Undersea Biomedical Research, Vol. 4, No. 2, June 1977

Alterations in long-bone regional blood flow associated with inadequate decompression in dogs

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Bove, A. A., F. C. Famiano, L. L. Levin, R. A. Carey, A. L. Pierce, and P. R. Lynch. 1977. Alterations in long-bone regional blood flow associated with inadequate decompression in dogs. Undersea Biomed. Res. 4(2): 169–182.—The relationship of bone blood flow abnormalities to symptoms of decompression sickness (DCS) was studied in 9 dogs before and after a 220-ft (98 psig), 20–25-min hyperbaric air exposure with inadequate decompression. Flow distribution in the humerus and femur was measured with the use of isotope-labeled 15-μm diameter microspheres injected into the proximal aorta. To account for effects of anesthesia and for possible emotional factors, five animals were studied awake and four were studied under pentobarbital anesthesia (25 mg/kg). Of the four anesthetized animals, three had evidence of reduced blood flow in one or more long bones, and only one of the animals with a flow abnormality had clincial decompression sickness. Of the five awake animals, two had reduced blood flow in one or more long bones, and only one of these had clinical decompression sickness. Thus, five of the nine animals studied after inadequate decompression had evidence of abnormal blood flow, and two of these five had symptoms of decompression sickness. Although five dogs had symptoms of decompression sickness, only two had abnormal flow distribution. In the predive control study absolute bone blood flow averaged 18 ± 2.3 ml/min/100 g, and there was a significant ($P < 0.005$) difference in flow distribution between the proximal and distal ends of the bones with the distal bone regions having lower flow. The lower flow regions were the areas most involved with flow abnormalities. These data indicate that inadequate decompression from an air dive produces abnormalities in regional blood flow to the ends of long bones which can be detected shortly after diving exposure and correlate poorly with clinical evidence of decompression sickness in dogs.

dysbaric osteonecrosis
aseptic bone necrosis
decompression sickness
diving medicine

Although aseptic necrosis of bone has been associated with exposure to air at pressures above atmospheric for over 60 years, the cause of this malady remains unclear. Chronic lesions of the long bones which manifest clinically as juxta-articular collapse and ultimate loss of joint function have been found in caisson and tunnel workers and more recently in deep air divers and oxygen–helium divers. Recent surveys from several countries where diving or tunnel work under pressure has been done for 30 to 40 years reveal that 20% to 60% of exposed workers may show some evidence of bone injury (McCallum 1974; Fagan, Beckman, and

Galletti 1974; Elliott 1974). The disease has been named dysbaric osteonecrosis, and resembles to a large degree the bone lesions found in aseptic bone necrosis.

The process by which compressed air workers sustain bony lesions is unclear. Indeed, overt evidence of decompression sickness (DCS) has often been absent in divers who are found to have bony lesions (Elliott 1974; Ohiwa and Itoh 1975). Gas embolism is usually considered to be the etiologic factor in decompression sickness, although changes in blood clotting, hemodynamics and capillary permeability are also known to occur (Hallenbeck, Bove, and Elliott 1973; Bove, Hallenbeck, and Elliott 1974b). It is likely that a combination of processes produces the clinical syndrome of decompression sickness; nevertheless, gas bubbles appear to be the initiating factor for all of the known alterations which occur.

Studies of the localization and effect of gas emboli in decompression sickness indicate that mild disease is associated with venous gas emboli which arise from an unknown location in peripheral tissues (Spencer 1976). Gas trapped in the pulmonary circulation is eliminated from the body via the lungs in mild decompression sickness, and only when the embolic load becomes great does gas pass through the pulmonary bed and enter the systemic circulation to produce arterial embolization (Bove, Hallenbeck, and Elliott 1974a).

Present knowledge is thus confronted with the paradox that divers with mild decompression sickness probably have no arterial emboli, yet this population shows evidence of vascular bone disease, with an incidence ranging from 5–75% (Jaffe 1972a). Because the mechanism of dysbaric osteonecrosis is not yet clear, it is worthwhile to evaluate the blood flow to bone in exposures of diving and diving with decompression sickness. This study describes such measurements in dogs exposed to air at pressures equivalent to a depth of 220 fsw. The results indicate that blood flow reduction does indeed occur but is not correlated with clinical signs of decompression sickness.

