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Effects of Halothane, Anoxia, and Hemorrhage upon Canine Whole-body, Skeletal Muscle, and Splanchnic Excess Lactate Production

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Dogs anesthetized with halothane were subjected to stress by increased depth of anesthesia, arterial hypoxemia, or hemorrhagic hypotension in stages leading ultimately to death. Excess lactate (XL) in the whole body, splanchnic circulation, and skeletal muscle did not change significantly until the final period just preceding death. At this time XL for the whole body and the splanchnic circulation increased. Muscle XL did not increase in any circumstance tested despite compromise of O_2 delivery sufficient to decrease muscle $\dot{V}_{O_2}$. Overall, changes in arterial blood pH, buffer base, lactate, and lactate/pyruvate ratio were small, metabolic acidosis was minimal to absent, and XL was insensitive and fallible as an index of regional and whole-body hypoxia. These findings are believed to be directly related to the relative suppression of activity of the sympathetic nervous system during halothane anesthesia. (Key words: Halothane; Anoxia; Hemorrhage; Excess lactate; Muscle lactate production; Splanchnic lactate production.)

THERE IS GENERAL ACCEPTANCE of the thesis that as the system for delivery of oxygen to the tissues becomes inadequate, relative to metabolic requirements, a shift from aerobic to anaerobic metabolic pathways occurs.[1] As a consequence, tissue lactate production is said to increase and lead to increased blood levels of hydrogen ion and lactate and development of metabolic acidosis. Skeletal muscle has been thought to be particularly active in this regard, and these events have been demonstrated to occur in muscle with vigorous exercise and with electrical stimulation of the isolated nerve-muscle preparation.[1, 2] As a result of these theoretical considerations and experimental observations, various indices of tissue hypoxia have been proposed, including whole-body and organ excess lactate, arterial blood lactate, and lactate/pyruvate ratios.[3-6] However, our studies and those of others have suggested that these indices may be insensitive as indicators of developing hypoxia during halothane anesthesia,[7-10] and additional studies seemed indicated. In the present study, dogs anesthetized with halothane were subjected to stress by deep halothane, arterial hypoxemia, or hemorrhagic hypotension, and whole-body, splanchnic, and skeletal muscle excess lactate were determined, in addition to arterial blood lactate, lactate/pyruvate ratios, and muscle $\dot{V}_{O_2}$. The results suggest that as tools for diagnosing tissue hypoxia during halothane anesthesia excess lactate, lactate, and lactate/pyruvate ratios are fallible, and that increases in these modalities may reflect increased activity of the sympathetic nervous system more directly than tissue hypoxia, *per se*.

Material and Methods

Eighteen unpremedicated dogs weighing 20 ± 3 kg were anesthetized with halothane and the trachea of each was intubated with the aid of succinylcholine (20 mg), which was continued at 150 mg/hr. Ventilation by a Harvard pump with O_2 in N_2 and halothane as desired was adjusted to result in a Pa_{CO_2} of 40 ± 3 mm Hg, with the relative concentration of O_2 adjusted initially to result in a Pa_{O_2} of 150 ± 10 mm Hg. Esophageal temperature was maintained at 37.0 ± 0.2 C by external means. The carotid artery was can-

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TABLE 1. Responses to Progressive Increases in Halothane Concentration*

