Chapter 3

The Mechanism

The manifestations of inadequate decompression are sufficiently undesirable to leave little doubt that prevention is better than cure, raising again the all-important problem of predicting the adequacy of a decompression before it is used in the field and consequently the following questions: how slowly should decompression be carried out?; what gas mixes should be breathed during decompression and when?

To try to answer these questions, it is most desirable to know the mechanism so that the *primary event* leading to a pain-provoking insult or to chronic changes to the tissues can be avoided or controlled.

The basic questions

The symptoms alone offer no obvious aetiology for decompression sickness as a whole but their wide diversity does suggest that the primary event occurs at a fairly fundamental level of physiological function. Moreover, the relative ease of placing most of the symptoms into different categories is perhaps a warning against assuming that the same primary event is responsible for each, or that it leads to the same *critical insult* or level of insult which precipitates decompression sickness in all of its clinical forms.

The operational urgency to predict the adequacy of a diving table focuses attention upon certain specific questions which need to be answered in a definite order if a fundamental basis for prevention is to be found. These are:

(1) What is the primary event?
(2) What is the critical insult to which the primary event can lead?
(3) Do the primary event and critical insult coincide, or does the degree of insult need to exceed a certain threshold for a particular clinical manifestation to be provoked?
(4) Are the primary event and critical insult the same for each category, or do some symptoms represent higher thresholds on the same scale and, if so, in how many tissues?
(5) What are the critical levels of insult and how can they be defined by environmental parameters and factors describing individual susceptibility?
(6) Since a primary factor is the inert gas content, what determines its distribution in tissue and the kinetics of uptake and elimination?

It is very easy to find questions to ask about decompression sickness but the foregoing sequence offers a framework for rational deductions to be attempted from the mass of information which is available.

The Primary Event

The large influence of many environmental factors on the incidence of symptoms offers the best lead to the primary event and points to a combination of two factors—the extent of decompression and the quantity of inert gas in tissue prior to decompression.

Decompression

Since the same symptoms can be produced by decompression alone, e.g. by aerial ascent, there is no doubt that it is the decompression

rather than any other stage of the environmental excursion which leads to symptoms. There is, however, the possible exception of dysbaric osteonecrosis which, apart from one case (Fryer, 1969), does not seem to occur with aerial exposure alone (Allen *et al.*, 1974). Although unlikely, it is conceivable that these category IV symptoms could be caused by some aspect of the excursion other than decompression. There is also doubt that decompression is necessary for producing the primary insult(s) leading to the groups of clinical manifestations known colloquially as 'skin bends' and 'vestibular bends' since both of these have been produced under isobaric conditions (p. 211). Otherwise decompression *per se* is the major factor in precipitating symptoms.

Tissue gas

The other necessary ingredient is a reasonable quantity of inert gas in the body at the time of decompression. This is shown by: the greater incidence with deeper exposure and with more time to assimilate inert gas; the decreased incidence on aerial exposure with longer pre-oxygenation and hence longer nitrogen wash-out, any substituted oxygen being consumable by metabolism; the increase in minimum bends depth with decrease in tissue solubility of the inert gas; and the increase in susceptibility with obesity and hence with more lipid in which the five-fold greater solubility for nitrogen should greatly increase total body nitrogen.

Gas separation

The combination of decompression and the amount of dissolved gas leads to the obvious conclusion that the gas will tend to separate from solution. This is further supported by the fact (p. 36) that a greater uptake of inert gas, or less wash-out, requires less decompression to precipitate symptoms and *vice versa.*

Cavitation has been stated or implied as the primary event since Lyttleton (1855) attributed the symptoms he observed in Cornish caisson workers to 'extricated air' while, in France, Pol and Watelle (1854) reasoned that 'la maladie de caisson' could be attributed to bubbles forming in blood and tissues—in fact, similar to those subsequently demonstrated in animals after hypobaric exposure by Paul Bert (1878). With the subsequent publication of the pathological findings of Boycott and Damant (1908), there has been little dispute that the primary event leading to symptoms of decompression sickness is the separation of gas from solution.

However, before passing to the much more controversial questions of whether this is also the critical insult or how gas phase formation leads to the critical level of insult, it is as well to consider whether there might be any reasonable alternatives.

Possible bubble-free alternatives

An effect first described by Swindle (1937) and demonstrated in decompressed animals by End (1938), is the agglutination of erythrocytes in which various blood elements lose their mutual repulsion, so tending to agglomerate and adhere to vessel walls. Consequently End (1939, 1971) has put forward the concept that the bends are due to ischaemia induced by infarction with agglomerates caused by stress-induced elevation of fatty acids and the deposition of microgels on lipid-rich platelets and red blood cells. He points out that recompression, particularly while breathing oxygen, can reverse agglutination prior to a point at which 'true thrombosis occurs'. Inert gas bubbles, when they appear, are then a secondary effect probably arising in regions where the circulation has been impeded by agglutinated cells.

End also emphasizes the effect of elevated carbon dioxide in promoting agglomeration (Swindle, 1937) but there is some doubt that the role of carbon dioxide *per se* in decompression sickness is as pronounced as he implies (see p. 46). Moreover, Walder (1969) makes the very pertinent point that the 'sludging' of blood occurs in many other clinical situations without provoking bends-like symptoms.

Even so, there is little doubt that the micro-

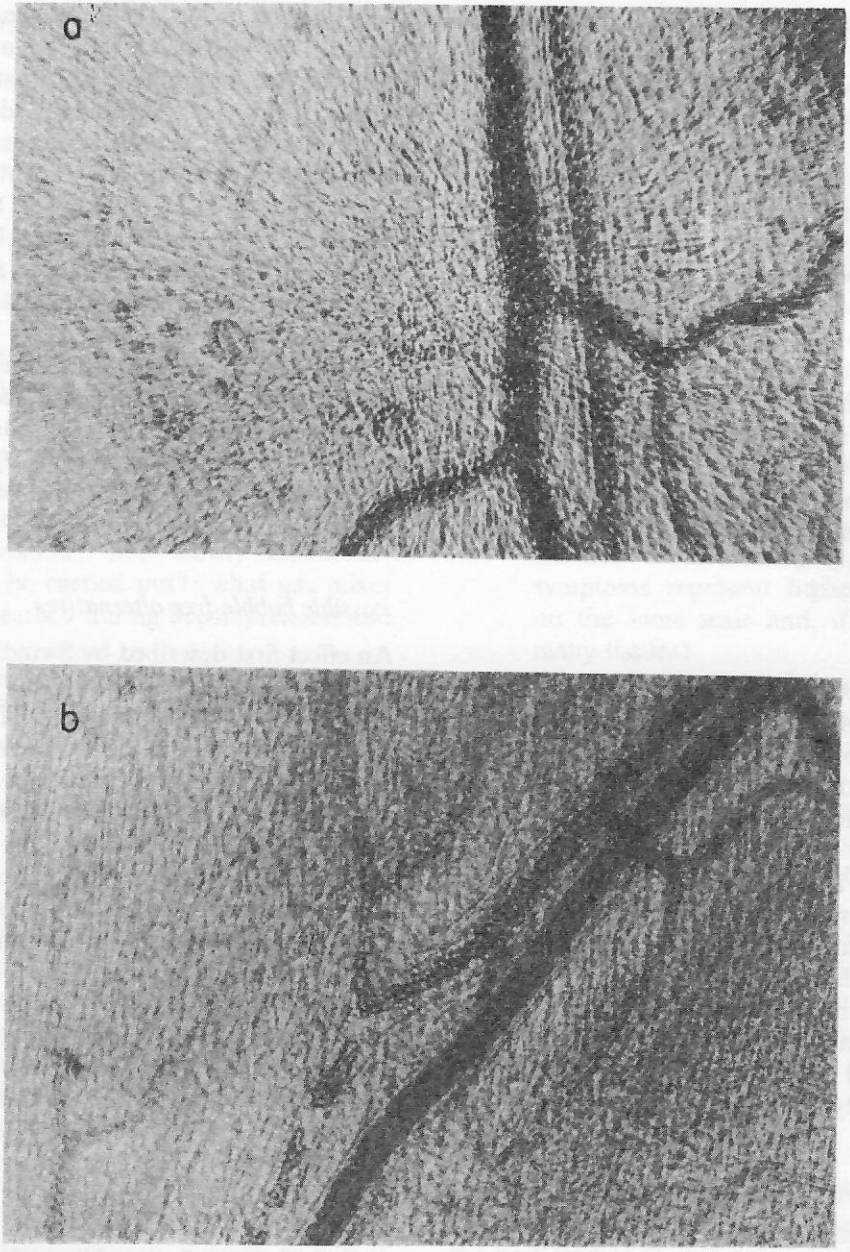

Fig. 16 Photomicrographs of the omental vessels of the dog (a) before exposure to air at 90 psi for one hour and (b) after decompression—note the granular appearance of the blood. Reproduced by permission of Dr. C.H. Wells

circulation can be altered by decompression (Heimbecker *et al.*, 1968; Wells *et al.*, 1971). These changes can be attributed to increased blood viscosity (fig. 17) and erythrocyte aggregation (fig. 16) rather than to any circulating bubbles lodging in the smaller vessels (Guest *et al.*, 1974). A similar 'rheological' approach has been proposed by Walder (1965) to explain the ischaemic pain which people with poor circulation experience when they immerse their fingers in cold water (Raynaud's disease), so this mechanism can easily account for the

adverse effect of very cold conditions during decompression. The alternative approach that micro-disseminated intravascular coagulation (Holland, 1969; Philp *et al.*, 1971) is actually induced by bubbles is discussed later (p. 55).

However, returning to the purely rheological hypothesis, it is convenient to attribute the increase in blood viscosity to the haemoconcentration known to occur on decompression (Cockett and Nakamura, 1964; Jacobs and Stewart, 1942) but this still leaves the vital question of identifying the factor initiating plasma loss. In brief, where does the fluid go and what makes it shift? The possibilities fall into two broad categories—those with a physical basis and those mechanisms mediated humorally.

The features of decompression sickness which would seem most difficult to explain by any hypothesis in which bubbles are absent, or play no active part, is the dominance of the inert gas content in determining the incidence of symptoms. Possible interpretations of the role of nitrogen are afforded by gas-induced

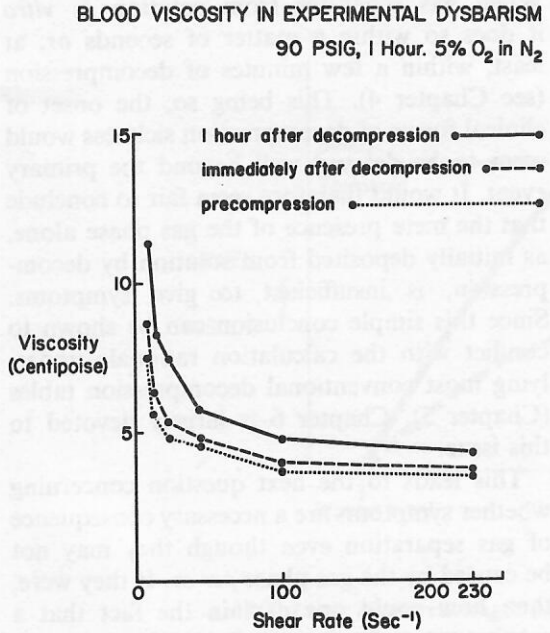

Fig. 17 Blood viscosity at various shear rates immediately after decompression and one hour thereafter. From Guest *et al.* (1974)

osmosis and by a mechanism which has received consideration in the field of artificial internal organs. Abdulla (1967) has suggested that platelet aggregation may be due to disturbance of a clathrate structure of water around platelets—a gas hydrate principle analogous to that proposed by Miller (1961) for the mechanism of gaseous anaesthesia. In this case, denaturation of plasma proteins should be a function of molecular size and groupings of the gases present. Some suggestion that this may be the case is afforded by the work of Vervloet *et al.* (1967) who show minimal blood damage in a membrane oxygenator when the gas mixture has a composition of 21% oxygen, 73% nitrogen and 6% carbon dioxide. However, the protection offered by elevating the carbon dioxide would appear contrary to the potentiating action of this gas in inducing the agglutination which is a major factor in the approach of End and Swindle.

