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Professor Brian Hills, the guest speaker for the 1983 Scientific meeting, has kindly provided this paper, the manuscript of a chapter in the now abandoned Volume II of his book "Decompression Sickness", which covers most of the topics he discussed in Fiji. "Decompression Sickness Volume I" was published by John Wiley and Sons in 1977 and is an excellent discussion of decompression sickness, the theories of its causation and its treatment. Professor Hills now works at the Department of Anesthesiology, The University of Texas Health Science Center at Houston.

Professor Hills also presented a paper on Surfactant, which is his current major interest, in Fiji. It is hoped to publish this in a future issue.

DECOMPRESSION PHYSIOLOGY

Brian Hills

Physiological changes during decompression can be divided into those associated with bubble formation and those directly attributable to the changes in alveolar partial pressures of the various gases which decompression must entail. Reversal of nitrogen narcosis for air diving or oxygen toxicity are described in standard texts of those diseases, while the manner in which these can influence the formulation of decompression is outlined in Decompression Sickness Volume I[1] (Chapter 8). This paper is directed towards the physical forms and locations for gas separated from solution by decompression and the physiological modes by which each form can then insult the body.

THE GENERAL ISSUES

Perhaps the most difficult task in pursuing the pathophysiology of decompression sickness in the literature is that of identifying the established facts and separating them from the numerous controversies and assumptions. Before entering into specific issues such as whether diffusion or blood perfusion limits the rate of uptake of inert gases, there are more general questions to be addressed. These include:

1. Is there just one mode of insult or many?
2. If more than one, do the mechanisms follow sequentially or proceed independently?
3. Are bubbles really the underlying cause or just a red herring?
4. What are the mechanisms for the various categories?
5. If current decompression tables and other means of preventing decompression sickness do not achieve their avowed intention of avoiding bubble formation, then what do they do? Do they achieve their goal, but only in the tissue(s) which can provoke symptoms?
6. What is really occurring at the tissue level during treatment?

One insult mode or many?

The wide diversity of symptoms resulting from inadequate decompression might be construed as indicating that there is a single mode of insult which occurs at such a basic level of physiological function that it can become manifest clinically in a most diverse manner. This is, perhaps, the sentiment underlying the statements often overheard, more often in Aviation Medicine, in that a subject starting with a limb "bend" can then "develop" into a neurologic case. It is indeed very common for neurologic symptoms to be preceded by limb pain but this does not necessarily mean that each reflects a different stage in the same underlying mechanism.

Considering the wide diversity of the list, the symptoms can be slotted particularly neatly into six categories consistent with a different physiological mediation of each insult (Fig. l). The best example is the Menière group of symptoms in Category IV whose occurrence as an end-organ injury immediately implies dysfunction of the vestibular apparatus. The classification adopted in Fig. 1 is an extension of the Medical Research Council (MRC) system of dividing cases into essentially local manifestations (Type I) and those with obvious neurologic involvement (Type II) in which, as Griffiths[2] aptly states, the subject really "feels and appears to be ill". With such relatively well defined categories, it would be short-sighted just to look for one mechanism for decompression sickness. Rather, there could be as many as six mechanisms or, at least, for there to be that many combinations of insults and target organs.

Sequential or simultaneous?

The concept that each mechanism can be triggered and proceed independently of the others is consistent with some ability to select the presenting symptom by changing conditions. Examples include:

1. A short deep "bounce" dive upon air is more likely to produce a CNS "hit" than a longer shallower dive for the same overall incidence of decompression sickness.
2. It is well known in commercial diving that a switch from helium to nitrogen as the inert gas breathed, such as often occurs in transferring a diver from a diving bell to a deck decompression chamber, can often precipitate vestibular (Category IV) symptoms (See Decompression Sickness Volume I)[1]
3. Spinal symptoms (III) occur more often than cerebral (II) in divers, about 3:1 as Hallenbeck, et al.[3] point out, and yet the reverse is true for aerial decompression sickness.
4. The percentage of spinal symptoms is much lower in heliox diving than air diving.[4]
5. In experimental animals undergoing the same decompression from the same exposure, a limb "bend" or neurologic "hit" can be selected as the presenting symptoms by the extent of the upward excursion interposed between the exposure and the same decompression,[5] the model adopted by Hallenbeck et al.[3] to ensure spinal injury in their dogs.

Many more examples can be cited of means by which the symptom category can be influenced by the conditions

CATEGORIES OF DECOMPRESSION SICKNESS

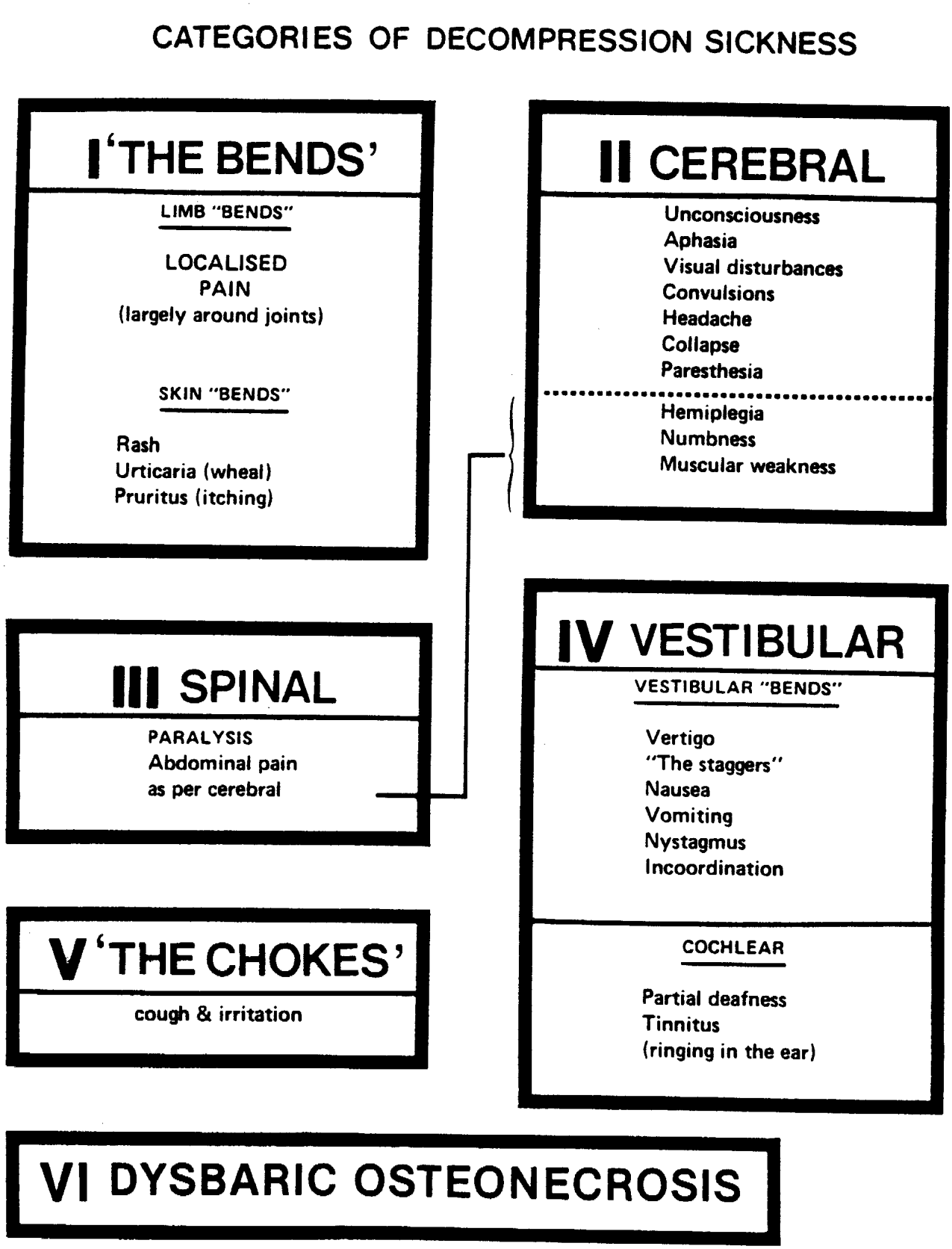

FIGURE 1

The numerous symptoms of decompression sickness arranged in categories of similar physiological mediation of the underlying insult and, hence, indicating as many mechanisms as categories.

prevailing during decompression. Thus it would appear that several insult processes are triggered by decompression and probably develop simultaneously and independently. The presenting category, if any, would then be determined by the relative kinetics of the various mechanisms and how prevailing conditions might tend to emphasize one over the others.

While emphasizing the point that different insult mechanisms *can* proceed simultaneously and independently, not all may do so. A particular example would occur where the production of large numbers of venous bubbles by decompression would produce the "chokes" when they were filtered by the lung. There is little doubt that these Category V symptoms are caused by massive pulmonary gas embolism.[6] In such quantity, the gas is more likely to overload the filtration capability of the lung[7,8] permitting arterial bubbles to embolise vital organs and produce the cerebral (Category II) symptoms or other neurologic forms of decompression sickness which commonly follow onset of "the chokes", a category which, understandably, seldom occurs alone.[9]

The above examples belabour the simple point that we should not be looking for just one mechanism by which to explain decompression sickness or to design measures for its prevention.

Are bubbles a red herring?

If there are different mechanisms for eliciting different symptoms, it could be further asked whether all of these need to be initiated by bubble formation, or separation of gas from solution in whatever other shape it may prefer to assume.

