20

Biophysical Aspects of Decompression

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The decompression syndrome involves mechanisms which are undoubtedly more complex than were envisaged even a decade ago. Interest has now arisen in the biochemical and haematological aspects. In this chapter, however, only the biophysical approaches will be considered since these are still more likely to provide any fundamental basis generally adopted for designing safe diving tables.

The present wide diversity of approaches indicates that there are probably an infinite number of computational routines for safely decompressing a subject following just one particular hyperbaric exposure. If the truly optimal procedure is to be found other than by trial and error, it is therefore necessary to determine the true model. At least each feature established adds a further constraint to the present proliferation of calculation methods.

Vital issues

There are many interesting physical and physiological questions in hyperbaria to which one would like to know the answers, but there are a few which cannot be avoided. Answers must be found, or assumed, for each of these vital issues before any comprehensive mathematical model can be put forward on fundamental grounds for deriving safe decompression schedules. These are:

1. The number of tissue types which can give rise to marginal bends, since this determines the number of independent conditions to be satisfied and hence the number of separate equations to be used in calculating a format.

2. Whether there is a critical limit to the degree of supersupersaturation of a tissue by a gas, and thus whether the separation of the gas phase from solution can occur in the vital tissue(s) during any asymptomatic decompression. This is a rather more specific statement of the old issue concerning 'silent bubbles' (Behnke 1951), the term 'bubble' being avoided here since it tends to suggest a particular geometric form for the separated gas. This issue is the most important since it determines the driving force for tissue desaturation *during* decompression.

3. The kinetics for separation of the gas phase from solution once it is nucleated; is the onset of symptoms determined by the rate of transfer of gas to the gaseous phase or by coalescence or both?

4. Whether the rate-limiting process for the transfer of gas *in solution* is blood perfusion, bulk diffusion, membrane permeation or a combination thereof. This determines the nature of the time function to be used in the computation of tables.

A critical analysis is therefore needed of the evidence considered relevant to each of these vital issues.

SITE AND MECHANISM OF DECOMPRESSION SICKNESS

Number of tissue types involved

To establish the features of the true mathematical model for calculating diving tables, we are concerned with avoiding any discomfort to the diver and must therefore consider the *marginal*

case where decompression has caused some critical insult to one or more 'sensitive' tissues. If these vary in function, they are also likely to do so in both the nature of their reaction and their time response to the exposure. Hence, for a multi-tissue system, we could reasonably expect a correlation between the time-course of the dive and the type of symptom observed. However, this does not appear to be the case, although one exception is sometimes quoted. This concerns a propensity for pain to occur in the lower limbs of caisson workers (Golding et al. 1960; Rose 1962) as opposed to the upper limbs of divers (Rivera 1964; Slark 1962), but may still involve *one* tissue type.

It can be argued that the similarity of Type I symptoms arises since the most sensitive tissue has one anatomical identity, but is kinetically heterogeneous, so that a wide spectrum of response times needs to be considered, as in the original Haldane calculation method (Boycott, Damant & Haldane 1908). However, it is then difficult to envisage the physical basis for a parallel spectrum of degrees of critical insult needed to explain the varying ratio (or M value) required by subsequent workers (Workman 1965; Schreiner 1968) in order to force a better fit of the Haldane model to practical data.

Experimental approaches

It is particularly difficult to design an experiment to differentiate conclusively between the involvement of one or more tissues in Type I decompression sickness (DCS). However, an ingenious attempt by Rashbass (1954) invoked the relationship between equivalent combinations of pressures (P_1 and P_2) of two consecutive exposures, each of constant duration. It can be shown by a simple mathematical argument, which does not require any specific transport model to be assumed, that the linear relationship actually found by Rashbass provides strong evidence of the involvement of no more than one tissue type. Subsequent repetition of this experiment by Hempleman (1957) essentially confirmed these findings except in the region where $P_1 \gg P_2$. Deviation in this particular region can easily be explained by the lower driving force for tissue gas transfer arising from gas phase formation during the second exposure (P_2) due to the large decompression (P_1–P_2) immediately preceding it. This concept is discussed in detail later.

It can also be argued that if one tissue supersedes another as the closest to its respective threshold for provoking marginal symptoms, there should be a transition point in the parameters defining safe decompression limits. Selecting exposure pressure and time as the two parameters most interdependent in determining the imminence of symptoms, no such transition point (kink) could be detected in any bounce dive curves. Data examined include the no-stop decompressions of Duffner, Van der Aue and Behnke (1946) for oxy-helium mixtures, Van der Aue et al. (1951), Albano (1962) and many goat curves obtained in the author's laboratory for air diving.

Yet another feature in favour of the one-tissue concept is the ability to express the empirical time function depicted by the bounce dive curve (Hills 1969b) by a single bulk diffusion equation (see Fig. 20.8).

Although the evidence is far from adequate for any conclusion, it would tend to favour a one-tissue model for Type I DCS as classified by the MRC Decompression Panel.

Other symptoms

Although Type II DCS obviously represents different physiological manifestations to Type I, there is the mathematical problem of deciding whether they represent a further development of the same basic mechanism or whether they are derived in a different tissue or from a different form of insult to the body. CNS symptoms can invariably be produced by extreme decompressions from exposures well beyond the safe limits such as the bounce dive curve for no-stop decompression. Usually Type I symptoms develop first, so that it would be convenient to dismiss Type II from our modelling considerations as not representative of a marginal case.

However, a method has now been found for producing Type II DCS as *marginal symptoms* by interposing an upward excursion between the exposure and a regular decompression (Hills 1972a) This technique is illustrated in Fig. 20.1, and now provides a convenient model for studying the treatment of CNS symptoms, in goats at least. The particular case when the upward excursion

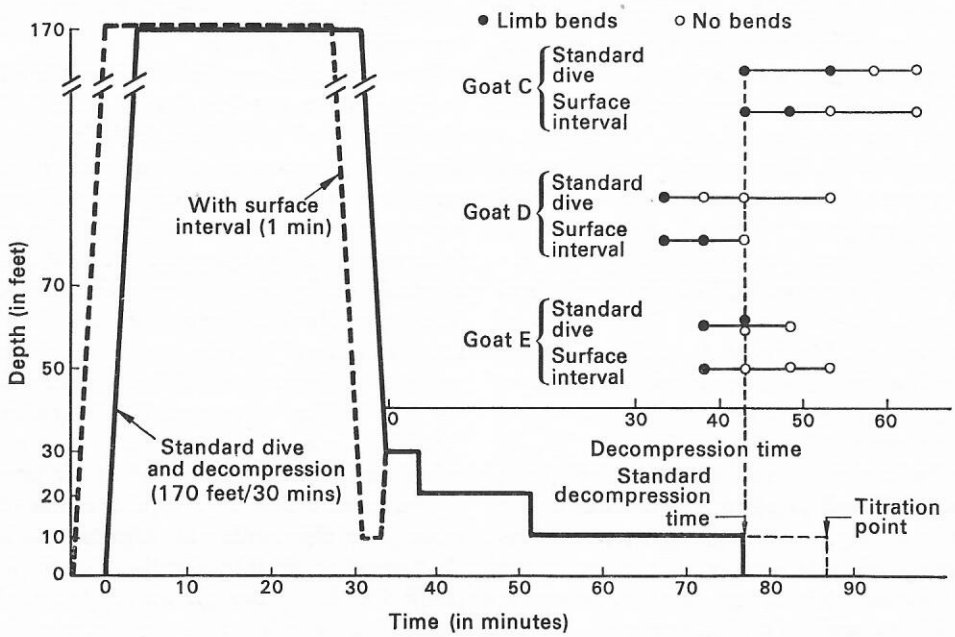

FIG. 20.1. Comparison of 'titrations' of the standard US Navy decompression table for an exposure of 30 min at 170 ft, both with and without an 'upward excursion', depicted as a stop at 10 ft in this particular case (after Hills 1971d)

pressure coincides with normal atmospheric represents the popular naval practice of 'surface decompression' or 'decanting'. However, for normal diving, decompression schedules which eliminate Type I DCS are likely to avoid all but the most minimal of Type II, but this reasoning should not be extrapolated from prevention to treatment, particularly for a CNS manifestation.