A second possible interpretation of the role of nitrogen is its potential for inducing fluid shifts by osmosis (Hills, 1971b). This could lead to haemoconcentration and hence aggravation of the blood disorders already mentioned, or they could lead to undesirable local mechanical stresses (see p. 58). It is conceivable that large quantities of extravascular inert gas could maintain gas concentration gradients caused by decompression until those reservoirs were depleted by diffusion. Those gradients would then tend to effect an osmotic shift of water out of the blood into the cell, or into the extravascular space in general, to build up a positive hydrostatic pressure-difference and to cause haemoconcentration.

The other category of possible explanations for the plasma loss essentially revolves around a change in vasoactivity induced by one or more humoral factors liberated by decompression. Chryssanthou and co-workers (p. 134) have emphasized the kinins, while Hilton and Wells (1976) suggest that prostaglandins may be important in the later stages of plasma extravasation. Their evidence is based largely upon the partial reduction in the plasma loss observed upon decompression when indomethacin or

nicotinic acid are administered—two enzymes which inhibit the synthesis of prostaglandins from fatty acids (Sorrentino *et al.*, 1972; Carlson, 1971).

There are various means by which vasoactive humoral factors could reduce plasma loss; these include elevating the effective oncotic pressure or, kinetically, by increasing the resistance of the vessel walls to fluid extravasation when the driving force is provided by a physical mechanism such as gas-induced osmosis. This could explain the fact that indomethacin blockade is only about one-third effective in reducing the fluid loss while the increase in plasma volume upon *compression* in the absence of inhibitors (Hills, 1973c) is only about one-third of the decrease upon decompression. Such a hybrid explanation could also account for the marked dependence of the incidence of decompression sickness upon the tissue inert gas content.

This line of reasoning still offers no key to the mechanism triggering the release of the humoral factor in the first place. Although Wells and co-workers observe no bubbles in their mesenteric window, they are primarily concerned with the role of blood flow changes in the potentially disabling chronic effects of grossly inadequate decompression so that humoral factors could have been released by gas separating from solution elsewhere in their animal preparations.

Conclusion

While it may be entertaining to theorize how inert gas *remaining in solution* can initiate various processes leading to decompression sickness, most mechanisms would seem unlikely. Moreover, most of the intermediate processes already outlined could also be initiated by gas bubbles, as described later (p. 55). It is difficult to envisage how any mechanism based on inert gas in solution can be reversed as rapidly as bends-pain is usually relieved by recompression. This also applies to gas-induced osmosis where it is difficult to see how a sufficient water shift could be induced by a nitrogen concentration gradient as small as that arising from the aerial decompression needed to produce symptoms. However, osmosis induced by the much larger gas concentration gradients anticipated at much higher pressures could make a minor, yet still significant contribution to the critical insult in diving, depending upon the nature of the primary mechanism.

Hence there are no serious contenders to the separation of gas from solution as the primary event leading to all symptoms with the possible exception of dysbaric osteonecrosis.

The Critical Insult

The next question to consider is whether gaseous cavitation alone is also the critical insult or by what mechanisms it can lead to a critical degree of insult. In other words, is the mere presence of the gas phase in tissue all that is needed to give symptoms, or to ensure their subsequent occurrence?

Gaseous cavitation alone

When gas separates from solution *in vitro* it does so within a matter of seconds or, at least, within a few minutes of decompression (see Chapter 4). This being so, the onset of clinical forms of decompression sickness would seem to be delayed well beyond the primary event. It would therefore seem fair to conclude that the mere presence of the gas phase alone, as initially deposited from solution by decompression, is insufficient to give symptoms. Since this simple conclusion can be shown to conflict with the calculation rationale underlying most conventional decompression tables (Chapter 5), Chapter 6 is largely devoted to this issue.

This leads to the next question concerning whether symptoms are a necessary consequence of gas separation even though they may not be caused by the gas phase *per se*. If they were, then how could one explain the fact that a regular recompression 'treatment' for an unsafe dive avoids symptoms if given *before* their onset? This strongly suggests that the mechanism by which the primary event leads to the

critical insult is reversible—or in part, at least. To emphasize this point, consider the caisson worker who is decanting (p. 11) or the diver who is undergoing surface transfer to a decompression chamber (p. 162): they have returned to normal atmospheric pressure from an exposure which is sure to give symptoms and has, therefore, initiated the primary event. However, provided they return to the first stop of a safe decompression table within 5 min, or longer (Gouze, 1944), they can follow that schedule and emerge free of overt symptoms.

It would therefore seem fair to make the further conclusion that the critical insult is not a necessary consequence of the primary event. Rather, it would appear that there is a *critical level* to an insult imposed by a mechanism which can be reversed, in part at least, by recompression and sometimes by other treatments (p. 232). Moreover, it would appear that reversal can occur whether the process has reached the symptom-provoking level of insult or not, this threshold representing a somewhat arbitrary point on a continuous scale of development.

The amelioration of limb bends with time alone strongly suggests that the level of insult grows to a maximum and then regresses, the occurrence of overt symptoms being determined by whether the pathological process 'peaks out' before or after reaching the critical threshold. The latter is then a somewhat arbitrary point on a continuous scale as envisaged in fig. 18.

This raises the further problem of identifying the process by which the initial cavitation can induce delayed symptoms; hence the critical parameter represented on the ordinate of fig. 18, the magnitude of which determines the imminence of bends.

Possible induction mechanisms

The following possibilities have been put forward:

(1) The separation of gas from solution continues to expand the initial nuclei into bubbles of a size at which they can occlude the circulation. These gas emboli may be grown *de novo* in blood (Bert, 1878) or released into it from extravascular sites by vascular haemorrhage

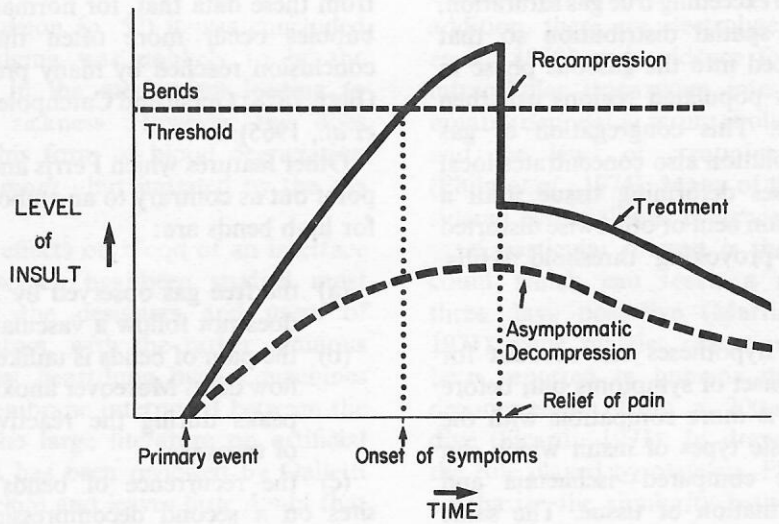

Fig. 18 The time course envisaged for the level of insult following a 'bounce' (no-stop) dive, where symptoms of Type I decompression sickness will occur if the threshold is exceeded. Recompression can reduce it to subsymptomatic levels. If left untreated, a mild bend will eventually disappear as the insult subsides

(Heller *et al.*, 1900). In either case, symptoms would then be produced by the ischaemia resulting from vascular occlusion.

(2) The formation of circulating gas emboli introduces a blood–gas interface which can then initiate various degredation processes whose products could then cause infarction of the vascular bed with subsequent ischaemia. This is similar to the pattern originally suggested by End (1938, 1939) but with the vital difference that gas separation is now the primary event causing the haematological changes. From a simplistic viewpoint, the blood itself cannot differentiate between the gas in a bubble and the air to which it is exposed at a cut and therefore initiates the first stages of clotting as though they were leading to wound healing.

(3) Extravascular gas nuclei, or those lodged in closed blood vessels, grow into bubbles until they assimilate sufficient gas by diffusion from adjacent supersaturated tissue that their expansion bends a nerve ending beyond its threshold for provoking pain (Nims, 1951).

(4) Gas nuclei, pre-existing in tissue or formed immediately upon exceeding true gas saturation, have a random spatial distribution so that gas rapidly dumped into the gaseous phase in the more densely populated regions can then start to coalesce. This congregation of gas separated from solution also concentrates local mechanical stresses deforming tissue until a nerve ending is again bent or otherwise distorted beyond its pain-provoking threshold (Hills, 1966).

Each of these hypotheses can account for the delay in the onset of symptoms but, before discussing which is more compatible with the facts, the two basic types of insult which can result should be compared—ischaemia and mechanical deformation of tissue. The same critical insult need not be responsible for all symptoms, however, so the comparison needs to be made in the context of each of the categories defined (p. 30) to classify the manifestations of inadequate decompression.

Limb Bends

Intravascular bubble hypothesis

Ischaemia resulting from bubbles lodging in the peripheral vessels of the arterial tree has long been implied as the cause of bends pain (Hoppe-Seyler, 1857), Armstrong (1939) going so far as to refer to the syndrome as 'aeroembolism'.

However, gas emboli occluding the arterial system would need to form in arterial blood, since the lungs appear to provide quite an effective filter for venous bubbles (p. 66). Therefore, it is difficult to see how arterial blood, arriving within 30 sec of virtual equilibration with the environment in the lungs, can contain sufficient gas in excess of saturation to form gas emboli. At least, this would apply for normal decompression rates as opposed to explosive decompression when there is little doubt of their presence in the arterial system (Wagner, 1945; Pudenz, 1945).

There is some controversy concerning whether bubbles first form in the arterial or venous system or whether they form in blood at all during a normal decompression (see p. 147). However, it would seem fair to conclude from these data that, for normal rates, venous bubbles occur more often than arterial—a conclusion reached by many previous authors (Bert, 1878; Gersh and Catchpole, 1951; Mclver *et al.*, 1965).

Other features which Ferris and Engel (1951) point out as contrary to an embolic mechanism for limb bends are:

(a) the free gas observed by X-ray (p. 142) does not follow a vascular distribution;
(b) the pain of bends is unlike that of blood flow debt. Moreover anoxic pain usually peaks during the reactive hyperaemia of recovery;
(c) the recurrence of bends in the same sites on a second decompression 4–6 hours after the first is highly suggestive that a bend is not related to intravascular bubbles. There is strong evidence to show that arterial bubbles can be cleared by extensive recompression (Waite *et al.*, 1967; Grulke and Hills, 1976).

Other reasons for querying the ischaemic approach include the mild protection afforded by hypoxia (p. 38) while hyperoxia tends to potentiate (p. 38). There is also the fact that circulating gas emboli may not be detected until a late stage in the development of the distress induced by decompression (Behnke *et al.*, 1936).