There has been the occasional implication that bubble formation may not be a necessary step in the aetiology of decompression sickness. One of the first was based upon the agglutination of red cells demonstrated in decompressed animals by End,[10] also noted by Wells et al.[11] who have emphasized increased blood viscosity as a possible source of tissue ischaemia leading to pain. However, Walder[12] makes the very pertinent point that blood "sludging" occurs in many other clinical situations without provoking bends-like symptoms.

Another no-bubble hypothesis was proposed for dysbaric osteonecrosis only[13] on the basis that bones are good osmometers for dissolved nitrogen; while the mineralisation process is particularly sensitive to the fluid shifts which might therefore be induced by gases. This approach had the primary advantage that it could explain the particularly long induction time of the first radiographic evidence of a bone lesion.[14] However, if gas-induced osmosis were the true mechanism, then one would expect aseptic osteonecrosis to be induced without decompression by the more potent osmotic gases such as nitrous oxide, but there is no record of any correlation between bone lesions and gaseous anaesthesia.

The primary event

The major evidence in favour of gas separation as the *primary event* in decompression sickness is that no other process has so far been conceived which could be so dependent upon the particular combination of two dominant features for its incidence and intensity, the syndrome being more likely to occur with

1. a greater decompression, and

2. a greater *inert* gas content of tissue prior to that decompression.

Other primary events could be conceived which are dependant upon one or other of the above factors, eg. gas-induced osmosis upon inert gas concentration, but none of these are so uniquely dependently upon the *combination* as the separation of the gas phase from solution, the vital first step to bubble formation.

In finding evidence to support the two principal features listed above, it is tempting to study very deep dives or the latest record for time or depth. From a decompression standpoint, however, this can be misleading since there are so many factors influencing the outcome of a long decompression that the basic trends can easily be obscured. For elucidating basic relationships, it is easier to consider a simple 'bounce" dive where the subject is returned directly to the surface, ie. with no-stop decompression as depicted in Fig. 2.

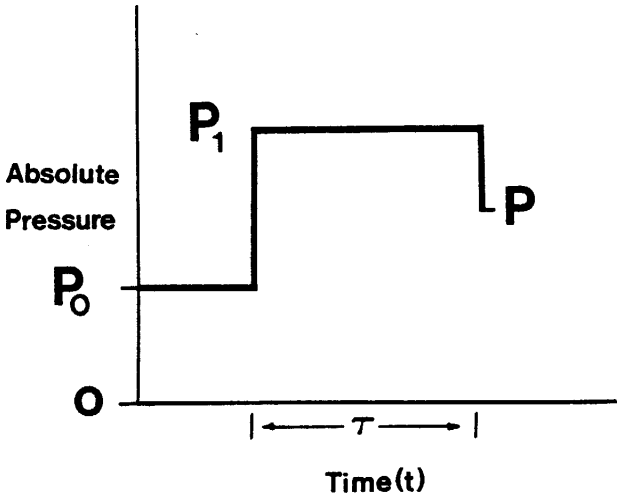

FIGURE 2

A simple exposure followed by no-stop decompression

Decompression per se

The evidence for decompression *per se*, ie. that greater decompression potentiates decompression sickness, is overwhelming with data from diving, tunnel work and aviation. This also applies to each category of decompression sickness with the possible exception of Category VI, dysbaric osteonecrosis. This possible exclusion is based upon the argument that for every decompression, there is also a compression and we should

therefore be sure to eliminate compression per se as an aetiological factor. This is easily done for categories I to V, since each can be induced at altitude, ie. after decompression only. However, bone lesions are not observed in aviators,[15] not even in those seriously incapacitated by other categories of decompression sickness. Thus the absence of Category VI from altitude DCS could be related to the fact that decompression precedes compression in this mode, but is more likely a consequence of the lower absolute pressures involved.

Inert gas content

Any factor which increases the *inert* gas content of the body prior to decompression increases the incidence of decompression sickness. Referring to the simple exposure depicted in Fig. 2, these include:

1. Deeper exposure (P_1 in Fig. 2).

2. Longer time at depth.

3. *Substitution* of a more soluble for a less soluble inert gas at a given depth, eg. He fi H_2.[16]

4. Substitution of inert gas for oxygen at a fixed depth.[17]

5. Increasing transport of inert gas to the tissue by selectively raising temperature,[18] selectively exercising that limb at pressure[19] and effecting other less obvious physiological changes designed to increase perfusion of the critical tissue by blood.

Recompression

Further to the above evidence, it can also be argued that gas separation must be the primary event in mechanisms where the phase gas also constitutes the critical insult, whether it needs to reach its critical state for clinical awareness by growing in volume, coalescing or undergoing any other transformation. Since the vast majority of symptoms are resolved or ameliorated with recompression, it is very difficult to argue that the insulting entity is not compressible and, hence, not in the gas phase. Thus gas separation is again overwhelmingly indicated as the primary event. Moreover this applies to all categories of symptoms since all are relieved by recompression, albeit with different success rates. The only possible exception is again dysbaric osteonecrosis in which there is no way of knowing whether recompression ever treated a potential bone lesion.

To summarise the above discussion, there is very little doubt that bubble formation is the primary event in all categories of decompression sickness with a remote possibility that dysbaric osteonecrosis may be an exception.

Primary event to critical insult

The reader might well ask why it is necessary to differentiate between the primary event as the initiating process and the mode of insult precipitating each category of symptom. In the past it has been argued by the mathematically inclined designers of diving tables that if you can avoid gas formation in the first place, ie. the primary event, then no harm can come to the diver anyway. However, the scientific evidence reviewed in Decompression Sickness, Volume I,[1] indicates that bubbles are formed when following many of the safest schedules and that what determines the occurrence of symptoms is not their presence but how far each mode of insult has progressed along its course towards its critical threshold for clinical awareness or injury. Since the extent of these progressions can be influenced by the overall decompression procedure, it is therefore most desirable to know the individual mechanism for each symptom category; while it is these progressions, rather than the primary event, which the clinician seeks to reverse by the treatment he prescribes.

To return to specifics, we therefore need to address the question that, if gas phase formation is the *primary event*, what are the modes by which it can then insult the body?

MODES OF INSULT

Gas can separate from solution as bubbles in blood, as gas in extracellular sites of various tissues or in the natural potential cavities of the body such as the peritoneal cavity or the joint capsule.

Extravascular gas can form within cells, in the interstitium or within the lymphatic system; but it remains in essentially the site where it was formed. Intravascular bubbles, by comparison, have the capability of mobility and therefore have many opportunities for occluding vessels and producing either general hypoxia or local ischaemia, depending upon their location. Potential occlusion sites include the bifurcating vascular beds of the systemic arterial and pulmonary arterial systems. Venous occlusion has also been postulated.

There are three basic questions to apply to any site of separated gas in determining whether it could produce clinical symptoms of decompression sickness. These are:

1. Could the bubbles occlude a vessel to cause tissue ischaemia or oedema and do other diseases producing other emboli, or otherwise obstructing the same vessels, produce the same symptoms?

2. Is there any opportunity for degradation of fluids in contact with the gas and are the products, eg. aggregates or humoral factors, likely to persist after the bubble has dissolved?

3. Is the bubble in a location where it can press upon a nerve ending to provoke pain, upon an axon to disrupt impulse transmission or upon a vessel to occlude flow and, if so, does the compliance and overall morphology of the tissue prevent the gas from expanding or otherwise dissipating the local pressure which it might otherwise generate to induce these dysfunctions?

These questions can be applied to each of the bubble locations outlined earlier to produce a list of at least eight cases warranting closer scrutiny as possible mechanisms for the six categories of symptoms. There are:

1. Bubbles formed in the natural body cavities, eg. the joint capsule, causing pain.

2. The products of blood-bubble interaction occluding vessels or otherwise disrupting function.

3. Occlusion of lymph vessels.

4. A "venous" bubble occluding the pulmonary arterial system.

5. Occlusion of the venous system for a particular tissue.

6. A bubble in the arterial system directly occluding flow and so causing tissue ischaemia.

7. Bubbles pressing against a nerve ending to produce pain.

8. The same autochthonous bubble pressing against an axon to interfere with transmission.

9. An extravascular bubble pressing against a vessel to compromise either perfusion of the tissue or blood supply to a nerve, again compromising transmission.

Pathology

Before pursuing each of the above as a possible mechanism for each of the six categories of symptoms (Fig. 1), the next logical step might seem to be one of turning to the pathological evidence to try to reduce the number of likely combinations. Three of the most comprehensive pathological studies are those of Boycott et al.[20,21] Haymaker[22] and Rozsahegyi.[23] These and others are discussed in some detail in Decompression Sickness, Volume I[1] but, basically, pathological evidence from autopsy reports or studies of sacrificed animals can be found to support all nine of the above mechanisms and possibly more. The problem lies in knowing what is cause and what is effect. This is aptly described by one of the most eminent decompression pathologists[22] who wrote "from this vast mass of material, nothing really pertinent to establishing a model or mechanism can be extracted." This may be an understatement since, to take one example, the *absence* of bubbles in skeletal muscle, liver and heart[20] is good reason to look at other tissues for the source of the problem. However, it does mean that we must rely primarily upon physiological reasoning to try to reduce the fifty-four possible combinations of mechanism and symptom category. Let us therefore consider each of the mechanisms in the above list individually.

