Diving Mammals

Paul J. Ponganis[*1]

ABSTRACT

The ability of diving mammals to forage at depth on a breath hold of air is dependent on gas exchange, both in the lung and in peripheral tissues. Anatomical and physiological adaptations in the respiratory system, cardiovascular system, blood and peripheral tissues contribute to the remarkable breath-hold capacities of these animals. The end results of these adaptations include efficient ventilation, enhanced oxygen storage, regulated transport and delivery of respiratory gases, extreme hypoxemic/ischemic tolerance, and pressure tolerance. © 2011 American Physiological Society. *Compr Physiol* 1:517-535, 2011.

Introduction

Gas exchange, both in the lung and in peripheral tissue, is fundamental to the ability of diving mammals to successfully forage and exploit the ocean depths. Efficient respiratory gas exchange at the surface allows for the rapid uptake of oxygen and removal of carbon dioxide between dives. Although continued pulmonary gas exchange at shallow depths allows depletion of the lung oxygen store, the cessation of lung gas exchange at greater depths is essential to prevent complications from excess nitrogen absorption. Alterations in tissue gas exchange during dives are also important to control the depletion rate of body O_2 stores. This is accomplished primarily through cardiovascular responses and changes in end-organ O_2 delivery. These demands on the respiratory and cardiovascular systems are typified by the diving behavior of the northern elephant seal (*Mirounga angustirostris*) (128). During 2-month periods at sea, the seal gains an average of 1 kg d^{-1} in body mass and spends over 85% of its time underwater at an average depth of 400 m. Surface intervals are only 3 min, and routine dive durations are 20 min.

Before considering the anatomical, physiological, and biochemical adaptations underlying gas exchange and dive capacity, it is important to emphasize that diving mammals are a diverse group and that they exhibit a wide range of diving behaviors (174). Marine divers are represented in four mammalian orders. The Cetacea, perhaps the best known and most aquatically adapted, include the toothed whales (odontocetes) and baleen whales (mysticetes). Sea lions and fur seals (otariids), true seals (phocids), and walruses (odobenids) comprise the order, Pinnipedia. And the Sirenia include the herbivorous manatees (*Trichechus manatus*) and dugongs (*Dugong dugon*). Although several species of otter utilize the marine habitat to various degrees, probably the best-known marine diver of the order, Carnivora, is the sea otter (*Enhydra lutris*). The polar bear (*Ursus maritimus*) is considered a marine mammal and is an excellent swimmer (215). It will not be included as a diver in this review because reported dive durations are very short. During underwater fishing, mean dive durations were 13 s (46).

Dive Behavior

The development of microprocessor-based data loggers in the past two decades has allowed documentation of remarkable diving behaviors in many marine species. Table 1 contains representative dive durations and dive depths in free-diving mammals. Among the cetaceans, the most notable dive depths and durations are those of the large toothed whales, specifically sperm whales (*Physeter macrocephalus*) and beaked whales (family: Ziphiidae) (4, 90, 225, 230). Routine depths and durations range from 400 to 800 m and 40 to 60 min, respectively, with maximum depths and durations greater than 2000 m and 120 min, respectively. In contrast, the well-known bottlenose dolphin (*Tursiops truncatus*) typically dives for less than 5 min to shallow depths of less than 20 m (140). Recent studies of pelagic spotted dolphins (*Stenella attenuata*) reveal that foraging dives are also up to 5 min in duration but can be as deep as 200 m (140, 204). The large baleen whales typically have dive durations under 5 min; they too, however, can reach depths of 200 m (36, 247).

Large phocid seals are the longest-duration divers among the pinnipeds (Table 1). These include Weddell seals (*Leptonychotes weddellii*), hooded seals (*Cystophora cristata*), and northern and southern elephant seals (*M. angustirostris, M. leonina*). Maximum depths are in the range of 600 to 1500 m (27, 66, 85, 214). Weddell seals dive in bouts, with long rest periods on the sea ice between bouts. This

[*]Correspondence to pponganis@ucsd.edu

[1]Center for Marine Biotechnology and Biomedicine, Scripps Institution of Oceanography, University of California San Diego, La Jolla, CA

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Table 1 Dive Characteristics of Some Cetaceans and Pinnipeds

Species	Duration, min		Depth, m		Reference
	Common	Maximum	Common	Maximum	
Harbor porpoise *Phocoena phocoena*	1	5	14-40	226	237
Bottlenose dolphin *Tursiops truncatus*	1	8	20	390	140, 192
Spotted dolphin *Stenella attenuata*	1-2	5	22	203	204
Pilot whale *Globicephala sp.*	5-15	21	100-800	1019	3, 83, 153, 211
Northern bottlenose whale *Hyperoodon ampullatus*	40	70	800	1483	90
Cuvier's beaked whale *Ziphius cavirostris*	58-70	95	1070-1334	1888	4, 225
Blainville's beaked whale *Mesoplodon densirostris*	47-55	84	835-1099	1599	4, 225
Sperm whale *Physeter macrocephalus*	40-60	138	400-900	2250	97, 158, 166, 230, 232
Humpback whale *Megaptera novaeanglieae*	1-4	–	23-118	~160	247
Blue whale *Balaenoptera physalus*	3-5	–	180-200	–	36
Northern fur seal *Callorhinus ursinus*	2	8	65	256	75
Antarctic fur seal *Arctocephalus gazella*	<2	5	30	101	75
Galapagos fur seal *A. galapagoensis*	<2	5	26	115	75
California sea lion *Zalophus californianus*	2	10	62	274	62
New Zealand sea lion *Phocarctos hookeri*	4	11	123	474	72
Steller sea lion *Eumetopias jubata*	<2	8	9-24	250	143
Harbor seal *Phoca vitulina*	1-2	17	5-19	59	14
Hooded seal *Cystophora cristata*	5-25	>52	100-600	>1016	66
Weddell seal *Leptonychotes weddellii*	10-12	82	150-400	726	27, 203
Northern elephant seal *Mirounga angustirostris*	23	119	437	1581	128, 214
Southern elephant seal *Mirounga leonina*	20-29	120	269-552	1256	85

interrupted pattern of diving contrasts with that in the latter three species. During their several month long trips to sea, these seals are underwater 80% to 90% of the time. Surface intervals are less than a few minutes. Accordingly, these species have been termed "surfacers" in contrast to the Weddell seal, which has been considered a "diver" (126). Routine dive durations of most other phocid seals are less than 10 min. Otariids have even shorter routine dive durations, typically less than 3 to 4 min (62, 72, 75). Walruses (*Odobenus rosmarus*) dive for under 4 to 6 min during underwater territorial displays and during foraging activity (12, 159, 239). Manatees and dugongs usually dive for 2 to 3 min to depths of about 12 m at most (33, 73, 74, 139, 189, 190). Most dives of sea otters are 1 to 3 min in duration and less than 30 m in depth (184, 248).

Airway and Lung Anatomy

Research on respiratory anatomy and respiratory mechanics in diving mammals stemmed from Scholander's observations of cartilaginous distal airways in whales, and his hypothesis that more rigid airways would allow (i) movement of air

into those airways during compression of the lungs at depth, (ii) alveolar collapse, and (iii) the cessation of gas exchange, and, in particular, N_2 absorption at depth (199). In a series of anatomical and histological studies (41, 108, 109, 112, 219), Kooyman and colleagues documented the airway reinforcement of diving mammals in comparison to terrestrial mammals. This is most prominent in cetaceans and sea lions, with cartilaginous reinforcement of the airways from the trachea to the level of the alveolar sac. Respiratory bronchioles are absent. In phocid seals, tracheal reinforcement is minor and ranges from flexible cartilaginous rings to ventral bars of cartilage in some species. Although cartilage is absent in the distal airways of phocids, the presence of oblique muscle fibers in the bronchial walls is thought to reinforce these segments. In walruses and sea otters, distal airways are reinforced with a mix of cartilage or muscle elements. Conceptually, more rigid airways should allow alveoli to empty and collapse more fully (no gas trapping) during compression.

The extensive cartilaginous reinforcement of the airways in cetaceans and sea lions should also allow higher flow rates and faster gas exchange during the brief surface intervals of these animals. Indeed, in cetaceans, it has been found that (i) the trachea is relatively short, (ii) there is little change in the proximal versus distal cross-sectional areas of the primary bronchi, (iii) secondary bronchi are more numerous, and (iv) cross-sectional areas of quaternary bronchi are high, 50% to 80% of those of the primary bronchi (44).