	Control		First Stress, Period 1		Second Stress, Period 2		Third Stress, Period 3	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Halothane expired (per cent)	1.10	0.04	1.65†	0.03	2.32†	0.03	3.23†	0.03
Mean arterial pressure (mm Hg)	110	5	88†	5	69†	4	36†	2
Pa_{O_2} (mm Hg)	154	1	155	1	163†	2	177†	2
$Paco_2$ (mm Hg)	39	1	35†	1	34†	1	28†	1
Arterial *p*H	7.41	0.02	7.44	0.01	7.45	0.01	7.50†	0.01
Arterial buffer base (mEq/l)	50	1	49	1	49	1	49	1
Arterial lactate (μmole/ml)	2.76	0.18	2.19†	0.20	2.26†	0.12	2.76	0.21
Arterial lactate/pyruvate	14.3	0.9	12.3	0.6	14.9	0.7	20.8	2.9
Whole-body excess lactate (μmole/ml)	0	0	−0.37	0.20	0.02	0.24	0.87	0.37
Muscle								
Blood flow (ml/min/100 gm)	15.1	3.0	8.3†	2.1	5.6†	1.2	2.7†	0.6
$P_{V_{O_2}}$ (mm Hg)	57	5	39†	4	34†	3	22†	1
$\dot{V}_{O_2}$ (ml/min/100 gm)	0.52	0.09	0.49	0.09	0.46	0.09	0.33†	0.08
Venous lactate (μmole/ml)	3.03	0.22	2.42†	0.17	2.34†	0.11	2.52	0.13
Venous lactate/pyruvate	19.2	1.1	16.7	0.8	19.4	0.9	26.0†	3.1
Excess lactate (μmole/ml)	0.73	0.10	0.61	0.10	0.55	0.05	0.54	0.33
Hepatic vein								
P_{O_2} (mm Hg)	53	3	38†	4	29†	2	9†	5
Lactate (μmole/ml)	2.95	0.28	2.42	0.28	2.42	0.26	4.47†	0.60
Lactate/pyruvate	10.4	1.1	9.9	0.7	11.9	0.8	37.2†	5.3
Splanchnic excess lactate (μmole/ml)	−1.04	0.19	−0.62	0.17	−0.68	0.35	2.00†	0.45

* Series of six dogs studied at 37 C.
† Significantly different ($P < 0.05$) from control period value.

nulated for sampling, measurement of blood pressure by strain gauge, and blood letting. The external jugular vein was cannulated for infusion of succinylcholine and return of collected blood. For the skeletal muscle studies, either the gastrocnemius or the gracilis muscle was prepared for total collection and measurement of venous outflow, as described previously.[11] For the splanchnic circulation studies, a catheter was passed with fluoroscopic guidance into a hepatic vein. At autopsy, muscle weight and hepatic venous catheter position were determined.

After these preparations and control measurements, three groups of six dogs each were studied during three periods of progressively-increasing stress occasioned by halothane, arterial hypoxemia, or hemorrhagic hypotension, accomplished by stepwise changes in inspired halothane concentration, inspired O_2 concentration, or blood volume by bloodletting, respectively. Actual conditions are specified in the presentation of results. Ventilation was unchanged and there was no therapeutic intervention in any experiment. Conditions of the final period were arranged to provide opportunity for observations just before death. Observations were begun 15 minutes after the change and continued for 30 minutes, or until death occurred.

During the control period and each of the three succeeding periods after stresses of increasing severity, blood P_{O_2}, P_{CO_2}, and *p*H were determined by electrodes at 37.0 C. Buffer base was estimated from the Singer-Hastings nomogram. Blood O_2 content was calculated from P_{O_2} and oxyhemoglobin concentration (I-L, Co-Oximeter), as previously described.[12] Muscle $\dot{V}_{O_2}$ was calculated from muscle venous flow rate and A-V_{O_2}. Arterial

TABLE 2. Responses to Progressive Arterial Hypoxemia*

	Control		First Stress, Period 1		Second Stress, Period 2		Third Stress, Period 3	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Pa_{O_2} (mm Hg)	152	3	49†	2	26†	2	17†	1
Mean arterial pressure (mm Hg)	106	6	102	4	110	3	95	11
Pa_{CO_2} (mm Hg)	38	1	36†	1	35†	1	34†	1
Arterial *p*H	7.40	0.01	7.43	0.01	7.44	0.02	7.41	0.02
Arterial buffer base (mEq/l)	48	1	49	1	49	1	46†	1
Arterial lactate (μmole/ml)	2.95	0.55	2.60	0.46	3.75†	0.60	6.33†	0.72
Arterial lactate/pyruvate	14.4	0.9	12.5†	0.7	18.4	1.9	34.0†	3.6
Whole-body excess lactate (μmole/ml)	0	0	−0.40	0.13	0.77	0.36	3.87†	0.43
Muscle								
Blood flow (ml/min/100 gm)	13.8	2.9	14.7	3.4	20.2	5.2	20.8	9.6
$P_{v_{O_2}}$ (mm Hg)	56	3	37†	2	21†	2	13†	1
$\dot{V}_{O_2}$ (ml/min/100 gm)	0.52	0.08	0.51	0.10	0.42	0.05	0.19†	0.07
Venous lactate (μmole/ml)	3.42	0.64	3.18	0.48	4.18†	0.70	5.96†	0.66
Venous lactate/pyruvate	18.7	1.4	17.0	0.7	19.9	1.0	27.8†	2.1
Excess lactate (μmole/ml)	0.77	0.22	0.79	0.11	0.42	0.29	−1.23†	0.26
Hepatic vein								
P_{O_2} (mm Hg)	52	2	34†	1	16†	3	5†	1
Lactate (μmole/ml)	3.24	0.61	2.98	0.45	3.82	0.26	7.35†	0.51
Lactate/pyruvate	10.9	0.5	10.6	0.6	14.5	3.1	42.4†	6.0
Splanchnic excess lactate (μmole/ml)	−1.21	0.33	−0.76	0.25	−1.76	0.59	1.17†	0.22