Gas in the body cavities

The natural body cavities are only so termed because it is easy to separate the surrounding tissues in forming them. Thus they do not resist the formation of this extravascular gas and are easily pushed aside without creating any significant pressure with which the enclosed gas can disrupt function. In fact, in a pneumothorax, the gas in the pleural cavity is at a negative pressure relative to atmospheric. The above argument also applies to the joint capsule where gas can easily escape from between the articular surfaces without deforming a nerve ending in the adjacent tissue as a rigid solid, such as sodium ureate crystals, can do in the case of gout. In fact, large volumes of gas can be injected into the synovial cavity without producing symptoms; while the same applies to gas formed by decompression and confirmed radiographically,[9] a condition more appropriately termed "aeroarthrosis".

Blood-bubble interaction

Potential infarcting agents which are incompressible and known to be associated with decompression include fat emboli[24] and microthrombi.[25] The whole subject of blood-bubble interaction became one of great interest a decade or so ago when some thought it held many of the answers to decompression problems. This may still be true for chronic cases but there is one inescapable fact which limits its relevance. This is the relief obtained by recompression which is effective in at least 99% of limb bends and 90% of neurologic cases. It is very difficult to envisage any mechanism whereby the application of hydrostatic pressure can restore blood flow to a vessel infarcted with an incompressible embolus.

When extensive coagulation or other degradation of blood is seen in pathological studies, eg. in vertebral venous lakes[3,22] it must be asked whether the observations are cause or effect.

Although the products of blood-bubble interaction may not be the primary agents in the aetiology of decompression sickness, they may have important secondary roles by way of the humoral factors released during those interactions. One example is the release of serotonin[26] which can sensitise nerve endings to other pain-provoking stimuli such as adjacent bubbles.

Although the products of blood-bubble interaction are likely to play no more than secondary roles in most categories of decompression sickness, the compressibility argument does not detract from their providing the primary mechanism in dysbaric osteonecrosis, as proposed by Jones et al.[27] This category (VI) is chronic only, since there is no way of telling whether recompression ever prevented a potential bone lesion.

Lymphatic bubbles

Bubbles have been found in the lymphatics of most organs in decompressed animals.[1,28,29] It is easy to envisage their occluding the lymph vessels to produce the oedema occasionally seen in decompression sickness and the "orange peel" appearance of the skin distal to the occlusion.

Venous bubbles

Venous bubbles are often produced in large number during decompression and usually remain asymptomatic. In decompressed animals they are seen mostly in the veins draining the fatty tissues in which nitrogen is six-fold more soluble than in water. The question concerning whether the bubbles form *de novo* within the vessels of those tissues or enter them pre-formed by rupture of the endothelial wall is an issue of largely academic interest, but the fact that, in either case, they are primarily derived from the large amount of nitrogen dissolving in adipose tissue must be borne in mind when interpreting the signals from precordial Doppler monitors.

In sacrificed animals it is tempting to speculate that the bubbles observed in the veins, or the products of blood-bubble degradation often seen adjacent to them, are responsible for any stasis observed. However, it must be asked whether these are effect rather than cause, since bubbles would remain in veins without flow whatever the cause of stasis, ie. they will reach systemic veins anyway but cannot be washed away without flow. Moreover, it is difficult to conceive bubbles occluding a flow system continuously converging into vessels of ever-increasing diameter. One exception to this confluence of blood flow is the vertebral venous lakes often implicated as the cause of spinal symptoms (Category III).[3] However it is difficult to envisage all of the many outlets to these lakes being occluded simultaneously, especially when they are not constricted by the valves common to veins elsewhere in the body.

Venous bubble detection in humans is particularly easy utilising ultrasonic probes which exploit the Doppler principle,[30,31] since it is non-invasive and the simple audio output can be interpreted with little training. When used in the precordial position, ie. looking down the pulmonary artery, there is the particular advantage that one is then scanning total venous return and, moreover, is doing so at the highest velocity of venous blood at which bubbles are more easily detected.[32] There have been many attempts to correlate Doppler signals with overt symptoms of decompression sickness with varying degrees of success. It is probably fair to summarise that data by concluding that the correlation is good for simple no-stop decompressions but very poor following a long, complex stage-decompression. This could reflect the fact that venous bubbles are derived largely from fatty depôts whereas an aqueous tissue is more likely to be responsible for the common forms of decompression sickness, ie. limb bends, with one becoming a poorer analogue for the other as the dive proceeds.

Pulmonary arterial bubbles

In tunnel workers, Nashimoto and Gotoh[33] have found a good correlation between "the chokes" and large numbers of venous bubbles as indicated by pre-cordial Doppler monitoring. This is consistent with the widely held view that these Category V symptoms are the result of extensive pulmonary air embolism.[6] This aetiology has been challenged by Ferris and Engel[34] on the basis that air accidentally introduced into the venous system does not elicit the same response, but such gas is more likely to resemble a bolus than the many microbubbles produced by decompression. It can then be argued that many smaller emboli could stimulate J-receptors in the respiratory exchange region of the lung more than a bolus by producing more local oedema or releasing a humoral factor as an intermediate step. Microbubbles can penetrate further into the pulmonary vascular bed by virtue of their size and, presumably, closer to the J-receptors. A good description of these receptors and the reflexes which can be invoked to elicit a laryngospasm are given by Paintal.[35]

Systemic arterial bubbles

There have been many pathological studies of arterial air embolism and a few in which the vessels have been observed following a bolus injection,[36] but the real question concerns bubbles of the sizes produced during decompression.

These have been measured in the venous blood of live decompressed dogs as ranging from 29-700 μm in diameter[37] with a median size in the region of 60 μm. When individual bubbles have been observed[38] in the middle cerebral artery of a guinea pig through a cranial window, they tend to reduce flow. They can be seen to proceed through bifurcations into arteries of smaller diameter until they reach those of comparable diameter. There is then a fairly sudden dilation of the arterial system distal to the bubble, diameters sometimes increasing two-fold. The bubble then proceeds until it is again of comparable diameter to the vessel when it now deforms and proceeds much more slowly. It may pass one more bifurcation, never splitting up, and then lodges at the next. The leading edge is rounded while the trailing edge is flatter and pulsatile. The bubble may remain for several minutes and then proceed to the next bifurcation where it will stop. When gas forms such a column following a bolus injection, it proceeds similarly, but gives the impression of not penetrating the vascular bed as deeply. This may be due to the absence of the trailing edge as a forward-propelling surface force. In other words, the trailing edge is now removed to such a large vessel ($r \neq\neq$) that the forward surface thrust (DP) as estimated by the Laplace equation ($DP = 2g/r$) is now very small. g is the surface tension.

When more microbubbles enter the cerebral arteries before the first has lodged, the first gives the appearance of slowing more than usual and letting the others catch up. When adjacent to each other, they then coalesce to form "slugs" of gas with a length about 1.5 times the diameter of the vessel which they slightly distend. These slugs then close upon each other until a thin liquid film separates them. If the bubbles are oxygen or the animal is ventilated upon oxygen during this phase of embolisation, the process can be reversed and fluid starts to enlarge the separating films as the slugs decrease in size until they finally move on. Otherwise, if left, the slugs will suddenly 'pop' together as though a shock wave had passed down the vessel. The time for this to occur is very variable but is of the order of 20 minutes from the initial slug formation. About this time, the venous blood can be seen to be noticeably more blue. Columns of gas do not reverse themselves and it requires a drastic procedure such as recompression to do so.

In terms of death or survival, the brain is slightly more tolerant to gas as microbubbles than as a bolus,[38] and can certainly tolerate more gas when administered at slower rates.[7] It still does not give us much of a handle on the awesome question of the rate at which the brain can disperse microbubbles asymptomatically or whether they have any chronic effects, ie. are there really "bubble heads" as some offshore communities somewhat callously refer to the divers.

The only hard figures readily available refer to bolus injection of gas into the arterial system of dogs. 0.5 ml/Kg of air injected into a dog's pulmonary veins cause death[39,40] or 0.25ml/Kg in the common carotid artery.[41] On the other

hand, 0.025 ml injected into the coronary circulation can cause myocardial ischaemia while 0.05 ml/Kg causes death.[42]

There is little doubt from autopsy findings on patients with air embolism or baboons with experimental air embolism[43,44,45] that the insult is ischaemic. Where there has been known arterial embolisation, eg. from pulmonary barotrauma following submarine escape,[46] the symptoms are the same as those listed for cerebral decompression sickness, see Fig. 1. Hence there is little doubt that arterial bubbles are responsible for Category II decompression sickness. Whether they are also responsible for other categories is quite another matter which is discussed later.

Role of the lung

The low tolerance of the body to arterial gas indicated by the above figures is in sharp contrast to the large tolerance of the venous system to air where dogs have survived after infusion of a litre.[47] This implies that the lung is a very efficient filter for the gas phase in all forms and direct experimental work upon dogs using both boluses and calibrated microbubbles has confirmed this.[8] If the lungs were not such a superb bubble trap, diving would probably be impossible.

This raises several unique situations, the first concerning anyone with a patent foramen ovals where accidental venous embolisation has been known to cause the patient to become comatose immediately. A somewhat similar situation would occur in the woman diving during pregnancy when the foetal brain would not be protected from venous bubbles in the manner afforded by the filtering capability of the lungs in adults.