METHODS

Animal preparation

Mongrel dogs weighing between 9 and 15 kg were studied both anesthetized (5 animals) and unanesthetized (5 animals). Unanesthetized animals were prepared as follows: one week prior to study each dog was placed in a small hyperbaric chamber (Bethlehem Steel Co. Model NB 791) and acclimatized to the sound of compression by simultaneously opening the air supply and exhaust valves to maintain the chamber at 1 ATA. This 1-ATA chamber exposure was done for 5 min daily for 3–5 days. Two days prior to study the animal was anesthetized; under sterile conditions, two polyethylene catheters were inserted into the left carotid artery. One catheter was placed in the left ventricle, the other in the descending aorta near the diaphragm. The proximal ends of the catheters were brought through a skin tunnel to the posterior neck and exteriorized. The neck wound was closed and bandaged, and the animal was allowed to recover. Both catheters were filled with heparin solution, flushed each day, and refilled to prevent clotting. On the day of the study the animal was brought to the laboratory and placed on a flat table in left lateral position. The catheters were cleared, left ventricular and aortic pressure were measured and preparations made for the measurement of bone blood flow. To eliminate the possibility that undetected psychological stress altered flow distribution, five acute studies were done under pentobarbital anesthesia (25 mg/kg). After induction of anesthesia, a carotid artery was exposed and catheters placed in the left ventricle and descending aorta, and the animal positioned as described above.

Bone blood flow

Measurement of regional distribution of blood flow to the long bones was carried out using the radioactive microsphere technique. This method assumes that the tissue distribution of isotope-labeled microspheres is proportional to the blood flow to the tissues (Sapirstein 1958), and that microspheres are evenly distributed in the arterial blood and do not pass through the peripheral capillaries. Adequate mixing of microspheres is attained by injecting them into the left atrium or left ventricle. For bone flow studies, a ventricular injection is adequate. The myocardium is the only tissue which may be improperly labeled with a left ventricular injection (Kaihara, VanHeerden, Migita, and Wagner 1968). To assure complete trapping in the capillary circulation, 15-μm diameter microspheres (3 M Co., Minneapolis, Minn.) were used. These were labeled with ^{85}SR, ^{169}YB, and ^{141}CE in various experiments. Injecting two different labels allows flow distribution at two states of the experiment to be measured.

For different experiments, different pairs of labels were used and the order of injection for each pair was reversed from one experiment to the next to eliminate possible errors due to counting statistics and energy separation among isotopes. The choice of isotope labels for microspheres was dictated for the most part by their availability from the manufacturer and by their gamma emission characteristics, which must be suitably different to allow for separation of one isotope from the other. Calibration of blood flow in ml/min/100 g was done by withdrawing blood from the descending aorta at a fixed rate of 8.0 ml/min using a constant flow withdrawal pump (Harvard Apparatus Co.). Since the reference flow is a portion of the cardiac output, the number of microspheres in the withdrawal syringe will be proportional to the reference flow. To find the flow to any other tissue, a simple proportion is established:

$$\frac{\text{Tissue flow}}{\text{Reference flow}} = \frac{\text{Tissue activity, cpm}}{\text{Reference activity, cpm}}$$

where flow is in ml/min, and activities represent the total activity of both the reference sample and the tissue sample. To measure the reference sample activity, five 2-ml samples of well-mixed reference blood were counted in an automatic gamma counter. From these data, the total reference counts were calculated.

For flow measurements, 100 μCi of ^{85}SR, 60 μCi of ^{169}YB, or 200 μCi of ^{141}CE were injected in the left ventricle. Total numbers of microspheres injected were 4.3 million for SR, 2.6 million for YB, and 8.6 million for CE. These proportions were established to provide nearly equal counting rates for each isotope. When there is much more of one isotope than others, separating each channel of data is difficult; it is thus desirable to have nearly equal absolute count rates for each isotope. These isotope proportions provide a minimum of 500 microspheres/g of bone tissue. According to Katz, Blantz, Rector, and Seldin (1971) this concentration of microspheres should reduce sampling errors to less than 5%.

Tissue sample preparation

Tissue samples were prepared by removing the right and left humerus and femur within 30 min of killing the animal. Each bone was surgically cleared of muscle and tendon remnants. When sectioning was delayed more than 12 h, the bones were frozen. To produce multiple bone segments for counting, the bones were cut with a saber saw into sections of 0.5 to 1.5 g weight. Cutting was performed in a completely enclosed, vented, negative pressure isotope handling hood to avoid inhalation of isotope-ladden bone dust. For ease of cutting the bones were clamped in a specially designed jig. Each bone section was placed in a previously labeled

and weighed isotope-counting vial. Figure 1 shows the bone regions analyzed. A total of 88 bone sections from the 4 long bones were counted, and 44 samples were used for analysis of the bone ends. Care was taken to remove all bone dust from the cut samples before placing them in the counting vials. After all counting vials were filled and tested for external contamination, each tube was weighed to 4 significant digits with an analytic balance. The empty tube weights were subtracted from the tube with sample weights. This weighing procedure was necessary to avoid contaminating the scale and surrounding laboratory with fine radioactive bone particles.