* Series of six dogs receiving 1 per cent halothane, studied at 37 C.
† Significantly different ($P < 0.05$) from control period value.

and venous (muscle and hepatic) blood lactate (L) and pyruvate (P) concentrations were determined by enzymatic methods. Excess lactate (XL) was calculated as suggested by Huckabee[3]:

$$XL = (L_E - L_C) - (P_E - P_C)\ (L_C/P_C)$$

where the subscripts E and C refer to experimental and control conditions, respectively. For whole-body XL, only arterial values were used. Control values were those of the initial control period and experimental values were those of each subsequent period. For muscle and splanchnic XL, control and experimental values were those of arterial and either muscle or hepatic venous blood, respectively, for that particular period.[1] Statistical significance was determined by Student's *t* test for paired and unpaired data, with $P < 0.05$ considered significant.

Results

The responses to increasing halothane, arterial hypoxemia, and hemorrhage hypotension are summarized in tables 1, 2, and 3, respectively. Control values in the three groups did not differ significantly. As halothane was increased stepwise from approximately 1 per cent to more than 3 per cent, mean arterial blood pressure decreased progressively, averaging 36 mm Hg during the final period of study just preceding death. During this time Pa_{O_2} increased and Pa_{CO_2} decreased despite unchanged frequency and tidal volume of ventilation and Fi_{O_2}. Whole-body XL, arterial blood buffer base, and L/P ratio did not change significantly during this time. Arterial lactate decreased initially and was not greater than control at any time. Arterial *p*H increased as a result of hypocapnia and an unchanged metabolic component. Muscle blood

TABLE 3. Responses to Progressive Hemorrhagic Hypotension*

	Control		First Stress, Period 1		Second Stress, Period 2		Third Stress, Period 3	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Blood removed, total (ml/kg)	0		19†	2	31†	4	39†	7
Mean arterial pressure (mm Hg)	102	4	70†	1	53†	3	37†	2
Pa_{O_2} (mm Hg)	144	4	131†	4	128†	5	128†	6
Pa_{CO_2} (mm Hg)	37	1	37	1	39	1	39	1
Arterial *p*H	7.43	0.01	7.42	0.01	7.39†	0.01	7.34†	0.01
Arterial buffer base (mEq/l)	50	1	49	0	48†	1	44†	1
Arterial lactate (μmole/ml)	3.33	0.62	3.09	0.50	3.51	0.43	4.94†	0.69
Arterial lactate/pyruvate	15.8	0.9	14.3	0.9	18.4†	1.5	27.8†	3.1
Whole-body excess lactate (μmole/ml)	0	0	−0.35	0.16	0.48	0.20	2.08†	0.49
Muscle								
Blood flow (ml/min/100 gm)	10.5	1.6	4.6†	0.6	3.3†	0.4	2.4†	0.4
P_{v_2} (mm Hg)	50	2	32†	4	26†	3	22†	1
$\dot{V}_{O_2}$ (ml/min/100 gm)	0.56	0.08	0.48	0.06	0.48	0.07	0.39†	0.06
Venous lactate (μmole/ml)	3.81	0.72	3.62	0.62	4.28	0.76	5.65†	0.94
Venous lactate/pyruvate	19.9	1.0	20.1	0.9	24.1†	1.7	28.4†	1.6
Excess lactate (μmole/ml)	0.75	0.13	0.94	0.07	0.64	0.32	−0.13	0.75
Hepatic vein								
P_{O_2} (mm Hg)	51	5	37†	6	27†	4	20†	4
Lactate (μmole/ml)	3.18	0.78	3.33	0.59	4.23	0.84	5.78†	0.80
Lactate/pyruvate	12.5	2.0	12.3	2.1	15.2	2.5	37.8†	10.0
Splanchnic excess lactate (μmole/ml)	−0.90	0.31	0.26	1.23	−0.91	0.48	0.70	1.33