This is certainly not the case for dysbaric osteonecrosis which may not result from inadequate decompression or even from decompression per se (Hills 1970a). This major worry to the designer of diving tables is discussed in detail later. However, in the absence of more specific knowledge, his essential task is still the estimation of the imminence of limb pain.

MECHANISM OF 'LIMB BENDS'

The concept that the pain is ischemic in origin has been dismissed by Ferris and Engel (1951) for numerous clinical and physiological reasons, which they list.

More likely, perhaps, are the implications derived from the simple experiments of Inman and Saunders (Inman & Saunders 1944; Saunders & Inman 1943). When they injected Ringer's solution through fine hypodermic needles into various tissues, they found that there was a well-defined pressure threshold for inducing pain. This pressure differential was about 15 cm water gauge (0·015 ATS) irrespective of the fluid flow required to maintain it. Related to decompression, this indicates that the pressure differential between the separated gas phase and tissue (δ) which can bend, or otherwise distort, a nerve ending can do so without effect until it reaches a pain-provoking threshold corresponding to a critical pressure differential (δ'), i.e. bends pain occurs if:

$$\delta > \delta' \simeq 15 \text{ cm w.g.} = 11 \text{ mm Hg} \qquad (1)$$

This simple mechanical concept has been adopted by Nims (1951) and Hills (1966) for their very different approaches in relating the critical degree of embolism to parameters of the hyperbaric exposure.

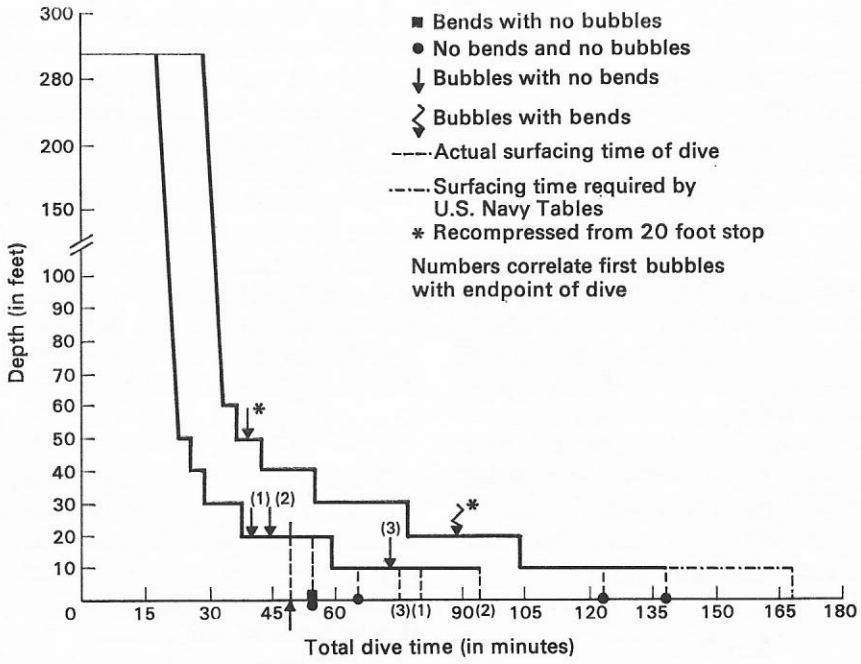

FIG. 20.2. Two standard US Navy decompressions showing the points at which bubbles were first heard and whether symptoms occurred (after Vann et al. 1973)

Intravascular versus extravascular site

Ferris and Engel (1951) list the clinical and physiological evidence on this issue, all of which tends to favour extravascular sites for the gas giving rise to '*limb bends*'. Their chief point is that extreme recompression should reduce any gas emboli to a size at which they could be expected to pass through the capillary bed if they were intravascular, so that symptoms would not be expected to re-occur in the same sites as they are found to do upon subsequent decompression (Blankenhorn et al. 1942).

It is also difficult to cavitate blood *de novo* (Harvey 1951) so that, overall, it means that intravascular bubbles are probably derived from gas initially deposited from solution in extravascular sites, vascular lesions having been first demonstrated after decompression by Chase (1934) and Tureen and Devine (1936). The likely origin of circulating bubbles would then be tissues with a predominance of lipid in which nitrogen is 5 times more soluble than in water. This implied tissue disruption by gas is compatible with the appearance of fat emboli (Shim, Patterson & Kendall 1967) and the remains of endothelial cells (Philp, Inwood & Warren 1972) in the circulating blood upon decompression.

Along this line of reasoning, intravascular bubbles therefore have little meaning in determining the imminence of 'limb bends', as several surveys of different decompressions with ultrasonic Doppler detectors have shown (Spencer & Campbell 1968; Evans, Barnard & Walder 1971; Vann et al. 1973 [see Fig. 20.2]).

This then raises the question of where to look for the relevant gas and, therefore, what is the anatomical identity of the tissue type responsible for marginal limb bends?

Identification of critical tissue

Pathological investigations have, on the whole, yielded surprisingly little information pertinent to establishing the true tissue model (Haymaker 1957), except to eliminate liver, heart and skeletal muscle from the list of possibilities as bubble-free after decompression. Previous discussions (Ferris

& Engel 1951) point to a well-innervated predominantly aqueous tissue occurring around joints and associated with the locomotor system, but not muscle. This suggests a connective tissue.

Hence it is interesting that Gersh, Hawkinson and Rathbun 1944) found that the incidence of 'bends' in small animals offered a better correlation with the gas content of excised tendon than with that of any other tissue. Other parameters which yield values compatible with tendon include the bulk modulus (Hills 1966), the ratio of 'elastic' to 'plastic' components for its load bearing, and the time for passive relaxation of the 'plastic' fraction (Hills 1969c) as a mechanical interpretation of known acclimatization (Walder 1966). These determinations of mechanical aspects were all based upon equation (1) in which the gas pressure differential (δ) can be related to the modulus (K) and the volume of gas (v) congregated in unit volume of tissue as:

$$\delta = Kv \qquad (2)$$

This expression is compatible with the linear increase in susceptibility with age described by Gray (1951), since the elastic modulus K is known to increase with age in most tissues, particularly the aorta (Hallock & Benson 1937). Thus the subject should be able to tolerate a lesser degree of embolism (v) as aging increases K, provided his pain threshold for δ remains the same.

However, this raises the next vital issue concerning whether 'limb bends' are, in fact, determined by a critical degree of embolism or by critical supersaturation.

PHASE CONDITIONS DURING DECOMPRESSION

Significance of this issue

An essential feature of all calculation methods is a critical condition to apply to the time response to determine whether a 'trigger point' has been reached for either the formation of the gas phase or the precipitation of a state which will lead to symptoms. In the case of the Haldane calculation method, and its many empirical modifications (Workman 1965; Schreiner 1968), these conditions are assumed to coincide since the same time functions are used to describe gas elimination during decompression as were employed to estimate gas uptake at pressure. This 'mathematical symmetry' is only valid provided the physics of the system is unaltered and, hence, all tissue gas has remained *in true physical solution*. If the gas phase *is* present, then not only is it inadequate just to change a time constant, but the popular exponential is no longer the appropriate function.