Isotope counting and flow calculation

All isotope counting was done in a two-channel automatic gamma counter (Searle Nuclear Div.) programmed to separate isotopes by differential gamma spectrometry. All tubes were counted in one machine run, which took 20–24 h. The automatic counter produced a typewriter listing of the total counts for each channel and the counting time. Adequate counting time was allowed to accumulate 10,000 total counts per sample to minimize random counting error. In addition to the numerical output, a punched paper tape for computer input was also produced. Data on this tape were entered into a PDP–9 digital computer (Digital Equipment Corp.) which was programmed to construct data files on magnetic tape for the isotope data and bone sample weights, then to calculate the actual counts/minute for each sample after correcting for background and channel overlap by differential spectrometry. A printout of actual counts per minute, blood flow in ml/min/100 g, and percent distribution of flow was produced from the data. These data were grouped for analysis of specific regions of each bone.

Experimental protocol

Blood flow was determined from the microsphere technique with the dog in the left lateral or supine position. The first determination was done after the animal was prepared and connected to the blood-withdrawal apparatus. The awake dogs rested quietly and showed no evidence of apprehension during the study. Upon completion of the first microsphere injection, the catheters were flushed with heparinized saline, capped, and wrapped in a soft cervical dressing. The animals were placed in the hyperbaric chamber and exposed to a pressure of 220 fsw (98 psig) for 20–25 min, using a descent rate of 75 ft/min and an ascent rate of 60 ft/min. All animals were subjected to the dive protocol shown in Fig. 2. The use of this protocol results in a high incidence of limb bends and has been used in previous studies (Bove et al. 1974a). The second dive followed a maximum surface interval of 4 min. The surface time

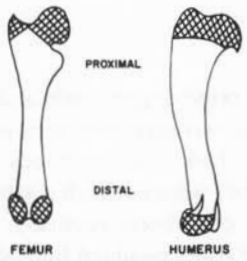

Fig. 1. Diagram of regions of long bones studied for blood flow distribution; shaded areas were divided into a total of 44 bone samples.

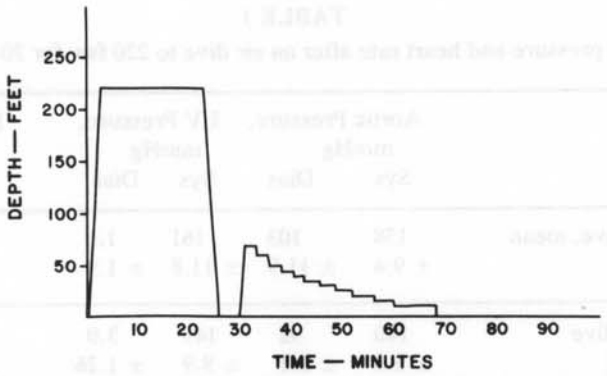

Fig. 2. Dive profile used to produce decompression sickness (DCS). Rapid decompression after initial 220-fsw (98 psig) exposure produced DCS within minutes after reaching surface. Second dive to 70 fsw is a treatment dive, controlled by observing animal for evidence of DCS during staged ascent.

was shorter if the animal showed signs of decompression sickness (dyspnea or in the awake animals, a limb disorder). This second exposure to pressure was, in essence, a treatment regime in which the animal was slowly returned to the surface while being observed for increasing severity of decompression sickness symptoms. Upon arrival at the surface after the second dive, the animal was returned to the experimental laboratory where the second microsphere injection was performed for flow measurement. Prior to each microsphere determination, aortic and left ventricular pressure and heart rate were recorded with a multichannel recorder (Electronics for Medicine) using electronic transducers (Statham P23Dd). Following the second study the unanesthetized animals were killed with pentobarbital anesthesia to eliminate discomfort caused by cardiac arrest from potassium chloride. The four bones to be studied were removed by dissection within 30 min after the animals died.