A unique feature in the lungs of most dolphins and some odontocete whales is the presence of bronchiolar myoelastic sphincters (6, 109, 112, 123). The function of these sphincters is unknown, although they have been postulated to (i) regulate gas distribution during diving, (ii) play a role in alveolar reexpansion during ascent from depth, or (iii) contribute to the rapid flow rates during exhalation.

Respiratory mechanics

The changes in respiratory mechanics suggested by the anatomical and histological findings in the above studies were investigated in the 1960s and 1970s. Almost all of this research, which focused on flow rates and emptying of the lung, was conducted at or in association with Scholander's Physiological Research Lab at Scripps Institution of Oceanography.

In studies on excised lungs, it was found that dog lungs contained 27% of total lung capacity (TLC) at their relaxation volume (pleural pressure = 0) whereas sea lions lungs had a smaller relative relaxation volume (18% of TLC) (42). Furthermore, when pleural pressure on the dog lungs was increased to +5 cmH_2O, only another 1% of TLC was expulsed before emptying stopped. In contrast, the sea lion lungs continued to empty with application of pleural pressures as high as +30 cmH_2O (the limit in the study). At that point, the mean gas volume of the lungs was 6% of TLC. A relaxation volume of less than 17% of TLC in harbor porpoise lungs (*Phocoena phocoena*) (123) and low volumes in fin whales (*Balaenoptera physalus*) and sei whales (*B. borealis*) (130) have also been reported. These studies support the concept that reinforcement of the distal airways in diving mammals allows for the movement of air from the alveoli into the bronchi during lung compression, thus promoting collapse of the alveoli and cessation of gas exchange at depth.

Maximum expiratory flow rates, as high as 162 liters s^{-1} in bottlenose dolphins and 202 liters s^{-1} in young gray whales (*Eschrichtius robustus*) (115, 119), are necessary in cetaceans since exhalation and inhalation occur in less than 1 s (115, 119, 163, 164). Such flows allow for a tidal volume as high as 88% of TLC in the pilot whale (*Globicephala melena*) (163, 164). Such a high-volume turnover is probably similar in other whales. In terms of vital capacity (VC), maximum expiratory flow rates in cetaceans and sea lions are in the range of 5 to 8 VC s^{-1} (106, 115, 123). Exhalation is not active, as elastic recoil of the lung has been found to be the sole driving force during expiration of the pilot whale (163, 164). These high flow rates minimize the time for exhalation/inhalation and allow animals to porpoise through the water. With such rapid breaths, the animals can spend most of their travel time below the surface where drag is less (241).

Flow volume curves of the bottlenose dolphin and of excised harbor porpoise lungs are remarkable for the maintenance of high flows at low lung volumes (115, 123). This contrasts with human flow volume curves, in which expiratory flow decreases as volume decreases. This difference, which contributes to the short exhalation time, is considered secondary to the cartilaginous reinforcement of distal airways in the dolphin.

Lung volumes

Lung volumes of diving mammals are in the general range of terrestrial mammals (Table 2). Notable exceptions are the small lungs of the deep-diving bottlenose whale (*Hyperoodon ampullatus*) and the large lungs of the shallow-diving sea otter. Inflation of excised lungs revealed lung volumes of 28 ml kg^{-1} in the bottlenose whale and 345 ml kg^{-1} in the sea otter (133, 199). The high lung volume in the otter presumably contributes to its buoyancy at the surface, where it feeds, grooms, and cares for its young. Such buoyancy in the otter also elevates more of the body out of the water while the animal is at the surface; this should reduce body heat loss due to conduction in water. In cetaceans and manatees, tidal volumes are large, 80% to 90% of TLC (190, 192), and, in Weddell seals, postdive volumes are 75% of VC (117). The large postdive tidal volumes and increased ventilatory rates of Weddell seals allow for a maximum postdive minute ventilation that is 10 times the minimum value at rest and a postdive O_2 uptake rate that is 8 times that at rest (117, 118). Harbor seals (*Phoca vitulina*) and California sea lions (*Zalophus californianus*) swimming vigorously in a water flume and taking a breath at each surfacing are able to attain maximum O_2 uptake rates that are 8 to 10 times that of the animals at rest (176, 177). These maximum O_2 uptakes in seals and sea lions are less than those of highly aerobic animals such as dogs and horses

Table 2 Lung Volumes in Diving Mammals

Species	TLC, ml kg^{-1}	Reference	DLV, ml kg^{-1}	Reference
Harbor porpoise *Phocoena phocoena*	80-130[a]	123		
Bottlenose dolphin *Tursiops truncates*	50-91[a,b]	115, 195	40-50[c]	208
Sei whale *Balaenoptera borealis*	61-126[a]	130		
Fin whale *Balaenoptera physalus*	61-126[a]	130		
Pilot whale *Globicephala melena*	100[d]	164		
Northern bottlenose whale *Hyperoodon ampullatus*	28[a]	199		
Sperm whale *Physeter macrocephalus*			28[c]	148
Manatee *Trichechus manutus*	65[e]	200		
Northern fur seal *Callorhinus ursinus*	145[a]	133		
Steller sea lion *Eumetopias jubata*	110[a]	133		
California sea lion *Zalophus californianus*			48[f]	124
Walrus *Odonbenus rosmarus*	116[a]	133		
Harbor seal *Phoca vitulina*	91[a]	133	23-39[f]	122, 124
Hooded seal *Cystophora cristata*	80[a]			20
Ribbon seal *Histriophoca fasciata*	86[a]	133		
Weddell seal *Leptonychotes weddellii*	48[g]	117	22[f]-27[g]	118, 122
Elephant seal *Mirounga angustirostris*			20[f]	122
Sea otter *Enhydra lutris*	345[a]	133	207[f]	174

[a]Inflation of excised lungs.
[b]Tidal volume measurement.
[c]Buoyancy—swim velocity calculations.
[d]Helium dilution.
[e]Inspiratory capacity.
[f]Compression during simulated dives.
[g]Nitrogen washout.
Abbreviations: TLC, total lung capacity; DLV, diving lung volume.

but are equivalent to those of less specialized species such as goats and calves (221).

Diving lung volumes, defined as the lung volume at the start of a dive, are important determinants of the size of the respiratory O_2 store during a dive. Cetaceans appear to dive on inspiration, while pinnipeds usually dive on expiration (111, 192). Consequently, the diving lung volumes of cetaceans are probably near TLC. This assumption is supported by the similarity of the calculated diving lung volume of the sperm whale, a deep-diving odontocete, to the measured TLC of another deep diver, the bottlenose whale (148, 199). Determinations of diving lung volumes in pinnipeds during free dives and simulated dives have yielded values that are 40% to 50% of TLC (117, 122, 124).

Effects of Pressure

Decompression sickness, N_2 narcosis, high-pressure nervous syndrome

These three syndromes, which seriously limit human diving performance, are all complications of diving to depth. These complications in human divers typically occur during compressed air diving. Decompression sickness (DCS) has been reported in human breath-hold divers (37, 65, 167). It results from excess N_2 absorption at depth and inadequate N_2 washout during ascent. The resulting elevations in P_{N_2} are associated with the onset of symptoms and bubble formation. Symptomatic bubble formation in cats requires a minimum P_{N_2} of 2476 mmHg (330 kPa or 3.3 ATA) (82), although asymptomatic venous gas emboli have been detected in humans on decompression from steady-state pressure exposure of 1023 mmHg (135 kPa, 1.35 ATA, or <5 m depth) (47). Nitrogen narcosis begins in humans at a depth of 30 m; this would correspond approximately to a P_{N_2} of 2400 mmHg (320 kPa or 3.2 ATA) (80). The onset of high-pressure nervous syndrome (HPNS) occurs at 190 m (20 ATA) in human divers (80). Many cetaceans and pinnipeds not only dive below this HPNS threshold but also descend faster than safe compression rates for humans. They are also below that symptom threshold depth for time periods well beyond that required for HPNS to occur in humans (7, 174). It is unknown whether unique anatomical or physiological adaptations protect against HPNS in deep-diving mammals. However, since N_2 is known to suppress the onset of HPNS in human divers, a tissue P_{N_2} in marine mammals that is less than that associated with N_2 narcosis may be an important factor in the prevention of HPNS in these animals (174). However, in order to avoid N_2 narcosis and DCS in deep-diving mammals, excess N_2 absorption at depth must be minimized, hence the significance of Scholander's hypothesis of alveolar collapse at depth.

