Elicitation of the H-reflex shows promise of being a useful method for investigating muscular relaxation and anesthetic "depth" during general anesthesia in man. Alterations in amplitude of the reflex H-wave provide a quantitative measure of changes in excitability of the motoneuron pool; while the simultaneously recorded direct electromyogram (M-wave) detects alterations in myoneural transmission.

We are indebted to Dr. Edward Perrin for his advice on and review of statistical methods. Mr. Edwin Boldrey, Jr., participated as a medical student summer research fellow. This investigation was supported by NIH grants GM-08013 and 5-T1-GM-63-06, by University of Washington General Research Support grants 11-9610 and 11-9614 and by a Research Support grant (Muscular Relaxation) from the Abbott Company.

References

1. Larrabee, M. G., and Posternak, J. M.: Selective action of anesthetics on synapses and axons in mammalian sympathetic ganglia, J. Neurophysiol. 15: 91, 1952.
2. Carpenter, F. G.: Alteration in mammalian nerve metabolism by soluble and gaseous anesthetics, Amer. J. Physiol. 187: 573, 1956.
3. Ngai, S. H., Hanks, E. C., and Fahrie, S. E.: Effects of anesthetics on neuromuscular transmission and somatic reflexes, ANESTHESIOLOGY 26: 162, 1965.
4. Somjen, G. G., and Gill, M.: The mechanism of the blockade of synaptic transmission in the mammalian spinal cord by diethyl ether and by thiopental, J. Pharmacol. Exp. Ther. 140: 19, 1963.
5. Magladery, J. W., and McDougal, D. B.: Electrophysiological studies of nerve and reflex activity in normal man. I. Identification of certain reflexes in the electromyogram and the conduction velocity of peripheral nerve fibres, Bull. Johns Hopkins Hosp. 86: 265, 1950.
6. Eger, E. I., Saidman, L. J., and Brandstater, B.: Minimum alveolar anesthetic concentration: A standard of anesthetic potency, ANESTHESIOLOGY 26: 756, 1965.
7. Siegel, S.: Nonparametric Statistics for the Behavioral Sciences. New York, McGraw-Hill, 1956, p. 184.
8. Bradford Hill, A.: Principles of Medical Statistics, ed. 7. New York, Oxford University Press, 1961, p. 176.
9. Magladery, J. W., Porter, W. E., Park, A. M., and Teasdall, R. D.: Electrophysiological studies of nerve and reflex activity in normal man. IV. The two-neurone reflex and identification of certain action potentials from spinal roots and cord, Bull. Johns Hopkins Hosp. 88: 499, 1951.
10. Lloyd, D. P. C.: Neuron patterns controlling transmission of ipsilateral hind limb reflexes in cat, J. Neurophysiol. 6: 293, 1943.
11. Angel, R. W., and Hofmann, W. W.: The H-reflex in normal, spastic and rigid subjects, Arch. Neurol. 8: 591, 1963.
12. Dundee, J. W.: Alterations in somatic pain associated with anaesthesia. II. The effect of thiopentone and pentobarbitone, Brit. J. Anaesth. 32: 407, 1960.
13. Magladery, J. W., Teasdall, R. D., Park, A. M., and Languth, H. W.: Electrophysiological studies of reflex activity in patients with lesions of the nervous system. I. A comparison of spinal motoneurone excitability following afferent nerve volleys in normal patients and patients with upper motor neurone lesions, Bull. Johns Hopkins Hosp. 91: 219, 1952.
14. Thomas, J. E., and Lambert, E. H.: Ulnar nerve conduction velocity and H-reflex in infants and children, J. Appl. Physiol. 15: 1, 1960.
15. Eccles, R. M., and Lundberg, A.: Supraspinal control of interneurones mediating spinal reflexes, J. Physiol. 147: 565, 1959.
16. Feldman, S., and Wagman, I. H.: Hypothalamic effects on spinal reflexes and their alteration by pentobarbital, Exp. Neurol. 5: 250, 1962.
17. Brooks, C. McC., and Eccles, J. C.: The study of the effects of anaesthesia and asphyxia on the monosynaptic pathway through the spinal cord, J. Neurophysiol. 10: 349, 1947.
18. Austin, G. M., and Pask, E. A.: Effect of ether inhalation upon spinal cord and root action potentials, J. Physiol. 118: 405, 1952.
19. Somjen, G. G.: Effects of ether and thiopental on spinal presynaptic terminals, J. Pharmacol. Exp. Ther. 140: 396, 1963.
20. Wyke, B. D.: Principles of General Neurophysiology Relating to Anaesthesia and Surgery. London, Butterworth & Co., 1960.