The possibility that occlusion may occur on the venous side has also been mentioned—such as by bubbles lodging in the convoluting cortical passages draining large medullary venous channels (Fryer, 1969). This may explain why bends and bone lesions tend to occur in the same limbs and around the same types of joint but it still suffers from the other objections to a mechanism based upon occlusion by gas emboli.

Other manifestations of Type I decompression sickness are easily explained on the basis of bubbles in the lymphatic vessels and at the nodes, their presence at these sites having been demonstrated in decompressed animals by Boycott and Damant (1908a), Blinks *et al.* (1951) and Lever *et al.* (1966).

Blood degradation by bubbles

In earlier discussion (p. 52) it was concluded that blood-sludging was unlikely to be the primary event in the mechanism leading to decompression sickness. However, this does not preclude this form of blood degradation as the *critical insult*—but initiated by the gas phase.

The adverse effects on blood of an interface with air or oxygen has been studied most extensively by the designers and users of blood oxygenators, with the rather ominous result that most heart/lung bypass machines now have a membrane interposed between the two phases. The large literature on artificial internal organs has been reviewed by Galletti and Brecher (1965) and leaves little doubt that the extent of blood degradation increases with surface area. The force associated with the interface is the primary source of damage to blood components (Pierce, 1967), leading to denaturation of plasma proteins by destroying their tertiary and/or secondary structure (Lee and Hairston, 1971).

The denaturation of plasma proteins results in a fall in colloid osmotic pressure with subsequent loss of vascular fluid and interstitial oedema in the patient maintained on a blood oxygenator without transfusion (Galletti and Brecher, 1965). A similar process could, therefore, occur in the subject in whom bubbles formed by decompression had initiated the degradation process. This approach is certainly compatible with haemoconcentration observed on decompression and the fact that its reversal by infusion of low-molecular-weight dextran can sometimes relieve bends pain (Cockett and Nakamura, 1964).

Many haematological measurements have consequently been made in divers during and after decompression and a number of excellent reviews of the many studies have been published within the last few years (Ackles, 1973; Philp, 1974). Among numerous significant findings are a decrease in platelets, evidence for micro-disseminated intravascular coagulation (Holland, 1969) together with fibrinolysis (Bonin *et al.*, 1973), increased blood lipids (Philp *et al.*, 1967), and the presence of endothelial cells in blood (Philp *et al.*, 1972). In addition, there are electrolyte shifts (Schaefer *et al.*, 1968) and evidence for the release of intracellular isoenzymes into the circulation, notably depressing serum cholinesterase activity and the level of creatinine phosphokinase (Philp *et al.*, 1974). Many of these can be considered essentially as evidence of cell damage.

Of particular interest is the fall in platelet count which can reach a maximum some three days post-dive (Martin and Nichols, 1971) while platelet reductions of 37% have been reported in humans immediately after decompression from a 200-metre (656-foot) dive (Sicardi, 1971). In drawing attention to the role played by platelets, Philp *et al.* (1971) emphasize the similarity between this mechanism and disseminated intravascular coagulation. Post-dive platelet depression can also occur following an asymptomatic dive and again raises the question whether humoral changes are a link in the aetiological chain or,

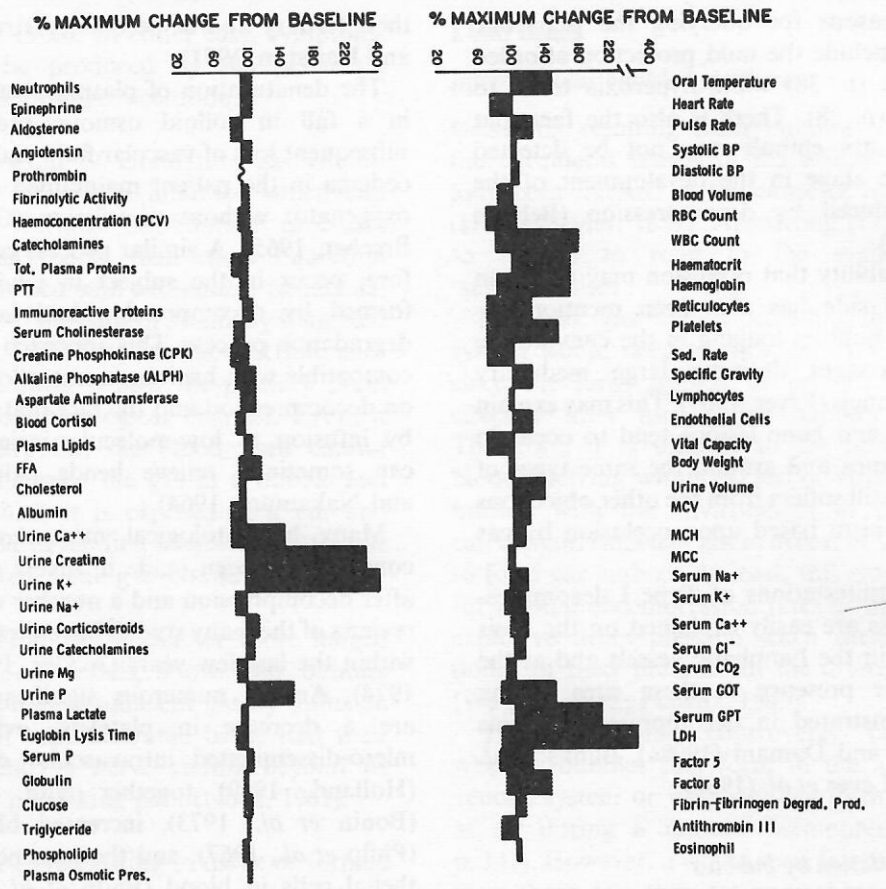

Fig. 19 A pictorial summary of the changes in many physiological and biochemical parameters of the body following exposure to compressed air. A great many reports are summarized here and conflicting results are indicated where the direction of the change is in question

as Martin and Nichols (1972) express it, 'a co-existing factor in some cases of decompression sickness'. While these observations offer strong implications that haematological factors are involved in the overall aetiology of decompression sickness, they do not prove that such factors affect the incidence and, hence, that they need to be considered in prescribing preventive measures—at least, for limb bends. Two pieces of evidence which do so indicate are the administration of an anticoagulant (heparin) which tends to protect rats (Philp, 1964) and act as a useful adjunct in therapy (Barthélemy, 1963); while elevated serotonin levels tend to increase the susceptibility of the individual (Philp *et al.*, 1971; Ross, 1976).

For those unfamiliar with the very complex processes involved in wound healing, a delightfully simple introduction has been written by Burton (1968). However, it may be said that platelets play a key role in the overall clotting mechanism and their release of serotonin is essential to the whole process. On the other hand, heparin is a powerful anticoagulant; although Philp (1964) has attributed its protective action more to its lipaemia-clearing activity. Both heparin and serotonin are physiologically active substances, so it must be borne in mind that they could be acting elsewhere on the system. For instance, serotonin is vasoactive and is believed to sensitize tissue to pain and may, therefore, reduce the threshold

for limb bends to be induced by another primary mechanism such as the mechanical approaches to be described later.

The concept that bends-pain is due to ischaemia induced by infarction caused, in turn, by blood denaturation initiated by intravascular bubbles certainly avoids many of the objections previously raised to its direct induction by gas emboli alone.

However, it would still appear incompatible with the other points, viz:

(a) the absence of a bends-like pain in other clinical situations where sludging occurs;
(b) the dissimilarity of the nature of the pain with that of known blood-flow debt;
(c) the indication that hypoxia protects against decompression sickness (p. 38), while hyperoxia potentiates;
(d) the ability to reverse pain so rapidly upon recompression.

In mitigation on this last vital point, it must be stated that direct observation of the vascular bed indicates partial restitution of the microcirculation within ten minutes or so of extensive recompression (Wells, 1976); although it does not restore the full flow pattern observed prior to decompression (see fig. 16).

The apparently marginal effects of agents specifically selected for their influence on the blood coagulation processes, suggest that haematological factors probably do not make the major contribution towards inducing limb bends but may play a prime role in other categories of decompression sickness to be discussed later.

Mechanical approaches

Cavitation between the articular surfaces of the joint capsule itself has been proposed as the source of decompression sickness (Matthews, (1939) with its possible initiation by tribonucleation (Ikels, 1970) and potentiation by other mechanical stresses on the joint (Vann and Clark, 1975). However, gas injected into the joint capsule, or occurring in such sites in the natural course of several disease conditions, does not cause a bends-like pain. The 'popping' of joints does not cause this pain even though these noises are fairly certain to result from cavitation by separation of the articular surfaces (Bradley and Vorosmarti, 1974). Moreover, large amounts of gas formed within the knee joint-space by aerial decompression (and confirmed radiographically) does not produce bends pain (Fryer, 1969). This supports the earlier conclusions of Evelyn (1941), Webb *et al.* (1944) and Bromley and Harvey (1944) whose X-ray studies have shown large volumes of gas in painless joints—a condition termed aeroarthrosis by Fryer and Roxburgh (1966). Further it would appear that any foreign material must be much less compliant than gas to penetrate the articular surfaces to the extent of stimulating nerve endings, requiring something with the hardness of sodium ureate crystals as in gout—and even this pain is quite unlike the bends. Hence the source of pain should be sought around the joint rather than within it.

A more likely mechanism is based upon the observations of Inman and Saunders (1944). They found that they could induce a bends-like pain by local injection of Ringer's solution into various connective tissues. However, it was not the volume of injected fluid which determined whether pain occurred or not but the *injection pressure*—which displayed a remarkably well defined threshold for both onset and relief in a given individual. This threshold for tissue pressure differential can vary from 35 cm (w.g.) down to 15 cm (w.g.) in 'tight' tissues (Saunders and Inman, 1943). The tissues investigated in this way included ligament, tendon and fascia.

In this way the critical condition for the onset of limb bends is conducive to mathematical description by the very simple equation stating that pain will occur if

$$\delta_f + \delta_g > \delta_t \simeq 11\text{–}26 \text{ mm Hg} \qquad (7)$$

where δ_f is the pressure differential induced by fluid imbalance, δ_g is that contributed by any gas phase attempting to push tissue aside and δ_t is the threshold known to be of the order of 15–35 cm (w.g.) (11–26 mm Hg) for tissues likely to be the site of bends (p. 59).

Fluid shifts represented by δ_f could be contributed by the effects of trauma, blood denaturation, gas-induced osmosis or the gas phase itself. Ferris and Engel (1951) elucidate the mechanisms whereby the mechanical distortion of tissue by bubbles may induce traumatic effects which cause secondary vascular reactions in either contiguous or distal sites.

Assessment of deformation concept

This very simple, yet readily quantifiable, mechanical concept has the great advantage of explaining the almost instantaneous reversal of pain with recompression of most cases of Type I decompression sickness. It simply involves compression of the bubble or locally congregated gas separated from solution in accordance with Boyle's Law, that is:

$$\delta_g = K(v/V) \qquad (8)$$

where v is the volume of gas separated from a tissue volume (V) and K is the bulk modulus of the tissue in attempting to resist expansion.

The occasional cases which do not respond to recompression (decrease in v), or do so more slowly, probably represent the situation where fluid pressure differential, i.e. δ_f alone, exceeds the threshold value δ_t.