Avoidance of barotrauma

Tissue trauma induced by descent to depth is due to mechanical distortion and tissue compression. In humans, this can occur in both breath-hold divers and compressed air divers (65). Air-filled cavities are especially susceptible to such injury. Air-filled cranial sinuses are absent in pinnipeds (107), and middle ear cavities are lined with venous plexuses, which

have been postulated to become engorged with blood and obliterate the air space at depth (162, 235). In cetaceans, the large pterygoid sinus that communicates with the middle ear via the Eustachian tube is also lined with prominent blood vessels (174).

Several adaptations appear to protect against barotrauma in the airways of marine mammals. First, actual narrowing of the flexible trachea, but not the more reinforced bronchi of seals, occurs during compression and has been demonstrated with air tracheograms and bronchograms obtained in a pressure chamber (116). Second, as found in the striped dolphin (*Stenella coeruleoalba*), the trachea, although stiffer than those in goats and pigs, has a higher breaking point and readily returns to its original shape after compression (34). In addition, large venous sinuses observed in the tracheal walls of striped dolphins may become engorged at depth to obliterate space and again prevent barotrauma (34). Such tracheal wall engorgement had also been previously suggested in sperm whales (131). An extensive vasculature observed in the terminal air spaces of beaked whales has also been postulated to become engorged at depth and again prevent "lung squeeze" (34,156). Such central pooling of blood within venous vessels of the thorax and the lung has been demonstrated in human divers (35,65,197) and has been postulated to also occur in the thoracic retia mirabilia of some cetaceans (141, 210, 229). However, in human divers, pulmonary edema and hemoptysis have been at least partially attributed to increased intrathoracic blood volume (135, 136, 229).

Lung collapse

In addition to mechanisms that protect the reinforced airways of diving mammals, volume-pressure curves of both the chest wall and lung of the ribbon seal (*Histriophoca fasciata*) demonstrated nearly limitless compression collapse (129). Such compressibility has also been demonstrated in the lungs of sea lions and cetaceans (42, 123, 129, 195). In these studies, relaxation volumes of isolated lungs were minimal and considered evidence of the collapsibility of alveoli. Actual compression of the chest wall has been photographically documented in the bottlenose dolphin at depth (195). In Weddell seals free diving to 80 m, however, chest circumference measurements during dives did not reveal chest compression (59). It was postulated that elevation of the diaphragm contributed to lung compression in this case.

Further support for Scholander's model of alveolar collapse and the cessation of gas exchange at depth are found in blood N_2 investigations of seals during both simulated dives and free dives (60, 122, 124). As demonstrated in Figure 1, with data from a free-diving Weddell seal (60), arterial P_{N_2} typically plateaus and gradually decreases despite further increases in ambient pressure. The level at which P_{N_2} plateaued corresponded to a depth of 20 to 50 m in elephant seals and Weddell seals (60, 122). Further review of blood and tissue P_{N_2} will be conducted in the final section of this article.

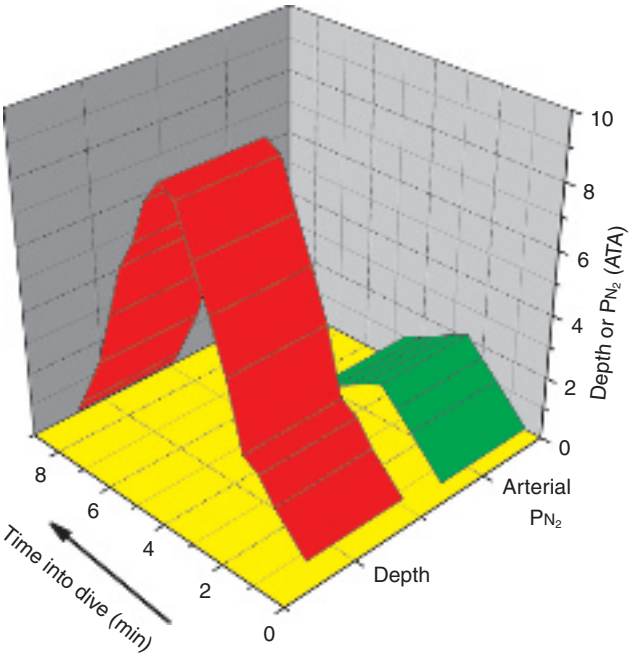

Figure 1 Depth and arterial P_{N_2} profiles of a Weddell seal. Data from reference 60. During this 8-min dive, samples collected during the first 4 min demonstrated that P_{N_2} peaked at 2.7 ATA and then declined despite depths as deep as 9.2 ATA (82 m) during sampling. A minimum 80% N_2 fraction in the lungs would correspond to an alveolar P_{N_2} of approximately 7.3 ATA at a depth of 82 m.

Pulmonary shunts

The degree of pulmonary shunt has been determined in one study of simulated dives in harbor seals and sea lions (124). Mean pulmonary shunt flow was 8% and 13% at rest in harbor seals and sea lions, respectively. The shunt progressively increased with depth of compression to 70% in harbor seals at 10 ATA (90 m depth) and to 57% in sea lions at 7.8 ATA (68 m depth). From these data, it was estimated that total lung collapse (100% shunt) would occur at depths of 170 m in harbor seals and 160 m in sea lions. These are much deeper threshold depths for lung collapse than those determined in Weddell seals and elephant seals and indicate that species differences probably exist. It was also notable that these depth thresholds for lung collapse were similar in harbor seals and sea lions, two species with very different terminal airways. As reviewed previously, sea lions have cartilaginous rings in the distal airway all the way to the alveolus whereas harbor seals lack such cartilaginous reinforcement. Although the harbor seal airway is more flexible, it was concluded that the muscle and fibrous tissue in the walls of the distal airway provide sufficient support to allow emptying and collapse of the alveoli at depth.

Surfactant

The routine collapse and reexpansion of alveoli during dives to depth raise the question of surfactant function and its role

in the maintenance of gas exchange in these animals. Analysis of bronchoalveolar lavage fluid from young seals and sea lions revealed a greater concentration of phospholipid and more fluidic species of phosphatidylcholine than in terrestrial mammals (213). This was consistent with more rapid spreading during alveolar reexpansion. Notably, surfactant from elephant seals, the deepest divers, produced moderately elevated minimum surface tension measurements. Poor surface activity and minimal reduction of surface tension were also later observed in analyses of lavage fluid from excised lungs of other pinniped species (145). In addition, further analyses of surfactant composition of pinnipeds revealed a relative decrease in anionic phospholipids, an increase in short-chain phospholipids and a decrease in surfactant protein B (146,147). Based on all these findings, it has been suggested that the primary function of surfactant in deep-diving mammals may be an antiadhesive function rather than only surface tension reduction (68). Antiadhesive function has been considered to include the facilitation of the unfolding of septal pleats and the reduction of adhesive interactions between respiratory surfaces due to variation in surface tension (68).

Regulation of surfactant production in diving mammals also requires further investigation. It has been found that phosphatidylcholine secretion of alveolar type II cells from California sea lions is less sensitive to increased pressure than that from sheep (144). In addition, it has been demonstrated that, in contrast to adult terrestrial mammals, leptin is expressed in the lung tissue of adult gray seals (*Haliochoerus grypus*) and harbor seals (81). Because leptin plays a role in stretch-induced surfactant production by alveolar type II cells during fetal development (224), it may be similarly involved in surfactant production in deep-diving mammals that undergo routine lung collapse and reexpansion.

Oxygen Transport and Storage

The transport and storage of O_2 within the bodies of diving mammals are primarily associated with the O_2-binding proteins, hemoglobin (Hb) and myoglobin (Mb). Blood O_2 storage is enhanced by large blood volumes, especially in phocid seals and some odontocetes such as the sperm whale and Dall porpoise (*Phocoenoides dalli*) (20, 168, 173, 207, 209, 223). Although slight elevations in neuroglobin and cytoglobin have been reported in some marine mammals (246), further evaluation and functional analysis of these proteins in brain and other tissues of diving mammals are needed.

Hemoglobin

The most notable aspect of Hb in diving mammals is its concentration in blood. Most species has exceptionally high values in comparison to terrestrial mammals. However, the O_2 affinity of Hb in these animals is not that different from many of their terrestrial counterparts (132,133,183). The P_{50}, the O_2 partial pressure at 50% Hb saturation, is in the range of 26 to 30 mmHg; the magnitude of the Bohr shift is also similar to that found in terrestrial mammals (132,133,183). As summarized in Table 3, Hb is most elevated in long-duration divers.

