

Physiologic Responses of the Anesthetized Dog to Oxygen at Five Atmospheres Absolute

Brett B. Gutsche, M.D.,* James R. Harp, M.D.,† C. R. Stephen, M.D.‡

Thirty-two dogs were subjected to inspired oxygen tensions of 3,860 mm. of mercury (60 p. s. i. g.) for one hour, or for 15 minutes after the onset of EEG convulsive activity. Seven control animals received only succinylcholine; the rest were given succinylcholine and one of the following: thiopental, halothane, methoxyflurane, nitrous oxide or a neuroleptanalgesic combination of droperidol and fentanyl. The anesthetic drugs afforded varying degrees of protection from oxygen toxicity, but no agent provided complete protection from the toxic effects. The means by which the anesthetic drugs conferred protection, as well as implications of anesthesia at high pressures of oxygen, are discussed.

OXYGEN at high pressures (OHP) has long been known to have toxic effects. In animals, death following exposure to OHP is usually related either to pulmonary changes¹ or to acute central nervous system hyperactivity characterized by convulsions.² In contrast to the acute signs of central nervous system toxicity, irreversible ataxia, postural disturbances, and spastic paralysis have followed repeated exposures to OHP in rats.³ These lesions have been referred to as delayed central nervous system toxicity.

Various anesthetics and central nervous system depressants, including chloroform, ethyl ether, barbiturates, paraldehyde and urethane, can delay or prevent the signs of acute central

nervous system oxygen toxicity.^{2, 4-6} However Van den Breuk and Jamieson^{4, 5} and Kidd⁶ state that depressant drugs can increase susceptibility to delayed central nervous toxicity. The purpose of this investigation therefore was threefold: (1) to determine in awake dogs the physiologic changes that occur during and after exposure to OHP; (2) to ascertain how anesthetic drugs may modify the responses; and (3) to determine the incidence and nature of oxygen toxicity in the several groups.

Method

Thirty-two mongrel dogs weighing from 9 to 15 kg. were studied. Seven dogs received only succinylcholine and served as controls. Groups of 5 animals were anesthetized with thiopental, halothane, methoxyflurane, nitrous oxide, or a neuroleptanalgesic combination of droperidol and fentanyl.

Approximately one hour before compression, all animals were given succinylcholine 4 mg./kg. intravenously and intubated with a cuffed endotracheal tube to assure an air tight fit. Ventilation with 100 per cent oxygen was provided with a Palmer or Harvard animal respirator, which delivered a minute volume of 300 to 320 ml./kg. at a rate of 16 to 20 per minute. The lungs were hyperinflated periodically by setting the ventilator to the maximum tidal volume for two or three inspirations.

Right femoral arterial and venous cutdowns were performed under local anesthesia and polyethylene catheters inserted to the level of the abdominal aorta and inferior vena cava. In most animals, an 18-gauge spinal needle was inserted under local anesthesia into the cisterna magna to record cerebrospinal fluid pressure. The catheters and needle were connected to Statham strain gauge transducers. Arterial pressure, venous pressure, cerebro-

* Formerly Public Health Service Fellow (1 F2 NB 23, 984-01), National Institute of Neurological Diseases and Blindness. Now Chief of Anesthesiology, Alaska Native Hospital, Anchorage, Alaska.

† Assistant Professor of Anesthesiology, West Palm Beach, Florida.

‡ Professor of Anesthesiology, University of Texas, Southwestern Medical School.

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spinal fluid pressure, lead 2 of the electrocardiogram (ECG), and fronto-occipital leads of the electroencephalogram (EEG) were monitored constantly on a Gilson direct writing polygraph.

Heparinized arterial and venous blood samples were taken before and after induction of anesthesia, at pressure, and during decompression. They were analyzed for P_{O_2} , P_{CO_2} and pH within five minutes at the pressure at which they were drawn, utilizing a modified Instrumentation Laboratories Model 113 analyzer. In some animals cerebrospinal fluid oxygen tensions were determined before and after going to pressure.