The feature of limb bends least conducive to interpretation by this simple mechanical model is the occasional relief of pain afforded by intravenous infusion of low-molecular-weight dextran (p. 232). However, if the bubble were located in an extravascular site, it is simple to envisage how the withdrawal of fluid ($\delta_f \downarrow$) could reverse the build-up of pressure due to any local fluid accumulation or even reduce the fluid present to a subnormal level to help accommodate the separated gas. Algebraically (Equation 7), this would amount to reducing δ_f to allow for a rise in δ_g which would otherwise exceed δ_t.

The feature which really favours this hypothesis over others is the ability to relieve bends by *local* recompression of the limb in pain—often by applying very small pressures of the same order of magnitude as quoted in Equation 7. These studies include local immersion in water (Fraser and Waters, 1942), or in mercury (Webb *et al.*, 1944) and use of various cuffs including a rubber bladder over a leg (Pask, 1942), sphygmomanometer cuffs (Anthony *et al.*, 1943; Lansing, 1944) and a particular type of flying suit (Fryer, 1966). This phenomenon is particularly difficult to interpret by any mechanism which does not postulate a critical degree of gas accumulation—as the gas phase. Moreover, the effects of humoral factors are easily explained by their sensitizing nerve endings; thus serotonin release would decrease the pain threshold (δ_t).

However, it leads to the next question concerning the point at which the mechanical stress induced by this gas needs to act in order to induce limb bends.

Site of limb bends

The discussion in the previous section has shown that the mechanical concept can offer a particularly plausible interpretation of the major features of limb bends provided the gas causing tissue deformation is either extravascular or is lodged in the micro-circulation to become effectively so. Then the question is: at what point in the nervous system does this local mechanical stress act in inducing pain? Does it act in bending a nerve ending by pressure applied on a nerve from outside or from within the nervous system itself—either in the nerve fibre, at a synapse or at some higher point within the brain? Pathological examination of sacrificed animals often shows extensive fenestration of nerve fibres—particularly of the myelin sheaths (Gersh and Hawkinson, 1944).

Bubbles acting on nerve fibres and higher nerve centres may well account for Type II symptoms (as discussed later) but limb bends appear to arise from an essentially *local* phenomenon. This is fairly well established on the basis of the effects of local analgesics and local compression in relieving pain—as discussed above.

It was thought at one time that there could be referred pain or involvement of some higher centre in the nervous system when a Royal Navy diver claimed to be experiencing bends

in his phantom limb—amputated above the elbow. However, closer interrogation revealed that he sometimes felt the same pain on days when he had not been diving (Workman, 1969).

Thus the concept of extravascular gas bending a nerve-ending beyond its pain-provoking threshold, possibly assisted by fluid shifts, is compatible with all of the qualitative features of limb bends. To model this system for quantitative analysis, it is then desirable, although not essential, to know the tissue type because this could provide some tissue dimensions and values for any other fundamental parameters which might be needed.

Tissue type

The reader might be surprised that, in comparing possible mechanisms, so little attention has been paid to the pathological studies. The great problem of interpreting such data is that many bubbles may be seen in animals but without any indication as to which, if any, could be responsible for limb bends. This frustration has been aptly described by Haymaker (1957) who, from his most comprehensive review of pathological approaches, admits that 'from this vast mass of material, nothing really pertinent to establishing a model or mechanism can be extracted'. While he emphasizes the occurrence of bubbles, perhaps their absence is more significant.

For all but extreme or explosive decompressions, bubbles are very seldom observed in heart, liver and skeletal muscle, suggesting that these organs should be eliminated from the list of possible tissues. Most gas is seen in fatty tissues, probably on account of the five-fold higher solubility of nitrogen in lipid than in water. However, adipose tissue has very few nerve-endings, if any, to sense the tissue deformation which is, therefore, unlikely to give pain. On the other hand, the formation of large volumes of extravascular gas could lead to vascular haemorrhage depositing both bubbles (Hill, 1912; Gersh and Hawkinson, 1944) and fat (Haymaker, 1957; Rait, 1959) into the circulation. In this connection it is interesting that both gas and lipid emboli have been found in blood after decompression (Shim *et al.*, 1967). In small animals sacrificed after decompression from an exposure of 60 min at 8 ATA on air, much gas has been seen in fatty cells, disrupting them and filling the adjacent blood vessels with columns of bubbles (Hill, 1912). The presence of endothelial cells in the circulation (Philp, 1972) could also be construed as supporting the concept that bubbles found in the circulation are derived from extravascular sites—probably from fatty cells since Philp also finds elevated blood lipids. This interpretation of the findings indicates that it is not important to pay much attention to lipid tissues in assessing the imminence of limb bends but it does leave the problem of what the cumulative effect of the repetitive release of fat emboli might be (p. 200), or their release in massive numbers by a decompression far in excess of the limits for marginal symptoms. In this connection it is interesting to cite studies on small animals in which limb bends cannot be detected but which go on to use death or recovery as the end-point. Lever *et al.* (1971a) have shown a correlation between the incidence of these severe manifestations of decompression and the lipid solubility of the inert gas (see also p. 193).

Returning to the subject of limb bends, less gas would need to separate from solution in order to exceed the critical threshold in less compliant tissues. In quantitative terms, this can be appreciated from the elimination of δ_g from Equations 7 and 8, when bends can occur if

$$v/V > (\delta_t - \delta_f)/K \qquad (9)$$

i.e. a smaller gas volume (v) is required for a tissue with a higher elastic modulus of expansion (K).

Again the various connective tissues suggest themselves as likely candidates. Moreover, critical mechanical thresholds (δ_t) have already been demonstrated experimentally in ligament, tendon and fascia (Saunders and Inman, 1943). Other factors favouring such sites include:

(1) All have a large number of nerve-endings,

especially tendon. (Everyone knows that an injured tendon can be particularly painful.)

(2) These tissues are all in close apposition to the locomotor system (p. 32), i.e. *around* joints.

(3) The nature of the pain from tendon which has been described by Stilwell (1957) as 'often poorly localized and referred distally, and its quality stated to be variably sharp and immediate, or else deep, unpleasant and burning, or boring, i.e. similar to painful sensation elicited from other deep tissues'. This summary compiled from many studies of tendon would also seem to offer a good description of limb bends (p. 32).

(4) The 20–30% increase in inert gas uptake calculated from the increased susceptibility to limb bends with heavy exercise (p. 46) would seem compatible with the anticipated increase in blood perfusion or vasodilatation in the tendon, ligament or fascia adjacent to the muscle being used.

(5) The cells of these connective tissues are arranged as fibres or in planes, so that it is not difficult to envisage how massage might shift gas to an adjacent site as it appears to do in some cases of bends pain.

(6) Connective tissues are predominantly aqueous and yet contain invested fat cells whose propensity is probably a reflection of total body fat and hence obesity (see also p. 41).

(7) Gersh *et al.* (1944) have compared the incidence of decompression sickness in guinea pigs with the fat content of some of their various tissues, finding a positive correlation in the case of tendon.

(8) Calculation of the modulus (K in Equation 9) from the known value of δ_t (p. 57) and those estimated for (v/V) from diving data gives a value for K very close to values determined by direct measurement on tendon (p. 253).

(9) Values calculated for (a) the plastic *versus* the elastic component of tissue resistance to deformation and (b) the half-time for passive relaxation calculated from acclimatization of caisson workers (p. 40) are both within 10% of those measured in human tendon (Hills, 1969c).

(10) The increase in susceptibility to bends with age is consistent with increases in the elastic modulus, i.e. K in Equation 9 increases with age such that less gas (v) is needed for the pain threshold (δ_t) to be exceeded.

In conclusion, although the critical tissue responsible for limb bends cannot be positively identified anatomically, it is most likely one of the 'tight' connective tissues—probably tendon.

Type II Decompression Sickness

Mechanism

Traditionally, damage to the central nervous system caused by decompression has been attributed to occlusion of the systemic arterial circulation by gas emboli (Bert, 1878; Boycott *et al.*, 1908). This interpretation for neurological manifestations does not provoke the same objections as it does when put forward as the possible mechanism for limb bends since:

(a) it involves a totally different set of symptoms more compatible with a process involving ischaemia;

(b) while Type II symptoms can be relieved by recompression, a larger proportion of cases fail to respond and most are not reversed as readily as limb bends (p. 229).

However, there do remain two outstanding

questions which need careful consideration before we can accept ischaemia, due to arterial occlusion by bubbles, as the critical insult.

(1) How can decompression produce *arterial* gas emboli?
(2) Do known arterial gas emboli, i.e. those unquestionably formed by air injection into arteries, produce the same manifestations as decompression?

Taking the second question as the least controversial, this requires a comparison of Type II decompression sickness with symptoms unequivocally caused by air emboli, i.e. due to unambiguous air embolism in the conventional use of this term.

Air embolism

Gas may be introduced into the circulation iatrogenically or as a result of pulmonary barotrauma (p. 66) or a change in the solubility of gas already dissolved in blood and tissues. The latter can arise from the warming of tissue following surgical hypothermia (Brierley, 1963). However, this will not be considered here since these bubbles also form essentially by a gaseous cavitation mechanism, so that their formation is therefore open to some of the same uncertainties as apply to those presumed to be formed by decompression.

On the other hand there is little doubt that lung-rupture due to inadvertent closure of the glottis during rapid decompression introduces air into arterial blood. Accidents occurring during submarine escape training (Gillen, 1968) therefore offer a particularly meaningful comparison, since air emboli in these cases occur in the absence of any significant degree of potential tissue supersaturation. For this reason it is interesting that the clinical symptoms were essentially those associated with insufficient cerebral blood flow (Ingvar *et al.*, 1973). Gillen describes these as characterized by a sudden loss of consciousness on reaching the surface, sometimes without warning but often preceded by dizziness, faintness or scotomata. Convulsions may occur either preceding or following loss of consciousness, while focal signs are common and may be the only symptoms.

A similar spectrum of symptoms has been described in surgical cases complicated by cerebral air embolism (Durant *et al.*, 1949; Brierley, 1963) although the complications and clinical course may be much more insidious (Sloan *et al.*, 1962). In experimental animals symptoms are more difficult to evaluate but neurological observations are consistent with the acute changes seen in humans (Fries *et al.*, 1957; Simms *et al.*, 1971).

Tolerance to intravascular air

Accidents occurring during general surgical or neurosurgical procedures usually result in air entering the venous rather than the arterial system; Chan and Yang (1969) have reviewed the variety of clinical situations predisposing towards air embolism. However, open-heart surgery is particularly prone to arterial air embolism because microscopic bubbles become entrained in blood circulating through the extracorporeal oxygenator. Using ultrasonic detection devices, Kessler and Patterson (1970) estimate that, *in vitro*, such systems regularly produce 500–15,000 suspended 'particles' of diameters ranging from 50 to 150 μm. At least a fair proportion of these 'particles' must be bubbles which have been identified by microscope in blood emerging from oxygenators (Selman *et al.*, 1967). This implies that either the body has quite a remarkable tolerance for small bubbles or that surgeons are most reluctant to diagnose air embolism in post-operative patients.

More impressive, perhaps, was the use of an ultrasonic technique to monitor bubbles in the common carotid artery of a patient during actual open-heart surgery (Spencer *et al.*, 1969). Bubble signals were detected sporadically at rates of up to 160 min^{-1} 'showers' being heard when cardiac function was restored. However, the patient subsequently showed no overt neurological symptoms.