RESULTS

Hemodynamic data

Blood pressure and heart rate were obtained pre- and postdive in all animals. Table 1 shows the heart rate and blood pressure response for all animals before and after the hyperbaric exposure. In all cases, data were recorded prior to the microsphere injection. A small, nonsignificant fall in aortic and left ventricular systolic pressure was found postdive. Left ventricular end-diastolic pressure and aortic diastolic pressure similarly showed small but nonsignificant changes. Heart rate fell from 155 to 130 beats per min (bpm) following the dive ($P < 0.001$). This change suggests that the second dive for control of decompression sickness symptoms was effective. We have shown previously (Bove et al. 1974b) that an increase in heart rate is an early sign of serious systemic involvement in decompression sickness and thus a reduction in heart rate in the absence of evidence of gross circulatory failure suggests that circulatory stress from serious decompression sickness was not significant enough to cause a tachycardia.

Anesthetized dogs

One of the five anesthetized dogs was studied without hyperbaric exposure to test the repeatibility of the measurements. In this animal, percentage of blood flow distribution to the

TABLE 1
Blood pressure and heart rate after an air dive to 220 fsw for 20–25 min

	Aortic Pressure, mmHg		LV Pressure, mmHg		Heart Rate, bpm
	Sys	Dias	Sys	Dias	
Predive, mean	158	103	161	1.6	155
SEM	± 9.4	± 11.9	± 11.8	± 1.9	± 13.7
Postdive	140	92	149	3.0	130+
SEM	± 8.6	± 9.1	± 9.9	± 1.26	± 10.6

Data are means ± SEM;+ = significantly different from control at $P < 0.001$ level; $n = 9$.

articular surfaces, trochanters, and midshafts of the long bones was unchanged when two injections 15 min apart were given (Table 2). These results suggest that repeated microsphere injections alone do not alter the pattern of distribution of blood flow in the bones.

Of the four anesthetized animals given hyperbaric exposure, two had observable dyspnea (chokes) upon surfacing from the 220-fsw dive. Although symptoms were alleviated by the return to 70 fsw and slow ascent to the surface, one of these animals had abnormal bone flow distribution. Both anesthetized animals without decompression sickness showed evidence of changes in flow distribution after the dive. Thus, abnormal flow distribution was present in three of the four anesthetized dogs. Table 3 shows the blood flow distribution in two of the anesthetized animals, one with and one without decompression sickness. These two animals showed substantial alterations in flow distribution to the distal humerus, and in the symptom-free dog, flow distribution was substantially altered to the distal femur as well. Except for these alterations, flow distribution was either unchanged or slightly increased.

Awake dogs

Five dogs were studied awake after surgical preparation 2 or 3 days prior to the experiment. Of these 5 animals, 3 had evidence of decompression sickness. One had a limb bend of the right foreleg, evidenced by guarding of the extremity and a mild limp, but there was no evidence of neurologic abnormalities. This animal showed a 25% reduction in blood flow to the proximal femur bilaterally, while flow to all other areas was unchanged.

Two dogs had evidence of chokes, and one of these showed signs of spinal cord decompression sickness with rigidity of the lower extremities and hyper-reflexia. Neither of these two animals showed changes in the distribution of blood flow to the long bones. However, one of the awake dogs without decompression-sickness symptoms showed a flow abnormality. Thus, of the five awake dogs, 2 had evidence of reduced blood flow to one or more regions of the long bones; only one of these, however, had clinical decompression sickness. No animal showed evidence of psychological stress during or after the dive. In both groups of animals, flow data are expressed as percent of total measured flow to each bone. Relative flow distribution is the most useful measure of regional flow because overall changes in flow may occur from alterations of cardiac output or generalized bone vascular resistance changes. These alterations occur in the total bone circulation and do not reveal local alterations in bone blood flow.

TABLE 2

Bone blood flow distribution in long bones of 1 anesthetized dog measured after 2 microsphere injections, no other intervention

	Injection 1	Injection 2
Proximal humerus	8.34	8.37
Humeral shaft	2.35	2.50
Distal humerus	1.22	1.11
Femoral head	8.17	8.49
Femoral trochanter	3.13	3.58
Femoral shaft	2.25	2.48
Distal femur	3.45	3.43

Values are percent of flow distribution.

TABLE 3

Blood flow distribution to articular surface of long bones in anesthetized dogs after an air dive to 220 fsw for 25 min

	Predive	Postdive	% Change
Animal without clinical DCS			
Humerus			
Proximal	7.27	9.12	+ 25
Distal	2.11	0.64	− 70
Femur			
Proximal	5.40	6.86	+ 27
Distal	3.53	1.88	− 48
Animal with clinical DCS			
Humerus			
Proximal	7.08	8.14	+ 15
Distal	3.52	1.87	− 47
Femur			
Proximal	4.27	4.49	+ 5
Distal	5.96	5.20	− 13

Values are percent of flow distribution; $n = 2$.

