Effect of Rapid Decompression and Associated Hypoxic Phenomena in Euthanasia of Animals: A Review

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SUMMARY

Documentation in the literature indicates that death is as painless following the induction of hypoxia by rapid decompression as by other methods that lead to hypoxia, such as exposure to high altitude, carbon monoxide, and inert gases (nitrogen, xenon, and krypton). Many of the signs and symptoms of hypoxia are the same as those for alcoholic intoxication and inert gas narcosis. Moreover, there is good evidence that analogous relationships or mechanisms may exist for hypoxia, inert gas narcosis, and anesthesia.

In 1972 and 1978, reports of the AVMA Panel on Euthanasia[1,2] included the utilization of hypoxic procedures in euthanasia of animals. The reports covered the effects of carbon monoxide, nitrogen gas, rapid decompression, and respiratory paralyzing concentrations of anesthetics, all of which result in death by inducing an acute hypoxia or acute oxygen deficiency.

Controversy has arisen regarding the humaneness of using hypoxic methods of inducing euthanasia in animals, especially those involving use of rapid decompression or nitrogen gas. Consequently, some cities and states have passed legislation banning the use of decompression or nitrogen gas. Because of the increasing interest of individuals desiring documented information on whether or not decompression and other hypoxic methods are humane procedures of killing animals, relevant literature was assembled and is reviewed here.

Comparative Effects of Decompression, Alcoholic Intoxication, and Inert Gas Narcosis

Decompression produces hypoxic effects similar to those observed during ascent in climbing high mountains or in flying at high altitudes in unpressurized aircraft.[3] The higher the altitude the lower the ambient pressure and the more severe the hypoxia. The percentage composition of the various gases of the atmosphere, however, remains the same as at sea level.[4] For example, the percentage of O_2 at sea level and at any given altitude above sea level is 20.96.[4] At sea level, the ambient or barometric pressure is 760 mm of Hg, whereas at 55,000 ft above sea level, the pressure is 68.8 mm of Hg. Thus, the partial pressure of O_2 at sea level is 760×0.2096 or 159 mm of Hg. At 55,000 ft, the partial pressure of O_2 is 68.8×0.2096 or only 14 mm of Hg (Table 1). The mean arterial blood of dog or man normally has an O_2 tension (P_{O_2}) of about 95 mm of Hg.[5] At 55,000 ft, the P_{O_2} (14 mm of Hg) is considerably below the physiologic level necessary to maintain proper oxygenation of tissues. This low or deficient P_{O_2} results in severe hypoxia, unconsciousness, and rapid death.

Ascent to high altitude and the resultant hypoxia may induce various effects such as excitement, exhilara-

TABLE 1—Altitude and Barometric Pressure Relationships Above Sea Level

Altitude (ft above sea level)	Barometric pressure (mm of Hg)
0	760
2,000	707
6,000	609
10,000	522
14,000	446
18,000	380*
22,000	321
26,000	270
30,000	226
34,000	187
38,000	155
42,000	128
46,000	106
50,000	87
54,000	72
58,000	60
63,000	47†

* Equivalent to one-half the pressure at sea level. † Altitude that ebullition occurs, or equivalent to water vapor pressure in lungs.

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TABLE 2—Comparative Potencies of Inert Gases and Gas Anesthetics Which Produce Equivalent Levels of Anesthesia or Neurologic Depression in Human Beings and Animals

Gas	Anesthetic pressure (ATA)*
Helium	> 261
Neon	88
Nitrogen	29
Argon	20
Krypton	2.9
Nitrous oxide	0.9
Xenon	0.85
Diethyl ether	0.02
Chloroform	0.015
Halothane	0.008

Data from Miller et al[50] and Saidman et al.[60] ATA = Atmospheres absolute.

tion, and euphoria followed by headache, lassitude, sensory dullness, visual impairment, neuromuscular weakness, dyspnea, and loss of consciousness.[4] It is well known that aircraft pilots flying at high altitude and exposed to a low O_2 environment will develop these hypoxic symptoms. Hypoxia may be so acute that loss of consciousness occurs rapidly without prior warning.[6,7]

All manifestations observed in alcoholic intoxication such as headache, drowsiness, severe respiratory depression and the associated O_2 deficiency, impaired vision, neuromuscular incoordination, and failure in mental tests also have been observed in human beings subjected to acute hypoxia[4] or exposure to decompression.[8] In all instances, these effects are induced by an insufficient P_{O_2} to the brain. Hypoxia or a deficient P_{O_2} should not be confused with suffocation, strangulation, or asphyxiation in which a deficiency in O_2 is combined with an increased CO_2 tension (hypercapnia) as that seen following the action of succinylcholine or *d*-tubocurarine[1] in paralysis of the respiratory musculature (intercostal muscles and diaphragm). Hypercapnia or suffocation is not a factor in ascent to high altitude or during decompression.