For the purpose of designing preventive methods for decompression sickness, it therefore becomes very important to determine what factors are likely to compromise this superb capability of the lung to filter or otherwise trap bubbles in venous blood. The first reaction is to look for any agents which might cause vasodilation, remembering that many drugs have the opposite effect upon the pulmonary vasculature to that observed in peripheral tissues. Thus it is most interesting to find that, when administered in clinical doses, aminophylline allows gas to escape into the arterial system.[8] This implies a possible warning to the use of such drugs as a bronchodilator for a case of "chokes", known pulmonary gas embolism. The situation is complicated, however, by the observation that aminophylline does not compromise the filtering capability of the lung if administered post-embolisation, ie. it does not seem to release those bubbles already trapped but just those continuing to enter the pulmonary artery.

Another factor which allows gas to escape entrapment is overloading the lungs with air[7,8] when there is a delay of 10-30 minutes in the appearance of systemic arterial bubbles, a delay which does not seem dependent upon the size of the infused bubbles. In fact, contrary to expectations, size of the venous bubble does not seem to be the primary factor determining whether or not it will be trapped. From this observation, the time delay and the rough indication from Doppler pulse heights, there is the impression that the size of arterial bubbles escaping entrapment bear little relationship, if any, to the size of bubble entering the lung. It is almost as though gas coalesced in the pulmonary vasculature, as observed and described above for the cerebral circulation, and was then later re-injected into the arterial system if the insult to the lung were enough. The overload mechanism can be attributed to occlusion of a vessel depriving the wall of blood-borne nutrients or the ability to lose released humoral factors which would then cause vascular smooth muscle to relax, either directly or indirectly. Indeed air embolism is used in many animal preparations as a means of inducing permeability oedema of the lung. There could also be a sympathetic or, possibly, parasympathetic response to embolisation.

Another insult which can compromise the capability of the lung to filter bubbles is pulmonary oxygen toxicity.[48] The effect is quite variable and the critical insult has not been characterised in terms of a number of UPTDs[49] or a threshold value for the COTi.[50] However, it poses an aggravating complication to the treatment of decompression sickness in divers who have already received a large exposure to oxygen before symptoms appeared. It is no good to treat a limb bend with even more oxygen if any resulting toxicity is simply going to allow venous bubbles to reach the arterial system with the risk of Category II symptoms.

There may be many other factors which can effect pulmonary vascular tone and, hence, the capability of the lungs to trap bubbles, but this field of investigation is just starting to attract attention. There may also be factors tending to release bubbles already trapped and one is recompression.

Bubbles in peripheral arteries

In an earlier section we discussed how bubbles in blood flowing to the brain afforded a very good explanation for cerebral (Category II) symptoms. The next question is whether bubbles in the arteries leading to other organs could explain other categories, eg. limb "bends" (Category I) or whether such symptoms are central anyway.

To address the last question first, there is good reason to believe that limb bends are derived from an essentially *local* insult since:

1. The pain can be ameliorated by local anaesthetics, eg. novalgin.[51]

2. The application of local pressure can usually reverse a mild limb bend, eg. by applying a sphygmomanometer cuff to the site of pain[52,53] or immersing the joint in mercury.

These key points and others leave little doubt that Category 1 symptoms stem from an essentially *local* insult but this leads to the next question, whether the symptoms of limb bends could be caused by arterial bubbles. Since the era of Paul Bert,[55] it has been generally assumed that bubbles occlude arteries to cause ischaemic pain. This mechanism, however, has encountered increasing criticism for the following reasons:

1. The argument that if recompression therapy is to relieve limb bends, it must dislodge the occluding bubbles and probably flush them out into the venous system as

observed in other organs.[36,38] However, if the subject is returned to the symptom-provoking pressure within a few minutes, the "bends" return to exactly the same sites with virtually the same intensity.[56] It is far too much of a coincidence to suppose that another bubble, or set of them, would lodge in precisely the same site a second time. It is much better explained by extra-vascular gas which cannot move but only change volume in the same site.

2. The pain of ischaemia is unlike bends pain. Other diseases which produce arterial emboli do not produce bends-like pain.[12]

3. Using tail-biting in kangaroo rats as a model to simulate limb bends in men, hypoxia following decompression was found to protect against "bends"[57] rather than potentiate them, which would be expected if the offending tissue were already deficient in oxygen.

4. In goats exposed to a marginally safe partial pressure of nitrogen, an appreciable increase in the oxygen partial pressure of the exposure caused extensive symptoms upon decompression.[58] It is hard to explain how an increase in PO_2 could exacerbate the pain if oxygen deficiency were causing it. However, while there were some Category I symptoms, most were spinal (Category III).

5. The fact that venous bubbles are a much more common occurrence than arterial in all but exceptionally fast decompressions[1] and that such bubbles would normally be trapped by the lungs, as described above, before they could become arterial emboli.

Further evidence for the incompatibility of the clinical symptom with a mechanism based upon bubbles in peripheral arteries have been discussed by Ferris and Engel.[34]

Arterial bubbles in other organs

It is easy to conceive bubbles occluding any arterial system provided they can reach those arteries in the first place. The more likely systems would be those with an end-artery type of circulation as occurs in the inner ear and the eye. This would appear to offer a very convenient explanation for Category IV symptoms until one asks the now-familiar question of why such symptoms do not occur much more frequently in cases of known embolic disease such as subacute bacterial endocarditis.

By far the most serious aspect of this question concerns the spinal cord, since Category III symptoms are currently the major cause of disablement in divers. Spinal cord decompression sickness, however, is restricted almost entirely to air diving, particularly in the range of 100-150 feet.[4] The popular explanation has been arterial bubbles as proposed for decompression sickness in general by Paul Bert[55] with specific reference to the spinal cord by Haldane and co-workers despite their clear demonstration of many extravascular bubbles in the white matter.[20]

Despite its continued popularity, arterial embolism would now seem an unlikely cause of spinal DCS for the following reasons:

1. Upon recompression most cases are relieved, indicating that any arterial bubble must have been dislodged but, upon return to the bends pressure, the symptoms return exactly as they were before. Thus the same argument invoked for limb bends can be used in that it would be a fantastic coincidence for another set of bubbles to lodge in precisely the same sites and cause the same symptoms with the same distribution of dysfunction as plotted on a neurologic atlas of the body. This is the same argument used earlier to discount other forms of embolism, eg. that of vertebral venous lakes.

2. It has been argued that the brain constitutes 98% of the spinal cord[59] and receives 78-85 times more blood flow than the spinal cord[60] and should therefore receive proportionately more arterial emboli. However the ratio is about 3:1 spinal:cerebral in divers, but not in aviators. Such reasoning has led Hallenbeck et al.[3] to discount arterial embolism, pointing out that, in other disorders producing systemic embolisation, the brain is the target organ with only 0.4% of cases involving the spinal cord.[61]

3. The almost total absence of spinal involvement in heliox diving[4] makes it very difficult to explain why systemic nitrogen bubbles would occlude the cord and yet helium bubbles would not do so for dives when the incidence of other forms of decompression sickness was comparable.

The above points would seem to make arterial embolisation just as unlikely as other embolic mechanisms for Category III symptoms. Care should also be exercised in reading standard neurological texts on embolic diseases not to invoke circular reasoning. The spinal cord is sometimes listed as a target organ for circulating arterial emboli but, often, this arises simply because the author has read a diving paper or two expressing the conventional (arterial) theory of spinal cord decompression sickness.

THE AUTOCHTHONOUS BUBBLE AND ENCASED GAS

The concept of the autochthonous bubble, forming de novo in the tissues, was probably first invoked by Haldane and co-workers to describe a bubble pressing onto a nerve or nerve ending, although the same authors still attributed decompression sickness to arterial bubbles. Theoretically, the extravascular gas bubble has the great advantage that it can explain the finding that symptoms, especially Categories I and III, can be relieved by recompression yet return in the same site upon return of the patient to the original symptom-provoking pressure. Thus it is most important to pursue all the ramifications of the remaining three possible insults, viz. those involving extravascular gas pressing upon a nerve ending, upon a nerve axon or upon a vessel.

Extravascular bubble pressing upon a nerve ending

The question of whether an extravascular bubble is going to elicit pain depends upon two factors: whether there are nerve endings which can give rise to "bends" pain and whether the gas in the bubble can generate the pressure needed to bend or otherwise distort that nerve ending to its pain threshold without being dissipated.

Most of these questions are answered by a very simple yet most fundamental experiment conducted by Inman and Saunders.[62] They inserted fine hypodermic needles into various tissues of Air Force cadets and found that, when they injected Ringers solution into many of the tight connective tissues, they could induce a pain virtually indistinguishable from "bends". This was particularly apparent for tendon. They found that the effect was reversible and that the pain threshold was determined by the pressure with which the Ringers solution was injected, the critical differential remaining the same for the same subject but varying between individuals within the range of 11-26 mmHg.

If a bubble can exert the same local pressure, then this offers a particularly attractive hypothesis for limb bends, since it can explain the titration of pain with decompression and its almost instantaneous reversibility with recompression. Many connective tissues are well innervated, particularly tendon in which other insults to the nerve endings produce a pain the description of which by Stilwell[63] virtually paraphrases the description of limb 'bends" given by diving physicians.