Table 3 Hemoglobin (Hb) Concentrations and Blood Volumes (BV) in Diving Mammals

Species	Hb, g dl^{-1}	BV, ml kg^{-1}	Reference
Bottlenose dolphin *Tursiops truncatus*	14	71	194
Pacific white-sided dolphin *Lagenorhynchus obliquidens*	17	108	194
Dall porpoise *Phocoenoides dalli*	20	143	194
Beluga whale *Delphinapeterus leucas*	21	128	205
Sperm whale *Physeter macrocephalus*	22	200	192,209
Manatee *Trichechus manutus*	15	80	10,74,238
California sea lion *Zalophus californianus*	18	96-120	175,234
Steller sea lion *Eumetopias jubata*		120	133
Northern fur seal *Callorhinus ursinus*	17	109	133
Australian sea lion *Neophoca cinerea*	19	178	69
Walrus *Odobenus rosmarus*	16	106	133
Harbor seal *Phoca vitulina*	21	132	19,133
Harp seal *Phoca groenlandica*	23	168	20
Hooded seal *Cystophora cristata*	23	106	20
Baikal seal *Phoca sibirica*	27	177	168,172
Weddell seal *Leptonychotes weddellii*	26	210	173
Northern elephant seal *Mirounga angustirostris*	25	216	207
Sea otter *Ehnydra lutris*	17	91	133

In some species, especially phocid seals, accurate estimations of total blood O_2 stores are complicated by a variable hematocrit and Hb content due to large spleens. There is a possibility for low hematocrit and Hb measurements because of splenic expansion/red blood cell storage during the sedation/anesthesia required for such sampling **(**24,95,173,181**).** The California sea lion data in this table also serve to demonstrate differences between adults and juveniles.

Myoglobin

The P_{50} of Mb at 37°C is less than 3 mmHg in both terrestrial and diving mammals (2,155,198,218). However, Mb concentrations in diving mammals are 10 to 30 times that found in their terrestrial counterparts (Table 4). Since the early studies

Table 4 Myoglobin (Mb) Concentrations and Muscle Mass (% Body Mass) in Some Diving Mammals

Species	Mb, g 100 g^{-1}	Muscle, %	Reference
Bottlenose dolphin *Tursiops truncatus*	3.3	30 (assumed)	10
Pacific white-sided dolphin *Lagenorhynchus obliquidens*	3.5		157
Northern right whale dolphin *Lissodelphis borealis*	1.8		157
Indus River dolphin *Platanista indi*	2.6		9
Common dolphin *Delphinus delphis, D. capensis*	3.6		157
Striped dolphin *Stenella coeruleoabla*	5.8		157
Spinner dolphin *Stenella longirostris*	5.5		43
Spinner dolphin *Stenella attenuata*	2.5		31
Fraser's dolphin *Lagenodelphis hosei*	7.1		43
Harbor porpoise *Phocoena phocoena*	4.0		157
Beluga whale *Delphinapterus leucas*	3.4	30	157, 205
Pygmy sperm whale *Kogia breviceps*	4.3		157
Cuvier's beaked whale *Ziphius cavirostris*	4.3		157
Narwhal *Monodon monoceros*	7.9		157
Northern bottlenose whale *Hyperoodon ampullatus*	6.3		199
Sperm whale *Physeter macrocephalus*	5.4	34	137, 199
Sei whale *Balaenoptera borealis*	0.9		220
Fin whale *Balaenoptera physalus*	2.4		157, 220
Bowhead whale *Balaena mysticetus*	3.5		157
Manatee *Trichechus manutus*	0.4	35	10
California sea lion *Zalophus californianus*	2.7-5.4	37	175, 234
Steller sea lion *Eumetopias jubata*	2.7		191
Northern fur seal *Callorhinus ursinus*	3.5	30	133
Australian sea lion *Neophoca cinerea*	2.7		69
Walrus *Odobenus rosmarus*	3.0	30	133
Harbor seal *Phoca vitulina*	5.5	30	133
Harp seal *Phoca groenlandica*	8.6	25	20
Hooded seal *Cystophora cristata*	9.5	27	20
Baikal seal *Phoca sibirica*	6.0	30	154
Weddell seal *Leptonychotes weddellii*	5.4	35	70, 173
Northern elephant seal *Mirounga angustirostris*	6.5	28	16, 223
Sea otter *Ehnydra lutris*	2.6	30	133

The Mb concentrations are from primary locomotory muscles. Estimations of the muscle O_2 store are usually based on such concentrations and total muscle mass. It should be noted that there may be some error in such calculations because Mb concentrations can vary within the primary locomotory muscle as well as among different muscles (20, 101, 168, 170, 171, 191). As shown in the California sea lion, there is also a twofold variation between juveniles and adults.

of Scholander and colleagues (199, 201), such high concentrations have long been considered to serve as an O_2 store for ischemic muscle during diving. Because of incomplete Mb desaturation during dives of Weddell seals, it had also been proposed that blood flow was maintained to muscle and that the primary function of such high Mb concentrations was to facilitate O_2 diffusion (78).

During sleep apnea of seals, a state in which some muscle blood flow persists during the breath hold, ^{1}H NMR spectroscopy has revealed that, although Mb serves as an O_2 store, Mb-O_2 is depleted only to 80% saturation during the apnea and that, based on the Mb content and its translational diffusion coefficient, O_2 flux through the cell is mediated through Mb at all blood P_{O_2}s during the apnea (178). Thus, the role of Mb in O_2 storage versus facilitated diffusion of O_2 would appear to be dependent on the degree of muscle ischemia during a breath hold. Further investigation of Mb saturation and/or muscle blood flow during dives is needed to clarify Mb's role. In addition, other functions of the Mb molecule such as scavenging of nitric oxide and reactive O_2 species (165) may also be important in diving mammals.

Total body O_2 stores

Calculation of total body O_2 stores in diving mammals is usually based on several assumptions. These usually include diving lung volumes that are 50% of total lung volume in pinnipeds (109, 111, 117, 118, 122, 124), total lung volume in cetaceans (115, 123, 192), the inspiratory volume in manatees (74, 200), and 60% total lung volume in sea otters [Costa and Kooyman, unpublished data (120)]. A 15% lung O_2 extraction is usually assumed (111, 121). As for the blood O_2 store, it is usually assumed that (i) one-third of the blood volume is arterial and two-thirds venous; (ii) initial arterial Hb saturation is 95%, and final arterial Hb saturation is 20%; (iii) initial venous O_2 content is 5 ml dl^{-1} less than 95% saturated Hb,

Table 5 Magnitude and Distribution of O_2 Stores in Some Marine Mammals Based on Parameters in Tables 2, 3, and 4, and Assumptions as Described in Text

Species	Mass, kg	Total O_2, ml kg^{-1}	Lungs, %	Blood, %	Muscle, %	Reference
Bottlenose dolphin *Tursiops truncatus*	200	36	34	27	39	120
Beluga whale *Delphinapterus leucas*	1,000	51	17	51	32	205
Sperm whale *Physeter macrocephalus*	10,000	68	4	38	58	120, 148
Manatee *Trichechus manutus*	155	21	33	60	7	74
California sea lion *Zalophus californianus*	35-87	39-52	21-16	45-41	34-43	175, 234
Steller sea lion *Eumetopias jubata*	238	40	20	45	35	191
Australian sea lion *Neophoca cinerea*	88	56	10	70	20	69
Walrus *Odobenus rosmarus*	65	38	24	50	26	133
Harbor seal *Phoca vitulina*	24	57	13	54	33	133
Hooded seal *Cystophora cristata*	252	90	7	51	42	20
Weddell seal *Leptonychotes weddellii*	400	87	5	66	29	120
Northern elephant seal *Mirounga angustirostris*	400	97	4	71	25	120
Sea otter *Enhydra lutris*	28	55	55	29	16	133

Body masses are those of the subjects studied and are not always adult animals.

and final venous O_2 content is zero; and (iv) 1.34 ml O_2 g^{-1} Hb at 100% saturation (111,121). In muscle O_2 store calculations, it is assumed that Mb is fully saturated at the start of the dive, that there is 1.34 ml O_2 g^{-1} Mb at 100% saturation, and that Mb fully desaturates during the dive (111, 121).

Based on the above assumptions, total body O_2 stores of diving mammals on a mass-specific basis range from two to five times that of human O_2 stores (111). One exception is the manatee with a mass-specific total body O_2 store equivalent to that in humans (Table 5). Also notable is the change in the distribution of O_2 stores among species. The role of the lungs as an O_2 store is minimized in deep, long-duration divers such as Weddell seals, elephant seals, and sperm whales. In these species, as much as 96% of the O_2 store is in the blood and muscle.