The conventional 'symmetrical' approach is only valid if there is a metastable limit to the saturation of a solution beyond equilibrium, a concept originally proposed for crystallization studies by Ostwald, a contemporary of Haldane.

Metastable limit versus random nucleation

A survey of the disciplines in the physical sciences where suppressed transformation occurs has shown that the concept of the metastable limit has been replaced by theories based upon random nucleation, with a finite probability for any condition in excess of equilibrium.

In justifying limited supersaturation, most proponents of theories of decompression sickness tend to quote values for the degree of supersaturation obtained by decompressing liquids in vitro. These are often designated 'tensile strengths', the values of which have been obtained under both static and dynamic conditions by a wide variety of methods. These are listed in Table 20.1.

The variation of values quoted in Table 20.1 needs no comment. Moreover, typical values (Table 20.2) for small animals indicate that cavitation is equally random in vivo.

Hydrophobic interfaces

It would seem most significant that bubbles formed by simple decompression in vitro almost invariably appear at the walls of the container (Wismer 1922). Moreover Harvey (1951) commented that nucleation is more profuse when the solid surface is hydrophobic.

This has also been found to hold at the liquid–liquid interface, which is significant since fat is fluid at body temperatures. A study of 580 decompressions of a hydrophobic fluid in contact with various aqueous fluids (Hills 1967d) has shown that cavitation is random and, when it occurs, invariably does so at the interface, ap-

TABLE 20.1

Recorded tensile strengths' of various liquids

Tensile strength (ATS)	*Liquid*	*Reference*	*Method*
300	Water	Bethelot (1850)*	Static
4·8	Water	Reynolds (1870)	Dynamic
30	Water	Meyer (1911)	Static
40	Ether	Meyer (1911)	Static
150	Water	Dixon (1914)	Static
207	Cell sap	Dixon (1914)	Static
2·38	Water	Vincent (1941)	Static
2·94	Mineral oil	Vincent (1941)	Static
2·9–114	Mineral oil	Vincent (1941)	Static
100–1000	Water	Harvey (1944)	Static
0·8	Water	Dean (1944)	Dynamic
100–200	Water	Pease & Blinks (1947)	Static
280	Water (10°C)	Briggs (1947)	Dynamic
20	Water	Willard (1953)	Ultrasonic
200	Water	Galloway (1954)	Ultrasonic
140	Benzene	Galloway (1954)	Ultrasonic

* Quoted and checked by Meyer and Dixon using the same method.

TABLE 20.2

Bubbles observed in resting cats

Time at pressure (P_1)	*Initial pressure (P_1) (ATA)*	*Final pressure (P_2) (ATA)*	*Number of cats in trial*	*Number displaying bubbles*
∞	1	0·14	37	4
∞	1		11	1+2?
2 to 5 hours	3·5	1	18	9
	3·14	1	10	7
	2·64	0·14	10	4
	3	1	12	3
	2·5	1	6	0
	2·0	1	5	0
	9	2	10	4
	6·8	2–3	8	0

This table gives a summary of data from Harvey et al. (1944) and McElroy et al. (1944).

parently with no significant metastable limit (Fig. 20.3).

Direct searches in intact tissue

The development of ultrasonic techniques for detection of the gas phase is described in another chapter (22), but those approaches invoking the Doppler principle seem to be emerging as the most successful. As stated earlier, these instruments often detect intravascular bubbles during asymptomatic decompressions using naval tables based upon the supersaturation concept—sometimes as early as the 50 ft stop (2·5 ATA; Fig. 20.2). However, in all fairness to the Haldane calculation method, one has no idea whether these *intravascular* bubbles detected are related to the state of the critical tissue in any way.

If the gas responsible for marginal DCS is deposited in extravascular sites or is lodged in capillaries as effectively extravascular, then we

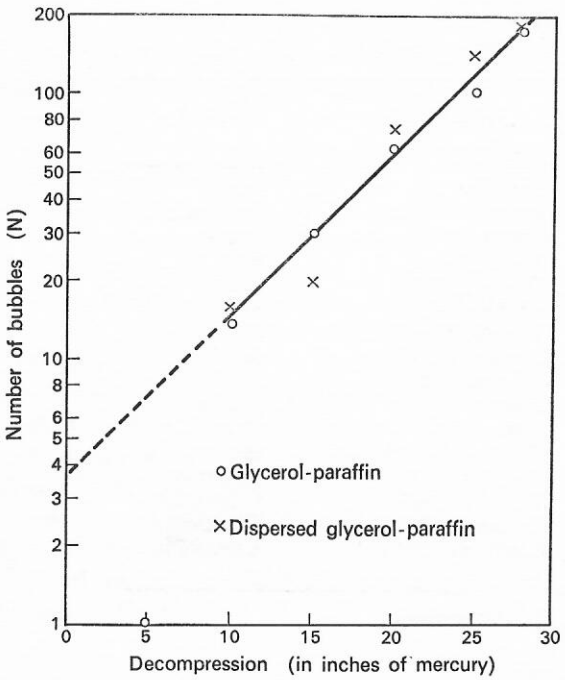

FIG. 20.3. The frequency of bubble formation at a hydrophobic-hydrophilic phase boundary in twenty runs for each extent of decompression (ΔP) from atmospheric

would need to seek other means of detection for answering this vital supersaturation issue. Other methods which have been used include conductance measurements, X-rays (Webb et al. 1943; Blankenhorn & Ferris 1944; Thomas & Williams 1944), monitoring cerebrospinal fluid volume, and the density measurements of Gersh, Hawkinson and Rathbun (1944) already discussed when implicating tendon as a likely critical tissue for limb bends. Details of the X-ray studies are given elsewhere, but two points require mention here:

Repetition of this work with modern X-ray equipment at Duke University, North Carolina, has essentially confirmed these early findings, but the nature of the streaking along tendon or muscle bundles becomes less regular with time or exercise, indicating coalescence.

Ryder et al. (1945) found the first indications of this 'streaking' to occur at an altitude of about 3950 m, i.e. an absolute pressure of about 483 mm Hg. This pressure is considerably higher than the value of 307 mm Hg corresponding to 7550 m which is the minimum bends altitude for the most susceptible individuals (Gray 1944), and certainly much closer to the value of 497 mm Hg calculated as the pressure for phase equilibration on the basis of equation (6) (Hills 1966). Thus the X-ray data would certainly favour the concept of gas separation occurring closer to the saturation point than to any predicted on the basis of critical supersaturation.

Conductance measurements

Electrical resistance of tissue has been monitored during decompression (Hills 1971c) since it is a parameter which can be measured very accurately and should be sensitive to both intravascular and extravascular gas, particularly if deposited in a finely dispersed state at lipid-aqueous boundaries. The results (Fig. 20.4) show a clear transition point upon decompression from ambient pressure, i.e. a point of sudden increase in the resistance between electrodes deposited subcutaneously across a rat tail. These points occurred for decompressions from normal atmospheric pressure of only 96, 127 or 145 mm Hg depending upon whether the animal had been breathing 80% He, N_2 or N_2O mixed with 20% O_2. There was little doubt that the changes were caused by the gas phase since the resistance increased more rapidly the greater the solubility of the inert gas present and the effect was reversed by recompression. Each transition point occurred when the extent of decompression was slightly greater than the inherent gas unsaturation arising in tissue by virtue of metabolism (see equation (6) and Fig. 20.6), whether the latter is predicted theoretically or measured experimentally (Hills & LeMessurier, 1969). This implies that the gas phase was first formed for a decompression much closer to the pressure for saturation than to any which could have been predicted by any ratio used in diving tables to describe a hypothetical limit to supersaturation.