Bone samples

The total number of bone samples analyzed from the ends and midshaft of the 4 bones from each dog was 88. Figure 1 shows regions analyzed in the humerus and femur. Average sample weight was 0.96 ± 0.05 g.

Bone blood flow

Normal blood flow in all dogs averaged 18.5 ± 2.3 ml/min/100 g of bone. A difference in flow was noted between the proximal and distal ends of the bones. Figure 3 demonstrates

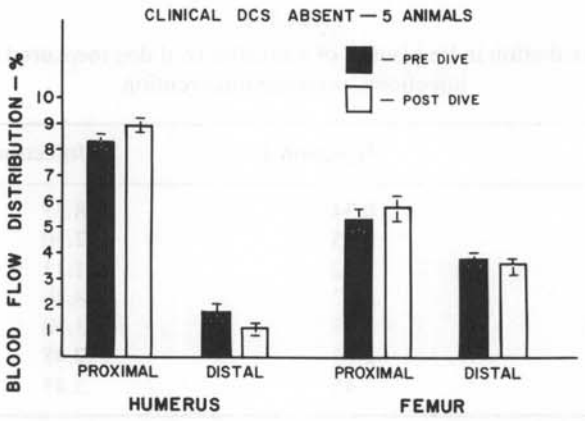

Fig. 3. Distribution of blood flow in % of total for all bones studied in 5 animals with no clinical evidence of DCS. No significant effects were noted after inadequate decompression and recompression treatment. A significant difference ($P < 0.005$) between proximal and distal bone regions was noted in both humerus and femur. Data are means ± SE.

dominance in flow distribution in the proximal ends of the bones. This difference was noted in both humerus and femur and was significant at the $P < 0.005$ level.

Flow distribution expressed as the percent of measured flow to each bone is shown in Table 4. The upper panel contains average data from 5 animals who showed no evidence of decompression sickness. The distribution was strikingly consistent for all bones studied and showed little change when evidence of decompression sickness was noted (lower panel). These overall data indicate that clinical symptoms (chokes or limb bends) are not well correlated with changes in bone blood flow. Note particularly the difference in flow between the proximal and distal ends of the long bones shown in Table 4. The ratio between proximal and distal flows in the humerus averages 4.8 (6.0, no decompression sickness; 3.8, decompression sickness), and in the femur averages 1.3 (1.50, no decompression sickness; 1.12, decompression sickness). In the animals with clinical decompression sickness, a relative increase in distal flow was noted in both humerus and femur. These changes are small and nonsignificant. Table 5 summarizes the relationship between symptoms and presence of bone flow abnormalities.

Although no clear pattern of flow alteration was noted in relation to decompression sickness, when the whole experimental population was examined individual animals showed local abnormalities in flow. These data suggest that regional alterations in flow to the long bones occur after inadequate decompression, but the changes may not produce symptoms and may occur in areas other than the location of a symptomatic limb bend. In this study of 9 animals exposed to a 220-fsw hyperbaric air exposure for 20–25 min, 5 showed reduced blood flow in one or more bone regions compared to predive measurements. Of these 5, however, only 2 had clinical evidence of decompression sickness, and of the 5 animals with clinical decompression sickness which were exposed to the same dive profile, only 2 showed alterations of bone flow in one or more ends of the long bones.

DISCUSSION

This study indicates that regional reduction of bone flow can occur following an inadequate decompression, but clinical evidence of decompression sickness need not be present when flow is impaired. The data thus suggest that silent bone ischemia may occur in association with

TABLE 4

Blood flow distribution to articular surfaces of long bones related to clinical evidence of DCS

	Humerus		Femur	
	Predive	Postdive	Predive	Postdive
	Animals without clinical DCS			
Proximal	8.03 ± 0.28	8.82 ± 0.18	5.27 ± 0.40	5.69 ± 0.41
Distal	1.69 ± 0.29	1.10 ± 0.24	3.77 ± 0.23	3.54 ± 0.36
	Animals with clinical DCS			
Proximal	7.42 ± 0.32	7.53 ± 0.31	5.08 ± 0.55	4.63 ± 0.61
Distal	2.05 ± 0.34	1.76 ± 0.24	4.17 ± 0.65	4.51 ± 0.50

Values are percent of flow distribution and means ± SEM; $n = 5$.