* Series of six dogs receiving 1 per cent halothane, studied at 37 C.
† Significantly different ($P < 0.05$) from control period value.

flow and venous P_{O_2} decreased progressively as halothane was increased, and muscle $\dot{V}_{O_2}$ was significantly diminished during the final period. Despite compromise of O_2 delivery to muscle of this degree, neither muscle venous lactate nor muscle XL increased, and the final increase in the muscle venous L/P ratio was approximately the same as that which had been present in the arterial blood entering the muscle. More marked changes in hepatic venous blood occurred during this time and during the final period, when hepatic venous P_{O_2} averaged 9 mm Hg, there were significant increases in hepatic venous lactate concentration, L/P ratio, and splanchnic XL.

During progressive arterial hypoxemia, arterial blood pressure was maintained without significant change until death. During the final period, when Pa_{O_2} averaged 17 mm Hg, arterial buffer base was decreased slightly, and whole-body XL, arterial lactate, and L/P ratio were increased. However, the slight reduction in the metabolic component was balanced by mild hypocarbia, and arterial *p*H was unchanged. Muscle blood flow tended to increase as Pa_{O_2} decreased, but the average changes were not significant and were insufficient to prevent a progressive decrease in muscle venous P_{O_2}, and in the final period muscle $\dot{V}_{O_2}$ decreased. Despite the development of arterial hypoxemia of this degree, the increases in muscle venous lactate and L/P ratio of the final period were less than in the arterial blood perfusing the muscle, and muscle XL was less than that observed at a normal Pa_{O_2}. While more marked changes occurred in hepatic venous blood during this time, it was not until the final period, when hepatic venous blood P_{O_2} averaged 5 mm Hg, that there were significant increases in he-

patic venous blood lactate, L/P ratio, and splanchnic XL.

During progressive hemorrhagic hypotension, as blood was removed and arterial blood pressure decreased, Pa_{O_2} decreased in the presence of unchanged Pa_{CO_2}. The significant decrease in arterial buffer base of the final period was associated with increases in whole-body XL, arterial lactate, and L/P ratio, and a slight decrease in arterial *p*H. As arterial blood pressure decreased, muscle blood flow and venous P_{O_2} diminished, and during the final period muscle $\dot{V}_{O_2}$ was reduced. Despite this degree of compromise of O_2 delivery to the tissues, muscle venous blood lactate and L/P ratio increases were approximately similar to those in the arterial blood perfusing the muscle, and muscle XL was lessened. During this time, hepatic venous blood P_{O_2} decreased progressively, and in the final period hepatic venous lactate, L/P ratio, and splanchnic XL increased significantly.

Discussion

Exposure to a variety of conditions compromising delivery of O_2 to tissues resulted in only minimal changes in the indices currently suggested to be appropriate for detection of tissue hypoxia, including whole-body XL, muscle and splanchnic XL, and arterial blood *p*H, buffer base, lactate, and lactate/pyruvate ratio. Each of the conditions was extended until the animal died. The least changes occurred with progressive increases in halothane concentration. Small but significant changes were observed in the final periods with arterial hypoxemia and hemorrhagic hypotension. During increased halothane concentrations and arterial hypoxemia, small reductions in buffer base were associated with reductions in Pa_{CO_2} such that arterial *p*H either increased (with halothane) or was unchanged (with hypoxemia). The development of hypocarbia in this circumstance is considered to reflect a reduction in CO_2 production and unchanged or reduced physiologic deadspace, since frequency and tidal volume of ventilation were unchanged. In the other circumstance, hemorrhagic hypotension, arterial *p*H decreased slightly, due to the combination of a small decrease in buffer base and a slight increase in Pa_{CO_2}. The latter presumably reflects an increase in physiologic deadspace, as has been observed during hemorrhagic hypotension previously.[12]

Although with each stress tested O_2 delivery to skeletal muscle was sufficiently compromised in the final period to result in a decrease in muscle $\dot{V}_{O_2}$, there were no indications of increased reliance on anaerobic metabolic pathways. These findings cannot be considered peculiar to a single, unique skeletal muscle, since results were similar in two separate muscles which differed significantly in resting $\dot{V}_{O_2}$, blood flow, and composition.[11] The muscle venous P_{O_2}'s at which $\dot{V}_{O_2}$ decreased were somewhat less (13, 22, and 22 mm Hg) than that previously observed by others (25 mm Hg) for resting canine gastrocnemius muscle.[14] Contrariwise, anaerobic metabolic activity apparently increased in organs drained by the splanchnic circulation during the extreme compromise of O_2 delivery in the final period just preceding death.