The next question concerns whether the gas separating from solution in a tendon would dissipate before it could reach a pressure of 11-26 mmHg in excess of tissue pressure. Obviously a bubble formed in a very compliant tissue would simply push the tissue aside rather than allow its formation to generate any excess pressure. It would therefore seem particularly meaningful that Inman and Saunders found their pain-pressure threshold in the "*tight"* connective tissues. Moreover, simple calculations based upon the compliance of these tissues and the volume of gas which could form in a diver with a minimum bends depth of 33 fsw on air provides quantitative confirmation of the 15 mmHg pain threshold.[64]

There are other factors in favour of extravascular bubbles in tendon as the cause of Category I symptoms, these including the effects of exercise and the location of bends pain as arising *around* the joints but not within the joint capsule itself. Regarding exercise, Behnke[19] quotes 25 minutes as the safe working time at 100 feet to be followed by no-stop decompression by comparison with 35 minutes for the same subject at rest. These values are much too close to reflect the 20 to 40-fold change in blood flow in muscle, but could well reflect the change in tendon. Thus an extravascular bubble pressing upon a nerve ending in a tight connective tissue offers a simple mechanism for Category I decompression sickness for which there would seem to be no adverse evidence. Bubbles are certainly seen in these tissues upon decompression, either directly in living animals[65] or as revealed by X-rays in humans.[1]

Extravascular bubbles pressing upon an axon

The spinal cord is another organ in which many extravascular bubbles can be seen following decompression from an air dive, particularly in the white matter and in those sections where the white/grey ratio is highest.[20] This probably reflects the much higher solubility of nitrogen in lipid, although there is some question whether the solubility in white matter is the same as in depôt fat. It can also explain why Category III symptoms are so much more common diving on air than on heliox and why neurological examinations tend to reveal a preponderance of lesions at T4 and L1. The preponderance of motor dysfunctions is also consistent with the greater myelination of nerves in the motor tract of the spinal columns, again reflecting the greater volume of gas separated from solution in those areas with a higher lipid content.

While all of these correlations may strongly implicate the numerous extravascular bubbles seen in the cord, and especially within myelin where Haymaker[22] remarks upon the propensity of bubbles as "fenestration", there is still the question of whether so much gas can actually press upon the axon with enough force to interfere with impulse transmission. This requires a close look at the complex anatomy of the spinal cord from which it can be seen that there are various mechanical barriers to gas expansion all acting in mutual support of each other, rather like an onion with many skins.

In order to determine whether transmission could be impaired by a bubble formed in the myelin adjacent to the axon or by gas formed outside the myelin sheath, we need to estimate the local distorting pressure and, hence, address the following questions:

1. Taking the outer shell first, we must ask by how much CSF pressure can rise during decompression.

2. Can extracellular gas dissipate and so reduce its local pressure by tracking along the cord between nerve fibres?

3. By how much can the pia and other membranes expand to accommodate the volume increase?

4. Can gas formed within the myelin sheath track along the axon to dissipate its local pressure and how compliant is the myelin sheath in resisting its expansion?

Mechanics of the spinal cord

Cerebro spinal fluid (CSF) pressure is normally about 11 mmHg[66] but can be raised by various physiological stimuli such as elevated PCO_2. In both men[67,68] and goats[6] with a lumbar spinal tap the volume of CSF was found to increase with decompression. If this fluid had not been allowed to expand then, presumably, it would have elevated the CSF pressure. Although lumbar puncture has produced remarkable relief from decompression sickness in some cases,[69] these were cerebral rather than spinal. Moreover the elevations measured in CSF pressure were inadequate to cut off blood flow to the cord. Thus elevation of CSF pressure can be regarded as a contribution to spinal cord pressures rather than a potential hazard in itself.

To take the second of the above questions, it was found that the ability of gas to track along the cord between nerve fibres was very variable but, on some occasions, back-pressures well in excess of 50 mmHg were found upon air injection into an open-ended dog cord.[70] When the cord was tied and fluid injected to eliminate capillarity effects from simple compliance of the adhering cord *in situ,* the back-pressure was related to injected volume as shown in Fig. 3. This is particularly interesting since the back-

pressure remains effectively zero until cord volume is increased about 11-19% and then rises very steeply, presumably when the convolutions of the pia are taken up and/or the non-compliant membranes of the arachnoid and dura also start to resist expansion. After an 11-19% cord expansion the "encased" gas now raises tissue pressure.

The gas *within* the myelin sheath has also been studied recently[70] by decompressing excised spinal cords and then raising and lowering its pressure when the gas itself must obey Boyle's Law. Any deviation offers a very simple means of estimating the pressure differential of the gas adjacent to the axon. Some of these autochthonous bubbles have estimated pressures up to 50 mmHg which would seem adequate to explain the occasional unilateral dysfunction of the cord after decompression. However, symptoms are usually bilateral and the pathology is more consistent with ischaemia and a vascular mechanism for Category III symptoms.

Encased gas closing a blood vessel

It is quite conceivable that a single bubble could press upon a blood vessel with sufficient force to close it, but only if the gas had a higher pressure than the perfusing blood *after* the bubble had indented the vessel. However it is difficult to envisage this occurring in most tissues since these are generally so compliant and, in any case, allow ample opportunity for the gas to expand in directions away from the vessel.

The most likely situation for a bubble to compress a blood vessel is where both the vessel and the bubble(s) are contained within a non-compliant structure. The bubble(s) would then not need to be adjacent to the vessel but their formation could act synergistically to cause a cumulative rise in local pressure which could be transmitted to the vessel wall by both the gas and the extravascular fluid acting as a hydraulic medium. This concept has been compared to a waterfall in explaining some aspects of pulmonary blood flow[71] where flow stops if the sill of the weir is raised above the upstream level just as perfusion ceases in the lung when alveolar pressure is raised above pulmonary arterial.

In bone the rigid walls provide the ideal non-compliant "casing" from which the many bubbles formed in the fatty marrow can raise intramedullary pressure and reduce blood flow proportionately. This has been confirmed experimentally.[72] Similar trends have been found upon decompression to simulated altitude.[73] Thus large volumes of extravascular nitrogen deposited in fatty marrow have been implicated as the cause of dysbaric osteonecrosis,[74] a concept compatible with the thin walls of bone blood vessels[75] and the remarkably symmetrical distribution of bone lesions.[23] However the occlusion should occur at the

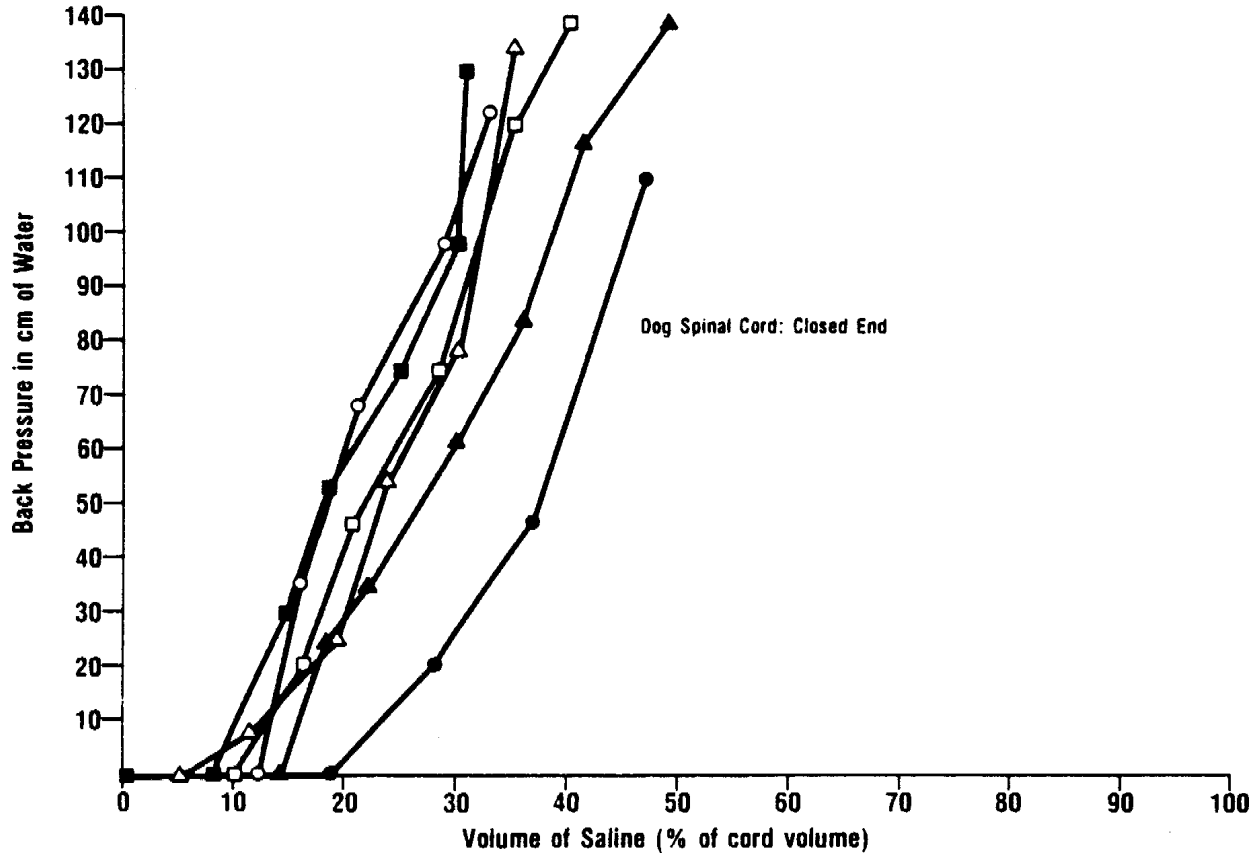

FIGURE 3

The relationship between the volume of ligated spinal cords of dogs and the internal pressure. Note the steep rise in pressure as soon as the convolutions are taken up and further volume increase requires deformation of the tough, non-compliant, encasing membranes such as the dura and arachnoid.

time of decompression and, along with embolic theories for Category VI symptoms, it is difficult to explain the long delay of several months[76] in the appearance of the lesion compared with the appearance of aseptic bone necrosis only weeks post-fracture.