Interestingly, many of the signs and symptoms of hypoxia described here are the same as those for compression in air and for inert gas narcosis.[9] Narcosis induced in human beings by their compression in air was reported as early as the last century. Symptoms resembling alcoholic intoxication were observed in 1835 by Junod.[9] This adverse effect on mental perceptivity and on the ability of the human being to perform in compressed air can range from the euphoria first observed in caisson workers, to amnesia, dangerous hyperconfidence, difficulty in decision making, and lapses in consciousness in divers.[9] In 1935, it was learned that this compressed-air intoxication was due to the nitrogen content of air.[10] A narcotic effect occurs in human beings in air at 3 atmospheres and greater. Euphoria, retardation of the higher mental processes, and impaired neuromuscular function are observed.[10] The study of Behnke et al[10] led to the realization that nitrogen narcosis was just one example of a more general phenomenon also characteristic of other inert gases.[11,12] The difference between the narcotic actions of these gases is primarily one involving potency rather than the nature of the symptoms they elicit.[9] According to Hills and Ray,[9] the best index for quantitating this difference is probably provided by the "equinarcotic partial pressure" and can be extended to include gaseous anesthetics.

Values are available for an assortment of gases and provide a comparative basis for their relative narcotic potencies (Table 2). The more potent inert gas requires the smallest partial pressure in order to elicit the same degree of narcosis.[9] Such a comparison infers that inhalant anesthesia is an extension of inert gas narcosis; in fact, there is good evidence that an analogous relationship or mechanism exists in both conditions.[13]

Similar to the symptoms induced by decompression or alcoholic intoxication, manifestations of inert gas narcosis or compressed air narcosis include euphoria, loquacity, hallucination, temporary loss of memory, difficulty in assimilating facts or in making decisions, overconfidence, delayed response to visual, auditory, olfactory, and tactile stimuli, and impaired neuromuscular coordination leading to stupefaction and loss of consciousness.[9] Exposure to compressed air at 2 atmospheres absolute (ATA)[a] or 2 × 760 mm of Hg results in delta activity of the EEG.[13] At 7 ATA, signs and symptoms of "nitrogen narcosis" are evident in a large number of individuals, accompanied by a slight decrease in the amplitude of the alpha rhythm. At 10 ATA, this decrease is more marked and the signs of the narcosis are more severe. If the pressure is increased further, unconsciousness occurs.[13]

Major Effects Observed Following Exposure to Decompression

The effects of decompression on the dog are summarized as follows[14-18]: Immediately after exposure to an ambient pressure of 30 mm of Hg, respiration becomes deep and rapid. This hyperventilation lasts for a matter of seconds. Marked abdominal distention occurs immediately. This is due to the expansion of gases present in the gastrointestinal tract. The animal collapses in about 8 seconds. Convulsions generally occur in from 10 to 12 seconds and last for several seconds. Decerebrate rigidity also may be observed. It occurs in animals following recompression or return to normal atmospheric pressure.[15] Following a convulsive seizure, the animal is quiescent except for occasional respiratory gasps which are ineffective in ventilating the lungs. Usually lacrimation, salivation, and urination occur.

In the monkey, gastric contents are suddenly and forcibly ejected at the time the animal is decompressed to altitudes above 55,000 ft.[19] Thirty to 40 seconds after the reduction of pressure, secondary swelling begins. This swelling occurs first in the rear limbs and lower abdomen and progresses headward. Animals will survive and completely recover if exposure to 30 mm of Hg is for less than 90 seconds. Exposures of 2 minutes or longer are usually fatal.

In the human being, pain from gas expansion in the gut has been uncommon during ascent in altitude, although most subjects notice a "boiling" sensation in

[a] ATA = Unit of pressure (760 mm of Hg) equal to the pressure of air at sea level at 0 C.

the abdomen.[3] Some individuals have complained of pain presumably by esophageal origin following inadvertent attempts to eruct during ascent. In addition to abdominal pain prior to unconsciousness, generalized chest pain has been reported by human subjects a few seconds before loss of consciousness.[20]

Neurologic Influence of Decompression

Of the tissues in the body, nervous tissue is the least capable of withstanding the effects of hypoxia.[4] In the human being, acute hypoxia resembles alcoholic intoxication because of the marked O_2 deficiency and respiratory depression that develops. The symptoms are headache, mental disorientation, drowsiness, depressed respiratory activity, neuromuscular weakness, and incoordination.[21] According to Van Liere,[21] "A person exposed to a low oxygen tension often passes through an initial stage of euphoria, accompanied by a feeling of self-satisfaction and a sense of power. The oxygen want stimulates the central nervous system so that the subject may become hilarious and sing or shout, and other emotional disturbances often manifest themselves."