It should also be noted that, as shown in Table 5, the blood O_2 store of the elephant seal has been calculated with the highest blood volume measured in that species, 250 ml kg^{-1}, about 16% greater than the mean value (207). This value has been used in order to provide a minimal estimate for a pregnant elephant seal (174) because (i) the longest routine dive durations of elephant seals are exhibited by female elephant seals during their final months of pregnancy (128) and (ii) the magnitude of the increase in blood volume with pregnancy is unknown in the elephant seal.

One other factor that may increase the magnitude of the blood O_2 store in these animals is an elevation in predive venous O_2 saturation due to the potential use of arteriovenous shunts (17, 149, 150, 202). This could account for elevations in venous Po_2s and O_2 contents that have been recorded at the start of sleep apneas and dives in elephant seals (142, 216). Such processes may well occur before diving and increase the magnitude of the blood O_2 store.

Circulatory Responses and O_2 Consumption

Cardiovascular regulation is critical during diving because changes in heart rate and cardiac output contribute to not only the rate of O_2 uptake from the lungs but also the magnitude of O_2 delivery and O_2 consumption in tissues (89, 127, 138, 221, 226), hence the significance of the severe bradycardia and peripheral vasoconstriction that Scholander observed during forced submersion of seals (199). With heart rates as low as 10 beats min^{-1} (bpm), blood flow and blood O_2 levels were conserved for the heart and brain while muscle and other organs were isolated from the circulation (199, 201). In short, heart rate and perfusion controlled the rate of depletion of the blood and lung O_2 stores. In the 1960s, Elsner demonstrated

that the degree of bradycardia during the breath-hold period was less during trained versus forced submersions (48, 51). Since that time, a key question in diving physiology has been the magnitude of the reduction of heart rate, blood flow, and tissue O_2 consumption during unrestrained dives at sea.

Forced submersion

Doppler blood flow and labeled microsphere studies have documented the lack of blood flow to peripheral organs and tissues during forced submersions (11, 50, 227, 249). During the latter portions of long submersions, O_2 uptake from the lung was minimal, as blood O_2 content in the hepatic sinus (the principal source of venous return to the heart) was greater than that in the aorta (54). The rate of blood O_2 depletion was also slow under such conditions (about 1-2 ml O_2 dl^{-1} min^{-1}) (49, 54, 104, 199). This was about one-fourth the rate of blood O_2 depletion during asphyxia in dogs (104). During forced submersions, muscle O_2 was depleted at a rate of 6 to 10 ml O_2 kg^{-1} min^{-1}, about three to five times the metabolic rate of muscle at rest (8, 199, 201). Lactate accumulated in muscle once muscle O_2 was depleted but washed out into blood only during the postsubmersion interval when heart rate and muscle perfusion were restored (199, 201). Whole-body O_2 consumption prior to submersions was 7 to 8 ml O_2 kg^{-1} min^{-1} and was estimated to be one-third that value during the submersion (199).

Sleep apnea

Phocid seals exhibit prolonged, spontaneous breath holds during sleep (25, 29, 30). In contrast to forced submersions, during such apneas in elephant seals, heart rates were 40 to 50 bpm, cardiac output was not depressed, and muscle blood flow declined but persisted throughout the breath hold (1, 29, 180). During eupneic intervals between the breath holds, heart rates were elevated at 60 to 80 bpm. Rates of blood O_2 depletion during apneas were 2 to 2.3 ml O_2 dl^{-1} min^{-1}, which were greater than during forced submersions (216). Muscle Mb saturations declined to 80% but remained at that level throughout the apnea (178). NMR spectroscopy revealed no evidence of muscle lactate accumulation or phosphocreatine breakdown during the breath hold (178). There were no changes in blood lactate concentrations (25). The depletion of the blood and muscle O_2 stores during the breath-hold period yielded a mass-specific metabolic rate that was 26% greater than the resting metabolic rate predicted by allometric equations (178, 216). Whole-body O_2 consumption rates, averaged over the eupneic and apneic periods, ranged between 2 and 6 ml O_2 kg^{-1} min^{-1} in young elephant seals (223). Mean metabolic rate measured similarly during sleep apneas of Weddell seals was 4.1 ml O_2 kg^{-1} min^{-1}, which was again greater than the allometrically predicted rate at rest (28).

The maintenance of cardiac output and oxygen consumption (as measured from blood and muscle O_2 store depletion) during sleep apnea when heart rate is 40 to 50 bpm raises the question as to what the normal resting heart rate is for these animals. Rather than considering heart rate depressed during sleep apnea, is it more appropriate to consider heart rate normal during sleep apnea and elevated during eupnea (1, 29, 30)? Because heart rate during sleep apnea is equivalent to that observed during the slow phase of the sinus arrhythmia pattern associated with breathing, it has been suggested that this be considered the normal resting heart rate (29, 30).

Exercise

Cardiovascular responses and swim patterns during exercise in a swim flume have been studied in both seals and sea lions. As workload increased in phocid seals, percentage time submerged decreased but surface heart rate and submerged heart rate remained constant, and distinct (61, 245). In harbor seals, for example, submerged and surface heart rates averaged 50 and 137 bpm, respectively, regardless of workload (245). The high surface heart rate and an increased stroke volume at the surface resulted in a fourfold greater cardiac output at the surface (177). However, similar to sleep apnea in seals, the submerged (apneic) cardiac output and stroke volume remained typical of seals and other mammals at rest. In flume-swimming sea lions (245), the swim pattern and heart rate responses differed from those in harbor seals in that percentage time submerged did not decrease with workload. Instead, both surface and submerged heart rates increased with workload. There was a constant, but small, difference between surface and submerged heart rates.

The increase in submerged heart rate of the sea lion in relation to workload contrasted with the constant submerged heart rate of the harbor seal. This raised the question as to whether muscle blood flow and oxygen delivery during the submergence differ between the two species. Theoretically, the higher Mb concentrations in the longer-diving harbor seal might make it less reliant than the sea lion on muscle blood flow and O_2 delivery during submergence. The differences in heart rate also emphasize potential differences in the magnitude of pulmonary gas exchange during submergence between the two species. Greater cardiac output and gas exchange during submergence may be necessary in the sea lion because of its short surface periods at high workloads.

Regardless of the differences in cardiovascular responses in flume-swimming harbor seals and sea lions, they both exhibited about an 8- to 10-fold metabolic scope that were normal to high for most mammals but less than those of "elite" athletes such as dogs and horses (176, 177, 221, 245). Maximum O_2 consumption in the flume was in the range of 35 to 40 ml O_2 kg^{-1} min^{-1}.

Exercise research on cetaceans has focused on the bottlenose dolphin. Maximum O_2 consumption in exercising dolphins (pushing against a load cell) was about 30 ml O_2 kg^{-1} min^{-1} (242). At low workloads and swim speeds, heart rate oscillated between a short postinspiratory tachycardia and an apneic bradycardia near 50 bpm (241, 242). This difference

disappeared as heart rate increased at higher workloads and swim speeds. This cardiovascular response paralleled that in the sea lion.

These exercise studies in cetaceans and pinnipeds have resulted in calculations of transport costs that are two to five times that of a hypothetical similarly sized fish (241, 245). The marine mammal values, which are four to 10 times less than that similarly calculated for humans (241), demonstrate the importance of the hydrodynamic shape of these animals.

Locomotory costs and the metabolic demand of muscle during exercise and diving also emphasize the importance of muscle's contribution to oxygen consumption and O_2 store depletion during these activities. Readers are referred to detailed studies of muscle fiber type, enzyme activities, and mitochondrial distribution in these animals (71, 100-103, 171, 179, 186, 231). In general, muscle was remarkable for a large percentage of oxidative fibers [fast-twitch, oxidative glycolytic (type IIa) and slow twitch oxidative (type I) fibers] and for oxidative enzyme activities and mitochondrial densities that were normal to high. The latter were considered to be an adaptation to hypoxia, with a decrease in oxygen diffusion distances to mitochondria. Muscle capillary density, however, was not increased in harbor seals (102). This was consistent with the low heart rate and presumably low muscle blood flow previously described during submergences in these animals.