However, it may be argued that the gas monitored was an artefact produced when a hydrophobic interface was introduced in the form of an electrode. Recent development of an electrodeless device (Searle & Hills 1975), based on the principle of the inductive conductivity meter, essentially

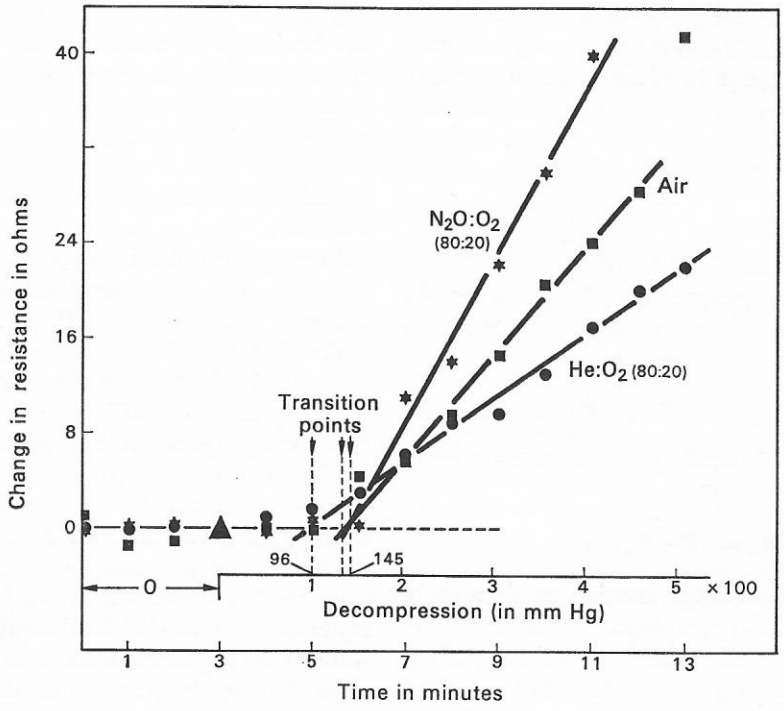

FIG. 20.4. The change in the electrical resistance across the tails of rats that had been breathing mixtures of 80% He–20% O_2, 80% N_2O–20% O_2 or air at normal pressure for 6 hours before death immediately followed by decompression (after Hills 1971c)

confirms these earlier findings. This device also appears most promising for further development into a non-invasive means of detecting that first onset of the separation of the gas phase from solution in divers.

Even though the rat tail used in these experiments is largely tendon, it can easily be argued that none of the direct approaches need have been detecting the gaseous phase relevant to Type I DCS. However, before discussing the indirect approaches which have been developed to try to overcome this objection, it might be as well to consider the importance of the presence of the gaseous phase in influencing gas elimination *during* decompression.

Driving force during decompression

Let us consider a tissue zone in which gas has been deposited from solution (Fig. 20.5). It has been shown from studies of the composition of gas pockets in animals (Campbell 1924; Van Liew et al.

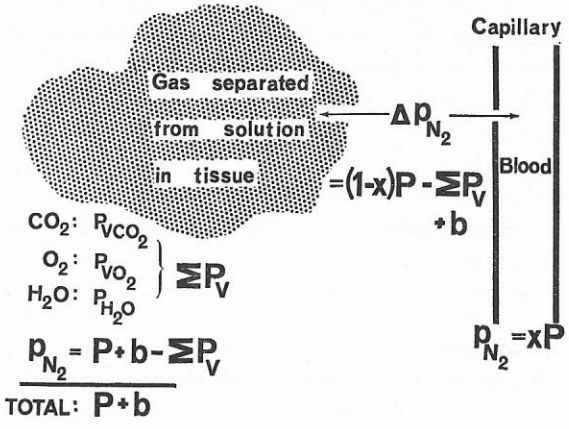

FIG. 20.5. Illustrating the driving force (ΔP_{N_2}) for the elimination from tissue of the nitrogen in gas separated from solution (equation 6). Absolute pressure of this gas is $(P+b)$ where b is a small factor allowing for surface tension and tissue distensibility (equation 4), while x is the wet volume fraction of inspired nitrogen

1965) that the partial pressures of CO_2 and O_2 in those pockets rapidly revert to near-venous values following any change in external pressure. Since gas separated from solution must be in mechanical equilibrium with its surroundings, the partial pressure of nitrogen (P'_{N_2}) can be deduced by difference as:

$$P'_{N_2} = P - P_vO_2 - P_vCO_2 - P_w + b = P + c \quad (3)$$

where b is a small term to allow for tissue compliance (δ) and curvature (radius $- r_b$) of the gas–tissue interface (tension $- \gamma$) i.e.

$$b = \delta + 2\gamma/r_b = c + P_vO_2 + P_vCO_2 + P_w \quad (4)$$

At the adjacent capillary, the nitrogen tension (P_{N_2}) will be given by:

$$P_{N_2} = (P - P_w)F_{I_{N2}} \quad (5)$$

where $F_{I_{N2}}$ is the volume fraction of nitrogen in inspired air on a dry gas basis.

Hence we can derive the driving force (ΔP_{N_2}) for nitrogen transfer from the gaseous phase to the capillary simply by subtracting equations (3) and (5), and eliminating b, when:

$$\Delta P_{N_2} = P'_{N_2} - P_{N_2} = P(1 - F_{I_{N2}}) + c' \quad (6)$$

where

$$c' = c - P_w . F_{I_{N2}} \quad (7)$$

For the comparison with the conventional supersaturation approach, if the nitrogen had remained in solution it would have a tension P''_{N_2}, say, higher than P'_{N_2}, and given by:

$$\Delta P''_{N_2} = P''_{N_2} - P_{N_2} = P''_{N_2} - (P - P_w)F_{I_{N2}} \quad (8)$$

Below convulsive limits of oxygen, P_vO_2 is approximately independent of pressure and hence so is c'—the term: $b - P_vO_2 - P_vCO_2 - P_w(1 - F_{I_{N2}})$. Thus the very important feature emerging from equation (6) is that ΔP_{N_2} *increases* with P since $F_{I_{N2}}$ must be less than 1. This suggests a *greater* driving force for resolution of separated gas provided the *gas phase is present.*

Equation (6) emphasizes the importance of knowing whether the gas phase is present since, if it is not, then it is better to decompress further and so obtain a greater driving force for nitrogen elimination intended by the first long 'pull' towards the surface in Haldane-type schedules ($\Delta P''_{N_2}$ increases with *decreased* P in equation (7)). However, once the gas phase forms, further decompression is the worst action possible since one is now not only forming more gas, but is reducing the driving force for its elimination according to equation (6), since ΔP_{N_2} is now *decreasing as* P *decreases.*

Equation (6) also expresses quantitatively the known benefit of oxygen treatment, where a decrease in F_{IN_2} increases ΔP_{N_2}.

Proof of the validity of equation (6) in vivo has been provided by considering what would happen if the separated gas in Fig. 20.5 were now encased in a rigid yet permeable capsule. As steady state conditions were reached, a partial vacuum would develop by virtue of the *inherent unsaturation*—a concept depicted in Fig. 20.6. This has been found to vary with change of $F_{I_{N2}}$ and absolute pressure (P) exactly as predicted for ΔP_{N_2} in equation (6) (Hills & LeMessurier 1969). If the walls of the capsule were suddenly removed, there would be a sudden increase in total pressure of the contained gas. The O_2, CO_2 and water vapour would adjust rapidly to new venous values leaving an increase in the P_{N_2} equal to the inherent unsaturation whose characteristics can thus be taken as those of ΔP_{N_2} in equation (6).

Hence, in any calculation, it is vital to know when the gas phase is first formed.