Arterial concentrations of halothane and methoxyflurane in blood were estimated just before compression and at pressure, utilizing the method described by North.⁹

Anesthesia was maintained in light to moderate planes, according to the EEG and vital signs. The initial dose of thiopental was 15 mg./kg. intravenously, and further fractional doses were injected as needed. Halothane was vaporized with oxygen at a constant flow rate through a Fluotec vaporizer; methoxyflurane was similarly vaporized using a Pentec vaporizer. After anesthesia was established, the Fluotec was set at 1 per cent and the Pentec at 0.3 to 0.5 per cent; these settings were not changed during the experiment. Nitrous oxide analgesia was induced and maintained with 50 per cent nitrous oxide and 50 per cent oxygen. Just before compression, the mixture was switched to a pre-mixed cylinder containing 9.5 per cent nitrous oxide and 90.5 per cent oxygen. For neuroleptanalgesia, an intravenous dose of droperidol 2.0 mg./kg. was followed in three minutes by fentanyl 0.04 mg./kg. No further doses of these drugs were administered.

When vital signs were stable, the control animals were given an additional dose of succinylcholine 4 mg./kg. and the anesthetized animals 2 mg./kg., to assure that there would be no extraneous movements during compression. The pressure of the Duke Pilot Hyperbaric Chamber was raised to insure a minimum inspired oxygen tension of 3,860 mm. of mercury (60 p.s.i.g.). The control dogs and those receiving only intravenous drugs were maintained at pressures of 60 p.s.i.g. (5

atmospheres absolute), while the animals anesthetized with the inhalation drugs (vaporizer in chamber) were maintained at slightly higher pressures. Twelve to 14 minutes were required for compression.

Once the desired pressure was reached, it was maintained for 60 minutes, or for 15 minutes after the onset of convulsive activity as recorded by the EEG, whichever event occurred first. If no convulsive activity occurred at pressure, the animal was decompressed to 4.4 p.s.i.g. over a ten minute period on oxygen and then to atmospheric pressure on air. Animals which showed convulsive activity by EEG were allowed to convulse for 15 minutes, after which oxygen was discontinued and the animal was decompressed on air, according to standard naval decompression tables.

When convulsive activity began, or after the animal had been at pressure for 35 minutes, the investigators underwent compression and entered the main chamber with the animal. Appropriate drugs were administered including barbiturates or thiobarbiturates to control convulsions, THAM buffer or sodium bicarbonate to counteract metabolic acidosis, and vasopressors, cardiac glycosides, or cardiac stimulants to avert or treat shock. When ventricular fibrillation occurred, external cardiac compression and external d.-c. defibrillation were employed in efforts to restore effective cardiac output.

Following decompression, the animals were ventilated on air until the return of adequate spontaneous respirations or until death. Frequently, the animals developed inspiratory convulsive movements, which were controlled with intravenous pentobarbital as needed. Many surviving animals were unable to take oral nourishment for periods of up to four days after exposure. They were maintained on appropriate parenteral fluid therapy.

Results

Central Nervous System. Succinylcholine masked all motor signs of convulsive activity. Onset, duration and nature of the convulsions were ascertained from the EEG. Table 1 summarizes the findings pertaining to the onset and frequency. Convulsive activity was always the first sign of oxygen toxicity noted.

TABLE 1. Data on Convulsions

Anesthetic	Animals (1)	Mean Exposure Time (minutes) (2)	Animals Convulsing (3)	Time to Onset of Convulsions (minutes) (4)	CSF Pressure Increase with Convulsions* (mm. Hg) (5)
Control (succinyl- choline alone)	7	30 ± .8	7	14 ± 11†	52 ± 11†
Thiopental	5	60 ± 1.0	0	—	—
Halothane	5	47 ± 11	5	29 ± 9	No change
Methoxyflurane	5	50 ± 15	3	27 ± 19	14 ± 2
Nitrous oxide	5	19 ± 6	5	1.8 ± 3.1‡	21 ± 11
Neuroleptanalgesia	5	51 ± 7	4	39 ± 16	27 ± 14
Total	32		24		

* Number of observations given by column 3.

† Four determinations only.

‡ See text.

No dog receiving thiopental developed convulsions during exposure to OHP. The EEG recordings remained essentially normal throughout the experiment. All animals in the control, nitrous oxide and halothane series developed EEG evidence of convulsive activity within the prescribed one hour period of exposure. Three and 4 animals, respectively, in the methoxyflurane and neurolept groups also developed EEG evidence of convulsive activity. The time of onset of convulsions was slowest with neuroleptanalgesia and fastest with nitrous oxide.