Diving: Heart rate

The physiological hallmark of diving is a decrease in heart rate during dives. This has been observed in free-diving Weddell seals, elephant seals, gray seals, California sea lions, fur seals, and bottlenose dolphins (1,15,61,84,175,222,244). Typically, heart rates are 30 to 50 bpm during the dive. Even in the manatee, heart rate declines from a predive heart rate of 50 bpm to 30-40 bpm during diving (74). These moderate heart rates during many dives again raise the question of the normal heart rate at rest in these animals and the magnitude of reduction of tissue perfusion and oxygen consumption during dives. Variation in heart rate due to the sinus arrhythmia associated with breathing as well as the effect of body mass on heart rate complicate the estimation and comparison of heart rates at rest among marine mammals.

Nonetheless, as already emphasized, the degree of bradycardia and peripheral vasoconstriction will affect the rate of blood O_2 depletion through regulation of tissue blood flow and subsequent delivery of O_2 to tissues. Perhaps, a most extreme example is the 7-bpm average heart rate of a gray seal during a 14-min dive (222). There would be no argument that tissue gas exchange was minimized in this dive, with cessation of hepatic and renal blood flow and function and with isolation of muscle from the circulation. In many dives of gray seals and other divers, however, heart rates are higher. This allows hepatic and renal clearances to be maintained during repetitive foraging dives of Weddell seals (38). In contrast, in prolonged dives of these seals, hepatic and renal clearances are reduced (77). Presumably, hepatic and renal blood O_2 uptakes are also reduced in these long dives.

A common characteristic of heart rate profiles during dives is an increase in heart rate during ascent, the so-called ascent or anticipatory tachycardia. It has been suggested that this increase in heart rate allows increased muscle blood flow and O_2 extraction so that blood O_2 is depleted by the end of the dive in order to enhance the alveolar-to-blood P_{O_2} gradient during eupnea, maximize respiratory gas exchange, and minimize the duration of the surface interval (222). Increased heart rates and pulmonary perfusion during the final phase of ascent may also allow uptake of any available O_2 in the reexpanded lung. This could supplement arterial P_{O_2} and, along with increased cerebral blood flow secondary to the tachycardia, decrease the risk of shallow water black out in these animals.

Heart rates during the surface intervals between dives are characterized by tachycardias, usually in the 120- to 150-bpm range (1, 15, 84, 113, 172, 175, 222, 244). In the elephant seal, heart rates during surface intervals between dives at sea were 20 to 40 bpm greater than those during eupneic intervals between sleep apneas on the beach (1). Such high heart rates maximize cardiac output, respiratory gas exchange, and refilling of blood and muscle O_2 stores between dives.

Diving: O_2 consumption

The O_2 consumption during dives has usually been measured as the O_2 consumption during the surface interval divided by the sum of the dive duration and surface interval duration (28). In Weddell seals, diving metabolic rates correlated inversely with dive duration and ranged from 2 to 9 ml O_2 kg^{-1} min^{-1} (28). The average diving O_2 consumption, 4. 5 ml O_2 kg^{-1} min^{-1}, was greater than that during sleep apnea (3.5 ml O_2 kg^{-1} min^{-1}) and 1.8 times greater than the resting value predicted by allometric equations (2.5 ml O_2 kg^{-1} min^{-1}). The difference in metabolic rate between sleep apnea and diving is at least partially secondary to the cost of swimming. These costs are minimized in divers, however, due to hydrodynamic shapes, efficient stroke-glide patterns, and periods of prolonged gliding, during which the animals take advantage of changes in buoyancy (240).

More recent studies in Weddell seals have confirmed the above metabolic rates and also documented that (i) locomotor costs increased linearly with the number of strokes during a dive and (ii) dives associated with feeding events had a 44% higher metabolic rate than nonfeeding dives of similar duration (243). In comparison to nonfeeding dives, the increased metabolic costs of feeding and digestion are presumably associated with increased heart rates, greater splanchnic perfusion, and faster rates of blood O_2 depletion. There have been few studies of blood O_2 depletion in diving mammals. Arterial blood O_2 depletion rates in diving Weddell seals and elephant

seals are about 0.8 to 1.7 ml O_2 dl^{-1} min^{-1} (142, 181). Depletion rates in the hepatic sinus and extradural vein of diving elephant seals are near 2 ml O_2 dl^{-1} min^{-1} (142). In comparison, arterial blood O_2 depletion rates in the Korean ama (human divers) are about 6 ml O_2 dl^{-1} min^{-1} (182).

Metabolic rates of captive gray seals and elephant seals diving in tanks, and of captive California sea lions during trained submersions, also decreased with dive duration and were in the same range of values as that for Weddell seals (96, 187, 233). Metabolic studies for up to 5 days have also revealed that metabolic rate can be elevated sevenfold during extended surface intervals of captive gray seals (212). It has been suggested that these animals are capable of delaying food processing until these periods of inactivity at the surface, thus decreasing metabolic costs during dive activity. During at-sea dives of captive Steller sea lions, mass-specific O_2 consumption rates not only had a greater range of values but also demonstrated similar relationships to dive duration and predicted rates at rest (58). During 40- to 192-s dives of captive sea otters (248), mean diving O_2 consumption was 17 to 18 ml O_2 kg^{-1} min^{-1}, about 1.3 times the rate of animals resting at the surface. As in Weddell seals, foraging during dives increased the metabolic rate in the otter. On average, foraging dive metabolic rate was about 22 ml O_2 kg^{-1} min^{-1} in the sea otters.

These diving metabolic rates, although measured over both the surface and the submerged periods, reflect the variability of the actual blood O_2 depletion rate during dives and, again, are probably a function of the magnitude of heart rate and cardiac output reduction during different types of dives. All these findings continue to emphasize the central importance of the heart rate response during diving.

Blood Gases, O_2 Store Depletion, and Lactate

The most remarkable aspect of blood gas analyses from samples during free dives of marine mammals is the low blood P_{O_2} that they can tolerate. Certainly, P_{CO_2} increases and pH declines during dives. However, these values are within ranges tolerated by human patients with severe lung disease and by patients during permissive hypercapneic ventilation protocols (5, 160, 236). The P_{CO_2}s measured during dives are also less than that associated with CO_2 narcosis in humans (160). As reviewed below, the changes in blood P_{CO_2} and pH during the dive are limited by (i) the finite size of the body O_2 store, (ii) the continued decline in heart rate and metabolic rate as a dive progresses ever longer, and (iii) the isolation of CO_2 and lactate in tissues that are not perfused at such low heart rates. The largest changes in blood pH in diving mammals, as demonstrated by the lactate washout in Scholander's original work, occur during the postdive interval when tissue perfusion is restored (199).

P_{O_2}, P_{CO_2}, and pH: Forced submersion

During forced submersions of harbor seals, arterial P_{O_2} and P_{CO_2} reached 42 and 70 mmHg at 10 min, respectively, and were 10 and 98 mmHg at 22 min (104). Corresponding venous values were 30 and 84 mmHg at 10 min and 3 and 105 mmHg at 22 min. Arterial and venous pH values were near 7.3 at 10 min and 7.2 at 22 min. With end-of-submersion arterial and venous Hb saturations near 10% and 0%, almost all of the blood O_2 store was consumed during a 22-min submersion. These data and the earlier results of Scholander (199) provide the criteria with which available O_2 stores are calculated (111, 133). Similar observations were made in Weddell seals. During 8- to 12-min forced submersions of Weddell seals, mean arterial P_{O_2}, P_{CO_2}, and pH were 32 mmHg, 59 mmHg, and 7.25 pH units, respectively (249). At 55 min of submersion of Weddell seals, corresponding arterial values were 10 mmHg, 84 mmHg, and 7.11 pH units (53).

P_{O_2}, P_{CO_2}, and pH: Sleep apnea

Changes in blood gases are not as extreme during sleep apneas of phocid seals. In Weddell seals and young elephant seals, end-of-apnea arterial and venous P_{O_2}s were 18-26 and 15-31 mmHg, respectively (125, 216). The corresponding arterial and venous P_{CO_2}s were both 55 and 72 mmHg in range and resulted in pH values near 7.3. For 7-min apneas of young elephant seals, 56% of the initial blood O_2 store was consumed.

