EVALUATION OF HYPOXIA, HYPERCARBIA AND ASPHYXIA IN THE PRODUCTION OF CARDIAC ARREST DURING SURGICAL ANAESTHESIA

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Sudden death due to cardiac arrest during anaesthesia has been known to occur ever since the first death occurred about fifteen months after the introduction of ether in anaesthesia and about two months after Simpson used chloroform in obstetrical practice. This and other subsequent deaths provoked a storm of controversy as to the cause of death and resulted even in legal inquiry. The attention of the various workers was naturally directed towards resuscitation of the heart. It was only during the last three decades that the workers endeavoured to look into the etiological factors of this catastrophe. Downs (2) observed that the reflex cardiac inhibition from the carotid sinus is sensitised during hypoxia. Gesell *et al* (3) observed cardiac irregularities during hypoxia both in human and animal subjects. Young *et al* (6) found that inhalation of 20% CO_2 enhanced the effect of vagal stimulation on the heart. Stephenson *et al* (5) suggested that the use of multiple premedication and anaesthetic agents could be a factor causing cardiac arrest. Whatever may be the etiological factor it is quite logical to believe that a certain amount of respiratory depression must accompany the use of anaesthetics leading to hypercarbia, hypoxia or a combination of the two. It was with this end in view that dogs anaesthetised with one drug without any premedication, were subjected to hypercarbia, hypoxia or asphyxia till such time that their effects proved fatal. An endeavour was finally made to assess the extent of cardiac damage done during any of the procedures.

MATERIALS AND METHODS

Apparently healthy and well fed mongrel dogs of both sexes weighing 8 to 13.5 kg were anaesthetised with Nembutal (pentobarbital sodium) given intravenously at a rate of 30 mg/kg body weight as a 1% solution in normal saline. No premedication was used. A tracheal cannula was introduced for adminstering the desired mixture of gases. Respiration was recorded from a balloon placed and inflated between the liver and diaphragm and connected to a tambour. Femoral blood pressure was recorded. The other femoral artery was cannulated for periodically collecting samples of blood under liquid paraffin. Electrocardiogram in Lead II was intermittently taken. In some dogs the heart beat was also recorded by a Hurthle's membrane manometer.

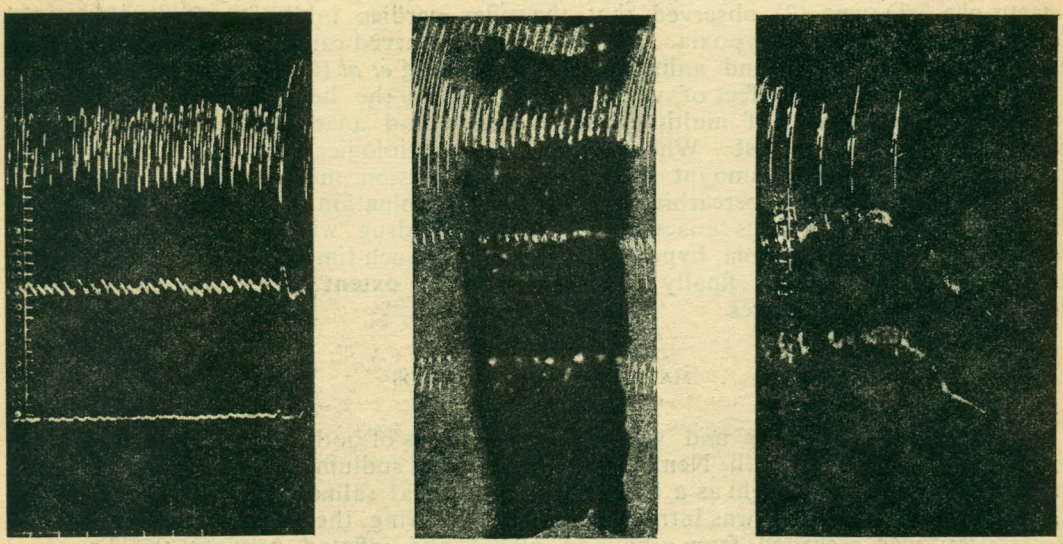
In nine dogs gradual asphyxia was produced by letting the animal rebreathe into a 1/4 inch bore tube of a capacity of 200 ml. In seven dogs hypoxia was produced by absorbing the exhaled carbon dioxide and making the animal rebreathe about 4 litres of air in a Benedict-Roth spirometer. In five dogs hypercarbia was produced by making the animal breathe a mixture of 20% CO_2 and 80% O_2 from a Boyle's machine. The expiratory valve was kept open so that practically no rebreathing occurred. In all dogs

samples of blood and electrocardiogram were periodically taken. The last sample of blood was taken when the respiration just stopped. From this time onward electrocardiograms alone were taken till cardiac arrest occurred.