In the control and nitrous oxide animals, EEG evidence of convulsions consisted of a sustained 400–600 μ v., 12 to 15 cycle per second spiking pattern lasting 30 to 60 seconds, then a pause of electrical inactivity, followed by another sustained seizure pattern. This type of activity repeated itself, but the periods of electrical inactivity and convulsive activity decreased in duration. This pattern contrasted markedly with that seen in the halothane, methoxyflurane and neuroleptanalgesia dogs, which showed initially short half-second bursts of 100–200 μ v. spikes, which over several minutes increased in duration, amplitude and frequency. Finally, a pattern of 15- to 20-second bursts of sustained high voltage spikes, separated by periods of electrical inactivity, predominated.

During EEG seizure activity, there were marked increases in cerebrospinal fluid pressure in the animals receiving only succinyl-

choline. These increases in pressure were less in the neurolept, nitrous oxide, and methoxyflurane animals. Convulsions were not associated with increase in cerebrospinal fluid pressure in the halothane group.

Cardiovascular System. Cardiovascular reactions are summarized in table 2. After compression, and before the onset of convulsive activity, the arterial pressures in all groups remained relatively stable. Moderate bradycardia developed in the halothane and methoxyflurane groups, which may have been related to an increased depth of anesthesia accompanying compression.

Marked increases in both arterial pressure and pulse rate were associated with EEG convulsive activity in the control, nitrous oxide, and neuroleptanalgesia groups. In the methoxyflurane group, convulsions were associated with moderate increases in arterial pressure, but a reduction in pulse rate. In the halothane animals, EEG seizure patterns were not accompanied by significant cardiovascular changes.

The control, nitrous oxide, and neurolept animals developed severe cardiac arrhythmias, including premature ventricular contractions, bigeminy, and ventricular tachycardia, with the onset of convulsions. The ECG remained unchanged during convulsions in the halothane and methoxyflurane dogs.

Figure 1 illustrates the variations in cerebrospinal fluid pressure and circulation observed in a control experiment.

TABLE 2. Vital Signs and Cardiovascular Reactions

Anesthetic	Animals	Vital Signs at Ambient Pressure		Vital Signs at Pressure		Animals Convulsing	Vital Signs During Convulsions*		Reactions During Convulsions
		Average Blood Pressure (mm. Hg)	Average Pulse Rate	Average Blood Pressure (mm. Hg)	Average Pulse Rate		Average Blood Pressure (mm. Hg)	Average Pulse Rate	
Control (succinylcholine alone)	7	186 \pm 28 111 \pm 27	111 \pm 12	190 \pm 46 111 \pm 30	97 \pm 50	7	309 \pm 64 198 \pm 52	215 \pm 99	Severe cardiac arrhythmias: ventricular tachycardia in 4 animals.
Thiopental	5	158 \pm 18 104 \pm 12	129 \pm 24	157 \pm 32 111 \pm 26	129 \pm 31	0	—	—	Stable cardiovascular system.
Halothane	5	146 \pm 28 98 \pm 21	125 \pm 22	121 \pm 28 81 \pm 23	77 \pm 16	5	121 \pm 28 81 \pm 23	71 \pm 15	Stable cardiovascular system.
Methoxyflurane	5	152 \pm 27 98 \pm 17	129 \pm 35	171 \pm 70 110 \pm 51	94 \pm 42	3	215 \pm 47 99 \pm 13	60 \pm 21	Bradycardia and moderate hypertension.
Nitrous oxide	5	172 \pm 21 108 \pm 23	124 \pm 16	187 \pm 14 130 \pm 23	124 \pm 26	5	285 \pm 41 198 \pm 27	143 \pm 56	Severe cardiac arrhythmias: ventricular tachycardia in 3 animals.
Neurolept-analgesia	5	147 \pm 7 77 \pm 19	65 \pm 26	160 \pm 19 85 \pm 21	60 \pm 10	4	302 \pm 53 190 \pm 46	203 \pm 99	Severe cardiac arrhythmias: ventricular tachycardia in 2 animals, one proceeding to ventricular fibrillation.