TABLE 5

Relationship of bone flow changes to clinical DCS in animals studied after an air dive

	Normal flow	Abnormal flow
No DCS, $n = 4$	1	3
DCS, $n = 5$	3	2
Total, $n = 9$	4	5

Values are numbers of animals.

clinical decompression sickness, and more importantly, may be present when decompression sickness is not evident clinically. The epidemiologic data obtained to date on a diverse population of divers (McCallum 1974, Fagan et al. 1974, Elliott 1974, Ohiwa and Itoh 1975) indicate that this may indeed be the case. McCallum and Walder (1966), in their review of bone lesions in tunnel workers, point out that many cases of dysbaric osteonecrosis are found in tunnel workers who have no history of decompression sickness. The data of Ohta and Matsunaga (1974) indicate that divers will also develop bone necrosis. In their study, 30 of 95 divers (32%) without a history of decompression sickness showed bone lesions, while 122 of 206 (59%) with a history of decompression sickness had bone lesions. Their data showed a statistically significant relationship between a history of decompression sickness and bone lesions. Although a relationship between clinical decompression sickness and bone lesions is evident in their data a substantial number of divers with bone lesions were identified who had no such history. It is therefore important to consider means of detecting bone injury associated with decompression and decompression sickness other than clinical symptoms.

Spencer, Clarke, and Simmons (1971) have shown that bubbles occur in the venous system in the absence of clinical evidence of decompression sickness. These silent bubbles, however, have an uncertain relationship to lesions in bone, since at present the mechanism of production of bone lesions is unknown. Although these lesions might be caused by arterial emboli,

evidence for arterial gas emboli in mild cases of decompression sickness is lacking. Stegall, Huang, and Smith (*in press*) have studied bone microstructure in swine who developed dysbaric osteonecrosis. They suggest that altered platelet and coagulation function causes occlusion of bone circulation when bubbles are present in the microcirculation. The relationships among clotting changes, bubbles, and reduced blood flow, however, are still unclear, and the cause of the circulatory changes in bone in response to decompression sickness remains obscure.

That this disease is a significant occupational health problem has been established by several recent studies. In Japan, the incidence of bone injury in divers may be as high as 60% (Ohiwa and Itoh *in press*). This population also has a high incidence of clinical decompression sickness, and according to Ohta and Matsunaga (1974) would be expected to show a high incidence of osteonecrosis. In other studies from England (McCallum 1974; Elliott 1974; Fagan et al. 1974; Kindwall 1974), the incidence is in the 20–35% range among tunnel or caisson workers and deep oxygen–helium divers. In the American and British studies, a poor correlation was found between the presence of bone abnormalities and a history of clinical decompression sickness involving the extremities. These data again indicate that divers need not sustain clinical decompression sickness to develop long-term bone injury.

From this study, the mechanism which produces chronic bone changes appears to involve obstruction of the circulation to bone. A detailed analysis of bone circulation is provided in a monograph by Brookes (1971). He describes three different circulations for the long bones. The epiphysis is supplied by extra-osseous arteries which penetrate the bone in the epiphyseal region. At present there is little evidence that epiphyseal arteries anastomose with medullary arteries in either growing or mature bone, although some data to support the existence of such anastomoses exist. These vessels are usually considered end arteries which anastomose minimally within the bone, although externally they contain many anastomoses. Bubbles occluding these vessels would produce epiphyseal ischemia and might produce the clinical syndrome of dysbaric osteonecrosis. Most bone lesions related to hyperbaric exposure are thought to be combined diaphyso-metaphyseal lesions (Edeiken, Hodes, Libshitz, and Weller 1967). Thus, involvement of metasphyseal vessels must also occur. Brookes (1971) describes the metaphyseal blood supply as dual in nature. A number of vessels penetrate the metaphyseal region directly and lie transversely in the cancellous bone of this region. Others are arranged longitudinally and are branches of the intramedullary artery which enters the nutrient foramen (Edeiken et al. 1967). The nutrient artery may be absent, however, and metaphysis, diaphysis and marrow will then be totally supplied by metaphyseal arteries. The two arterial supplies of the metaphyseal region are known to anastomose, and a significant degree of vascular occlusion would therefore be necessary to cause metaphyseal ischemia. It is difficult, however, to find even minimal evidence of arterial gas embolism in limb bends, and the likelihood of metaphyseal ischemia from arterial embolization seems remote.