To avoid the major objection to the direct methods described earlier for determining this point, it is necessary to ensure that one is dealing with the tissue type(s) responsible for marginal symptoms. One means of guaranteeing this condition is to use the occurrence of symptoms as the outward indication of the methods employed to differentiate between the possible thermodynamic states of the critical tissue(s).

Indirect methods

Hempleman (1960) performed a number of double exposures upon goats, 'titrating' the pressure of the second exposure to a bends point. By varying time intervals, he was able to show that gas elimination from the critical tissue(s) was slower than uptake for the corresponding pressure differences. This would indicate a basic asymmetry between uptake and elimination indicative

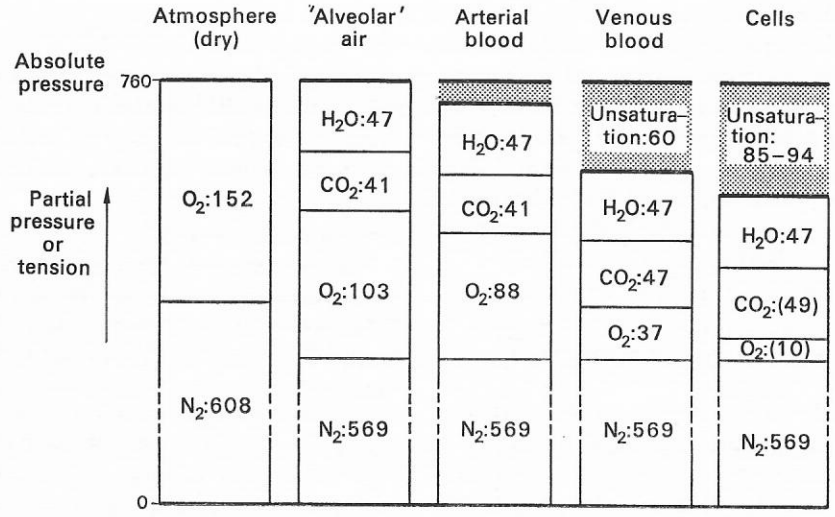

FIG. 20.6. Typical partial pressures of the respiratory gases and their tensions in solution (in mm Hg) for a day when the absolute atmospheric pressure is 760 mm Hg. The deficit in the total represented by the shaded areas represents the inherent unsaturation (after Hills 1974)

of asymptomatic gas in the critical tissue, such as a switch from equation (8) to (6).

A somewhat similar experiment has been performed recently in which the interval between two fixed exposures to pressure was changed (Griffiths et al., 1971). They found that the bends incidence in small animals increased as the interval increased—which they conclude is the opposite to the trend predicted by the critical supersaturation concept.

An experiment to determine the state of the tissue has exploited the difference between equations (6) and (8) (Hills 1968, 1970b). Goats were given an exposure to compressed air (60 min at 160 ft; 53 m) followed by a standard US Naval decompression calculated by conventional methods based upon the concept of critical supersaturation (Workman 1965). Total decompression time was then 'titrated' for each animal by cutting back upon the time spent at the last (10 ft) stop until bends occurred. When these 'titrations' were repeated upon the same animals, using the same procedure apart from carrying on at the 20 ft stop and 'surfacing' directly from this pressure, it was found that less total decompression time was needed for each goat. This indicates more effective elimination of gas at 20 ft than at 10 ft and is consistent with equation (6) where (ΔP_{N_2}) increases with P. It is directly opposed to equation (8) by which the reverse should hold and must therefore add strong support for the presence of the gas phase in the critical tissue(s).

Taking a different approach, it was found that in 3 goats which had just completed marginally safe decompressions, symptoms could not be induced by exposure of their limbs to high intensity ultrasound (Hills 1970b). This indicates that their critical tissues were already equilibrated or that any increase in the number of equilibrated regions did not increase the local volume of separated gas per unit volume of nucleated tissue. These results are hard to reconcile with a metastable limit to supersaturation.

Conclusion

With so much evidence from both direct and indirect approaches to this problem, there is now little doubt that, during an asymptomatic dive, there can be not only intravascular bubbles, but the gas phase present in the critical tissue for limb bends. Moreover, it would appear that the gas phase starts to form soon after the position of phase equilibrium is exceeded. Thus, for calculation purposes, it remains a purely academic

question whether there is a negligible decompression threshold to nucleation in vivo (Hills 1966) or there are always macronuclei present under ambient conditions (Evans and Walder 1969) when they could be stabilized by shear forces of the type which have been used to predict bubble stabilization in isotropic media (Gent and Tompkins 1969). The evidence on this vital issue has been reviewed more recently (Hills 1970c).

GROWTH OR COALESCENCE

While the above conclusion would eliminate conventional calculation methods based upon critical supersaturation, it raises the question of whether the period between initiation of the gas phase and the onset of symptoms has any significant influence upon the incidence. This poses the further question concerning whether the rate of onset of marginal symptoms is determined by the rate of transfer of gas to the gaseous phase from solution, i.e. growth, or by the coalescence or congregation of separated gas into a bubble of critical size. Theories for the former argument have been put forward by Nims (1951), while Bateman (1951) includes further nucleation upon a semi-empirical basis and Albano (1962) allows for the presence of nuclei. However, when expressing their driving force for N_2 elimination mathematically, these approaches do not allow for the desaturation of tissue which bubble growth must cause. This does not invalidate the growth-rate-limiting concept in which interest has recently been revived by Griffiths et al. (1971), but leaves a need for a comprehensive analytical treatment.

The second approach (Hills 1966) largely avoids these kinetic aspects by considering only the 'worst possible case' or those few regions where nucleation is so profuse as to permit total local desaturation within a few minutes. This gas then coalesces. It has been claimed that the random onset time of symptoms is more compatible with the random nature of coalescence than with any time course based upon continuous growth.

Before developing this zero supersaturation approach further, it is necessary to have a physical model for gas transfer in the absence of the gas phase.

TRANSPORT

When a subject starts breathing a different inert gas, its macro-distribution over the body must be effected by the circulation, while beyond the capillaries it must then proceed by diffusion.

Conventional approach

The physiological literature in general favours blood perfusion as the rate-limiting process (Kety 1951; Jones 1951). However, there is at least one disquieting fact which forces one to question what would otherwise be a simple model giving a single exponential function for each tissue, a form which has proven so easy to handle in the Haldane calculation method, yet tends to be retained in subsequent approaches largely for its mathemetical simplicity.

Helium versus nitrogen

Hempleman (1967) has indicated, that for corresponding partial pressures of inert gas, the air and oxygen–helium 'bounce dive' curves intersect for both goats and men. For long exposure times, greater pressures can be tolerated when the inert gas is helium than when it is nitrogen. This is compatible with the lower solubility of helium in tissue, whether aqueous or lipid. However, for exposure times of less than 20 min, resulting in a predecompression state further from saturation, and hence emphasizing the kinetics, the same subject can be exposed to a greater pressure upon air than $He:O_2$. This can easily be explained on the basis of the slower diffusion of nitrogen, where Graham's Law would predict a ratio of coefficients ($He:N_2$) of 2·65:1 which would override the solubility effect over this range. Hempleman points out that a similar ratio (3:1) of time constants can be predicted on the basis of the perfusion-limiting model, but only if the faster tissue were lipid—a most unlikely situation.