Greater tolerance to intra-arterial air in the form of such microscopic bubbles has been demonstrated in guinea pigs (Grulke and Hills, 1976). They can survive two to three

times the volume of air introduced into the common carotid sinus as carefully calibrated microbubbles selected over the range 50–120 μm diameter compared with air injected as a bolus. However, most experimental studies have employed bolus injection with particular emphasis on determining the lethal air dose and the target organ. Injection of air into the femoral veins has shown that dogs can tolerate boluses of 100 ml of air repeated every 5–10 min up to a total of one litre (Durant *et al.*, 1947). Death eventually resulted from obstruction of the pulmonary circulation.

In the *arterial* system, irreversible changes can be produced by a much smaller bolus of air. Tolerance is naturally dependent upon the rate and site of injection, the gas composition and the position of the animal. Death from coronary embolism resulted when as little as 0·5 ml/kg of air was injected into the pulmonary veins of dogs (Van Allen *et al.*, 1929; Kent and Blades, 1942). Larger volumes were tolerated when the animal's body was tipped head downwards because air was then trapped in the left ventricle.

Experimental cerebral air embolism

Injection of air into the common carotid artery of dogs (0.25 ml/kg) produced marked neurological changes including convulsions and loss of consciousness (Geoghegan and Lam, 1953), while doses of 1–2 ml/kg resulted in rapid deterioration and death (Gomes *et al.*, 1973). Much larger doses were tolerated when the air was injected into the ascending aorta. Fries *et al.* (1957) found that slow injections produced the same mortality rate but produced only minor physiological changes.

Physiological changes

Physiological parameters showed remarkably little change when quite large volumes of air (1 ml/kg) were injected as microbubbles (diameter < 100 μm) into the common carotid artery of guinea pigs (Grulke, 1975; Grulke and Hills, 1976). Changes were also quite minor when the air was injected as a bolus. Heart-rate was generally unaffected but there was a brief period, 10–15 sec after injection, in which there was a rise in blood pressure, a slightly widened pulse pressure and tachypnoea followed by prolonged apnoea and return of blood pressure to normal—all within three minutes. These findings are essentially the same as those reported on dogs by Fries *et al.* (1957) using bolus injections alone. This large tolerance of the gross physiological parameters to arterial air emboli would seem compatible with the course of Type II decompression sickness.

Looking specifically at the brain, a total arrest of isotope clearance is observed acutely in primates following embolization (Meldrum *et al.*, 1971). Electroencephalographic (EEG) records show both acute and late changes with about half of the baboons showing bilateral 'silence' persisting for 4–80 sec after a short latency period. Complete return to pre-embolism patterns took one to three hours. The remaining animals in this study showed no EEG changes even though simultaneous isotope clearance techniques indicated marked alternations in cerebral blood flow in all cases.

Late EEG changes begin 1–12 hours after embolization and indicate irritative foci, predominantly in the boundary zone regions, which sometimes progress to status epilepticus (Naquet, 1966). This is particularly interesting because convulsions can be induced by both decompression and exposure to high partial pressures of oxygen and raises the possibility of synergistic action of high P_{O_2} and decompression. The writer has found some evidence to this effect in goats exposed to 200 fsw on air for six hours. EEG abnormalities have also been observed in men after submarine escape training, sometimes when there are no overt neurological symptoms (Ingvar *et al.*, 1973).

The foci of electrical activity have been correlated with neuropathological changes in the same areas.

Pathology of cerebral air embolism

The gross appearance of the brain following an acute surgical death due to air embolism is striking, according to Chase (1934). Long columns of air were seen in branches of the

pial arteries extending into the cortical convolutions, predominantly in the frontal and parietal areas. Similar columns of air separated by fluid blood were dispersed more proximally throughout the anterior and middle cerebral artery distributions and the Circle of Willis. The vessel segments containing air appeared to be locally distended. No gas was seen in the meningeal veins or venous sinuses but the venous system was engorged with blood. Diffuse, bilateral, subarachnoid haemorrhages were noted in the frontal and parietal regions.

Neuropathological findings in patients dying within several hours to several days following open-heart surgery have been described by Brierley (1963, 1967). Gross examination of the brain revealed irregular areas of discolouration, some petechiae, occasional subcortical haemorrhages, and subarachnoid or subdural haemorrhage in a few cases. Microscopically, the discoloured areas corresponded to focal perivascular regions or larger irregular geographical lesions in which ischaemic cell change and glial proliferation was evident. These changes were felt to be consistent with air emboli in many cases. More diffuse neuronal loss and gliosis was attributed to hypotension.

Experimental cerebral air embolism in dogs given air injections via the carotid artery produced similar histological changes of neurotic foci with glial proliferation (Benjamin *et al.*, 1957). In studies by Fries *et al.* (1957), it was noted that air remained in the pial arteries in all animals examined up to 48 hours following air injection. Acute perivascular haemorrhage was evident and cortical atrophy was observed in dogs which survived for several days. Perivascular haemorrhage following air embolism has been found to occur predominantly in the vicinity of capillaries and venules (Chase, 1934).

Fluorescein injections into the cerebral circulation following air embolization revealed impaired perfusion which was limited to the grey matter and most noticeable at the boundary of the major artery distributions in the frontoparietal region (Fries *et al.*, 1957). In another study where carotid air injections in baboons were used to demonstrate early pathological changes (Brierley *et al.*, 1970), ischaemic cell damage consisting of cell shrinkage, hyperchromasia and swelling of the mitochondria, was seen predominantly in the same boundary regions or 'watershed zones' between the major artery territories.

The predominant pathological changes are therefore early perivascular haemorrhagic events and ischaemic damage or frank necrosis in affected tissue areas which have time to respond. Since the air formations in pial arteries appear to be stable for periods of many hours, it is significant that the boundary zones (or collateral regions) of the vascular bed are most susceptible to perfusion deficits and tissue injury (Grulke, 1975).

Implications

The foregoing account is just a brief outline of the major types of pathological change to be found in the brain following unambiguous arterial air embolism. It leaves little doubt that the clinical symptoms coincide with some of the rarer yet more serious forms of decompression sickness.

The most disquieting aspect to this writer was the apparently normal behaviour of a 'diving' goat which, when sacrificed several weeks after its last exposure, was shown to have a brain in which pathological examination showed over one half to be effectively nonfunctional. The impression of personality changes in certain professional divers gives cause for wondering whether the brain is really so tolerant to large numbers of microbubbles as the gross physiological examination of patients and animals would indicate. Are there subtle cumulative changes and, if so, are such 'punch-drunk' divers then less tolerant to an acute insult? How would such chronic effects influence the ability of anyone needed to exert extreme mental effort, such as a mathematician who takes up SCUBA diving as a recreation or an engineer who regularly visits the workface in pressurized tunnel construction? It is easy to ask questions to which there are no obvious answers at this time and, until there are, it would seem unwise to suggest

any changes in protocol based on mere impression.

Target organ for air emboli

The preceding discussion of Type II decompression sickness has centred around the brain because it constitutes 98% of the central nervous system (Truex and Carpenter, 1969). Moreover, it receives some 75–85 times more blood flow than the spinal cord (Kety, 1960) and should therefore receive proportionately more arterial emboli. However, spinal cord involvement is dominant in Type II decompression sickness (about 77%, p. 32).

Such reasoning has led Hallenbeck *et al.* (1975) to question the assumption that spinal cord lesions are associated with arterial embolization. They point out that in clinical disorders involving known systemic embolization, such as subacute bacterial endocarditis, fat embolism, or the presence of a thrombus in the left atrium, the brain is a major target organ. Spinal cord involvement is of the order of 0·4% in these diseases (Blackwood, 1958). Indeed, it is only listed by neurologists as a target organ for circulating arterial emboli on account of their assumed role in decompression accidents.

Hallenbeck *et al.* produce pathological evidence in dogs to support their hypothesis that spinal cord lesions arise by obstruction of the epidural vertebral venous system. This is in basic agreement with the suggestion of Haymaker (1957) that gaseous embolism could embarrass the venous drainage from the spinal cord. Attractive as this hypothesis may sound in attempting to explain the predominance of spinal cord lesions, it is still difficult to see why these are restricted to the white matter; one would have thought that venous obstruction at the level of the epidural vertebral system would have affected grey matter also. However, the fact that perfusion is impaired primarily in the grey matter in brain is suggestive of a different mechanism in spinal cord compared with brain. There is also some query whether the lesions in the white matter of the cord are consistent with the symptoms observed.

Another point also raised recently by Behnke (comment at 6th Symposium, Underwater Physiology) in this connection is the old question: why do aviators not show more spinal cord involvement? If the *absolute* pressure change is a factor, then perhaps the gas remaining in solution is exerting an effect on the processes leading to a spinal cord 'hit', along the lines that have already been outlined for the possible influence on limb bends (p. 49).

Ischaemic versus mechanical mediation

It is possible that a mechanical process similar to those discussed for Type I decompression sickness also applies to the spinal cord. Whereas arterial embolization implies ischaemic mediation of the primary insult, venous obstruction could also become manifest through the build-up of CSF pressure. Indeed, relief of CSF pressure by lumbar puncture was considered by Halbouty and Long (1953) to be an important part of therapies which they administered for these forms of decompression sickness.

Returning to the question of the mechanism whereby bubbles can induce dysfunction of the nervous system within the cord, Elliott (1969) cites the 'oxygen bends' of Donald (1955) as cases where Type II decompression sickness occurred under conditions where there should be a surfeit of oxygen rather than the hypoxia otherwise associated with deficient blood flow. Moreover, a physico-chemical analysis of Donald's data (Hills, 1966) showed that the inert gas would still predominate in a bubble formed in a venous 'pool', again suggesting a mechanical rather than an ischaemic insult. On the other hand, occlusion of a vessel by a bubble can still cause ischaemia even though that bubble may contain pure oxygen.

Even so, this concept has a particular appeal to any designer of decompression tables since it would mean that one set of equations should be sufficient to avoid both limb bends and spinal cord lesions; but does the pathological evidence support this?

Spinal cord pathology

The concept of loss of neurone function due to

distortion by a bubble expanding at its site of formation, the 'autochthonous' bubble, is not new (Behnke and Shaw, 1937). Boycott and Damant (1908) found extravascular bubbles in the CNS but still considered the primary cause of symptoms to be arterial gas embolism. In the peripheral nerves, at least, these bubbles are confined to the myelin sheath (Gersh *et al.*, 1945). However, since this is predominantly lipid, it raises the questions of whether to base preventive measures on an aqueous or lipid tissue; or under what conditions one will supersede the other as the more likely to precipitate symptoms. This point is better pursued later from a quantitative standpoint (see p. 192).

For detailed accounts of the pathology of spinal cord lesions, the reader is advised to consult the comprehensive reviews of Haymaker (1957) and Rozsahegyi (1959).

Arterial occlusion

Before turning from the conventional concept of arterial occlusion to any other in explaining spinal cord 'hits', one simple fact must be remembered. The vascular systems in brain and spinal cord are different, particularly with regard to the collateral circulation available to each. In addition, by simple statistical reasoning, it is potentially several orders of magnitude more dangerous to send two bubbles to a system with two arteries than to send twenty bubbles to a system with twenty arteries all interconnected at more distal levels of bifurcation. A much reduced blood flow supplied collaterally can maintain tissue in a viable condition but no blood flow must result in tissue damage.

There is no purpose, however, in pursuing any hypothesis based upon arterial occlusion if arterial emboli are not produced by decompression.