As exposure to low P_{O_2} levels is increased, loss of consciousness occurs. An aircraft pilot exposed suddenly to an altitude of 45,000 ft above sea level will become unconscious in 13 to 16 seconds.[22] Unconsciousness can only be avoided if 100% O_2 is inspired within 5 to 7 seconds. Pilots subjected to 33,000 ft and breathing 100% O_2 and immediately exposed to 52,500 ft for less than 6 seconds and then recompressed to 33,000 ft do not lose consciousness.[23] If exposure is longer than 6 seconds, unconsciousness will occur even while breathing 100% O_2.

In the human being, temporary arrest of the circulation to the brain without affecting the respiratory tract has been accomplished by means of a specially designed inflatable cervical pressure cuff.[24] Characteristic reactions resulting from acute arrest of the circulation to the brain for 5 to 10 seconds are fixation of the eyeballs, blurring of vision, loss of consciousness, and hypoxic convulsions. Loss of consciousness precedes the hypoxic convulsion. Convulsive seizures are of a generalized tonic and clonic type. Inasmuch as the convulsion is preceded by loss of consciousness, the person remains unconscious throughout the seizure and has no memory of it. Electroencephalographic recordings reveal the sudden appearance of large slow waves (delta waves) that are closely correlated with fixation of the eyes or loss of consciousness. Also, EEG and other electrical recordings have been made for human subjects made hypoxic by breathing nitrogen,[23,25] low O_2 concentrations,[26] and in those decompressed to simulated altitudes of 45,000 ft.[22] In animals, electrical cortical activity of the brain has been recorded following hypoxemia[27] and decompression.[28]

The cerebral circulation has been arrested for as long as 100 seconds in human beings.[24] All subjects regain consciousness within 30 to 40 seconds after restoration of circulation. During the arrest, loss of consciousness, convulsions, marked cyanosis, involuntary urination and defecation, bradycardia, and dilation of pupils are observed.[24] These signs are comparable to those observed in animals following the induction of hypoxia by decompression.

In the dog, arrest of brain circulation for 6 minutes or less recover neurologic function, whereas those subjected to periods of circulatory arrest for 8 minutes or longer usually have permanent brain damage.[29] Urination frequently occurs during the first minute of circulatory arrest. Respiratory activity ceases 15 to 20 seconds after arrest of brain circulation in most animals. This results in development of severe hypoxia.

During a period referred to as hyperactive coma following circulatory arrest, there are rapid running movements of all limbs, often accompanied by salivation and vocalization. These coordinated and rhythmic movements along with vocalization occur with the dog lying unconscious on its side.[29] Early in the period of hyperactive coma, extensor rigidity is seen, usually expressed as opisthotonos with the jaws closed tightly. During intervals between running movements, there is moderate extensor rigidity predominantly in the forelimbs.[29] Manifestations of the signs observed in dogs during the period of hyperactive coma are almost, if not identical, to what the author has seen in some dogs subjected to the early period of rapid decompression or exposure to lethal concentrations of carbon monoxide.

According to Kabat et al,[29] running movements during the period of hyperactive coma are similar to those that occur during recovery from barbiturate anesthesia. Veterinarians are well acquainted with these running movements and vocalization during the delirium period during recovery from pentobarbital sodium anesthesia.[30] The animal is comatose or unconscious during this period which is characteristic of stage-2 anesthesia.[30]

Pulmonary and Cardiovascular Influences of Decompression

The most consistent and outstanding response observed in animals (cat, dog, rat, rabbit, and guinea pig) following decompression is the development of abdominal distention.[31] Abdominal distention is greatest in the guinea pig and rabbit due to the relatively large amounts of gas normally present in the gastrointestinal tracts of these animals. As the distention increases, the diaphragm is forced up into the expiratory position, while the thorax is lifted into the inspiratory position. In the rabbit and guinea pig, these effects may be so prominent as to interfere seriously with, or actually prevent, respiratory movements. This distention and the pressure build up inevitably interferes with blood returning to the heart by way of the caudal vena cava. A positive intra-abdominal pressure of the magnitude observed at a simulated altitude of 55,000 ft must be sufficient to interfere with venous return to the heart.[32] A marked reduction in venous return results in a decrease in cardiac output and prompt lowering of arterial pressure. This reduces the latent period of the hypoxic response since, in addition, the arterial pressure and blood flow to the brain and heart also are reduced. Hypoxia impairs the heart as a circulatory pump. Cardiovascular depression is as prompt and the hypoxia as

complete following decompression to 55,000 ft as at higher simulated altitudes.[32]