When considering mechanisms for bone ischemia from hyperbaric exposure, the venous system must be discussed. Occlusion of the venous drainage of bones by obstructing the nutrient vein is known to slow or stop arterial circulation to the region drained by the occluded vein. In the epiphyseo-metaphyseal junction in mature bone, veins are known to anastomose (Brookes 1971; Vaughan 1975) while arteries do not. Since intramedullary pressures do not change in unison with ambient pressure during compression and decompression (Harrelson and Hills 1970), it is possible that venous occlusion could occur. In addition, since significant amounts of fat are present in the medullary cavity, bubble formation may occur and produce venous or arterial occlusion by extrinsic pressure. Little evidence is available at present to invoke either an arterial or venous mechanism for dysbaric osteonecrosis. Stegall et al. (*in*

press) recently reported the finding of bubbles within arterial vessels which cause intimal proliferation and thrombosis with subsequent occlusion. These data indicate that intra-arterial bubbles are a causative factor in osteonecrosis. Their findings are of interest because of the absence of any evidence of arterial embolization to other tissues in divers with bone lesions who have either a history of no or of one or more limb bends. The fact remains that flow was decreased in the epiphyseo-metaphyseal region in half of the animals studied in this experiment, and either venous or arterial occlusion could produce these findings. Further exploration of the mechanism, however, should address both arterial and venous hemodynamics, since explanations for occlusion by either can be put forth.

It is evident from the study of Stegall et al. (1976) and the work of Weatherley, Dale, McGurk, and Walder (1976) that changes in bone metabolism occur immediately after reduction of bone blood flow. Furthermore, is is noted in this study that these changes can occur immediately after a dive with inadequate decompression. It is not clear, however, how the immediate changes are related to the long-term development of osteonecrosis. It is reasonable, therefore, to develop a method for measuring these early changes in the hope of identifying divers who are prone to bone lesions.

Interest in measuring bone blood flow has developed recently because of changes which occur in several metabolic diseases, with fractures, and with other causes of aseptic bone necrosis (Jaffe 1972b; Semb 1969). Bone flow can be measured in several ways. Post and Shoemaker (1962) measured bone flow by cannulating effluent veins in chronically instrumented dogs. Although their method produces surgical trauma to the lower extremity which might alter flow, their values are in the range measured by the microsphere technique. More recent studies have used tracer techniques to measure flow. When a diffusible tracer is used, kinetic curves of uptake or washout are used to calculate flow (Kelly, Yipinstoi, and Bassingthwaighte 1971, Cofield, Bassingthwaighte, and Kelly 1974). With this method, using radioactive ^{18}F or ^{85}SR, flows in the range of 6–8 ml/min/100 g have been calculated. These methods can be questioned because of the problem of distribution of tracer within the bone. The ^{18}F tracer is useful clinically, and allows repetitive bone scanning for both flow calculations and for measurement of regional distribution of flow within the bone. The study by Kane and Grior (1969) demonstrated flows in canine femur of 14–17 ml/min/100 g using the diffusible indicator ^{44}K. Their values are higher than other reported values derived from diffusible indicators because they considered the extraction ratio of ^{44}K to be less than one. Many earlier studies reporting lower flow values used soluble indicators and assumed the indicator to be totally extracted from the blood in one passage. It appears that bone flows in the 15–20 ml/min/100 g range are correct when all possible errors in method are accounted for. The technique described by Sapirstein (1958) using measurement of fractional distribution of indicators to find flow has been developed intensively for several organs and tissues using radioactive, labeled particles (microspheres) which are trapped in the microcirculation and which are distributed in proportion to the flow. To date, this technique has been used to study flow in all the major circulations (Kaihara et al. 1968; Ryan 1969), and has been used specifically for measurement of bone blood flow. With this method, flows in the range of 18–20 ml/min/100 g are found (31). The disparity between the kinetic tracer method and the microsphere method has not been fully explained to date, but the data of Kane and Grior (1969) may provide an answer to this disparity. One disadvantage to microsphere flow measurement is that in order to count tissue samples, the animals must be killed to obtain the flow data. The values for normal bone flow (18.5 ml/min/100 g) found in this study agree with other data using the microsphere method (Brookes 1975) and thus appear reasonable. Of interest also are the data on flow distribution derived from these studies. It is evident from all long bones studied

that the distal end of the bone received a lower flow than the proximal end. The most striking difference was in the humerus. While the femur showed similar differences, the ratio of proximal to distal flow was not as large. The reason that flow is distributed in this manner is unclear; it is of interest to note, however, that the distal ends of the long bones were most often found to have a significant flow change following hyperbaric exposure. The data presented in this study represent epiphyseo-metaphyseal flows from both ends of the long bones in mature animals and should be representative of the regions of bone involved in dysbaric osteonecrosis. Bone lesions in man are usually located in the proximal femoral and humeral heads (McCallum and Walder 1966). This distribution is different from the areas of involvement found in dogs in this study, but bone structure, pattern of loading, and limb position are sufficiently different to make direct extrapolation between man and dog impossible.