Arterial gas emboli

It is very rare to find bubbles in the arterial systems of animals following any reasonable decompression procedure. They tend to be observed following explosive decompression or where the animals had been subjected to gross surgical interference (Gersh and Catchpole, 1951; Blinks *et al.*, 1951). On this last point, Fryer (1969) points out the marked contrast between reports of bubbles seen in unanaesthetized intact animals and those subject to operative interference before, during or immediately after decompression. This emphasizes the need for non-invasive techniques in bubble detection such as those described later in discussing the quantitative limits for the onset of cavitation in tissue and venous blood (p. 150).

It is very simple to interpret the need for explosive decompression in forming arterial bubbles by reasoning that blood leaving the lungs needs to be rapidly decompressed in order to be supersaturated within the 20 sec or so that it takes to reach the systemic microcirculation. Leaving the left ventricle with an excess hydrostatic pressure averaging 120 mm Hg and unsaturated because of the venous admixture of up to 20 mm Hg, supersaturation of arterial blood would occur if the ascent rate exceeded $(120 + 20)/20 = 7$ mm Hg/sec $= 18{\cdot}2$ fsw/min or roughly 20 feet of sea water per min. However, as discussed later in connection with the mechanism of cavitation (p. 139), it is difficult to form bubbles in blood—even with appreciable degrees of supersaturation.

It does raise a query with regard to free ascent in the ocean and submarine escape in particular, where ascent rates may be an order of magnitude greater than this conservative no-supersaturation figure of 20 fsw/min. Gaseous cavitation is dismissed on the grounds that the escaping submariner is under pressure for much too short a period for any tissue to take up enough gas to be released as bubbles. However, in this case, the source of potential bubble-forming gas is the *lungs* and not the systemic tissues. It does offer a possible interpretation for the man who suffers from air embolism following an ascent in the training tower yet claims not to have closed his glottis. It also queries the use of oxygen-breathing during these ascents (Moses, 1964) since, although oxygen is much easier to resolve in

the brain than air if embolized (p. 230), there is no longer any unsaturation of efferent blood imparted by ventilation: perfusion inequalities in the lung. Thus the inspiration of pure oxygen would increase the supersaturation of arterial blood by gases and hence the likelihood of arterial emboli.

Returning to the observation of arterial bubbles following explosive decompression, it must be remembered that these conditions are particularly conducive to classical air embolism. Even an 'air cyst' could offer sufficient resistance to the instantaneous expansion of distally occluded air to cause local rupture of the pulmonary membrane (Walder, 1963). However, normal decompression rates to the first stop, or between stops, are much slower than any which could be considered 'explosive'. Hence it is necessary to consider whether any arterial bubbles could have a venous origin under non-exceptional conditions, which immediately raises the following question.

The lungs: how effective as a bubble trap?

Pulmonary capillaries range in size from 4–15 μm so, at first sight, it would appear that no circulating particles of greater diameter would be permitted to pass from the pulmonary artery to the pulmonary vein. If larger bubbles were to deform in trying to 'squeeze through', then there could be a large frictional drag between the gas and the hydrophobic endothelial lining of the capillary wall to which it would tend to adhere. In fact, using a value of surface tension for blood of 50 dynes/cm, Walder (1948) has calculated that, for any gas to pass, the perfusion pressure needs to be at least 150 mm Hg—a value far in excess of normal right ventricular pressure. Such calculations do not, however, allow for any lung surfactant which is present within the alveolus anyway (Clements, 1957) or which could be attracted into it by air to help clear the obstruction. It also assumes a contact angle of zero, another question in doubt in the presence of lung surfactant (Hills and Ng, 1974). Even after allowing for these factors, it is still difficult to envisage the normal peak hydrostatic pressure of pulmonary arterial blood (20 mm Hg) as adequate to clear pulmonary emboli exceeding 10–15 μm in diameter.

This suggests that any bubbles entering the arterial system would need to do so by bypassing the pulmonary capillary bed and immediately raises the question of whether such shunts exist. Oxygenation studies which can differentiate between true shunt and partial venous admixture due to ventilation/perfusion inequalities in the lung (Cohen *et al.*, 1971) confirm a direct flow of blood from venous to arterial systems which bypasses any vessels capable of transferring oxygen from the air.

Morphologic basis for shunt

Anatomic evidence shows that arterial blood can receive direct venous admixture from Thebesian veins draining from the myocardium into the left side of the heart and from the bronchial circulation via the pulmonary veins. There is also the so-called Batson plexus of communicating veins which allow emboli, infection and thrombi to pass between the abdominal and pelvic veins, the spino-vertebral veins and the azygos system. Arterio-venous connections through fistulae can be regarded as abnormal, along with the large right to left shunts found in patients with atrial and ventricular septal defects and who develop pulmonary hypertension, while direct venous admixture is likely to increase with atelectasis (Stekhoven and Kreuzer, 1967). However, in normal humans, the total shunt is probably no more than two per cent of total cardiac output.

Unfortunately, such estimates derived from functional physiological studies give no indication of the calibre of the vessels bypassing the pulmonary capillary bed, so experimental observations of arterial blood following particle deposition in the venous system must be considered.

Experimental observations

There is a large literature concerning the lung as a filter which leaves little doubt that its effectiveness decreases with decrease in particle size. The cut-off diameter for rigid emboli is around 15 μm for both barium sulphate

granules (Colebatch, 1964), glass beads in rabbits and rats (Gordon *et al.*, 1953) and polystyrene spheres in dogs (Ring *et al.*, 1961). However, 5 min after their introduction, spheres of up to 80 μm diameter appeared in blood collected from the carotid arteries but less than 1% of particles larger than 15 μm still seemed to find their way across the lungs. Much larger (500 μm) cut-off diameters have been claimed for human lungs (Tobin and Zariquiey, 1950) but these studies used glass beads in excised preparations perfused at pressures far in excess of the normal physiological range.

Injecting glass beads with a wide diameter spectrum into the right jugular vein of dogs, Niden and Aviado (1956) found some with diameters up to 420 μm in arterial blood. However, the proportion transmitted varied with the oxygen partial pressure inspired under normobaric conditions. Very few were recovered in arterial blood when 100% oxygen was respired, while even mild hypoxia (10% oxygen in nitrogen) gave an appreciable increase over normal air breathing. Although the cut-off diameter differs greatly from those found by other workers, it does imply that great care should be taken to avoid even mild hypoxia during decompression. While it may protect against limb bends (p. 38), it may permit bubbles to pass from venous to arterial parts of the circulation, so provoking a Type II 'hit'.

The cut-off diameters found for rigid particles need not apply to anything as compliant as a bubble; although the smaller the bubble the less readily it is deformed and the closer its physical characteristics, e.g. terminal rise velocity, approach those of a rigid sphere. Unfortunately, most studies have not employed bubbles of known diameter but have sought to detect arterial gas following a bolus injection somewhere into the venous system. This tends to 'fracture' at vessel bifurcations (Curtillet, 1939), probably resulting in a spectrum of bubble diameters. Rangel (1942) summarizes a number of cases indicating either clinical or necropsy evidence to suggest arterial gas embolism following undoubted venous air embolism. It is difficult to be sure, however, that where such evidence is ischaemia it has not been caused by hypoxia due to pulmonary occlusion such as invoked by Tureen and Divine (1936) to explain cerebral damage.

In the case of bolus injection, there are several reports of air passing from the arteries to the veins of various tissues—as already described. In lung, Villaret and Cachera (1939) found bubbles in the arteries of about one-third of their dogs following intravenous injection but no cases were observed by Marchand *et al.* (1964). These apparently conflicting results may be reconciled by the observations of Mandlebaum and King (1963) who found that gas bubbles in the pulmonary vein were much more numerous following air injection into the pulmonary artery if the lung was sufficiently overloaded, i.e. 1·5 ml/kg in one bolus. For *continuous* infusion, gas can traverse the lung for rates of 0·15 ml. kg^{-1} min^{-1} and over (Oyama and Spencer, 1971).

After infusion, into the vena cava of guinea pigs, microbubbles of diameters carefully selected and calibrated according to the method of Grulke *et al.* (1973), this author has never been able to observe arterial bubbles. This study used bubbles of diameters down to 40 μm but did not permit the infusion rate to reach the 'overload' level of the previous studies.

In most venous infusion studies where arterial 'particles' have been observed, their appearance seems to have been delayed well beyond the blood transit time. It seems as though bubble overload of the pulmonary circulation cuts off the supply of some blood-borne nutrient, metabolite or other entity necessary to maintain vasomotor tone. When the consumption of this compound by parenchymal tissue reduces its concentration to a critical level, this could produce a relaxation of the lung as a filter in a manner similar to that induced much more rapidly by hypoxia due to the more rapid depletion of tissue oxygen.

Since carbon dioxide can provide a strong stimulus for vasodilatation in most tissues, it is interesting to consider whether it could change the calibre of pulmonary vessels to the extent that it could impede the effectiveness of the lung as a bubble filter. It is possible that

elevated levels of carbon dioxide could enable venous bubbles trapped by the lung to escape into arterial blood where they could precipitate a Type II 'hit'. This serious implication of increased P_{CO_2} is currently under rigorous investigation in the writer's laboratory.

The impaired-filter explanation may also extend to the goat study described on p. 38, since the lungs of those animals had received an oxygen exposure far in excess of the limits for chronic oxygen toxicity by the time they developed spinal DCS. This implies that the oxygen-poisoned lung may admit to the arterial system the otherwise-silent bubbles commonly detected in venous blood (p. 146). This possible explanation is also compatible with unconfirmed reports of divers who have developed CNS symptoms *after* complaining of substernal pains in the chest and, particularly, when also recompressed—another factor under investigation as a release for the bubble trap (p. 230).

In conclusion, it can be stated that in the absence of hypoxia, chronic hyperoxia, hypercapnia or severe overloading, the lung is a particularly effective filter of venous bubbles, trapping those of 40 μm diameter and probably many of those down to 15 μm in diameter. These conclusions lead the writer to the opinion that *arterial* gas emboli are a rare occurrence during decompression—certainly too rare to explain limb bends—but sufficiently frequent to account for cerebral symptoms and possibly other cases of Type II decompression sickness.

Other Symptoms

The remaining categories which need individual discussion include 'the chokes', the vestibular manifestations of inadequate decompression which are becoming much more common with very deep diving and dysbaric osteonecrosis. The last of these is so complex and different from the others that it requires separate consideration (Chapter 8).

The chokes

The 'chokes' is generally regarded as a form of decompression sickness attributable to pulmonary gas embolism *per se* (Armstrong, 1939). It probably requires an appreciable number of venous bubbles to be gathered in the lung by filtration before their presence becomes manifest. Little further accumulation of venous bubbles would therefore be needed to reach the 'overload' level described in the previous section, when this alone or the resulting coughing would release some of them as arterial emboli and lead to the neurologic symptoms which can follow soon after (p. 32).

This aetiology has been challenged by Ferris and Engel (1951) on the basis that accidentally introduced intravenous air, presumably as a bolus, does not produce 'chokes'-like symptoms. But they have been produced by continuous infusion of oxygen (Sanders and Isoe, 1947).