* Number of observations the same as that given by the number of animals convulsing.

Postexposure Course. Table 3 summarizes the postexposure course of the animals. Death was usually related to either circulatory changes or central nervous system signs. Death occurred rapidly in some animals following the development of hypertension and severe cardiac arrhythmias, and in 3 dogs was associated with pulmonary edema. This type of death was seen in 4 control animals and in one neurolept dog. While the nitrous oxide group showed severe cardiovascular abnormalities, no cardiovascular deaths occurred.

Dogs that succumbed with acute central nervous system signs developed convulsions in

the immediate postexposure period and succumbed within 24 to 48 hours despite vigorous anticonvulsant therapy. The convulsions could be temporarily alleviated by the use of pentobarbital or phenobarbital, but only in doses sufficiently large to require mechanical ventilation to assure adequate oxygenation. When the barbiturates were discontinued, the animal usually reverted to a convulsive state both clinically and on the EEG. Gradually the condition of the animal deteriorated, and it died in a state of shock. Only one of 924 animals showing these postexposure convulsions recovered. This type of death occurred

in 4 halothane animals and in several dogs receiving methoxyflurane, nitrous oxide, or succinylcholine alone.

Three animals died from causes believed not to be directly related to oxygen toxicity. Two dogs made a rapid recovery, but died within 48 hours from meningitis confirmed at autopsy. The third animal suffered a tension pneumothorax during decompression.

Of 15 animals which survived exposure to OHP, 8 revealed a weakness or spasticity of the extremities associated with generalized disequilibrium and incoordination. Seven of these animals made a complete recovery in one to seven days. The eighth animal which died seven days after exposure was showing improvement, but still had incoordination of the hind legs. This type of delayed oxygen toxicity was seen in 3 thiopental, 2 methoxyflurane, 2 succinylcholine and one halothane treated animal.

Seven animals, most of which had EEG convulsions and cardiovascular abnormalities during exposure to OHP, had a rapid and uneventful recovery. Three received neuroleptanalgesia and the other 4 were given thiopental, nitrous oxide, or methoxyflurane.

Blood and Cerebrospinal Fluid pH and Gas Determination. Table 4 lists the P_{O_2} , P_{CO_2} and pH values of the arterial and venous blood, and the P_{O_2} of the cerebrospinal fluid, both at ambient and increased pressures. At ambient pressure, the arterial blood gases were similar in all animals, except that the oxygen

OHP TO 60 PSIG IN SUCCINYLCHOLINE TREATED DOG (#773)

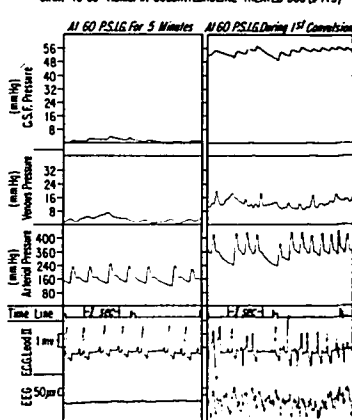


FIG. 1. Cardiovascular parameters and cerebrospinal fluid pressures in a control succinylcholine dog. Note marked elevation of the arterial and cerebrospinal fluid pressure, as well as the ECG arrhythmias associated with convulsive activity.

tension of the neuroleptanalgesic group was elevated and that of the nitrous oxide animals reduced. Only the lungs of the neurolept group were deep-breathed (sighed) three minutes before each determination. The nitrous oxide animals had only 50 per cent oxygen in the inspired air.

TABLE 3. Postexposure Data

Anesthetic	Animals	Deaths				Signs of Toxicity		
		Total	Cardiovascular	Convulsive	Not Related to Oxygen Toxicity*	Acute	Delayed	None
Control (succinylcholine alone)	7	5	4	1	0	7	2	0
Thiopental	5	0	0	0	0	0	3	2
Halothane	5	4	0	4	0	5	1	0
Methoxyflurane	5	2	0	2	0	3	2	1
Nitrous oxide	5	4	0	2	2	5	0	0
Neuroleptanalgesia	5	2	1	0	1	4	0	1
Total	32	17	5	9	3	24	8	4

* See text for explanation.