The blood samples were analysed for their oxygen and carbon dioxide content by the Vanslyke and Neill's manometric blood gas analysis apparatus. The oxygen capacity of all the samples was also determined.

RESULTS

The respiratory response to asphyxia consisted of an increase in rate and amplitude of breathing commencing almost immediately after asphyxiation (Fig. 1 *a* and *b*). This state of respiration continued till the arterial CO_2 rose from a mean resting value of 37.4 vol% to 45- 50 vol%, and the arterial O_2 content fell from a mean resting value of 15.2 vol% (93.3% saturation) to 5-10 vol%. With any further rise in arterial CO_2 and fall in arterial O_2 the respiration rate slowed down and then suddenly stopped (Fig. 1 *c*). During hypoxia the respiration rate increased without any increase in depth

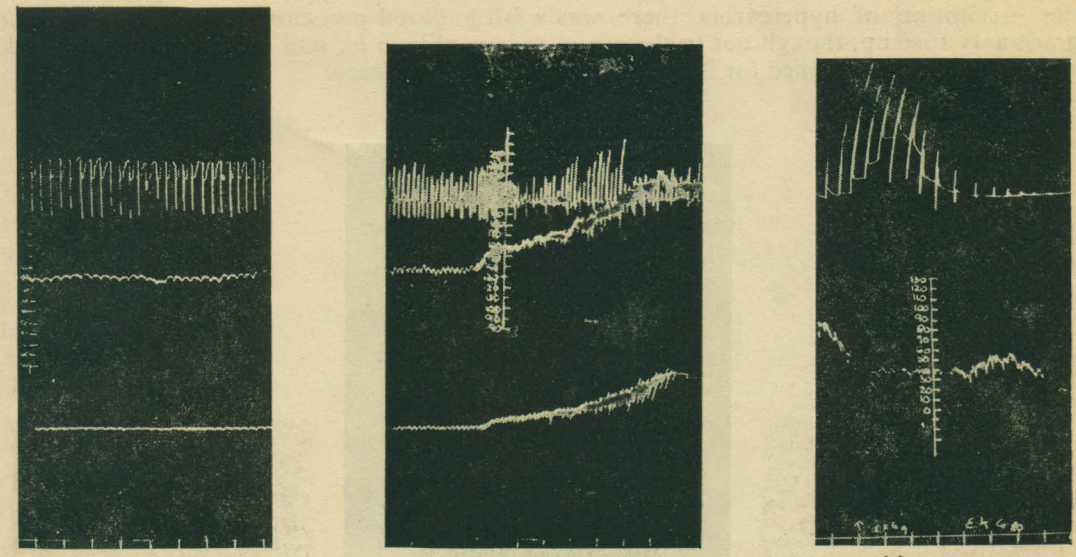


(a) (b) (c)

Fig. 1 From below upwards the records are of time (10 sec), Hurthle's Manometer, blood pressure, and respiration

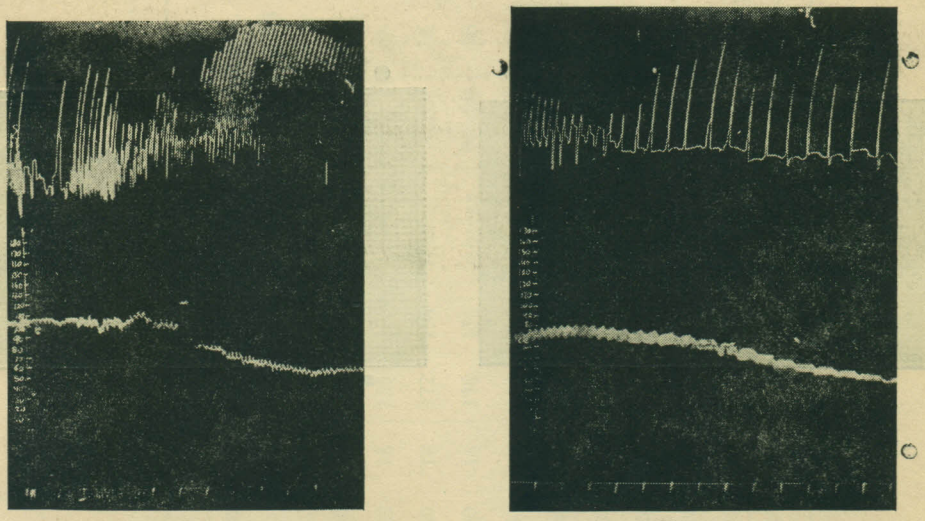
(Fig. 2 *a* and *b*). This state of respiration continued till the arterial oxygen content fell to 5-7 vol%. With any further decrease in arterial oxygen the respiration gradually failed and terminal apnoea developed (Fig. 2 *c*). The arterial carbon dioxide content also slightly decreased due to hyperpnea that developed due to hypoxia. During hypercarbia both the rate and amplitude of respiration increased (Fig. 3 *a*) till the arterial carbon dioxide content rose to 60-65 vol%. With any further rise in arterial