The many studies of intravenous air embolism have been collected by Fryer (1969). From these contradictory data, there is the impression that the 'chokes' may be associated with conditions predisposing towards more bubbles rather than more gas, i.e. towards the larger number of microbubbles likely to be released by the tissue during an inadequate decompression or continuous infusion of microbubbles rather than the release of a bolus of air into the venous system as a single event. Finer dispersion would enable the same gas to reach more lung receptors. From a morphological standpoint, it would be necessary for the bubbles filtered out in the pulmonary arterial system to reach these receptors sensitive to mechanical stimulation. The regular stretch receptors found in the bronchial tree are not located that far distal for them to encounter the pulmonary circulation (Fillenz and Widdicombe, 1971) but it is likely that such bubbles would irritate J-receptors—so named as juxta-pulmonary capillary. These have many interesting properties (Paintal, 1969) but one of particular relevance here is their ability to produce a powerful reflex contraction of the adductor (constrictor) muscles of the larynx (Stransky *et al.*, 1973). This can easily induce a laryngospasm and the coughing so characteristic of the 'chokes'.

Perhaps the most direct demonstration of the involvement of venous bubbles is provided by

Nashimoto and Gotoh (1975) who show a close correlation between the incidence of 'chokes' and the presence of large numbers of small bubbles detected in the pulmonary arteries of caisson workers by a Doppler bubble detector. There would now seem little reason, however, to dispute the popular belief that the 'chokes' are a manifestation of pulmonary gas embolism.

Otologic disorders

Otologic disorders occur quite frequently in diving and compressed-air work as a whole, so it is desirable to know that any category III symptoms (p. 31) are not simply barotrauma in one of its many forms. This point has been pursued in detail by Rawlins (1959) whose arguments leave little doubt that many vestibular symptoms are, indeed, manifestations of inadequate decompression. However, before discussing these in more detail, it is as well to be aware of the range of otologic disorders in diving, these having been conveniently grouped into the following list by Farmer and Thomas (1973).

(1) Hearing disorders related to the high background noise which has been demonstrated during certain diving conditions (Summit and Reimers, 1971). These have been well described by Coles and Knight (1961) and Zannini *et al.* (1975).

(2) Injuries occurring during *compression* which can be explained on a simple mechanical basis involving rupture of the round window or cochlear membrane disruption. Since this type of injury can occur in shallow water exposures during descent (Freeman and Edmonds, 1972), it is unlikely to be a manifestation of decompression sickness and will not be discussed here but the reader pursuing this problem should consult the work of Edmonds (1973).

(3) Vestibular manifestations of inadequate decompression described earlier as category III symptoms (p. 31).

(4) Otologic injuries incurred by switching inert gases at a stable and unchanging depth. Subjects in a helium:oxygen environment experienced the sudden onset of vertigo, nausea and nystagmus on breathing a nitrogen:oxygen mix by mask—at the same pressure and inspired P_{O_2} (Sundmaker, 1974; Lambertsen, 1975). These subjects at the University of Pennsylvania also showed the same skin lesions that were found in previous studies at Duke University involving the switch of inert gas but at lower pressures (Blenkarn *et al.*, 1971). The observations are particularly interesting because each set of symptoms is typical of those described as category III decompression sickness and yet they occurred at a time when there had been *no decompression*!

Vestibular decompression sickness

A decade ago, when dives beyond 200 feet were rare, these category III manifestations were not thought to occur without other symptoms of decompression sickness. In classical descriptions of the disease, they were mentioned only in association with CNS manifestations and considered of secondary importance to lesions which were probably centrally located. However, with regular diving to 500 feet and experimental exposures to 2000 feet, vestibular symptoms are not only becoming much more common but are now occurring largely in the absence of other manifestations of decompression sickness (Edmonds, 1973). For instance, Bühlmann and Waldvogel (1967) reported that, in 211 deep dives, the only 11 cases with neurologic symptoms consisted of vertigo, nausea, vomiting and tinnitus—the classical Menière-type complex. Moreover, these occurred not only during decompression from the greatest exposure but at considerable depth, e.g. 485 and 726 feet.

Other conditions which can predispose the subject towards vestibular dysfunction or potentiate category III symptoms include:

(a) changing to air following a marginally sub-toxic exposure to oxygen (Donald, 1947) (the 'oxygen-off' effect);
(b) elevating the oxygen, where vertigo has also been listed as a symptom of pre-decompression neurologic oxygen toxicity (Edmonds, 1973);
(c) switching to fresh air following a prolonged period of breathing in an environ-

ment with elevated carbon dioxide (35 mm Hg)—Blackwood and Edmonds (1971);

(d) elevated carbon dioxide, where disorientation and nausea are features of of carbon dioxide toxicity (p. 206); although Blackwood and Edmonds failed to verify this as a cause of vertigo and nystagmus;

(e) rest following heavy exercise at depth, although this may be the same basic effect as (c);

(f) breathing fresh air following prolonged carbon monoxide inhalation, e.g. the old case of the sailor from the engine room collapsing with vertigo after rushing on deck;

(g) changing inert gases, particularly from heliox to air, as often occurs in commercial diving when transferring men from the bell to a DDC at a pressure around 120–180 fsw (p. 90).

Most of these factors, together with many others unrelated to pressure or the gaseous environment, are described in detail by Edmonds (1973). Their potentiating actions are also fairly specific to vestibular manifestations of decompression sickness and therefore indicate that not only another tissue type but another mechanism may be involved in these category III symptoms. If this were the case, then there could be a range of exposures or a phase of the decompression where this mechanism or tissue (or both) could take over as the rate-limiting factor. Hence it could be particularly significant that Hempleman (1975) finds some evidence for this 'take over' in data collected largely from the work of Barnard (1975).

Vestibular limitations upon decompression

Earlier (p. 35) it was shown how the effects of decompression *per se* could be studied, largely divorced from other complicating factors, by allowing a subject to reach steady-state (so-called 'saturation') at a pressure P_1 before being rapidly decompressed to a lower pressure which was 'titrated' in consecutive runs until the value P_2 was found for marginal safety (see fig. 11). A linear relationship between P_1 and P_2 has been found for the imminence of limb bends over the range of normal air diving (fig. 35). However, Hempleman has indicated a sharp transition in the $P_1 : P_2$ relationship occurring in the region of 300 fsw (see fig. 20) above which symptoms tend to be of the Menière type, to which reference is sometimes made as 'the eighth nerve syndrome'.

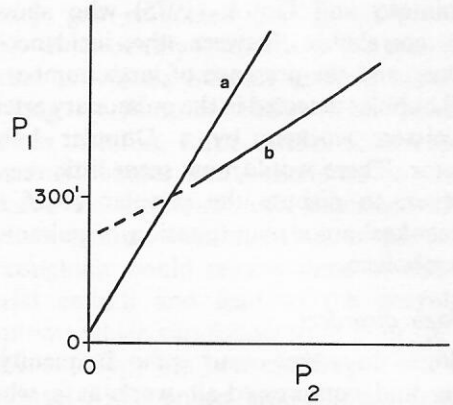

Fig. 20 The relationship between the maximum pressure needed to provoke decompression sickness (P_2) and the pressure (P_1) at which the subject attained steady state before rapid (no-stop) decompression to P_2. Limb bends are the marginal symptoms defining line (a), while line (b) indicates how vestibular symptoms tend to take over at greater depths. This line has a gradient near to unity but a large intercept on the P_1 axis (discussed p. 120). Redrawn from a slide presented by Hempleman (1975)

This indication is supported by many unconfirmed reports from commercial diving companies and from the higher incidence of category III symptoms in very deep chamber dives but interpretation of this supporting evidence is complicated by the many factors which can be varied in a staged decompression. However, this elegantly simple indication (fig. 20), together with the unique potentiating factors and the tendency for category III symptoms to occur alone, all provide good reason to invoke another tissue and possibly another mechanism in programming decompression. Avoidance of limb bends does not seem to provide automatic protection against vestibular decompression sickness at higher pressures in the same way that it is assumed to

do against Type II (CNS) symptoms. In other words, for dives in excess of a critical value of the order of 300 feet, vestibular symptoms can become manifest *before* the anticipated onset of other categories of decompression sickness. This means that different criteria must be used to programme at least that portion of the decompression in excess of this transitional depth. Once again, it is highly desirable to know the underlying mechanism.

Aetiology of category III symptoms

The gross aetiology is little understood but it is now becoming evident that lesions may occur anywhere within the vestibular pathway from the end-organ along the vestibulo-spinal tract to the cerebellar cortex (Winklemann *et al.*, 1975; Caruso *et al.*, 1977). Sometimes these are multiple, occurring in both the labyrinth and brain stem. Those in the higher centres of the brain seem to occur under the same conditions as the neurologic forms of Type II decompression sickness already described (p. 60) and are probably manifestations of cerebral air embolism.

Labyrinthine lesions are not quite so serious because, provided the brain is intact, the subject can make cerebral compensation, learning to walk or overcome most other disabilities within a few months. However, if treated soon enough by recompression, end-organ dysfunctions do not result in permanent disablement. Moreover, they are reversed so rapidly by recompression (Farmer and Thomas, 1973) that it is difficult to explain them by mechanisms involving haemorrhage into the inner ear, vascular spasms or thrombosis with subsequent ischaemia. End-organ dysfunctions are of two basic types: cochlear (involving hearing loss) and vestibular; but the two tend not to occur simultaneously (Edmonds, 1973), although Rubenstein and Summitt (1971) did report that out of 16 cases of category III decompression sickness, three had both vertigo and hearing loss.

Pathological investigations do not point to any obvious mechanism, although Money (1976) and co-workers have observed a deformation and some evidence of exudate and haemorrhage arround the cupulae of the cristae ampullares in several cases of vestibular disorders induced in monkeys. McCormick (1976) has observed a bubble through the round window of a guinea pig after decompression.

Mechanisms for vestibular DCS

Edmonds (1973) has proposed the following possible mechanisms for perturbation of the vestibular mechanism by decompression in elaborating upon the original hypothesis of Keays (1909) who attributed these dysfunctions to bubbles in the labyrinthine system. The writer has added two of the mechanisms (Nos. 5 and 6) to account for no-decompression symptoms to complete the following list.

(1) Diffusion of gas across the round or oval window of the ear. The inner ear can receive gas not only by a limited vascular supply but by diffusion from perilymph which can become saturated with the gas phase in the middle ear. It can thus reach a steady-state gas content quite rapidly and so cavitate during decompression, the bubbles causing a hydrostatic pressure differential which can then account for vestibular dysfunction. However, rapid saturation by diffusion would also imply rapid desaturation during decompression.

(2) Supersaturation by counterdiffusion (Graves *et al.*, 1973) across a membrane, such as the round or oval window, resulting in bubbles at the interface between the middle and inner ear. Any supersaturation arising by gas switching will thus be superimposed upon that caused simply by the decompression. Hence this hypothesis can explain the additive nature of the effects of inert gas switching and decompression. However, for counterdiffusion supersaturation to occur, an appreciable portion of the diffusion barrier needs to be lipid (see p. 210) and it is difficult to envisage this in any organ such as the ear which is virtually fat-free.

(3) Vascular emboli: being of the end-artery type, the vascular supply to the inner ear may be vulnerable to occlusion by circulating bubbles.

(4) Impaired perfusion due to a localized collection of perilymph or endolymph. This would have difficulty in eliminating inert gas during decompression and would therefore predispose towards bubble formation. This hypothesis is plausible but is incomplete in that it omits the explanation for the fluid accumulation initiating the whole process.

(5) Supersaturation of either of these fluids (perilymph or endolymph) by counterperfusion (Hills, 1976a); this does not require the lipid bilayer needed in the counterdiffusion mechanism postulated in No. 2 and permits the bubbles to form *within* the perfused fluid (see p. 212).

(6) Gas-induced osmosis (see p. 213), any shift of fluid between endolymph (perfused with blood) and perilymph (saturated with the gas in the middle ear) could result in vestibular derangement.