P_{O_2}, P_{CO_2}, and pH: Diving

There have been relatively few blood gas determinations during dives of marine mammals. Near the end of a 27-min dive of a Weddell seal (181), arterial P_{O_2}, P_{CO_2}, and pH were 18 mmHg, 55 mmHg, and 7.3 pH units, respectively. P_{O_2} rapidly increased to above 60 mmHg within the first few minutes of the postdive interval. End-tidal P_{O_2} profiles of Weddell seals after dives as long as 32 min revealed a similar range of P_{O_2} values and also a rapid recovery of P_{O_2} and presumed Hb saturation (173). The minimum P_{O_2}s during these dives in seals are less than the minimum end-of-dive arterial P_{O_2} values (near 30 mmHg) found in human breath-hold divers (65, 182). In translocated juvenile elephant seals with mean dive durations near 10 min, and occasional dives as long as 40 min (142), minimum P_{O_2}s recorded with an indwelling P_{O_2} electrode were 10 mmHg or less in the extradural vein in 51% of dives (lowest value, 2 mmHg), 10 mmHg or less in the hepatic sinus in 21% of dives (lowest value, 2 mmHg), and 30 mmHg or less in the aorta in 46% of dives ($\leq$20 mmHg in 10% of dives; lowest value, 12 mmHg). During the surface interval, mean times of recovery of arterial P_{O_2}, hepatic sinus P_{O_2}, and extradural vein P_{O_2} were 82, 149, and 123 s, respectively. These data from both Weddell seals and elephant seals

indicated that these animals are capable of almost complete blood O_2 depletion during some dives.

End-tidal P_{O_2}s for dives of other species are not always as low as in Weddell seals and elephant seals at sea. After dives up to 12 min in duration in captive gray seals (187), end-tidal P_{O_2}s were near 60 mmHg. Postdive end-tidal gas analyses from bottlenose dolphins after dives to 200 m depth also revealed a similar ranges of values, with mean P_{O_2}s as low as 39 mmHg and P_{CO_2} as high as 57 mmHg (195). After 25-s breath holds of harbor porpoises, end-tidal P_{O_2} and P_{CO_2} were 53-60 mmHg and near 58 mmHg, respectively (188). In the manatee, end-tidal values after 10-min dives were 27 mmHg (P_{O_2}) and 87 mmHg (P_{CO_2}) (74). In these examples, all P_{O_2}s are consistent with arterial Hb saturations of 50% or more and less than complete blood O_2 depletion under such conditions.

Myoglobin desaturation

Investigations of muscle O_2 depletion during breath holds of diving mammals are even fewer than those for blood O_2 depletion. In the studies by Scholander and colleagues, muscle O_2 was depleted in about 10 min at rates of 6 to 10 ml O_2 kg^{-1} muscle min^{-1} during forced submersions of seals (199, 201). In comparison, the O_2 consumption of terrestrial mammalian muscle at rest is 1 to 2 ml O_2 kg^{-1} muscle min^{-1} (8, 45). When harbor seals underwent a forced submersion training protocol in a near-infrared spectroscopy study (99), heart rate and muscle blood flow were higher and the Mb desaturation rate was slower in trained versus naive seals. In an NMR study of sleep apnea in young elephant seals, Mb desaturated at a rate of 1 to 2.3 ml O_2 kg^{-1} muscle min^{-1} for the first four min to about 80% saturation where it remained for the rest of the apnea (178). In diving Weddell seals equipped with a backpack near infrared spectrometer, Mb desaturated in the latissimus dorsi muscle at a rate of 2 to 4 ml O_2 kg^{-1} muscle min^{-1} but did not completely desaturate even in dives greater than 30 min in duration (78). It is unknown whether the primary locomotory muscle, the longissimus dorsi, desaturated at a faster rate. The slow desaturation rate and lack of complete desaturation in the latissimus dorsi suggested to those authors that muscle blood flow persisted during the dive and supplemented the muscle O_2 store. This would be similar to that observed during sleep apnea and trained submersions but contrast with that during forced submersion. The regulation of muscle blood flow remains a key question in the management of O_2 stores and the physiology of diving mammals.

Lactate and the aerobic dive limit

In the forced submersion studies of Scholander and colleagues, muscle lactate concentration in seals increased as muscle O_2 was depleted and reached concentrations as high as 44 mM (199, 201). Although arterial and venous lactate concentrations typically increased to 2 to 4 mM during submersions in these and other studies (87, 104, 134), peak blood levels [i.e., 14 mM (87)] occurred only after the submersion, consistent with intense peripheral ischemia during the submersion and washout of lactate afterward. In contrast, during sleep apnea of seals, muscle intracellular pH and blood lactate concentrations did not change during or after the apnea (25, 178).

Blood lactate concentrations during and after dives have been most intensively studied in Weddell seals. In a landmark study, Kooyman and colleagues documented that postdive arterial blood lactate accumulation did not begin to occur in Weddell seals until after dives of about 20-min duration (125). Blood lactates began to increase above baseline near 19 min, were definitely elevated by 26 min, and reached concentrations as high as 26 mM after a dive duration of almost 1 h. The dive duration associated with the onset of postdive blood lactate accumulation was termed the aerobic dive limit (ADL) (114). It has been found to vary with the age and size of an animal, as well as with the nature of a dive (18, 114, 243).

The existence of the ADL and the fact that most dives of Weddell seals are less than 20 min shifted the focus of the study of diving metabolism from glycolysis and anaerobic metabolism (87, 88, 206, 217) to oxidative metabolism and regulation of O_2 store utilization (26, 32, 86, 181). The ADL has since become an essential concept in the interpretation of diving behavior and foraging strategy (23, 110, 111). It has also been suggested by some authors that the ADL be called the diving lactate threshold or DLT (21-23).

Blood lactate levels do not change significantly during long dives. Although blood lactate concentrations began to increase slightly toward the end of long dives of Weddell seals and Baikal seals, those concentrations were less than 2 mM (77, 172, 181). As observed in the Weddell seals, these minimal increases in lactate concentrations may be secondary to onset of the ascent tachycardia and potential reperfusion of previously ischemic tissues (77). However, in the Baikal seal study, these small elevations in blood lactate concentrations occurred when heart rate was only 5 to 10 bpm (172). This suggests that these small changes in blood lactate concentrations during long dives may also be secondary to increased glycolysis in the heart and brain, which are still perfused at such low heart rates, but with blood with low O_2 content and P_{O_2}.

The washout of lactate after long dives or forced submersions is associated with a further decrease in blood pH. For example, after dives of 27 and 37 min, arterial pH values of Weddell seals were 7.29 and 7.16, respectively (181). These approached values measured after forced submersions (7.0-7.2) (53, 134). After a 61-min dive of a Weddell seal, arterial pH was 6.8 and P_{CO_2} 55 mmHg (125). These observations reinforce the significance and dynamic nature of the surface interval. Not only are blood and muscle O_2 stores restored but also CO_2 and lactate are washed out from underperfused tissues. The lowest blood pH values and greatest potential effects on the O_2 affinity of Hb are not during the dive but during the surface interval.

Aerobic dive limits have been determined with postdive blood lactate measurements in only two other pinnipeds in experimental situations. The aerobic limits of young California sea lions swimming submerged in a tank, and of captive Baikal seals lying quietly underwater in their tank, were 2.3 and 15 min, respectively (172, 175). In a study of captive sea otters, blood lactates did not increase after dive durations as long as 100 s (248).

Blood lactate concentrations have also been determined in exercise and diving studies of bottlenose dolphins and beluga whales (205, 242, 244). In the bottlenose dolphin, blood lactate concentration increased from 1.1 mM at rest to about 3 mM during routine swimming and reached a peak value of 11 mM during stationary maximum exercise at an oxygen consumption of 30 ml O_2 kg^{-1} min^{-1} (242). In the dolphin, postdive blood lactate concentrations gradually increased with dive duration but reached a breakpoint near 3-mM concentration and a dive duration of 220 s, after which blood lactate concentrations increased even more sharply (244). This inflection point was interpreted to be the ADL of the bottlenose dolphin. Similar to the dolphin, beluga whales increased blood lactate concentrations from less than 1 mM at rest to about 2 mM while swimming at the surface (205). Postdive blood lactate concentrations began to increase after a dive duration of 9 to 10 min, which again was interpreted as the ADL of the beluga whale.