carbon dioxide content the respiration rate decreased and then suddenly apnea developed. Three to four minutes after this apnea 1 to 6 gasps of respiartion appeared in all dogs (Fig. 3 *c*) before terminal apnea developed.



(a) (b) (c)

Fig. 2 From below upwards the records are of time (10 sec.), Hurthle's Manometer, blood pressure and respiration.



(a) (b)

Fig. 3 From below upwards the records are of time (10 sec.) blood pressure and respiration.

In all the three set of dogs death was primarily due to respiratory failure. Circulatory failure soon followed and finally asystole of the heart occurred. In asphyxic and hypoxic dogs the blood pressure was sustained till just before terminal apnea (Fig. 1 *c* and 2 *c*) when it suddenly fell to low levels. In hypercarbic dogs soon after the institution of hypercarbia there was a fall in blood pressure (Fig. 3 *a*), but then it gradually rose up, though not to the same degree (Fig. 3 *b*), and when apnea appeared, after remaining sustained for 2-7 min. it gradually fell to zero.

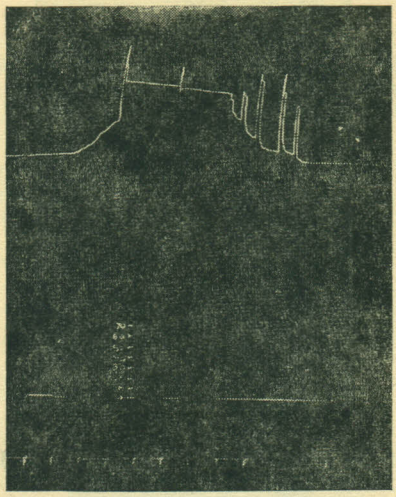


Fig. 3 (c)

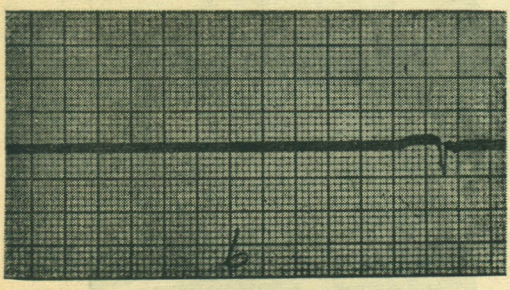


Fig. 4

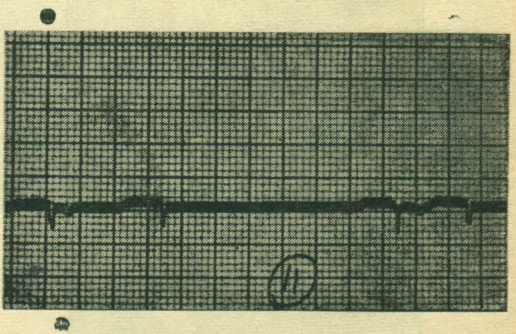


Fig. 5

In asphyxic and hypoxic dogs the heart rate started declining (Table 1 and 2) soon after the institution of asphyxia or hypoxia respectively, but in hypercarbic dogs there was an increase after a transient initial decrease which progressively developed into