The perfusion/diffusion confusion

Observations such as these have led the author to search back into the vast physiological literature based upon this assumption to see why blood perfusion was accepted as the rate-limiting process in the first place. This has led to a long and critical

TABLE 20.3
Analysis of inert gas elimination from man (data from Jones 1951)

Gas	*Method of enumeration of Jones*					*Time constants in order of extraction*				
	k_1	k_2	k_3	k_4	k_5	k_1	k_2	k_3	k_4	k_5
N_2	0·46	0·087*	0·024†	0·0047‡		0·0047‡	0·024†	0·087*	0·46	—
Xe	0·35	0·987	0·024	0·0038	0·0008	0·0008	0·0038	0·024	0·087	0·35
He	0·50	0·084	0·024	—	—	0·024	0·084	0·50	—	—
Ratio (N_2/Xe)	1·32	1·00	1·00	1·24	—	5·87	6·32	3·62	5·29	—
Ratio (He/N_2)	1·09	0·97	1·00	—	—	5·11	3·50	5·74	—	—

Nitrogen values given by Behnke (1951) are: * 0·085 min^{-1}, † 0·019 min^{-1}, ‡ 0·0054 min^{-1}.

review (Hills 1970d) from which several broad conclusions have been made:

1. The data is difficult to interpret on the basis of models advocating either simple homogeneous perfusion or simple linear diffusion in a homogeneous medium.

2. It is necessary to postulate that both of these processes are rate controlling or that diffusion occurs in a heterogeneous medium or that perfusion is heterogeneous. This involves either much more rigorous mathematical application of simple physical principles in the first two cases or postulating more complex physiological mechanisms to overcome the inadequacy of simple equations relevant to the last case, the latter proving more popular.

3. Most evidence is equally compatible with either heterogeneous perfusion or diffusion in a heterogeneous medium. A typical example often quoted in favour of perfusion limitation is the data of Jones (1951) who has argued that if blood perfusion is rate limiting, then all inert gases should have much the same time constants for gas elimination from aqueous tissues. When he extracts from two to four time constants (k) each by backward projection for He, N_2, Kr and Xe, he arranges them in a table such as shown on the left-hand side of Table 20.3. These do indeed tend to agree as laid out in this arbitrary manner.

However, when enumerated according to their order of extraction, these values offer a better correlation on a diffusion-controlling basis (Table 20.3, right-hand side).

Despite the ambiguity of interpretation of most data, there are a few points which afford a better chance to differentiate.

Critical experiments

From the vast mass of material, the following critical points have been selected.

During uptake, the highest inert gas tension must be the arterial value and the lowest must be mean tissue, with venous somewhere in between. Kety and Schmidt (1945) argue that if perfusion is rate limiting, the venous tension will approach mean tissue tension, while if diffusion is rate limiting, venous will approach arterial. They perform a series of experiments in which they estimate mean tissue values by arteriovenous differences to find that they approximate to venous values, implicating a perfusion controlling system. However, if allowance is made in the integration for the time for encumbent blood to be displaced, then the venous and mean tissue values no longer coincide. What is more disturbing are the values for blood perfusion which one derives from the time constants in Kety and Schmidt's experiments. These differ by factors of as much as 2 from the values derived independently from a–v differences, but in such a direction as to be compatible with a significant controlling influence exerted by diffusion (Hills, 1970d; Table 20.4).

Kety (1951), Cavert and Lifson (1958), Forster (1964) and Roughton (1952), using the same radial diffusion equation, have calculated that mean extravascular tissue tension should attain 95 to 99% of the asymptotic value within 1 to 5 sec of a 'step' change in the blood tension of that gas. Thus they dismiss diffusion as an insignificant factor in controlling blood–tissue gas exchange. However, to describe this *transient* situation, they use *overall* tissue values of 10^{-5} cm^2 sec^{-1} for the diffusion coefficient, as determined by a *steady*

TABLE 20.4

Comparison of cerebral blood flow ($\dot{Q}$) determined from the same experiments for the uptake of nitrous oxide by brain and calculated: (I) from the time constant, (II) by arteriovenous difference, and (III) by direct measurement (data from Kety & Schmidt 1945)

Time constant in min^{-1}	*Tissue: blood partition* ($1/\lambda$)	*Cerebral blood flow* ($\dot{Q}$) *in ml/(g tissue min)*		
		(*I*) $1/\lambda$ (*perfusion controlling*)	(*II*) *by a–v balance*	(*III*) *by direct measurement*
0·182	1·3	0·24	0·36	0·37
0·198	1·6	0·32	0·35	0·42
0·102	1·0	0·10	0·22	0·17
0·154	1·4	0·22	0·42	0·46
0·287	1·3	0·38	0·62	0·60
0·089	1·3	0·12	0·30	0·31
0·266	1·4	0·37	0·36	0·38
0·230	1·5	0·34	0·66	0·76
0·138	1·2	0·17	0·34	0·32

state method and therefore only acceptable in this context if tissue is uniform.

Determinations of diffusion coefficients in cytoplasm by truly *transient* methods have given very much lower values of $1{\cdot}5 \times 10^{-8}$ to $5{\cdot}0 \times 10^{-10}$ for water (Dick 1959), 3×10^{-8} to 3×10^{-10} for 10 polar solutes (Fenichel & Horowitz 1963) and $2{\cdot}3 \times 10^{-10}$ $cm^2\,sec^{-1}$ for certain gases (Hills 1967a). Recalculation of tissue saturation times using these values indicates much slower diffusion and hence a much greater diffusion limitation.

Rigorous mathematical analyses show that it is easier to differentiate between perfusion and diffusion as the rate-limiting process for small time intervals, but these, unfortunately, represent the range of greatest uncertainty in the practical data. Over the well-defined 'asymptotic' region (large time values) the respective time functions become similar, yet still tend to indicate bulk diffusion as the relevant mode of uptake, yielding diffusion coefficients within the range of 'transient' values quoted above (Hennessy 1971).

Very recent studies of the separation of multiple inert gases from solution in tissue (Hills 1975) have indicated that the empirical time functions, $\Phi(t)$ by analysis of practical data using equation (12), are almost identical for nitrogen and helium uptake in man. This would provide strong support for a perfusion-limited system if it were not for the equally close agreement which both functions show for the $\sqrt{t}$ relationship of Hempleman (1952)—the ultimate approximation of all models for bulk diffusion (Hills 1966). These apparently conflicting observations have been interpreted on the basis of bulk diffusion of gas through capillary bundles of alternating patency; this model gives the $\sqrt{t}$ effect.

THERMODYNAMIC (ZERO SUPERSATURATION) APPROACH

The foregoing reasoning leads to some fairly definite conclusions to some of the *vital issues*, while upon others such as the perfusion/diffusion controversy the answers are less obvious. This type of analysis of the evidence available led to a new quantitative approach to Type I DCS which was termed 'Thermodynamic' (Hills 1966), although it could have been more appropriately named 'Zero Supersaturation' to emphasize the major issue on which it diverged totally from conventional approaches at that time. On several points it is compatible with the 'Oxygen Window' concept developed more qualitatively and quite independently by Behnke (1967).

Features

The salient features of the thermodynamic approach may be listed as follows:

1. It involves only one critical tissue type for Type I DCS.

2. Nucleation of the gas phase in this critical

tissue upon decompression is presumed to be as random as found in tissues of known identity and in the multi-phase systems investigated in vitro, both in decompression threshold and in spacial distribution.

3. The relevant sites to be considered in estimating the imminence of decompression sickness are taken as the 'worst possible'. These are the few micro-regions, or may be only one in many million possibilities, where caviatation has occurred (a) soon after equilibrium conditions have been exceeded, and (b) in such profusion that any local supersaturation is soon dissipated by virtue of the short diffusion paths for the excess gas in reaching the nearest nucleus, i.e. excess gas is 'dumped'.

These conditions define the 'worst possible' since they represent not only the maximum volume of gas separating from solution per unit volume of tissue (v in equation 2), but the minimum driving force for its elimination via the circulation once formed (equation 6).