TABLE 4. Blood and Cerebrospinal Fluid pH and Gas Determinations*

Anesthetic		Ambient			At 60 p.s.i.g. O ₂ Pressure		
		P _a O ₂ (mm. Hg)	P _c O ₂ (mm. Hg)	pH	P _a O ₂ (mm. Hg)	P _c O ₂ (mm. Hg)	pH
Control (succinylcholine alone)	Arterial	475 ± 74	24 ± 4	7.46 ± 0.07	3003 ± 545	29 ± 18	7.34 ± 0.1
	Venous	130 ± 83	26 ± 5	7.44 ± 0.10	1419 ± 1015	49 ± 13	7.22 ± 0.0
	CSF	128†	—	—	2020†	—	—
Thiopental	Arterial	442 ± 30	28 ± 8	7.46 ± 0.05	2706 ± 650	32 ± 6	7.49 ± 0.0
	Venous	119 ± 53	40 ± 20	7.43 ± 0.07	1298 ± 282	36 ± 6	7.44 ± 0.1
	CSF	—	—	—	1815†	—	—
Halothane	Arterial	489 ± 89	28 ± 5	7.47 ± 0.03	2761 ± 733	36 ± 5	7.32 ± 0.0
	Venous	92 ± 43	33 ± 4	7.40 ± 0.05	494 ± 138	48 ± 10	7.30 ± 0.0
	CSF	—	—	—	2192 ± 318	—	—
Methoxyflurane	Arterial	499 ± 117	24 ± 8	7.48 ± 0.02	2764 ± 926	34 ± 6	7.38 ± 0.0
	Venous	60 ± 18	29 ± 9	7.43 ± 0.06	1168 ± 1120	48 ± 18	7.25 ± 0.1
	CSF	210 ± 49	—	—	†1482 ± 308	—	—
Nitrous oxide	Arterial	280 ± 58	30 ± 6	7.42 ± 0.05	2619 ± 396	36 ± 5	7.32 ± 0.0
	Venous	71 ± 16	37 ± 9	7.38 ± 0.04	922 ± 529	52 ± 11	7.21 ± 0.0
	CSF	141 ± 31	—	—	2108 ± 682	—	—
Neuroleptanalgesia	Arterial	622 ± 27	27 ± 5	7.50 ± 0.07	3523 ± 359	29 ± 7	7.46 ± 0.0
	Venous	72 ± 11	30 ± 6	7.49 ± 0.12	1909 ± 964	42 ± 9	7.32 ± 0.0
	CSF	188 ± 26	—	—	2761 ± 413	—	—

* All means result of seven determinations for control group or five determinations for other groups unless noted.

† Only two determinations made.

‡ Only four determinations made.

At pressure, the mean arterial oxygen tension was higher in the control animals (3,003 mm. of mercury). The theoretical value at 60 p.s.i.g. is 3,785 mm. of mercury.

Despite the fact that ventilation was kept constant throughout the experiments, an increase in both the mean arterial and venous P_cO₂ developed in all but the thiopental animals at pressure. Also in the thiopental group, in which no convulsions were observed, the pH changed little at pressure. However, in the remaining groups, pH values decreased consistently. Many animals in these groups were having EEG convulsive activity when the samples were drawn. On decompression, the animals which convulsed showed even more reduction in pH, frequently to values of less than 7.20; these animals required alkalinizing agents.

The cerebrospinal fluid oxygen tensions at pressure were markedly elevated, ranging from

a mean of 1,482 mm. of mercury in the methoxyflurane animals to 2,760 mm. of mercury in the neurolept group. The P_aO₂ of the cerebrospinal fluid was intermediate between that of the arterial and venous oxygen tensions.

The arterial levels of halothane and methoxyflurane were not consistent, either at ambient or increased pressures, despite the use of flow and temperature compensated vaporizers, similar induction and maintenance dosages of the drugs, and constant tidal and minute ventilation. The mean arterial concentration of halothane at atmospheric pressure was 9.9 ± 1.7 mg./100 ml. and at pressure was 15.1 ± 2.4 mg./100 ml. The arterial concentrations for methoxyflurane were 12.5 ± 4.4 mg./100 ml. and 13.8 ± 3.4 mg./100 ml., respectively. The one surviving halothane animal and the 3 surviving methoxyflurane animals had the highest arterial blood anesthetic concentration during OHP exposure.