TABLE 1

Dog No. 7 showing typical result under Asphyxia

Sr. No.	Time	Resp. rate/ min.	Mean B.P. mm Hg	Heart rate/ min.	Analysis of E. C. G.						Arterial Blood			
					P	PR	QRS	QT	ST	T	CO_2	O_2	O_2 Cap.	% Sat.
1	0	24	110	184	Up right	.06	.04	.20	Depressed	Up right	40.58	15.43	16.28	94
2	1.20	18	156	156	Up right	.08	.06	.20	Iso electric	Up right	48.95	11.27	17.73	63
3	4.40	18	172	134	Absent	Nodal	.06	.20	Iso electric	Flat	51.10	7.32	16.28	45
4	6.20	18	176	134	Absent	Nodal	.06	.20	Iso electric	Flat	—	—	—	—
5	9.30	6	186	134	Absent	Nodal	.06	.20	Iso electric	Flat	—	—	—	—
6	10.20	0	114	166	Absent	Nodal	.04	.20	Raised	Up right	52.20	3.90	16.28	24
7	11.00	0	72	150	Absent	Nodal	.04	.20	Flat	Flat	—	—	—	—
8	11.40	0	86	174	Absent	Nodal	.04	.20	Flat	Absent	—	—	—	—
9	12.20	0	52	134	Absent	Nodal	.04	.22	Raised	Up right	—	—	—	—
10	13.30	1	10	30	Absent	Nodal	.04	.24	Raised	Up right	—	—	—	—
11	17.40	0	0	10	Complex undifferentiated						—	—	—	—

TABLE 2

Dog 12 showing typical result under Hypoxia

Sr. No.	Time	Resp. rate/ min.	Mean B.P. mm Hg	Heart rate/ min.	Analysis of E. C. G.						Arterial Blood			
					P	PR	QRS	QT	ST	T	CO_2	O_2	O_2 Cap	% Sat.
1	0	24	130	200	Up right	.08	.06	.20	Iso electric	Inverted	35.03	20.35	21.59	95
2	1.30	30	150	200	Up right	.08	.04	.20	Depressed	Inverted	—	—	—	—
3	2.50	42	150	214	Notched	.08	.04	.16	Depressed	Inverted	33.46	14.97	21.59	69
4	7.50	36	159	187	Prominent	.10	.04	.16	Depressed	Inverted	—	—	—	—
5	10.10	42	240	125	Voltage low	.10	.04	.12	Raised	Flat	28.79	5.78	21.59	26
6	11.00	0	154	115	Flat	.10	.04	.14	Raised	Flat	—	—	—	—
7	12.20	1	104	150	Absent	Nodal	.04	.16	Raised	Up right	25.03	3.36	21.59	10
8	13.20	6	108	43	Absent	Nodal	.04	.20	Raised	Up right	—	—	—	—
9	14.30	6	104	214	Absent	Nodal	.04	.12	Raised	Flat	—	—	—	—
10	15.30	0	68		Irregular Sparse AV nodal complexes						—	—	—	—
11	16.50	0	0		Ventricular fibrillation									

TABLE 3

Dog 18 showing typical result under hypercarbia

Sr. No.	Time	Resp. rate/ min.	Mean B.P. mm Hg	Heart rate/ min.	Analysis of E. C. G.						Arterial Blood			
					P	PR	QRS	QT	ST	T	CO_2	O_2	O_2 Cap	% Sat
1	0	18	100	127	Up right	.08	.02	.20	Raised	Up right	40.99	10.31	12.12	85
2	1.20	36	50	94	Up right	.08	.04	.24	Iso electric	Up right	—	—	—	—
3	2.10	36	52	107	—	—	—	—	—	—	66.79	11.43	12.12	94
4	4.00	6	68	103	Up right	.08	.04	.20	Iso electric	Inverted	64.90	10.71	12.12	89
5	5.50	6	22	103	Up right	.08	.04	.20	Iso electric	Absent	—	—	—	—
6	7.30	0	0	93	Up right	.08	.04	.24	Depressed	Flat	65.60	10.01	12.12	82
7	8.30	0	0	92	Up right	.10	.04	.24	Depressed	Flat	—	—	—	—
8	9.50	0	0	45	Up right	.10	.04	.24	Depressed	Flat	—	—	—	—
9	10.10	0	0	1	Up right	.12	.04	.28	Depressed	Flat	—	—	—	—
10	11.10	6	0	0	Asystole						—	—	—	—
11	12.10	0	0	80	Up right	.16	.04	.28	Depressed	Flat	—	—	—	—
12	13.30	0	0	43	Up right	.16	.04	.28	Depressed	Flat	—	—	—	—
13	14.40	0	0	18	Up right	.18	.04	.28	Depressed	Inverted	—	—	—	—
14	15.50	0	0	8	Up right	.18	.04	.28	Depressed	Inverted	—	—	—	—

a progressive bradycardia ending in asystole (Table 3). In three of the five hypercarbic dogs an interesting feature was a return of the heart beat after asystole for 40-60 sec. (Fig. 4 and 5) and apnea of 3-4 min. The return of the heart beat synchronised with the appearance of a few respiratory gasps before terminal apnea develped. The heart beat was ineffective in raising the blood pressure. The heart showed either a normal sinus rhythm or an alternating sinus and nodal rhythm (Fig. 5).