Another situation where vessels could be compressed by gas encased by non-compliant mechanical structures is in the spinal cord. Upon decompression, the pressure within the various membranes, the dura, arachnoid and pia, could be raised by both the formation of extracellular bubbles and the distension of the myelin sheath by gas formed within the myelin. It can be seen from the mechanical studies illustrated in Fig. 3 that the net effect of the membranes is to allow distension of the cord to occur freely until the volume has increased by 7-19%, averaging 12%. After this, the pressure rises steeply and would reach the perfusion pressure of the cord, about 30 mmHg, for a volume increase of about 18%. For a fatty tissue reaching steady state before direct return to the surface, this volume of "encased" gas could be formed by an air dive to 100 feet. This is interesting, since it is just about the shallowest depth at which spinal "hits" start to become common in air diving.[4]

Thus the cumulative effect of extravascular gas in compromising blood flow could offer a simple mechanical explanation for the termination of motor function at a particular point in the cord. The system envisaged is thus a double waterfall where flow would stop when the extracellular fluid pressure exceeded capillary blood pressure. This is most likely to occur in the watershed zones and provide yet another reason for the preponderance of symptoms arising from T4 and L1.

It is impossible to assign a particular mechanism to each category of decompression sickness shown in Fig. 1. However, it is probably fair to say that although arterial bubbles are not the universal insult they were once thought to be, they are fairly certain to cause cerebral symptoms (Category II) while venous bubbles reaching the pulmonary arterial system are almost certain to produce "the chokes" (Category V). The autochthonous bubble would seem to offer the best correlation with the many features of limb "bends" (Category I) while many such bubbles, or "encased" gas, could be responsible for spinal decompression sickness (Category III), although more evidence is needed before arterial bubbles are definitely ruled out for the latter. Vestibular problems (Category IV) and dysbaric osteonecrosis (Category VI) remain open and several of the modes of insult could apply to each, remembering of course, that there could easily be more than one mechanism for each category.

PREVENTION

The prevention of decompression sickness is largely associated with the formulation of diving tables in which basic physiology is often obscured by mathematical complexity. Perhaps the most surprising fact is how little impact that basic research into the physics of bubble formation and the physiology of diving has had upon the decompression formats actually used in naval and commercial diving.

Conventional format

The vast majority of practical diving tables are based upon empirical calculation methods which are only loosely associated with the physiology of the body in so far as they are modifications of the original Haldane rationale.[20] Few of these calculated tables have not undergone further modification by pure trial and error. The Haldane rationale and the many calculation methods derived from it are described in detail in Decompression Sickness Volume I,[1] but it essentially consists of taking air as though it were one gas and then assuming that a tissue will take up that air exponentially. This means that the rate of uptake is proportional to the driving force (blood-tissue tension differential), ie. a linear relationship between the rate of "saturation" and the difference between the ambient air tension and the saturation value as represented by the depth of the dive. An exponential function is a particularly convenient one to adopt since it means, in effect, that this difference, ie. the deviation from "saturation", is continually halved in the same time interval. Thus it takes the same interval to proceed from 0% to 50% as from 50% to 75%, as from 75% to 87.5% "saturation" and so on. This interval for uptake is appropriately termed the "half-time" of the tissue and the same equation with the same half-time is used to calculate elimination of air from that tissue during decompression, such *linear* systems being particularly easy to program on computers.

Having calculated the tissue *(p)* at any instant, the next requirement for computing a diving table is to select some criterion by which to limit the decompression at that particular stage. In the original use of the Haldane method, *p* would be expressed as so many "footsworth of air". It was then argued that no air bubbles would form if the tissue was reduced to an *absolute* pressure (*P*) provided the decompression ratio *(p/P)* was less than 2. Many years later this critical value of the ratio was given the symbol 'M' with values other than 2 as it was redefined with *p* referring to inert gas tension only. Provided this 'M' value for the tissue was not violated, then it was assumed that the air remained in supersaturation solution. The same linear relationship was used to calculate the history of gas in that tissue during decompression as had been used to determine uptake.

This might seem a very simple means of calculating a decompression schedule but, unfortunately, no one equation has ever proved adequate for computing tables of widely differing bottom times. Hence Haldane invoked the concept of multiple tissues, in fact a spectrum of tissues from which he arbitrarily picked five with halftimes of 5, 10, 20, 40 and 75 minutes as representing almost equal geometric steps.

Upon diving deeper than 200 feet this calculation rationale was found inadequate and since then empiricism has run riot, with the numbers of hypothetical tissues reaching several hundred in some computer programmes, each tissue having an empirically determined 'M' value, an empirical half-time or even an 'M' value which is an empirical function of depth.[77]

In all of these approaches there is almost universal acceptance of the axiom that violation of the 'M' value can

cause gas to separate from solution. Conversely it represents a trigger point for bubble formation which, if not violated, implies that no gas has formed in that tissue. Thus most designers of diving tables take great care never to exceed any of their empirical 'M' values in the hope that they are not forming any gas phases and, therefore, they need not consider the mechanisms whereby the bubbles can provoke any of the insults discussed earlier. How nice it would be if decompression were that simple!

Fundamental assumptions

The development of decompression schedules has essentially followed a long series of modifications to the original "Haldane" calculation method necessitated by an unacceptable incidence of decompression sickness, usually found when venturing deeper or for longer than that rationale had previously been used to compute tables. With one notable exception,[78] the changes were not based upon physiological parameters. It is therefore interesting to consider that basic assumptions underly present commercial tables and why many of them seem to give an acceptable bends incidence.

Many questions arise but, on the whole, they can be reduced in number to include the following:

1. How is gas taken up by tissues?

2. If air cannot be regarded as one gas, how should allowance be made for the oxygen partial pressure?

3. Can tissue really retain any supersaturation and does the "trigger point" represent the primary event or the critical insult or what should replace it?

4. How is gas eliminated from tissue and is elimination really the mathematical reverse of uptake?

5. What modifications should be made to the tables to allow for the different categories of symptoms?

Gas uptake

Haldene's original adoption of the exponential function for describing gas transfer in a single tissue was based upon the realisation that this is the mathematical format followed if uptake is limited by blood perfusion. This means that the accumulation of gas in a tissue is limited entirely by the flow of blood to that tissue and not by its subsequent diffusion into extravascular tissue.

This assumption is generally accepted in physiology[79] and has only really been challenged in connection with the incidence of limb bends in divers where the no-stop limits for both air and heliox were found to follow a $\sqrt{t}$ relationship characteristic of diffusion limitation.[78,80] This has led to much argument in the literature, otherwise known as the perfusion-diffusion confusion described in detail in Decompression Sickness Volume I.[1] The controversy is somewhat academic but the conflicting evidence produced can be explained on the basis that blood perfusion is not a continuous process, especially in tendon[81] which has been implicated as the tissue responsible for limb bends and, hence, the tissue having the major influence upon decompression formulation. Thus, when a bundle of 20-140 capillaries in a tendon are closed with little collateral flow, gas transfer must be controlled by diffusion and this would apply particularly to dives of shorter duration and, hence, the $\sqrt{t}$ relationship for bounce dives.[78]

The observation that some tendon capillary bundles may close for long periods, as much as 2 hours or so,[81] queries the basic assumption in all calculations of diving tables that gas uptake and elimination are continuous processes even though the rates may vary depending upon the driving force. Thus one tissue zone may "saturate" in a series of curves with sharp breaks representing periods where the flow was diverted to other capillary bundles.

"Saturation"

Modifications of the Haldane approach have taken account of the fact that air cannot be regarded as one gas and that the inert gas and oxygen must be computed separately. The kinetics of inert gas uptake are such that the tissue nitrogen tension will eventually reach the alveolar nitrogen partial pressure if this is not changed. The question then arises as to what tension the metabolic gases will reach.

When microprobes are placed in tissues to try to measure $P0_2$, values can be obtained anywhere from zero to arterial values but most are at venous levels or below. The analysis of gas placed in the natural body cavities, eg. in the peritoneal cavity shows that it is saturated with water vapour at body temperature, but both oxygen and carbon dioxide soon attain venous values.[82] Let us consider the tissue in a diver who has been living in air at 100 feet for 24 hours. We find that the nitrogen tension has equilibrated with the alveolar N_2 partial pressure (2383 mmHg in this example) and the whole tissue was attained *steady-state*. If we now add up the total gas tensions in the tissue, the total is 2526 mmHg, which is 537 mmHg short of the total of alveolar partial pressures, see Table 1. By Dalton's law this must equal the absolute pressure since the gases are all in the gas phase in the alveolus. Hence, even after reaching *steady-state conditions*, there is a deficit of total gas tension in the tissue due to the metabolic assimilation of

TABLE 1

THE INHERENT UNSATURATION FOR STEADY STATE AT 100 fsw ON AIR

GAS	Alveolar partial pressures (in mmHg)	Tissue gas tensions (in mmHg)
N_2	2383	2383
O_2	593	50
CO_2	40	46
H_2O	47	47
	3063	2526
	↑	↑
	Absolute pressure	Total gas tensions

INHERENT UNSATURATION
= 3063-2526 = 537 mmHg

oxygen and the production of CO_2, a much more soluble gas. This difference or *inherent umsaturation* of tissue has been measured directly in tissue and found to increase with inspired oxygen partial pressure, whether this is effected by substituting oxygen for nitrogen at a fixed pressure or increasing pressure on a given breathing mix.[83]

This means that, whereas the inert gas may equilibrate, a tissue never comes to true saturation with the environment unless it is not metabolising and, therefore, is dead. Thus the diver with the typical gas tensions given in Table 1 who has reached steady-state could decompress by 537 mmHg, ie. from 100 to 77 feet before reaching saturation in the true physico-chemical sense of that word.