In dogs exposed to decompression, there is a rapid drop in systemic arterial pressure.[31] Also, in dogs decompressed to 30 mm of Hg (ie, equivalent to an altitude of 72,000 ft), circulation is completely stopped in less than 16 seconds after decompression.[16] This circulatory arrest results from vapor or bubbles due to the expansion of blood gases in the heart or vascular bed and corresponds to what an engineer refers to as vapor lock. Brief arrest of blood flow to the brain of the adult dog produces coma for 12 to 18 hours; after 6 minutes, for 24 hours or longer and; after 8 or more minutes, coma is permanent.[29]

More than 40 years ago, Lennox et al[33] reported that in human beings loss of consciousness occurs when O_2 saturation of the jugular venous blood drops to 24% or below. The percentage O_2 saturation has been determined in the dog 30 seconds following decompression to various barometric pressures.[34] Decrease in percentage saturation does not occur until pressures less than 510 mm of Hg are attained. Oxygen saturation decreases sharply at barometric pressures between 510 mm of Hg and 50 mm of Hg. The percentage saturation is zero at 50 mm of Hg ambient pressure. At an ambient pressure less than 52 mm of Hg intravascular, bubbles are a frequent finding in the dog but bubbles are not found at higher pressures.[34]

Evaporation of body fluids may lower the oral temperature below freezing and also may lower the internal body temperature several degrees in less than 2 minutes in dogs subjected to near vacuum (1 mm of Hg) conditions.[35]

Cardiovascular responses of dogs to nitrogen breathing at ground level and to hypoxia at 55 mm of Hg absolute are quite similar.[36] The systemic arterial pressure drops, and pulmonic arterial pressure increases due to the hypoxia produced by nitrogen or decompression. Venous pressure increases following decompression[37] but remains within a normal range throughout the hypoxic episode during nitrogen breathing.[36] Apnea occurs sooner during decompression to 55 mm of Hg within an average of about 60 seconds compared with about 80 seconds for dogs breathing nitrogen. Bradycardia occurs following the hypoxic episodes produced by both nitrogen breathing and decompression to 55 mm of Hg. However, the heart rate decreases sooner and falls to lower levels following decompression compared with animals breathing nitrogen.

Decompression of anesthetized dogs to near vacuum (4 mm of Hg) for 60 seconds causes severe reduction of arterial blood flow.[38] Hemodynamic effects produced at 4 mm of Hg are attributable largely to mechanical obstruction of the cardiovascular system by increased extravascular pressures, resulting from gas expansion and especially vaporization of water.

The effects of hypoxia produced by decompression to a simulated altitude of 30,000 feet for 90 minutes has been studied in unanesthetized dogs.[39] A consistent result of decompression was a marked decrease in plasma-potassium concentration. Plasma sodium concentration remains unchanged.

Otologic Influence of Decompression

The effect of decompression on the middle ear of the monkey has been studied.[40] In the course of decompression at a slow rate (50 mm of Hg/min), the eustachian tube opened periodically to keep the tympanic pressure open to the ambient pressure. Periodic opening of the eustachian tube occurred only when the decompression rate was slow. When the rate of decompression is higher than 120 mm of Hg per minute, a sustained patency of the eustachian tube results. Even at excessive rates of decompression, such as seen during explosive decompression, the middle ear pressure very quickly returns to that of the ambient pressure.

Explosive decompression occurs at a rate many times faster than that used in rapid decompression. For example, explosive decompression can occur in about 12 to 40 msec with a drop in barometric pressure from 740 mm of Hg to 25 mm of Hg or less.[15,17] Rapid decompression may vary in time from 10,000 msec and upward.[3]

Evidence indicates that tympanic hemorrhage and pain are caused by negative pressure ($>$ 600 mm of Hg) that develops in the middle ear during recompression whether the latter is gradual or explosive.[40] Hemorrhage in the frontal sinuses of dogs also has been observed and attributed to rapid recompression.[41]

Myringopuncture can prevent development of negative pressure and therefore can prevent the production of barotraumatic lesions to the ear. Puncture of both ear drums also completely eliminates bradycardia during recompression of the unanesthetized monkey brought down from 42,000 ft at a faster rate than free fall.[19] Apparently the bradycardia that occurs during recompression is due to the unequalized negative middle-ear pressure and is mediated reflexly by the vagus nerve. It has been suggested that impulses from receptors, possibly pain receptors, in the middle-ear or tympanic membrane, or both, initiate this reflex.

In human beings, ear discomfort and severe pain have been observed principally during recompression or upon descending to a lower altitude.[22,42,43] There are rare cases where barotrauma involving the ears or sinuses occur during ascent.[44] A predisposing factor in all such cases was upper respiratory infection. This is not surprising, for it is known that inflammation of the respiratory tract mucosa can interfere with ventilation of the middle ear and paranasal sinuses.[44]

Pathologic Effects Following Decompression

The gross pathologic lesions seen in dogs following decompression are hemorrhagic in nature.[45] Petechial to ecchymotic hemorrhages in the lungs occur. Cardiac damage occurs also with ecchymotic hemorrhages on the mitral valves of some animals. Ecchymotic hemorrhage occurs also under the dura mater encompassing the sagittal sinus of the brain.