Cardiac irregularities were observed during asphyxia and hypoxia. In asphyxic dogs the first change was always an increase in PR interval, followed by an increase in the duration of P, QT interval, and T waves. Terminally nodal rhythm developed (Fig. 6). When such irregularities developed arterial CO_2 varied between 39.1-53.2

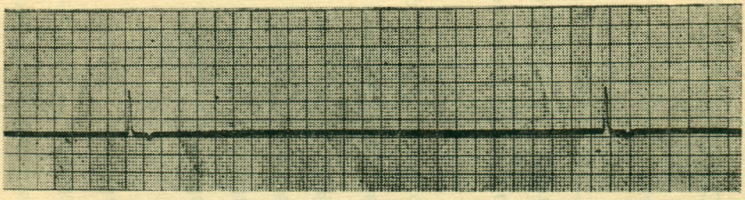


Fig. 6

vol% and haemoglobin was 27-75% saturated with oxygen. In hypoxic dogs apart from similar changes (Fig. 7) partial heart block (Fig. 8), changes in ST segment and

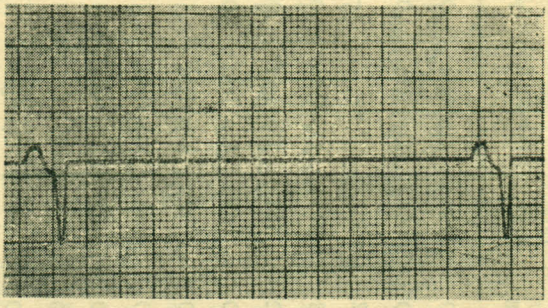


Fig. 7

ventricular extrasystoles (Fig. 9), and ventricular fibrillation (Fig. 10) also occurred in many animals. These irregularities appeared when haemoglobin saturation with oxygen varied between 44-69%. In hypercarbic animals the cardiac cycle presented no change as long as respiration was present, but when apnea developed nodal rhythm and

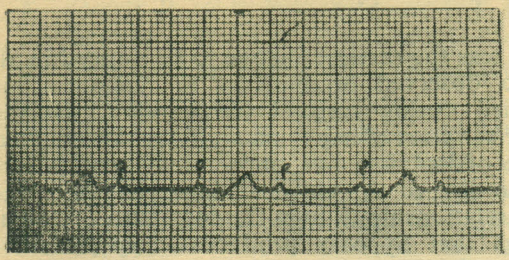


Fig. 8

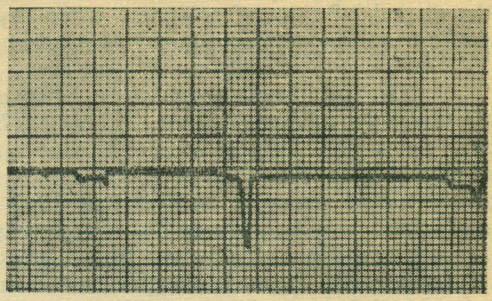


Fig. 9

changes in ST segment and T waves were seen (Fig, 11). At such time the arterial CO_2 varied between 54.2-68.5 vol% and haemoglobin was 89-99% saturated with oxygen.