Discussion

The purpose of the investigation was to study the modifying effects of anesthetic drugs, suitable for use in the hyperbaric environment, on the development of central nervous system signs of oxygen toxicity. A maximum of one hour exposure at 60 p.s.i.g. was chosen because it was known that few unanesthetized dogs could withstand such exposure without developing acute central nervous system signs of oxygen toxicity.¹⁰ Oxygen was discontinued after EEG evidence of convulsions for 15 minutes because earlier experience¹¹ had indicated that dogs convulsing a longer period would not survive. Muscle relaxant drugs were used in the control animals and with the anesthetic drugs to ensure that undue motor activity would not interfere with the basic design of the investigation.

In the past, investigators have argued that OHP causes central nervous system toxicity by "hyperoxic anoxia"; that is, OHP produces an anoxic state of the brain.¹² In the present experiments, the oxygen tension of the cerebral spinal fluid was markedly elevated at pressure. Although some doubt exists whether the cerebral spinal fluid oxygen tension accurately reflects that of the cerebral tissue, Jamieson and Van den Breuk¹³ have shown that oxygen electrodes placed in the subarachnoid space of the rat subjected to OHP gave similar responses to those in the brain substance. The present work adds credence to the hypothesis that the central nervous system toxic effects of OHP are due to the direct effect of increased oxygen tension on central nervous system tissues.

Exposure of the animal to central nervous system depressant drugs delays the onset of the EEG manifestations of oxygen toxicity. With the exception of nitrous oxide, all the anesthetic drugs studied delayed the onset of convulsive activity. Thiopental was most effective in this respect, followed by the neuroleptanalgesic combination, and then by methoxyflurane and halothane in close order. The ability of general anesthetics to delay or prevent seizures is likely related to their non-specific depression of the central nervous system. Why thiopental should be the most effective is unknown, but one can postulate

that it produces a greater depression of more susceptible areas. Certainly, the anticonvulsant properties of the barbiturates are well documented.

The appearance of cardiovascular changes with convulsions has been demonstrated in both man and animals.^{14, 15} Recent experiments in this laboratory have shown marked hypertension and cardiac arrhythmias associated with electroshock, pentylenetetrazol convulsions, and oxygen induced convulsions (at pressure) in succinylcholine treated dogs. Since muscular paralysis was complete in these studies, the cardiovascular changes could not be explained on the basis of muscular overactivity. A reasonable explanation would be the release of endogenous catecholamines following stimulation of the sympathetic nervous system by mechanisms in the overactive central nervous system. Both Woodbury¹⁵ and Gatgounis¹⁶ have presented evidence to add weight to this theory. None of the halothane animals in this series showed cardiovascular alterations during seizure activity at OHP. Since there is evidence that halothane exerts a blocking action on the sympathetic nervous system,¹⁷ and since Black¹⁸ has shown that halothane is capable of blocking vasoconstriction by norepinephrine, these observations support the concept that sympathetic discharge is responsible for the cardiovascular changes associated with convulsions.

A less dramatic aspect of central nervous system oxygen toxicity is the development of post exposure or delayed signs of oxygen toxicity. Bean³ first described this form of toxicity in rats and noted that the signs persisted until death. We have noted relatively transient neuromuscular disturbances in dogs, both anesthetized and unanesthetized.¹¹ Only recently have neuropathologic lesions been found which may shed light on the etiology of these delayed signs of oxygen toxicity.^{19, 20}

In this investigation, 8 of 32 animals demonstrated transient neuromuscular disturbances on recovery from anesthesia. All of these animals showed improvement, with 7 having complete clinical remission two to seven days following exposure. Of these 8 animals, four exhibited EEG convulsive activity during exposure to OHP. However, 3 thio-

penthal and one methoxyflurane dog showed no demonstrable signs of acute oxygen toxicity while subjected to OHP. These observations emphasize an important point: anesthetic drugs may prevent the occurrence of acute signs of oxygen toxicity, but they do not assure the absence of neurologic damage in the recovery period.