Numerous efforts have been made to detect tissue hypoxia by measuring various elements in the circulating blood. Most approaches have included determination of blood lactate and pyruvate, since there are intracellular biochemical pathways which can proceed anaerobically to ATP generation and result in altered levels of tissue lactate and pyruvate.[1-3] The limitations of using blood lactate levels alone in estimating the magnitude of hypoxia have been emphasized by Huckabee,[3] who demonstrated increases in blood lactate during a variety of conditions not expected to induce tissue hypoxia, including hyperventilation and infusion of pyruvate or glucose. These observations and various theoretical considerations led Huckabee to suggest that calculation of XL was a more reliable approach to estimating the presence and severity of tissue hypoxia. In Huckabee's studies, XL did not increase with hyperventilation, since the increase in lactate which occurred was accompanied by an increase in pyruvate appropriate to the ratio of lactate to pyruvate during control circumstances. Further, with arterial hypoxemia the appearance, magnitude, and time course of XL correlated with

these aspects of O_2 debt development, whereas changes in blood lactate levels did not.[4]

Initially the suggestion by Huckabee seemed to solve a difficult problem which had occupied the attention of many investigators. Accordingly, a great number of publications which emphasized the use of XL as an index of whole-body or individual organ hypoxia appeared. These developments were carefully reviewed and appraised by Olson,[15] who, while conceding the positive aspects of Huckabee's contribution, offered numerous reservations regarding the universal application of XL as an invariable indicator of tissue hypoxia. This limited view of XL appears to have been substantiated by subsequent events. There has been, however, a reappearance of publications stressing the reliability of blood lactate alone or blood L/P as an index of O_2 deficit.[5, 6] For these reasons, all three determinations (XL, L, and L/P) have been used in the present study. None proved to be a sensitive, reliable indicator of tissue hypoxia, and significant changes in each appeared only when the O_2 delivery system was subjected to stress to such a degree that death was imminent.

The modest responses of blood L, L/P, XL, and *p*H in the present study are believed directly related to the use of halothane anesthesia and, consequently, the relative mild to absent activation of the sympathetic nervous system to stress. The degree of sympathetic nervous system activity and consequent release of endogenous catecholamines can directly influence the responses observed, since both epinephrine and norepinephrine result in increased blood levels of lactate and increased rates of anaerobic glycolysis in skeletal muscle.[2, 16] These considerations are particularly relevant in considering the responses to anesthesia, hypoxia, and hemorrhage which are so dependent upon sympathetic nervous system activation and release of catecholamines.

The implications of this line of reasoning seem to offer a ready explanation of the differences between the findings of the present study and those of several previous studies by others. In the following comparisons I am assuming that activity of the sympathetic nervous system is suppressed with halothane, enhanced with cyclopropane, and intermediate with barbiturates.[17] In Huckabee's[4] studies of response to arterial hypoxemia by awake, unmedicated human subjects, blood lactate increased in each, with an average increase of approximately 0.5 μmole/ml during conditions which resulted in an average arterial blood O_2 saturation of 88 per cent. While Pa_{O_2} at this time was not reported, it was presumably considerably greater than 49 mm Hg, which was the average Pa_{O_2} during period 1 of our study and which did not result in increased blood lactate in any dog. Greene and Willenkin[18] detected increased arterial lactate and whole-body XL and the appearance of muscle XL in dogs anesthetized with pentobarbital and subjected to hemorrhage and hypotension of a degree similar to that of period 2 of our study, during which no significant changes in these values were detected.