Hemorrhagic lesions following decompression of the explosive type are found primarily in the lungs, brain, and heart.[45] Of these, the pulmonary lesions are most common.[45,46] It is thought that these lesions occur as a result of the sudden increase in intrapulmonary pres-

sure during decompression. The sudden rapid expansion of the lungs with stretching of the alveolar walls probably results in tearing of these structures.

Residual histopathologic changes in the central nervous system of dogs have been described following rapid decompression to 1 mm of Hg for 120 seconds.[47]

Effect of Decompression and Other Hypoxic Episodes on Survival Time

Unconsciousness or collapse in adult dogs exposed to simulated altitudes between 50,000 and 55,000 ft, whether breathing air or 100% O_2, occurs in less than 9 or 10 seconds following exposure.[14] "Complete anoxia" or "complete hypoxia" therefore occurs at these altitudes (ie, 52,500 ft) in animals breathing either air or 100% O_2.[32,48,49] In human beings, the potentially severe hypoxia encountered above 50,000 ft begins to become effectively reversed at the 50,000-ft level, improving rapidly with continued recompression to 40,000 ft or lower.[8]

Studies in animals have shown that survival time decreases with increasing altitude as the severity of hypoxia increases.[50] However, the survival time reaches a minimum and remains constant regardless of further increase in altitude. The minimal survival time of animals exposed to rapid decompression has been studied in O_2 and in air by Lutz.[51] In animals breathing O_2, Lutz found that a minimal survival time of 25 seconds was attained when animals were decompressed to a simulated altitude of 52,000 ft. Following the same procedure to altitudes below 52,000 ft the survival times were longer, and to altitudes above 52,000 ft the survival times did not become significantly shorter but remained approximately 25 seconds. In animals breathing air, Lutz observed that a minimal survival time of 25 seconds was reached on decompression to 43,000 ft or above.

The survival time of unanesthetized animals (rats) after decompression in air, when cessation of respiration is used as the end point, is constant for all simulated final decompression altitudes above 52,000 ft.[49] In the rat, at simulated altitudes of 52,000 and above, rhythmic respiration ceased on the average of 17.8 seconds after decompression in air. Studies on the effects of decompression of dogs and rats from sea level to 30 mm of Hg (ie, 72,000 ft) revealed that respiration ceased at about 30 seconds. Also, it is of interest and noteworthy that respiration in dogs ceases in 15 to 20 seconds after sudden complete arrest of the cerebral circulation.[29]

As exposure to high altitude and the accompanying hypoxic environment increases, resistance or tolerance to hypoxia becomes less.[50] Tolerance to high altitude or decompression appears to vary with various animal species. Compared with the guinea pig, the cat and dog are more tolerant.[52] Cats, rabbits, cavies, hamsters, rats, and mice fail to survive a decompression of 100 mm of Hg (ie, 47,000 ft) for 3 minutes.[53]

The respiratory center is most resistant to hypoxia at birth, then declines through the 4th month of life in the dog.[54] Resistance to hypoxia induced by nitrogen at birth varies from 28 minutes in the ground squirrel to 16 minutes in the cat, to 6 minutes in the guinea pig.[55] The origin of hypoxic resistance in mammals has not been identified.

Adult rabbits can tolerate an anoxic atmosphere of 100% nitrogen for only 1.5 minutes before death, whereas the newborn rabbit can survive for as long as 27 minutes.[56] In the adult dog, acute occlusion of the cerebral circulation and resultant hypoxia produce cessation of spontaneous respiration after only 20 to 30 seconds; in the 8- to 10-day-old puppy, this effect occurs in 5 minutes, and in the newborn animal, occurs in 27 minutes. Reptiles and amphibians can tolerate O_2 deprivation to a much greater extent than the mammalian species; for example, the turtle can tolerate anoxia produced by 100% nitrogen for several hours and a dose of cyanide 50 times greater than that toxic to the mammal.[56,57]

Exposure of the dog to a near vacuum environment (less than 2 mm of Hg absolute) indicates that dogs exposed for less than 120 seconds are capable of survival upon recompression to 35,000 ft while breathing O_2.[14] In such animals, collapse occurs within 9 to 10 seconds after decompression along with a generalized muscle spasticity, a few gasps, momentary convulsive seizures, apnea, and gross swelling of the body and extremities.