4. The phase equilibration (growth of gas phase) of these profusely nucleated micro-regions is considered to occur within a few minutes of a change of pressure. Fortunately this avoids the insuperable mathematical complexity introduced by superimposing slow growth of nuclei upon their pattern of random distribution.

5. This gas separated from solution will then tend to coalesce, or to congregate by other means, until its local displacement of tissue bends or otherwise distorts a nerve ending beyond its pain-provoking threshold. Physically, this can be regarded as a concentration of mechanical stress (δ) until it exceeds the critical value (δ') as expressed by equation (1).

6. When the gaseous phase has formed, the driving force for its elimination via the circulation is provided by the *inherent unsaturation* alone (equation 6).

Quantitative description of general case

The bends-provoking stress (δ) is difficult to measure but, fortunately, it can be eliminated from equation (1) and (2) to give the critical condition for bends as:

$$v > \delta'/K \qquad (9)$$

where the total volume of all separated gases per unit volume of tissue (v) can be related to the nitrogen separated from solution in the gaseous phase from a simple balance for this gas in tissue as:

$$\underset{\text{(separated)}}{vP'_{N_2}} = \underset{\text{(initial)}}{S(P_O - P_w)F_{I_{N2}}} + \underset{\text{(uptake)}}{G_u} - \underset{\text{(eliminated)}}{G_e} - \underset{\text{(remaining in solution)}}{SP'_{N_2}} \qquad (10)$$

where S is the solubility of nitrogen, $F_{I_{N2}}$ is its inspired fraction and G_e is the nitrogen eliminated during gradual decompression, while the nitrogen taken up at the 'bottom' pressure (P_b) is given by the time function, $\Phi(t)$, such that:

$$G_u = S(P_b - P_O)F_{I_{N2}}.\Phi(\tau) \qquad (11)$$

where τ is the 'bottom' time.

Elimination of G_u, P'_{N_2} and v from equations (3), (9) and (10) gives the general condition for the occurrence of a limb bend as:

$$\frac{[P_O - P_w + (P_b - P_O).\Phi(\tau)]F_{I_{N2}} - (G_e/S) - P - c}{(P+c)} > \frac{\delta'}{KS} = f \qquad (12)$$

where f is the critical volume fraction and, if pressures are given in units of atmospheres, S is then the Bunsen coefficient for nitrogen. c is given by equation (4).

Assessment

In qualitative terms, this comprehensive expression (equation 13) can be seen to predict a greater likelihood of bends for a greater 'bottom' pressure ($P_b \uparrow$), greater decompression ($P \downarrow$), a longer exposure time ($\tau \uparrow$), more nitrogen in the O_2:N_2 breathing mixture ($F_{I_{N2}} \uparrow$), less decompression time ($G_e \downarrow$), a more soluble inert gas ($S \uparrow$) or a less compliant critical tissue ($K \uparrow$).

Quantitatively, this expression can offer a reason why a decompression ratio would appear to hold—at least, for the particular conditions of the experiments (Boycott & Damant 1908) which led to the introduction of this concept by Haldane, viz. saturation exposure, $\Phi(\tau) = 1$, followed by no-stop decompression ($G_e = o$), when equation (12) gives:

$$P_b = P(f+1)F_{I_{N2}} + c' \qquad (13)$$

Where f is a constant for a particular individual and c'' is a small constant (relative to diving values for P_b), given by:

$$c'' = c(f+1)/F_{I_{N2}} + P_w \qquad (14)$$

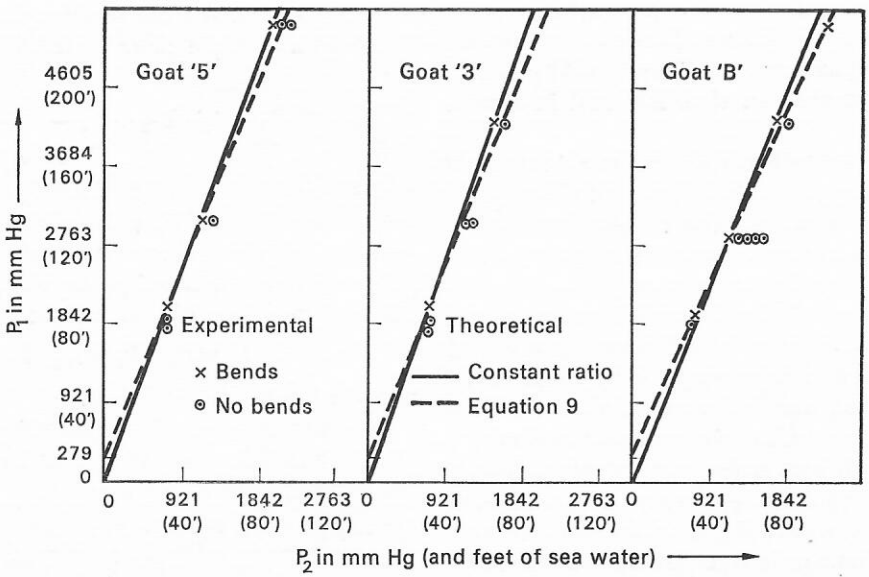

FIG. 20.7. Data from Hempleman (1957) for the outcome of the decompression of goats from an effective steady state at P_1 to a lower absolute pressure (P_2). It can be seen that the broken line (equation 13), based upon the total volume of separated gas offers a slightly better separation of 'bends' from 'no bends' points than a simple ratio as depicted by the full line

Thus equation (13) represents a linear relationship between P_b and P offering a slightly better correlation than the ratio for experimental data (Hempleman 1957) extending the test to higher pressures (Fig. 20.7 where $P_1 = P_b$ and $P_2 = P$). For these higher exposure pressures (P_b), c'' becomes negligible, when its omission from equation (13) gives an apparent ratio of $(f+1)/F_{I_{N_2}}$.

This omission cannot be made for aerial decompression when c' is now appreciable relative to the absolute pressure. Equation (13) can now be used to correlate aerial data with underwater to give the same values of f for pilots and divers of corresponding sensitivity to decompression, taking $c = 74$ mm Hg and $b = 200$ mm Hg (Hills 1969a). This includes a comparison of helium and nitrogen data for which the critical values of f are found to lie in the ratio of their solubilities (S) as predicted by equation (12).

General analysis

The test of this expression has been extended from these special yet important cases to an analysis of the bends incidence in 10 sets of exposures, each followed by a conventional decompression. It has offered a better prediction (Hills 1966) than the supersaturation ratio concept on which those trials were designed. This analysis departed markedly from Haldanian traditions by recognizing the presence of the gas phase following the typical long initial 'pull' to the surface and, moreover, refuting any connection between the gas elimination (G_e) and the uptake function $\Phi(t)$. Rather, G_e was taken as increasing linearly with ambient pressure (P) on the basis of the inherent unsaturation. ($G_e \propto \Delta P_{N_2}$ in equation 6).

However, before extending the thermodynamic approach from a general analysis of dives irrespective of their design to decompression optimization, it is first necessary to consider the transport model in more detail.

The transport model

Most approaches are synthetic in so far as they select one or more time functions for gas *uptake*, each with suitably chosen constants, and then use the same function to describe *elimination*. Others modify those constants empirically to allow for

some degree of asymmetry of gas transfer between exposure and decompression.