In studies during hemorrhagic shock, Drucker and associates[7, 8] observed a greater increase in whole-body XL in dogs during pentobarbital as compared with halothane anesthesia and a greater increase in whole-body XL and a decrease in arterial *p*H with cyclopropane as compared with halothane anesthesia. Price and associates[9] detected splanchnic XL production during cyclopropane but not during halothane anesthesia. The XL production could not be related to any condition predisposing to hypoxia, and could be abolished by a β-adrenergic blocking drug. These investigators concluded that ". . . 'excess' lactate apparently resulted not from splanchnic ischemia but from metabolic action associated with increased sympathetic nervous activity in these viscera." I agree with this interpretation and, further, support their suggestion that ". . . the calculation of either L/P ratios or excess lactate can be a fallible tool in the diagnosis of hypoxia."

References

1. Miller AT: Energy Metabolism. Philadelphia, F. A. Davis Company, 1968, 186 pp
2. Himwich HE: The rôle of lactic acid in the living organism. Yale J Biol Med 4:259–291, 1932
3. Huckabee WE: Relationships of pyruvate and lactate during anaerobic metabolism. I. Ef-

fects of infusion of pyruvate or glucose and of hyperventilation. J Clin Invest 37:244–254, 1958
4. Huckabee WE: Relationships of pyruvate and lactate during anaerobic metabolism. III. Effect of breathing low-oxygen gases. J Clin Invest 37:264–271, 1958
5. Neill WA, Jensen PE, Rich GB, *et al.*: Effect of decreased O_2 supply to tissue on the lactate:pyruvate ratio in blood. J Clin Invest 48:1862–1869, 1969
6. Weil MH, Afifi AA: Experimental and clinical studies on lactate and pyruvate as indicators of the severity of acute circulatory failure (shock). Circulation 41:989–1001, 1970
7. Drucker, WR, Davis HS, Burget DE, *et al.*: The effect of halothane on metabolism during hemorrhagic shock (abstract). Fed Proc 23:416, 1964
8. Drucker WR, Davis HS, Burget D, *et al.*: Effect of halothane and cyclopropane anesthesia on energy metabolism in hypovolemic animals. J Trauma 5:503–512, 1965
9. Price HL, Deutsch S, Davidson IA, *et al.*: Can general anesthetics produce splanchnic visceral hypoxia by reducing regional blood flow? ANESTHESIOLOGY 27:24–32, 1966
10. Theye RA, Sessler AD: Effect of halothane anesthesia on rate of canine oxygen consumption. ANESTHESIOLOGY 28:661–669, 1967
11. Theye RA, Brown AL Jr, Van Dyke RA: The effects of halothane and succinylcholine on oxygen uptake of the canine gracilis muscle. ANESTHESIOLOGY 35:304–308, 1971
12. Theye RA: Calculation of blood O_2 content from optically determined Hb and HbO_2. ANESTHESIOLOGY 33:653–657, 1970
13. Gerst PH, Rattenborg C, Holaday DA: The effects of hemorrhage on pulmonary circulation and respiratory gas exchange. J Clin Invest 38:524–538, 1959
14. Stainsby WN, Otis AB: Blood flow, blood oxygen tension, oxygen uptake, and oxygen transport in skeletal muscle. Amer J Physiol 206:858–866, 1964
15. Olson RE: "Excess lactate" and anaerobiosis. Ann Intern Med 59:960–963, 1963
16. Goodman LS, Gilman A (editors): The Pharmacological Basis of Therapeutics. Third edition. New York, The Macmillan Company, 1965, pp 492–493
17. Price HL: The significance of catecholamine release during anaesthesia. Brit J Anaesth 38:705–711, 1966
18. Greene NM, Willenkin RL: Skeletal muscle oxygen tension and metabolism during hemorrhagic hypotension and subsequent vasopressor administration. Yale J Biol Med 35:429–438, 1963

Anesthesia

MISADVENTURES IN ANESTHESIA "Negligence," in the words of Mr. Justice McNair, is described in the following way: "It is a term well-known to lawyers but liable to be misunderstood by the layman, to whom it may convey some sense of censure. But a finding of negligence does not in any way necessarily involve any finding of moral blame, indifference or recklessness, though in particular cases each of these may be present." In seeking a word which anesthetists would accept as fulfilling the definition of negligence in law, the word "stupidity" has been suggested, that is, all anesthetic accidents may be attributed to either "ignorance or carelessness." (*McConnell, W. S.: Misadventures in Anaesthesia, Proc. Roy. Soc. Med. 63: 691 (July) 1970.*)