Humane Considerations of Decompression

The rapid decompression technique for producing hypoxia (not the explosive decompression method) has been used for euthanasia of animals.[53,58] There have been many pathophysiologic studies involving the use of animals subjected to decompression. Most were conducted by high altitude or space research laboratories, so manned space flights could be accomplished with a minimum of hazard. Sufficient evidence as indicated by EEG recordings have revealed that hypoxia rapidly induces unconsciousness in both animals and man subjected to high altitude simulated by the use of decompression chambers or inhalation of inert gases. It is not known what the subjective perceptions of an animal in a chamber may be but when properly done, decompression is a painless procedure for all species.[53] Decompression at the rate of 4,000 ft per minute for 10 minutes, thus creating a simulated altitude of 40,000 ft (141 mm of Hg), and maintaining this pressure until respiration ceases are considered optimal for a mature dog.[58] For adults of other species such as cats, rabbits, cavies, hamsters, rats, and mice, a decompression of 100 mm of Hg (ie, 47,000 ft above sea level) for 3 minutes is adequate for induction of euthanasia following a decompression rate of 15 mm of Hg per minute.[53]

As emphasized in the 1978 AVMA Panel on Euthanasia report,[2] the successful use of decompression chambers is predicated on the proper operation and maintenance of the equipment. Personnel operating the equipment must be skilled and knowledgeable in its use as well as understand the esthetically unpleasant reactions manifested by animals during the period of hyperactive coma or unconsciousness prior to death.

Dogs under 4 months of age are more tolerant to hypoxia and require longer periods of decompression before respiration ceases.[54] Animals with respiratory complications and especially those with otitis media should not be subjected to decompression because of the possibility of the development of pain from unequalized positive middle-ear pressure.