Data similar to that obtained in this study may be obtained in man via one of the standard bone tracer methods currently used in clinical medicine. Use of ^{18}F-scanning, for example, may provide useful data on the pattern of flow in the bones of divers who show clinical evidence of limb bends. This method of using a soluble indicator may be repeated without harm to the subject and does not produce occlusion in the microcirculation; additionally, any microcirculatory obstruction produced by tracer doses of microspheres has been found to be insignificant (Kaihara et al. 1968; Katz et al. 1971). Using clinically acceptable bone-scanning techniques, therefore, it may be possible after decompression sickness or extreme diving exposures to identify those individuals who will develop dysbaric osteonecrosis before the clinical syndrome becomes evident either by X-ray changes or by clinical symptoms of bone and joint abnormalities.

In conclusion, this study has shown that localized reduction in blood flow can occur in the epiphyseo-metaphyseal region of long bones in association with exposure to the hyperbaric environment with inadequate decompression. The flow changes are poorly correlated with clinical evidence of decompression sickness, and in the dog are found mainly in the distal end of the long bones where flow is normally lower than in the proximal end. No mechanism can be identified from these data, but equal weight could be given to arterial or venous occlusion as the etiologic factor. The fact that flow abnormalities can be identified after a single hyperbaric exposure suggests that a bone scan using currently acceptable clinical techniques after certain diving exposures may be useful in identifying divers who are at risk for dysbaric osteonecrosis before overt evidence of the disease appears.

This study was supported in part by USPHS NHLI Grant HE 08886 and funds from the Southeastern Pennsylvania chapter of the American Heart Association.—*Received for publication December, 1976; revision received March, 1977.*

Bove, A. A., F. C. Famiano, L. L. Levin, R. A. Carey, A. L. Pierce, and P. R. Lynch. 1977. Altérations du debit régional sanguine des os longs qui accompagnent une décompression insuffisante chez le chien. Undersea Biomed. Res. 4(2): 169–182.—Les rapports entre des anomalies de la circulation sanguine des os et les symptomes de la maladie de décompression ont été étudiés chez 9 chiens avant et après une exposition à l'air hyperbare (220 ft, 90 psig, 20–25 min) suivie d'une décompression insuffisante. La distribution du débit sanguin dans le humérus et le fémur a été mesuré à l'aide de microsphères marqués (diamètre: 15 μm) injectés dans l'aorte proximale. Pour éviter les effets de l'anesthésie et des facteurs émotionnels éventuels, on a étudié 5 animaux en éveil, et 4 anesthésiés (pentobarbital, 25 mg/kg). Une réduction du débit sanguin dans les os longs a été constatée chez 3 des 4 chiens anesthésiés, tandis qu'une maladie de décompression ne s'est manifestée que chez un seul des chiens à débit anormal. Des 5 autres, un debit anormal a été observé chez 2 chiens, dont un a presenté une maladie de décompression clinique. Des débits

anormaux fémoraux et huméraux ont été observés chez 5 des animaux, dont 2 ont présenté des symptomes de la maladie de décompression. Quoiqu'une maladie de décompression ait apparu chez 5 chiens, 2 seulement avaient présenté un débit régional anormal. Avant la plongée, le débit moyen absolu était de 18 ± 2,3 ml/min/100 g, et la différence de distribution circulatoire entre les parties distale et proximale était significative ($P < 0{,}005$), la partie distale recevant le débit moindre. Les régions de débit réduit étaient celles de débits anormaux. Ces résultats suggèrent qu'une décompression insuffisante puisse produire des anormalités du débit régional sanguin aux entrémités des os longs, des anormalités qui peuvent être dépistées peu après la plongée, et dont les rapports avec la maladie de décompression clinique chez le chien ne semblent pas étroits.

ostéonecrose dysbarique
ostéonecrose aseptique
maladie de décompression
médecine de la plongée

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