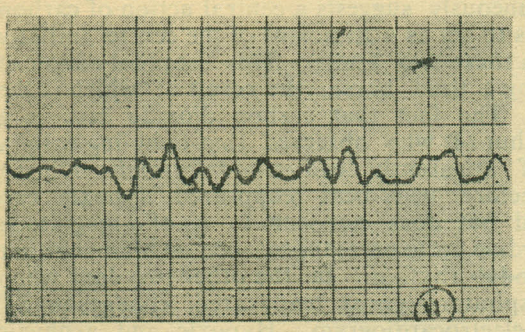


Fig. 10

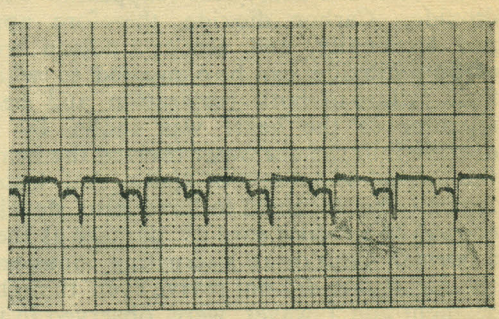


Fig. 11

DISCUSSION

In dogs exposed to hypercarbia the respiration remained stimulated upto an arterial CO_2 content of 65 vol%, but in asphyxic dogs such was the case upto 45-50 vol%. Though carbon dioxide stimulates the respiratory centre, in asphyxia the centre is depressed because of the central depressant action of hypoxia. It also becomes obvious at the same time that though carbon dioxide is a stimulant of the centre but beyond certain concentrations it acts like a protoplasmic poison and depresses the centre leading to development of sudden apnea. The hypoxic depression of the centre, on the contrary, is a slow one as signified by develpoment of gradual respiratory failure in such dogs. The fact that the blood pressure fell soon after respiratory failure in asphyxic and hypoxic dogs is suggestive of hypoxic depression of the mechanism responsible for the maintenance of blood pressure, as the cause of circulatory failure. During hypercarbia a fall followed by slight rise of blood pressure is suggestive of carbon

dioxide toning up this mechanism after an initial depression. Circulatory failure developed 2-7 min. after apnea when hypoxia can logically be assumed to have developed and led to depression of this mechanism.

In the heart progressive bradycardia was the earliest change to be noticed in all the three set of experiments. Ziegler (7) also observed bradycardia in nine out of his ten cases of cyanotic heart disease that died during surgical intervention. During asphyxia heart rate started declining soon after the start of asphyxia and could be related to the blood pressure only in the early stage of its rise, but once circulatory failure developed the heart rate did not increase according to the classical Marey's law. The heart rate did not follow the blood pressure relationship in hypoxic dogs also. Downs (2) concluded from his experiments on dogs that hypoxia produces a hypersensitive carotid sinus reaction resulting in inhibition of the cardiac activity. Although such an observation cannot be completely denied, it seems highly improbable that this hypersensitive reaction shall convert the normal inverse relationship of heart rate and blood pressure to a direct relationship. It is likely therefore, that the sinus effect, if any, remains in abeyance during hypoxic state. Hypercarbia after a transitory initial bradycardia increased the heart rate which then changed into progressive bradycardia till asystole occurred. Surprisingly in three of the five hypercarbic dogs the heart beat reappeared after an asystole of 40-60 sec.s and apnea of 3-4 min. The fact that both respiration and heart beat reappeared simultaneously suggests a central action of carbon dioxide. Carbon dioxide, therefore, appears to act as a stimulant of the centre initially and terminally, and acts as a poison within these two limits. This terminal action of carbon dioxide can be compared to whipping a tired horse, the result of which is the final failure of both respiration and heart. The fact that carbon dioxide acts as a stimulus to the heart was shown by Mathur (4) who observed that bubbling carbon dioxide into the sea water revived the heart of apparently dead *ciona intestinalis* During the period of 3-4 min of apnea that lasted before heart beat reappeared, hypoxia can logically be assumed to have also developed but does not seem to be of a magnitude enough to produce cardiac damage as the cardiac cycle on reappearance exhibited either a normal sinus or an alternating sinus and nodal rhythm. In the other two dogs when the heart rate did not revive even though respiratory gasps reappeared, changes in ST segment and T waves were observed in the electrocardiogram. Hypoxic and asphyxic dogs exhibited electrocardiographic evidence of severe cardiac injury leading to ventricular fibrillation in some of the animals. Gesell (3) also observed marked cardiac irregularities both in man and dogs exposed to hypoxic states.

Asphyxia, hypoxia or hypercarbia *per se* do not cause any primary cardiac arrest. It is the respiration that primarily fails and is followed by circulatory failure. Asystole occurs as a secondary but inevitable consequence. Hypoxia appears to be a more important factor for cardiac damage during anaesthesia. Dale (1) suggested that hypoxia possibly sensitises the myocardium to certain reflexes which necessarily originate from the site of operation or elsewhere. Obviously in this study the amount of tissue injury that occurred due to operative interference in setting up these experiments was not sufficient to precipitate cardiac arrest during hypoxia.

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