Hypoxemic tolerance

Cerebral hypoxemic tolerance, which is essential to make full use of the blood O_2 store, was investigated by Elsner and coworkers in Weddell seals and harbor seals. As indicated by electroencephalographic changes, both species appear to have an arterial hypoxemic threshold near 10 mmHg (53, 104). In harbor seals, the corresponding venous P_{O_2} was 2 to 3 mmHg (104). Weddell seals and elephant seals occasionally approach these limits in the wild. In studies of Weddell seals, the lowest end-tidal and arterial P_{O_2}s during dives have been 15 and 18 mmHg after 32- and 27-min dives, respectively (173, 181). During sleep apneas of juvenile elephant seals, arterial and venous P_{O_2}s reached 18 and 15 mmHg, respectively (216). In translocated juvenile elephant seals, arterial P_{O_2} was as low as 12 mmHg but usually was in the 15- to 30-mmHg range at the ends of dives (142). Hepatic sinus and extradural vein P_{O_2}s in these elephant seals were often below 10 mmHg; in fact, the extradural vein P_{O_2} commonly reached 2 to 3 mmHg just as during the forced submersions. Many of these arterial values in seals are below the mean arterial P_{O_2} (24 mmHg) of climbers on ambient air on Mt Everest and below human thresholds for shallow water black out (about 25 mmHg) (64, 65, 76). End-of-dive venous P_{O_2}s in the elephant seals are also often less than mixed venous and femoral vein P_{O_2}s during exercise at maximal O_2 consumption in terrestrial mammals (196, 221). These end-of-dive values also have implications for mathematical models of O_2 store depletion during diving because they are often less than assumed possible (39, 40).

Higher capillary densities and high glycogen concentrations in the brain as well as neuroprotection from mild hypothermia may contribute to the hypoxemic tolerance of diving mammals (67, 104, 105, 161, 185). Higher capillary densities would decrease the diffusion distance for oxygen, and increased glycogen content would allow for more glycolysis and anaerobic energy production. Alterations in neuroglobin/cytoglobin concentration or function, and scavenging of reactive oxygen species may also allow such extreme depletion of the blood O_2 store (52, 246). In addition, hypoxemic tolerance exists in other organs of the seal, such as the kidneys, which are much more resistant to ischemia and hypoxemia than those in terrestrial counterparts (79). Elevated tissue buffering capacities in marine mammals may contribute to tissue survival under such conditions (31). In addition, some protection may be afforded by reexpansion of the lung during ascent and supplementation of arterial P_{O_2} by blood uptake of the oxygen remaining in the lungs; this may contribute to end-of-dive arterial values that are slightly higher than venous values in the elephant seal (142). On the other hand, if P_{O_2} in the reexpanded lung is less than venous P_{O_2}, the reverse could occur. Because of the maintenance of gas exchange to greater depths in otariids than in elephant seals and Weddell seals (124), it has been suggested that Antarctic fur seals decrease lung P_{O_2} to near-zero values during dives (92) and that that is why these animals have been observed to actively exhale during ascent (to prevent lung reexpansion with subsequent transfer of O_2 from blood into the lung and a lowering of arterial P_{O_2}).

Nitrogen

Although there have been relatively few studies of blood oxygen and carbon dioxide levels in diving mammals, there have been even fewer studies of N_2 pressures. However, as already reviewed in this article, Scholander's model of lung collapse and cessation of gas exchange at depth has been well supported by anatomical and experimental evidence. It was therefore surprising that necropsies of beaked whales stranded in association with naval sonar exercises revealed findings consistent with, although not diagnostic of, DCS (63, 98). Pathologic findings consistent with dysbaric osteonecrosis in sperm whales also raised the same question as to the magnitude of N_2 absorption in deep-diving mammals (152).

Blood and muscle N_2 measurements

During simulated dives as deep as 14.6 ATA (equivalent to 136 m depth), arterial and venous P_{N_2} did not increase above 3 ATA in elephant seals and a Weddell seal with diving lung volumes of about 40% forced inspiratory capacity (122). These findings supported the concept that lung collapse occurred at shallow depths in these species. In one elephant seal that inhaled an unusually large air volume, venous P_{N_2}s were 2 to 3 ATA greater, providing evidence that the depth of

lung collapse was partially dependent on the magnitude of the diving air volume. During free dives of Weddell seals, arterial P_{N_2} did not rise above 3.9 ATA despite depths of 24.6 ATA (60), again confirming the prior compression chamber findings. Together, these studies were consistent with cessation of gas exchange at 20- to 50-m depth in both elephant seals and Weddell seals. During simulated dives of harbor seals (118), venous P_{N_2} reached 5 ATA. This suggests a deeper depth of lung collapse in harbor seals and is also consistent with the study of pulmonary shunts during simulated dives previously reviewed in this article (124).

In a N_2 study of bottlenose dolphins, a mass spectrometer was used to monitor intramuscular N_2 washout after a series of dives to 100 m depth (11 ATA) (193). The washout during the surface interval after the dive session was used to back extrapolate to an end-of-dive muscle P_{N_2} and a muscle washout half-time. End-of-dive muscle P_{N_2} was estimated to be 1.7 to 2.1 ATA. This suggested that muscle blood flow persisted during the dive, and, with several assumptions and calculations, that lung collapse occurred at 70 m in the dolphin. It should be noted that the data in this study of bottlenose dolphins were collected between 8 and 22 min after the dive. This reflects a significant assumption about the shape of the washout curve back to 0 min and the estimation of the end-of-dive muscle P_{N_2} value. This study has taken on more importance since the beaked whale strandings because its findings have provided the basis for the initial modeling of N_2 absorption and distribution in diving cetaceans (94, 193). In particular, the tissue washout time, the depth of lung collapse, and assumptions as to the magnitude and symmetry of N_2 wash in and wash out during a dive have all been used in such modeling efforts.

These physiological investigations in seals and dolphins are supportive of Scholander's model of lung collapse. Furthermore, these studies document that P_{N_2} is elevated in these animals at depth. Therefore, it is not surprising that computed tomographic scans of marine mammals that died at depth while trapped in gillnets revealed the presence of bubbles in blood and various organs (151). It is not questioned that P_{N_2} is elevated at depth. The debate is whether P_{N_2} is dangerously elevated at the surface, and, if so, why.

Modeling of N_2 absorption and distribution

Because of the difficulty of measuring gas exchange, and N_2 absorption and redistribution during dives, mathematical models have been developed to estimate these parameters and develop hypotheses and predictions (13, 55, 56, 94, 193, 250). These models are complex, have multiple assumptions, and are dependent on limited available anatomical and physiological data. For example, in many models, "lung collapse" or cessation of gas exchange was assumed to be an instantaneous, all-or-nothing process at the 70-m depth determined in dolphins (56, 94, 193, 250). Despite these limitations, many hypotheses have been generated and more refined models developed. One such hypothesis is that the previously measured blood N_2 levels in seals and dolphins can be accounted for by (i) a finite quantity of lung N_2, (ii) tissue N_2 uptake dependent on the blood flow patterns and the heart rate profile during the dive, and (iii) the progressive development of a pulmonary shunt with depth (13, 55). In other words, it was hypothesized that actual alveolar collapse may not be necessary for the cessation of gas exchange. With regard to pulmonary or right-to-left cardiac shunts, it should be noted that both the foramen ovale and the ductus arteriosus are closed in adult seals and cetaceans (210, 228).

Another modeling hypothesis, related to the beaked whale sonar issue, is that (i) whales are predisposed to DCS due to excess blood N_2 uptake not during deep dives but during shallow dives that are above the depth threshold for lung collapse, and that (ii) sonar avoidance behavior leads to such unusual repetitive, shallow dives and subsequent DCS (250). This hypothesis should be able to evaluated with dive data loggers (225) during controlled exposure experiments. In contrast to this model, however, other models make the opposite prediction, that is, that shallow dives are protective, allowing washout of excess N_2 (57), or that routine deep-dive profiles result in elevated P_{N_2} and increased risk of DCS (91).

Clearly, more biological data are needed to evaluate and refine such models. For example, a recent anatomical study of bottlenose dolphins and pygmy sperm whales (*Kogia* spp.) confirmed that mass-specific lung mass was greater in the shallow-diving dolphin and that the relative intrathoracic volume of the thoracic rete mirabile was greater in the deep-diving whale (169). The isolated lungs of the deep-diving whale were also much more flaccid than those of the dolphin. All these findings could contribute to more rapid collapse of the lung in the pygmy sperm whale than in the bottlenose dolphin. This should afford greater protection against excess N_2 absorption. It should also be noted that even in the bottlenose dolphin, a recent physiological investigation failed to find ultrasound evidence of asymptomatic intravascular bubble formation during the postdive period (93). In addition, heart rate profiles of that dolphin revealed that modeling assumptions with regard to cardiac output and tissue N_2 wash-in/wash-out times during descent, ascent, and the surface interval need to be revisited. In the future, continued physiological and behavioral experiments combined with modeling studies should further our knowledge of these N_2 questions and of gas exchange, in general, in diving mammals.

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