No. (3) would seem unlikely since the inner ear is not generally a target organ for circulating emboli; while (2) and (5) can be regarded as adjuncts to (1) and (4) respectively to account for their inability to explain how vestibular decompression sickness can occur under isobaric conditions.

Critical assessment

The mechanisms proposed so far can therefore be effectively reduced to three:

(A) Bubbles formed by decompression of the fluids of the inner ear which had taken up gas largely by diffusion across the round or oval window and which could be supersaturated under isobaric conditions by counterdiffusion of two different inert gases—one in the middle ear and the other inspired and hence in the blood;

(B) Bubbles formed by decompression of the same fluids which had taken up gas largely from the perfusing blood and which could be supersaturated under isobaric conditions by the counterperfusion of two different inert gases;

(C) Pressure differentials caused by fluid shifts between the various compartments induced by their different gas concentrations or the different osmotic potencies of the gases in these fluids.

For gas-induced osmosis to occur, there must be a partially selective membrane capable of allowing fluid to shift at an appreciable rate under an osmotic gradient. A likely candidate is provided by the vestibular (Reissner's) membrane (fig. 21) which is the thin unicellular barrier separating perilymph (whose composition resembles that of plasma) from endolymph which reflects intracellular concentrations (see fig. 22). Hence this membrane is physiologically active with respect to ion transport and is therefore also likely to display an appreciable degree of osmotic selectivity.

Gas-induced osmosis can easily explain the tendency for vestibular symptoms to occur on switching from heliox to air during decompression when endolymph saturated with blood-borne nitrogen would 'pull' water away from perilymph saturated with the helium remaining in the middle ear. This mechanism has the great advantage that it can explain both the 'on' and the 'off' effects of the various potentiating factors such as oxygen, carbon dioxide and carbon monoxide, fluid shifts in either direction causing vestibular derangement. In this regard, it is interesting that two of the symptoms of nitrogen narcosis after a rapid compression are nausea and dizziness (p. 204); while a potent osmotic agent such as alcohol gives a positive nystagmus on uptake but negative during elimination (Money, 1976) indicative of a reversal in fluid shift. An osmotic basis is further indicated by the fact that during 'recovery', balance can be returned to normal by administering 'a little of the hair of the dog that bit you'. Moreover, the osmotic approach is compatible with the successful use of alcohol in very deep dives by Krasberg (1976). The tendency for the P_1 versus P_2 line for vestibular symptoms (fig. 20) to approach a gradient

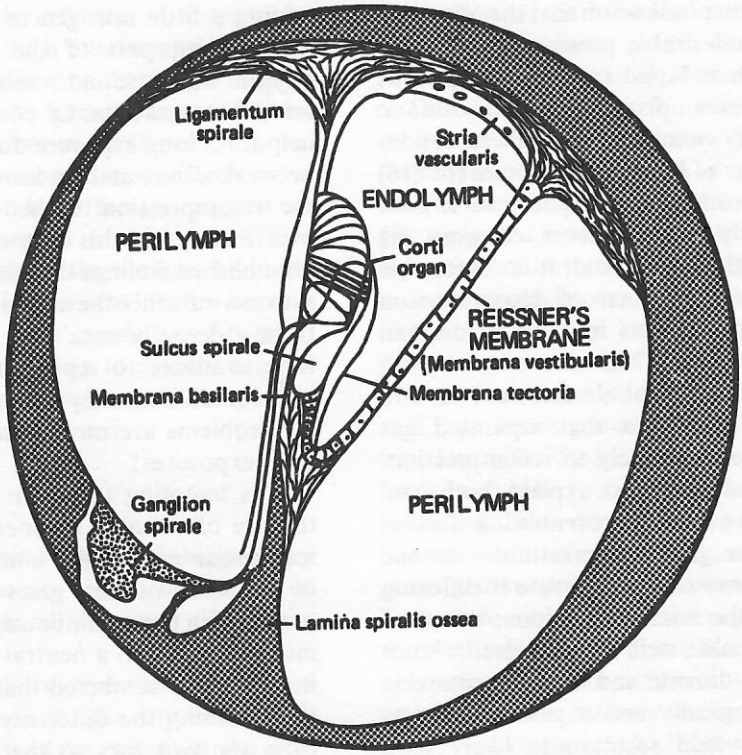

Fig. 21 A cross-section of the vestibular system showing endolymph separated from perilymph by Reissner's membrane. Redrawn from Lederer and Hollender (1951)

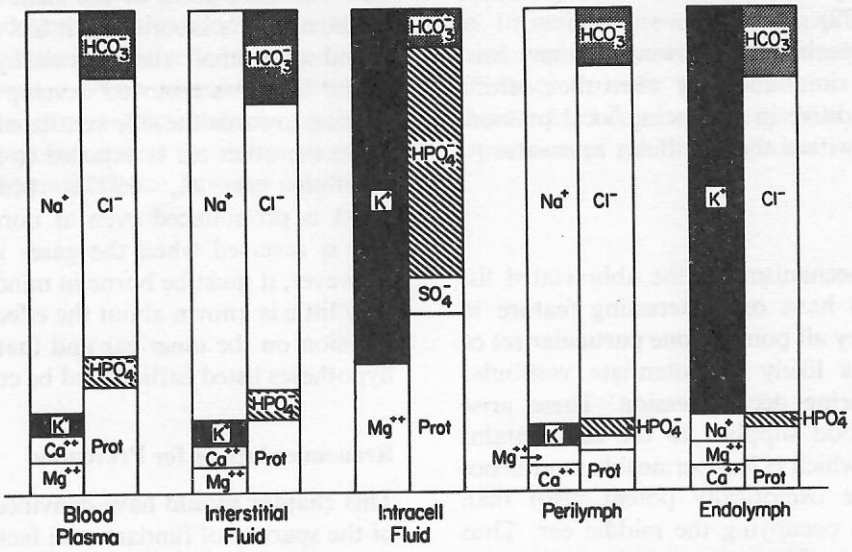

Fig. 22 Ionogram of intracellular and extracellular fluid, perilymph and endolymph of mammalia. Data from Keidel and Neff (1974)

of unity is a further indication that the offending fluid causing undesirable pressure differentials in the labyrinth is liquid rather than gaseous (p. 120). However, plausible as an osmotic mechanism may sound, it still faces fundamental questions of homeostatic forces (p. 216) and whether recompression could reverse fluid shifts as rapidly as it relieves category III symptoms. On the other hand, it is compatible with treatment of this form of decompression sickness with intravenous infusion of dextran (Youngblood *et al.*, 1975).

By comparison, the bubble theories ((A) and (B)) have the attraction that separated gas would respond immediately to recompression. However, it is difficult to explain both 'on' and 'off' effects of the potentiating factors because, if two gases supersaturate in one direction, they must undersaturate if diffusing or perfusing in the reverse directions; but other mechanisms could well be involved, since oxygen, carbon dioxide and carbon monoxide are all physiologically active gases. Counter-perfusion (B) would seem more likely than counterdiffusion (A) for inducing bubbles since not only is the ear lipid-free but it is easier to envisage gas separating from solution within a fluid compartment than at the interface within the hypothetical two-phase diffusion barrier needed before (A) can occur (compare figs. 71 and 72).

All three mechanisms, however, or any pair, could occur simultaneously when their effects would be additive in producing local pressure differentials within the vestibular apparatus.

Implications

All of the mechanisms in the abbreviated list ((A) to (C)) have one interesting feature in common; they all point to one particular set of conditions as likely to potentiate vestibular problems during decompression. These arise when the blood supplied to the ear contains an inert gas which is less permeable (and hence usually more osmotically potent also) than the inert gas occupying the middle ear. Thus some of the problems occurring on switching to air at 120–180 feet may be alleviated by adding a little nitrogen to the bottom mix or compressing part of the way on nitrogen : oxygen mixes to add more nitrogen to the middle-ear gas mix. Of course, this would not help for a long exposure during which it would be washed out and replaced by helium before the decompression reached the critical change-over to air, but this may explain some of the unpublished feelings that the mode of compression can influence the outcome of decompression from a deep 'bounce' dive. The much greater time available to replace nitrogen by helium in the middle ear may also explain why vestibular problems are more common after 'saturation' exposures!

It is tempting to go on to speculate about the use of valsalva manoeuvres to equilibrate middle-ear gas or the continuous adjustment of the blend of inert gases in a breathing mix to maintain the continuously monitored nystagmus of a diver in a neutral position. However, it must be remembered that the brain is essentially sensing the difference between the input from the two ears so that any compensating action which had a greater effect upon the wrong inner ear could worsen the situation. This indicates a simple means of testing the hypotheses ((A) to (C)) by ventilating the two middle ears of the same primate with different inert gases at the same temperature. In the author's laboratory, it has recently been found that small rhesus monkeys with their round windows removed develop a nystagmus beating towards the side ventilated with helium when the other ear is exposed to nitrous oxide (Griffiths *et al.*, 1977). Moreover, the effect is pronounced even at normal pressure and is reversed when the gases are switched. However, it must be borne in mind that, as yet, very little is known about the effects of decompression on the inner ear and that none of the hypotheses listed earlier need be correct.

Recommendations for Prevention

This chapter should have convinced the reader of the sparsity of fundamental facts with which to try to elucidate the mechanisms underlying the various manifestations of inadequate de-

compression. This is reflected in the almost total disregard for such fundamental aspects in the formulation of the mathematical expressions actually used to prescribe safe decompression schedules (Chapter 5). However, rather than abandon fundamental reasoning because the accumulation of basic facts is lagging so far behind the commercial need for deep diving tables, reasonable conclusions might be made on the basis of the data selected for its bearing upon deriving the true model(s). At least, since it would be foolhardy to present conclusions in such controversial areas, an opinion is the best that can be expected.

An overall opinion

The least controversial aspect is the primary event which appears to be the separation of gas from solution in all instances of decompression sickness.

The critical insult is probably mechanical in nature, arising from the autochthonous bubble pressing on a nerve ending in the case of limb bends or, possibly, against a nerve fibre in the case of spinal cord involvement. In this last case, interference with venous drainage from the cord, either directly or indirectly, by bubbles would seem an equally likely mechanism. Arterial gas embolism seems to offer an adequate explanation for cerebral symptoms and their relatively infrequent occurrence. However, both spinal and cerebral manifestations are nearly always preceded by Type I symptoms unless the decompression is grossly inadequate. Hence, at lower pressures, prevention of limb bends should prevent decompression sickness altogether—with the probable exception of dysbaric osteonecrosis.

The autochthonous bubble is unlikely to represent the whole picture but any blood degradation or ischaemia due to occlusion should also be proportional to the volume of gas separated from solution in tissue. Accordingly the volume of gas formed per unit tissue volume would appear to be a key factor in all likely mechanisms and thus conveniently provides the schedule designer with a fairly universal scale for grading the degree of insult.

If limb bends provide the criteria for depths less than 200–350 feet, then vestibular involvement must take precedence when the exposure is deeper. This must involve another set of factors—probably best superimposed upon the same general bubble description as used for Type I decompression sickness. This applies whether one believes in counterdiffusion supersaturation, counterperfusion supersaturation, or gas-induced osmosis or just takes a pragmatic view of the effect of inert gas switching—particularly at greater depths during decompression.

Prevention

Before seeing how such reasoning can be used to formulate preventive measures and how fundamental issues have largely failed to influence current techniques, a closer look should be taken at the *primary event*—the separation of gas from solution.