References

1. AVMA Council on Research: Report of the AVMA panel on euthanasia. *JAVMA* 160:761–772, 1972.
2. AVMA Council on Research: Report of the AVMA panel on euthanasia. *JAVMA* 173:59–72, 1978.
3. Bryan CA, Leach WG: Physiologic effects of cabin pressure failure in high altitude passenger aircraft. *Aerospace Med* 31:267–275, 1960.
4. Van Liere EJ, Stickney JC: *Hypoxia.* Chicago, University of Chicago Press, 1963, pp 1–381.
5. Tenney SM: Respiration in mammals (chapter 15), in Swenson, J Melvin (ed): *Dukes' Physiology of Domestic Animals,* ed 9. Ithaca, NY, Constock Publishing Associates, Division of Cornell University Press, 1977, p 186.
6. Busby DE, Higgins EA, Funkhouser GE: Effect of physical activity of airline flight attendants on their time of useful consciousness in a rapid decompression. *Aviat Space Environ Med* 47:117–120, 1976.
7. Busby DE, Higgins EA, Funkhouser GE: Protection of airline flight attendants from hypoxia following rapid decompression. *Aviat Space Environ Med* 47:942–944, 1976.
8. Bancroft RW, Simmons DG: Rapid decompressions up to 60,000 feet wearing the standard oxygen mask. *Aerospace Med* 35:203–211, 1964.
9. Hills BA, Ray DE: Inert gas narcosis. *Pharmacol Ther [B]* 3:99–111, 1977.
10. Behnke AR, Thomson RM, Motley EP: The psychologic effects from breathing air at 4 atmospheres pressure. *Am J Physiol* 112:554–558, 1935.
11. Behnke AR, Yarbrough OD: Respiratory resistance, oil-water solubility, and mental effects of argon, compared with helium and nitrogen. *Am J Physiol* 126:409–415, 1939.
12. Lawrence JH, Loomis WF, Tobias CA, et al: Preliminary observations on the narcotic effect of xenon with a review of values for solubilities of gases in water and oils. *J Physiol* 105:197–204, 1946.
13. Bennett PB, Glass MB: Electroencephalographic and other changes induced by high partial pressures of nitrogen. *Electroencephalogr Clin Neurophysiol* 13:91–98, 1961.
14. Bancroft RW, Dunn JE II: Experimental animal decompressions to a near vacuum environment. *Aerospace Med* 36:720–725, 1965.
15. Edelmann A, Hitchcock FA: Observations on dogs exposed to an ambient pressure of 30 mm Hg. *J Appl Physiol* 4:807–812, 1952.
16. Hitchcock FA, Kemph J: The boiling of body liquids at extremely high altitudes. *Aviat Med* 26:289–297, 1955.
17. Kemph JP, Beman FM, Hitchcock FA: Subcutaneous pressure developed in dogs following explosive decompression to 25 or 30 mm Hg. *Am J Physiol* 168:601–604, 1952.
18. Kemph JP, Hitchcock FA: Further studies of effects of high intrapulmonic pressure on dogs at 30 mm Hg. *Aviat Med* 25:227–234, 1954.
19. Gelfan S: Explosive decompression of macaque monkeys to extreme altitudes and recompression at free-fall rates. *J Appl Physiol* 3:254–281, 1950.
20. Holmstrom FMG: Collapse during rapid decompression. Report of three cases. *J Aviat Med* 29:91–96, 1958.
21. Van Liere EJ: *Anoxia, Its Effect on the Body.* Chicago, University of Chicago Press, 1942, pp 1–269.
22. Barron CI, Cook TJ: Effects of variable decompressions to 45,000 feet. *Aerospace Med* 36:425–430, 1965.
23. Luft UC, Clamann HG, Opitz E: The latency of hypoxia on exposure to altitude above 50,000 feet. *J Aviat Med* 22:117–136, 1951.
24. Rossen R, Kabat H, Anderson JP: Acute arrest of cerebral circulation in man. *AMA Arch Neurol Psychiatr* 50:510–528, 1943.
25. Gibbs FA, Davis H: Changes in the human electroencephalogram associated with loss of consciousness. *Am J Physiol* 113:49–50, 1935.
26. Davis PA, Davis H, Thompson JW: Progressive changes in the human electroencephalogram under low oxygen tension. *Am J Physiol* 123:51–52, 1938.
27. Sugar O, Gerard RW: Anoxia and brain potential. *J Neurophysiol* 1:558–571, 1938.
28. Stephens LM, Hartman JL, Lewis OF, et al: Electrophysiology of chimpanzees during rapid decompression. *Aerospace Med* 38:694–698, 1967.
29. Kabat H, Dennis C, Baker AB: Recovery of function following arrest of the brain circulation. *Am J Physiol* 132: 737–747, 1941.
30. Booth NH: Intravenous and other parenteral anesthetics, in Jones LM, Booth NH, McDonald LE (ed): *Veterinary Pharmacology and Therapeutics.* Ames, Iowa State University Press, 1977, pp 241–306.
31. Whitehorn WV, Lein A, Edelmann A: The general tolerance and cardiovascular responses of animals to explosive decompression. *Am J Physiol* 147:289–298, 1946.
32. Gelfan S, Werner AY: Cardiovascular responses following explosive decompression of macaque monkeys to extreme altitudes. *J Appl Physiol* 4:280–310, 1951.
33. Lennox WG, Gibbs FA, Gibbs EL: Relationship of unconsciousness to cerebral blood flow and to anoxemia. *AMA Arch Neurol Psychiatr* 34:1001–1013, 1935.
34. Kemph JP, Hitchcock FA: Changes in blood and circulation of dogs following explosive decompression to low barometric pressures. *Am J Physiol* 168:592–600, 1952.
35. Cooke JP, Bancroft RW: Some cardiovascular responses in anesthetized dogs during repeated decompressions to a near vacuum. *Aerospace Med* 37:1148–1152, 1966.
36. Bancroft RW, Cooke JP, Cain SM: Comparison of anoxia with and without ebullism. *J Appl Physiol* 25:230–237, 1968.
37. Cooke JP, Cain SM, Bancroft RW: High venous pressures during exposure of dogs to near vacuum conditions. *Aerospace Med* 38:1021–1024, 1967.
38. Pratt AJ, Stone HL, Stegall HF, et al: Circulatory impairment during exposure to ambient pressures of 4 mm Hg and 55 mm Hg. *J Appl Physiol* 29:177–180, 1970.
39. Ferguson FP, Smith DC: Effects of acute decompression stress upon plasma electrolytes and renal function in dogs. *Am J Physiol* 173:503–510, 1953.
40. Chang H-T, Margaria R, Gelfan S: Pressure changes and barotrauma resulting from decompression and recompression in the middle ear of monkeys. *Arch Otolaryngol* 51:378–399, 1950.
41. Cole CR, Chamberlain DM, Burch BH, et al: Pathological effects of explosive decompression to 30 mm Hg. *J Appl Physiol* 6:96–104, 1953.
42. Barron CI, Collier DR Jr, Cook TJ: Observations on simulated 12-second decompressions to 32,000 feet. *Aviat Med* 29:563–574, 1958.
43. Idicula J: Perplexing case of maxillary sinus barotrauma. *Aerospace Med* 43:891–892, 1972.
44. Lewis ST: Barotrauma in United States Air Force accidents/incidents. *Aerospace Med* 44:1059–1061, 1973.
45. Edelman A, Whitehorn WV, Lein A, et al: Pathological lesions produced by explosive decompression. *Aviat Med* 17: 596–612, 1946.
46. Dunn JE II, Bancroft RW, Haymaker W, et al: Experimental animal decompressions to less than 2 mm Hg absolute (pathologic effects). *Aerospace Med* 36:725–732, 1965.
47. Casey HW, Bancroft RW, Cooke JP: Residual pathologic changes in the central nervous system of a dog following rapid decompression to 1 mm Hg. *Aerospace Med* 37:713–718, 1966.
48. Gelfan S, Nims LF, Livingston RB: Cause of death from explosive decompression at high altitude (abstr). *Fed Proc* 6: 110, 1947.
49. Gelfan S, Nims LF, Livingston RB: Explosive decompression at high altitude. *Am J Physiol* 162:37–53, 1950.
50. Armstrong HG: Anoxia in aviation. *Aviat Med* 9:84–91, 1938.
51. Luft UC, Clamann HG, Adler HF: Alveolar gases in rapid decompression to high altitudes. *J Appl Physiol* 2:37–48, 1949.
52. Whitehorn WV, Lein A, Hitchcock FA: The effect of explosive decompression on the occurrence of intravascular bubbles. *Aviat Med* 18:392–394, 1947.
53. Barber BR: Use of a standard autoclave for decompression euthanasia. *J Institute Anim Technol* 23:106–110, 1972.