Phases of decompression

The next question to ask is by how much the decompression could overshoot the 77 foot mark (2526 mmHg in Table 1) before bubbles will actually form, ie. what is the degree of true supersaturation which the tissues can tolerate before bubbles form? Before addressing this question, however, we should be quite sure of what we mean by supersaturation and how this particular phase fits into the overall decompression since it has long been my contention that supersaturation has been unduly emphasized by popular calculation methods.[64]

Let us consider the diver at 100 feet on air who returns to the surface without stopping and then develops limb bends. His bends-provoking tissue must pass through the following three phases (Fig. 4):

I. Until he reaches 77 feet, this bends-provoking tissue must remain undersaturated by reason of the inherent unsaturation discussed above. If he had not attained steady state at 100 feet before starting his decompression, then he could carry on a bit further and ascend by the additional amount by which his tissue nitrogen had failed to reach the equilibrated value of 2383 mmHg given in Table 1. If the tissue were 80% equilibrated, this would amount to an additional 0.2 (2383-570) = 362 mmHg, or 16 feet closer to the surface.

II. After reaching 77-16 = 59 feet, any further decompression would then start to cause true supersaturation unless he were to stop and let the inert gas re-equilibrate with its new alveolar partial pressure. If the diver continues to ascend, then the degree of supersaturation will increase until, at some critical level, the solutions "breakdown" and a gas phase forms, ie. he has "triggered" the primary event. The growth centres, or nuclei, will form bubbles and, if left long enough, will take up all of the gas in supersaturated solution.

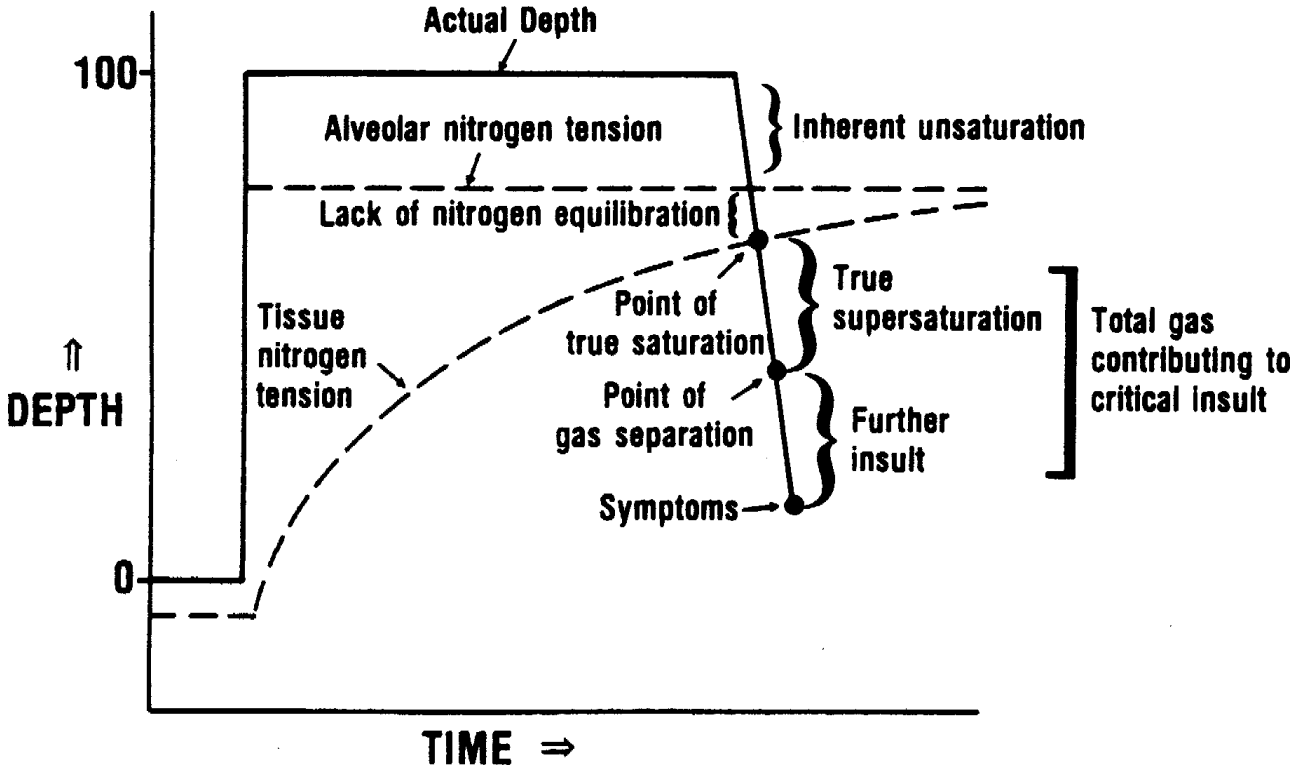

FIGURE 4

A no-stop decompression depicting the factors which can determine the degree of supersaturation and, when exceeded, how this and further decompression can contribute to the quantity of gas actually eliciting symptoms.

III. The diver would remain asymptomatic if he remained at the depth at which critical supersaturation broke down. By decompressing further, however, he now enlarges the gas phase which, in turn, increases the insult, by whichever mechanism applies, until it reaches its symptom-provoking threshold. It is during this phase of decompression that the mechanism becomes important and yet this is seldom considered in designing the table.

The above series of steps is depicted in Fig. 4.

True supersaturation

The physics of suppressed formation of the gas phase has been described in much detail in Decompression Sickness Volume I[1] but the discussion tends to become very academic as one pursues the questions of nucleation or what activates pre-formed nuclei into macro-nuclei which can then grow bubbles. Whatever the semantics involved, there does seem to be some degree of supersaturation needed before a fluid will start growing bubbles. The difficulty arises in trying to quantify this critical degree of supersaturation since the phenomenon seems fairly random and this tempts the investigator into using pure liquids to try to derive some underlying theme. Gelatin has been a popular model for many years[20,64,84] but this has no metabolism and does not reflect the many interfaces in tissue, especially a lipid-aqueous interface which is particularly conducive to bubble formation.[64]

The latter study has claimed that nucleation is very random and that, whereas about 70-80% of tissue can withstand substantial supersaturation,[57] some bubbles can form for negligible degrees of supersaturation, in fact much less than predicted by the Haldane ratio[20] or the fixed differential (*p-P*) first advocated by Hill.[85] The controversy essentially degenerates into a show of figures in which extremely high degrees of supersaturation can be shown in perfectly clean pre-pressurised pure liquids while some bubbles can be observed in animals following very small decompressions,[86,87] some barely exceeding the inherent unsaturation. Thus the controversy is transformed more into one of whether we should consider what the average tissue zone is doing or just the "worst possible case" of one bubble forming for a negligible level of true supersaturation.[64]

Alternating bubbles

The recent results on the tendon[81] would question the relevance of the above issue since gas will accumulate in non-perfused areas and soon exceed almost any published criterion for supersaturation. Thus bubbles should form whoever is correct in this academic argument. A bubble in living tendon, either intravascular or extravascular, can be seen to grow during decompression when the capillary bundle perfusing its site is closed and then shrink when that area is perfused. Thus one observes a whole range of bubble sizes as some shrink and others grow depending on the momentary distribution of blood flow. The important criterion then seems to be one of the sequence of perfusion, ie. vascular programming, rather than critical supersaturation. The same phenomenon can be seen on a much reduced time scale in the human hand[88] where areas do not change their boundaries but alternate in colour between pink and white. If one such area in a decompressed tendon misses its turn for perfusion, it can grow a bubble large enough to elicit pain. This assumes, of course, that the critical tissue for limb bends is tendon, but intermittent perfusion can offer a simple explanation why even the most conservative diving tables sometimes produce the odd limb 'bend". It would also provide a mechanism adding credence to the feelings of some designers of diving tables that the perfect bends-free table is either a myth or not cost effective. In fact it has been further suggested that it is the presence or otherwise of this phenomenon in a particular tissue type (eg. tendon, bone and skin) which determines whether that tissue is subject to insult and injury by decompression.

Practical diving tables

In the design of most diving tables, the inherent unsaturation and the growth of the insult are ignored. Ostensibly, the designer is avoiding the formation of the gas phase altogether by keeping on the safe side of his "trigger" points for the various hypothetical "tissues" he invokes. This is excellent providing the gas is remaining in true physical solution. In practice, however, it would appear that much of the gas is not remaining in solution but is forming bubbles and proceeding quite a way from the point of phase separation towards the critical insult for symptoms (Fig. 4). Thus even the much used tables of the US Navy would appear to be *treating* a gas phase rather than preventing it.[64] This may not be as serious a deficiency as it might sound since, according to my best estimates, it would take of the order of four times the total decompression time for the critical tissues to remain bubble-free. Thus, to be economically competitive, decompression schedules probably allow gas to separate from solution but prevent the insult from reaching the threshold for symptoms. This means, however, that the table was designed on the basis of preventing the gas phase from forming and yet, in practice, gas *did* separate from solution and, therefore, the table should have been formulated to minimise the insult. This is where it now becomes important to know the mechanism for provoking each category of symptom. Optimal conditions for preventing a gas phase which forms sooner than expected are unlikely to be the best for minimising development of the insult. This point is best illustrated by considering the effect of bubble formation upon the elimination of inert gas from a tissue.