Recently, several investigators^{4,7,8} have presented evidence that central nervous system depressant drugs, most notably pentobarbital, while delaying the onset of the acute signs of oxygen toxicity in the rat, hasten and augment the delayed central nervous system signs of oxygen toxicity as described by Bean.² We have not been able to corroborate this finding in rats exposed to oxygen at 57-58 p.s.i.g.²⁰ The results of the present study throw little light on the matter.

In all but the neuroleptanalgesic dogs, which were vigorously hyperventilated three minutes before each blood sample, the arterial oxygen tensions at pressure were considerably below the theoretical value of 3,785 mm. of mercury. Periodic hyperinflation tends to open collapsed alveoli through which blood is flowing but is not being oxygenated, and hence increases the arterial oxygen tension. These observations stress the importance of periodic hyperinflation or "sighing" of individuals on controlled respirations who are receiving high inspiratory concentrations of oxygen.

On the basis of these experiments, certain conclusions may be drawn. Exposure times to high pressures of oxygen should be brief if they are to be safe, both in awake and anesthetized animals. During such exposures, abnormalities in the EEG and ECG, both of which should be continually monitored, demand that oxygen be immediately terminated. Otherwise, rapidly fatal convulsions and/or associated cardiovascular abnormalities may develop.

Of the anesthetic drugs studied, thiopental afforded the greatest protection against the onset of convulsions, but it offered little guarantee against the development of delayed oxygen toxicity. Halothane and methoxyflurane, while delaying the onset of convulsions and protecting against the cardiovascular changes accompanying convulsions, did not prevent

death from convulsions following exposure or the development of delayed oxygen toxicity. The neurolept combination delayed the onset of convulsions and prevented the onset of post-exposure signs, but did not confer protection against the cardiovascular changes. In other words, none of the drugs studied afforded complete protection from the several manifestations of central nervous system oxygen toxicity.

Summary

Thirty-two dogs were subjected to inspired tensions of 3,862 mm. of mercury oxygen (60 p.s.i.g.) for 60 minutes, or for 15 minutes after the onset of EEG convulsions. Seven animals received only succinylcholine and served as controls. Five animals each were exposed to succinylcholine in combination with thiopental, halothane, methoxyflurane, 9.5 per cent nitrous oxide, or a neuroleptanalgesic combination of droperidol and fentanyl.

Some animals in all groups showed signs of central nervous system oxygen toxicity, which were classified as acute or delayed. The acute signs of central nervous system oxygen toxicity were demonstrated by the onset of convulsive activity on the EEG. Thiopental provided the most complete protection against acute toxicity. Associated with EEG convulsions were severe cardiovascular disturbances in the control, nitrous oxide and neuroleptanalgesic groups of dogs. Halothane provided the best protection in this respect. Delayed signs of oxygen toxicity, consisting of neuromuscular disturbances, were observed after decompression and recovery from anesthetic drugs.

The anesthetic drugs afforded varying degrees of protection from oxygen toxicity. The mechanisms of such action are discussed. The data suggests that exposures to high pressures of oxygen for even brief periods of time are hazardous in both awake and anesthetized animals.

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EPIDURAL HEMORRHAGE Three instances of spinal epidural hemorrhage are reported in patients on anticoagulant therapy with reduced prothrombin times. The presenting complaints were pain and paraparesis, none had had epidural or subarachnoid puncture. (*Jacobson, I.: Spontaneous Spinal Epidural Haemorrhage During Anticoagulant Therapy, Brit. Med. J.* 1: 522 (Feb. 20) 1966.)

PAIN CLINIC The management of patients with severe, intractable pain often requires a multiplastic approach, or the application of several therapeutic methods, each chosen specifically for certain desired effects. It is obvious that effective diagnosis and therapy may be possible only through the concerted efforts of the patient's doctor and specialists who contribute their individual skills toward a common goal. One of the best means of achieving these objectives is to form a pain clinic group represented by an anesthesiologist, neurosurgeon, psychiatrist, radiotherapist, physiatrist, orthopedic surgeon, general surgeon, internist, and a social worker, meeting at frequent intervals. The group provides consultative services to the referring physician and the patient. Face-to-face group discussions are much more effective and productive than communication by letter or phone. (*Bonica, J. J.: Management of Intractable Pain in General Practice, G. P.* 33: 107 (Jan.) 1966.)