54. Kabat H: The greater resistance of very young animals to arrest of the brain circulation. *Am J Physiol* 130:588–599, 1940.
55. Adolph EF: Regulations during survival without oxygen in infant mammals. *Respir Physiol* 7:356–368, 1969.
56. Cohen PJ: The metabolic function of oxygen and biochemical lesions of hypoxia. *Anesthesiology* 37:148–177, 1972.
57. Bellamy D, Peterson JA: Anaerobiosis and the toxicity of cyanide in turtles. *Comp Biochem Physiol* 24:543–548, 1968.
58. Smith DC: Methods of euthanasia and disposal of laboratory animals, in Gay WI (ed): *Methods of Animal Experimentation*. New York, Academic Press, 1965, vol I, pp 167–195.
59. Miller KW, Paton WDM, Smith EB: Site of action of general anesthetics. *Nature* 206:574–577, 1965.
60. Saidman LJ, Eger EI II, Munson ES, et al: Minimum alveolar concentrations of methoxyflurane, halothane, ether, cyclopropane in man: Correlation with theories of anesthesia. *Anesthesiology* 28:994–1002, 1967.

Canine Mycotoxicosis

Although many mycotoxicoses in domestic and companion animals remain undiagnosed, epizootics have occurred on a regular basis for many decades in the United States and other nations. In the southern United States where the climate is warm and humid, mycotoxicoses are more prevalent than in other regions. A mycotoxicosis in dogs, designated "hepatitis X," was first reported in the southeastern United States in 1952. Subsequent investigations traced the cause to commercial dog food which contained peanut meal as the principal protein source. A relationship also was established between this disease in dogs and "moldy corn poisoning" in cattle and swine.

A review of several epizootic mycotoxicoses occurring in the southeastern United States indicated that aflatoxin and aflatoxigenic strains of *Aspergillus flavus* were in most of the feed samples. Reportedly much of the feed-grade peanut meal purchased during this period on the open market in the United States was contaminated with aflatoxin. However, in the cases of hepatitis X in dogs and moldy corn toxicoses in cattle and swine, other toxigenic fungi, including *Penicillium rubrum*, were isolated. Furthermore, other toxic substances having a synergistic effect with aflatoxin were present in contaminated feeds. While similarities between experimentally induced aflatoxicosis and field cases of hepatitis X are impressive, there are differences, particularly in renal alterations.

Since hepatitis X in dogs generally has been associated with commercial feeds from which *A flavus* and *Penicillium* sp were isolated, a study was initiated to examine the effect of aflatoxin B_1 and rubratoxin B in dogs and to compare the experimental disease with spontaneous hepatitis X observed in field cases. Results indicated that the dog is sensitive to the toxic effects of both mycotoxins. Histologic changes were induced in the dog not only by aflatoxin but by rubratoxin. A striking similarity was observed between induced lesions when the 2 toxins were combined and lesions observed in dogs used in laboratory studies or affected in natural outbreaks of hepatitis X.

Based on these data and earlier reports, it would seem that there is little doubt of an association of hepatitis X and aflatoxin B_1, although it is apparent that the disease probably is not the result of a single toxic factor.—*A. W. Hayes and W. L. Williams in J Environ Pathol Toxicol, 1, (1977): 59.*

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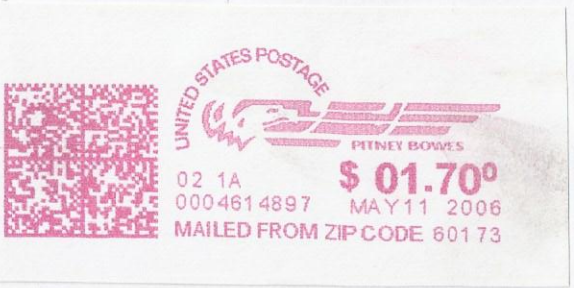

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