Gas elimination

In gas uptake, there is no doubt that the driving force is the difference between alveolar partial pressure and tissue tension. Upon lowering the alveolar partial pressure by substituting another gas for the inert gas, the gradient can be reversed and so the exchange of gas will not only be reversed but will follow the same kinetics. If, on the other hand, lowering the alveolar partial pressure of the inert gas was effected not by substitution but by decompression and, moreover, by a decompression which caused gas to separate in the tissue, then everything is different. The tissue may contain the same total gas in all forms, but only the gas in true physical solution determines the tissue tension of that gas and hence the driving force for its elimination.

This very important point is demonstrated in Fig. 5 where dissolved gas simulated by the liquid in one tank is flowing into a lower tank representing the lung. If all gas remains in solution, the driving force is the head (H_1).

If gas is 'dumped' into the gas phase, however, this is equivalent to opening the valve when liquid will rapidly flow into a third tank representing separated gas until they are at the same head, ie. at the quasi-equilibrium where partial pressure in the bubble equals the tension of gas remaining in solution. However, the driving force for liquid flowing into the lower tank has now decreased from H_1 to H_2. So the driving force for eliminating inert gas from the tissue will decrease and allowance must be made for this in the formulation of a decompression table, yet none do, despite the many studies showing bubbles present even in the critical tissues for limb bends.

When the gas phase is present, then the driving force for inert gas elimination is simply the inherent unsaturation, which is much smaller than the hypothetical supersaturation used to compute standard tables, ie. we should be using H_2 instead of H_1 (Fig. 5) in our calculations.

Other symptoms

The above discussion applies primarily to limb bends (Category I) since these are by far the most common symptoms and, historically, have been taken as the ones to avoid when it was thought that other more serious symptoms were a further development of the same overall insult process. The question then arises as to what procedures should be taken to ensure that other categories are also avoided or that these are primarily avoided since, unlike limb bends, they have the capacity to cause permanent injury.

The two categories which can be made to precede limb bends by selecting the conditions are cerebral[89] and vestibular.[90] Taking Category II first since cerebral symptoms are fairly certain to be caused by arterial bubbles, it would seem most desirable to avoid any insult to the lungs which could cause them not to trap bubbles. This would suggest careful control of the oxygen prescribed during the decompression so as not to cause pulmonary oxygen toxicity.

The fact that Category IV symptoms can be provoked without decompression by inducing counter gradients of the 'heavier' inert gases indicates that it is also desirable to avoid a situation where one inert gas is adjacent to one body surface and another inert gas is in contact with another surface, unless favourably orientated. This creates the conditions for steady-state counterdiffusion[91] or exchange by counterperfusion,[92] or both, which might result in bubble formation in the vestibular apparatus.

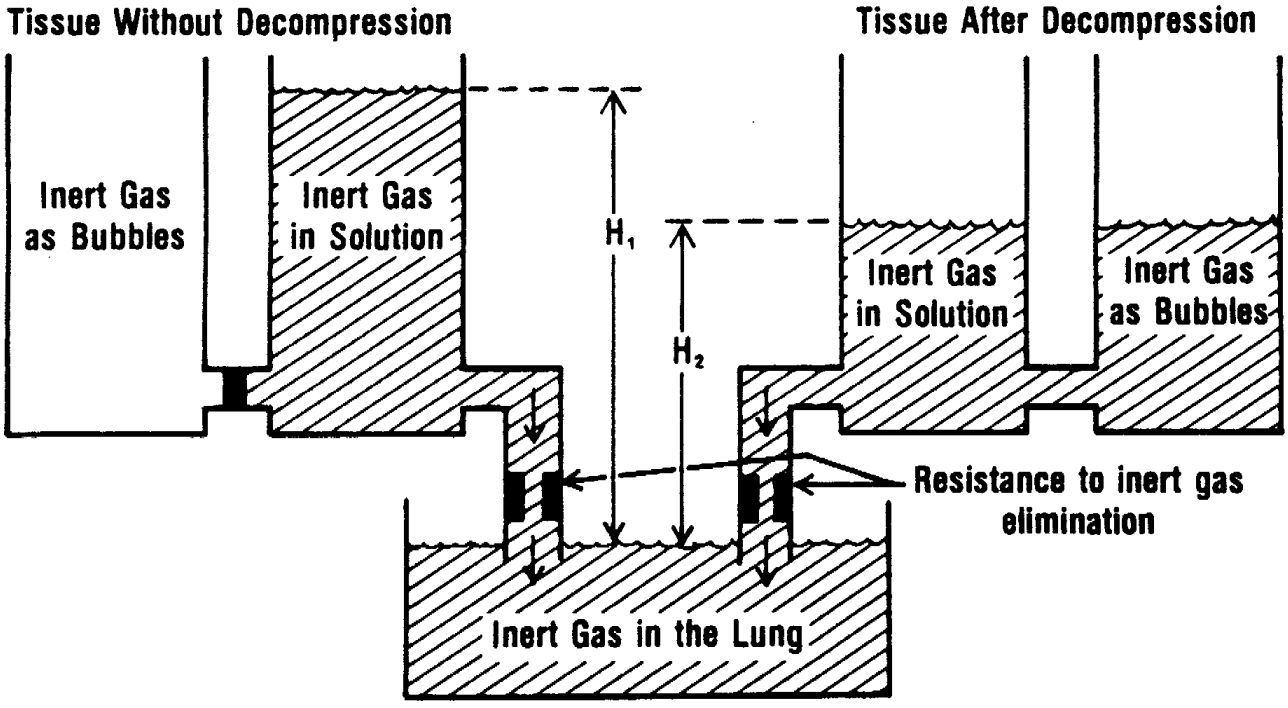

FIGURE 5

A hydraulic analogue for inert gas elimination from tissue, showing (on the left) how reduction of the alveolar inert gas partial pressure by substitution of another gas can produce a driving force for its elimination simulated by the head (H_1). On the other hand, reduction of the alveolar inert gas partial pressure to the same level by decompression *(on the right)* can also cause bubbles to separate from solution and so reduce the driving force for elimination, simulated by the head (H_2), even though the total gas in the tissue is the same as in the previous case depicted on the left.

Hence it is desirable not to switch from heliox to air rapidly as sometimes occurs in transferring divers from a bell ventilated with heliox to a deck decompression chamber pressurised with air.

These are some of the more obvious factors which can potentiate the more serious neurologic forms of decompression sickness which otherwise are produced by very few tables.

TREATMENT

Recompression

The resolution of a bubble depends upon its location. If it is extra-vascular, then it will be reduced in volume but remain in essentially the same site. Hence, if the diver is decompressed, the symptoms will return as before, as argued in favour of the extravascular mechanisms for Category I and Category III symptoms. Upon recompression, it is therefore necessary to hold the patient at pressure even though relief is complete in order to allow the much slower process of dissolving the gas to take effect.

The kinetics must be dependent upon any alternating patency of, say, a tendon for Category I or possibly the cord in Category III. It may be necessary to wait until the capillary bundle adjacent to the bubble is perfused before that bubble can be reduced in volume to any appreciable extent. The other factor influencing the kinetics is the driving force which is virtually the inherent unsaturation, as described in detail in Decompression Sickness, Volume I.[1] This inherent unsaturation can be greatly increased by breathing a high partial pressure of oxygen, in fact by roughly the elevation of the inspired PO_2. This offers a simple physical explanation for the efficacy of oxygen in resolving decompression sickness.

The other aspect of recompression is its effect upon intravascular bubbles, especially those occluding an artery from within. These require an appreciably larger volume change for complete dislodgment but are cleared most effectively by extensive recompression.[36,38] This may account for many unconfirmed reports of remarkable recoveries from neurologic symptoms upon a deep bounce with direct return to the surface. However, it is my experience with animals that, whereas most were cured, a few died. This could be attributed to the fact that recompression not only acts upon the occluded tissue but also upon the lung which is probably holding back many more trapped bubbles. If some of these were released, then the symptoms could be worse, depending upon where they happen to lodge.

Depth of recompression

According to the above argument, it takes a greater volume decrease to dislodge an intravascular bubble than it does to reduce the pressure with which a bubble is pressing upon a nerve ending to below the pain threshold. This is essentially reflected in the treatment tables where 165 feet (6 ATA) is the treatment depth for central nervous system involvement while 60 feet is recommended for limb bends only. In view of the possible effect of recompression releasing trapped lung bubbles,[93] lesser recompressions may be preferred for limb bends where there is complete relief shallower than 60 feet.

Gas for recompression

The last degree of freedom which the physician can prescribe in the treatment of decompression sickness is the gas mixture for recompression. For the reasons already discussed, the oxygen partial pressure should be high in order to increase the inherent unsaturation and, hence, the driving force for resolving the bubble. On the other hand, the overall exposure must not precipitate oxygen toxicity in any form. Naval treatment tables take account of the compromise necessary, but this is sometimes upset when the diver has already received an excessive oxygen exposure before the bend occurred.

The last question is which inert gas to use for diluting the desired oxygen to the point where adequate pressure can be applied to the bubble. This complex issue will not be discussed in this paper.

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