A different approach is the analytical one. This avoids uncertainties in mathematical symmetry by considering no-stop decompressions only ($G_e = 0$) and then invoking the comprehensive (equation 12) to derive the true uptake function, $\Phi(t)$. This has been done (Hills 1969b) and effectively assumes that the critical tissue contains the same quantity of gas at the start of decompression from all exposures described by the bounce dive curve. The analytical uptake function can then be compared with those derived by mathematical expressions describing blood perfusion limitation, diffusion into a flat slab and radial diffusion from a cylindrical capillary. It can be seen in Fig. 20.8 that no equation fits exactly, indicating that gas transfer is probably limited by both diffusion and the circulation as discussed earlier. However, by far the closest fit is afforded by a model representing radial diffusion from a capillary of radius (a) and intercapillary distance ($2b$), when:

$$\Phi(t) = 1 - \frac{4}{(b/a)^2 - 1} \times \sum_{0}^{\infty} \frac{e^{-\alpha_n^2 Dt}}{(a\alpha_n)^2 \{[J_0(a\alpha_n)/J_1(b\alpha_n)]^2 - 1\}} \quad (15)$$

where D is the diffusion coefficient and α_n is the nth root, real and positive, of the equation:

$$J_0(a\alpha_n) \cdot Y_1(b\alpha_n) = Y_0(a\alpha_n) \cdot J_1(b\alpha_n)$$

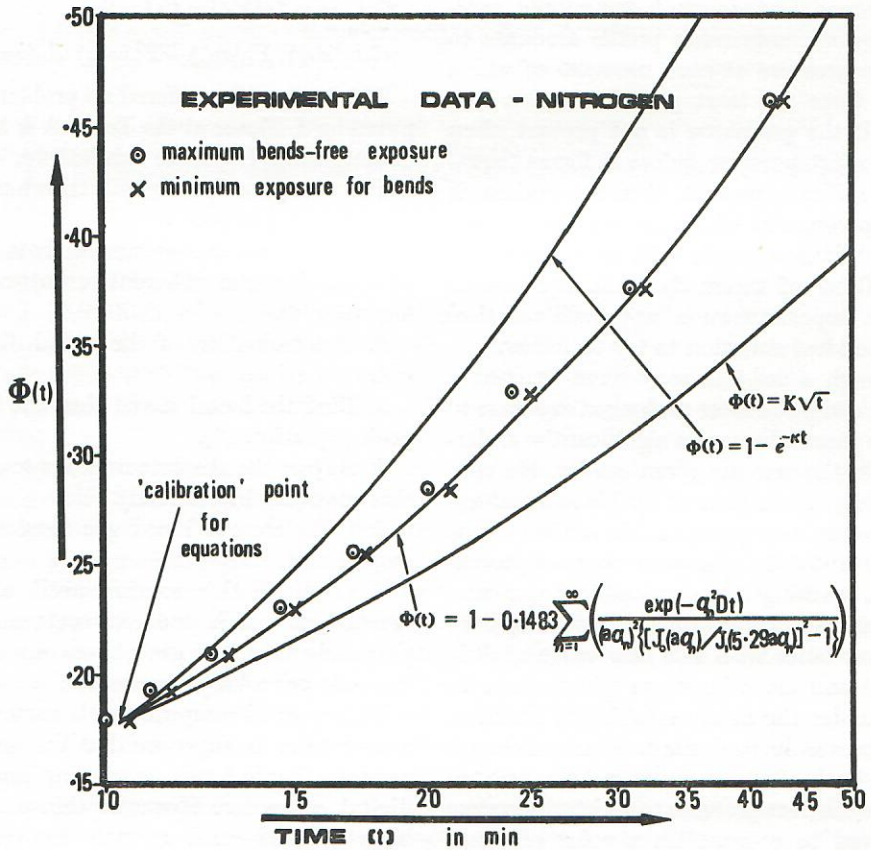

FIG. 20.8. A comparison of the uptake function for nitrogen, $\Phi(t)$, determined by applying equation (12) to the comprehensive bounce dive data of Albano (1962), with various theoretical functions. In descending order, those represent blood perfusion, radial bulk diffusion and linear diffusion, with one point being sacrificed as a 'calibration' to determine the one constant required by each model (after Hills 1969b)

J and Y represent Bessel and Neumann functions as defined by Watson (1944).

The above expression for $\Phi(t)$ can easily be derived from equations given in standard mathematical texts describing the inert gas tension (p) at a radial location (r) at time (t) following a sudden change from O to P_1 within the capillary ($r<a$) as:

$$\frac{p}{P_1} = 1-\pi \times \sum_{0}^{\infty} \frac{[J_0(r\alpha_n)Y_0(a\alpha_n)-Y_0(r\alpha_n)J_0(a\alpha_n)]\,e^{-\alpha_n{}^2Dt}}{[J_0(a\alpha_n)/J_1(b\alpha_n)]^2-1} \quad (16)$$

Optimization

Whatever model or approach one adopts, optimization of a decompression profile amounts to selecting the pressure at each moment at which the driving force for inert gas elimination is a maximum. If the gas phase is not present, then this is the lowest pressure before it forms (equation 8) while, if it *is* present, then the optimal is the highest pressure at which the gas phase exists (equation 6). These coincide with each other only at the position of thermodynamic equilibrium on the 'Zero Supersaturation' approach and thus represent the ideal situation to try to follow.

Even though a subject may have reached a steady state condition after prolonged exposure to pressure, he must always be significantly undersaturated for the reasons given earlier. He can thus be rapidly decompressed by his *inherent unsaturation* before any point in his critical tissue need be saturated in the true thermodynamic sense. Upon reaching this new ambient pressure, the unsaturation will re-establish itself in capillary blood in accordance with this new value of P in equation (6) and more inert gas will tend to be eliminated under the newly established gradient. This will decrease the peak gas tension and change its location, both of which can then be calculated to determine the next pressure to which the system can be moved to re-establish a point of phase equilibrium.

If the computation is correct, then no gas phase should have formed, so that the same time function can be used to describe inert gas elimination as uptake, i.e. successive steps described by equation (16) can be superposed to obtain the distribution of inert gas at any time.

In superposing the effects of successive changes of pressure, these are only additive for linear time functions, such as the simple exponential as used in the Haldane approach. In the above case of radial diffusion Hennessy has derived the expression (17) to describe the tension (p) at a general location (r) after a switch to a capillary tension (P_1) following any previous history resulting in a general distribution $h(r)$ at zero time.

$$\frac{p}{P_1} = P_1+\pi \times \sum_{1}^{\infty} \frac{[J_0(r\alpha_n).Y_0(a\alpha_n)-Y_0(r\alpha_n).J_0(a\alpha_n)]\,e^{-\alpha_n{}^2Dt}}{\{[J_0(a\alpha_n)/J_1(b\alpha_n)]^2-1\}} \times \int_a^b \frac{\pi}{2}.\alpha_n{}^2x[h(x)-P_1] \times [J_0(x\alpha_n).Y_0(a\alpha_n)-Y_0(x\alpha_n).J_0(a\alpha_n)]\,dx \quad (17)$$

This integral has offered no problem when computed by J. Moore at the Texas A & M Computing Center, using Legendre quadrature.

The computation routine therefore consists of the following steps:

1. Very rapid decompression from the exposure pressure by the inherent unsaturation at P_b (equation 6).
2. Determination of the radial distribution of gas.
3. Find the location and then the height of the peak (equation 16).
4. Adjust the absolute pressure to coincide with this peak (see Fig. 20.10d).
5. Calculate the blood gas tension and repeat steps 2 to 4.
6. Continue this routine until a pressure is reached at which one can surface directly and purposely form the gas phase, but to just below the pain-provoking dimensions.

This type of computation is very tedious since a new term is superposed with each change of pressure, 1-min intervals proving convenient on a digital computer. However this complexity has been avoided until recently by the use of an analogue.

Decompression analogues

The exact similarity in mathematical descriptions of diffusion and thermal conduction has led

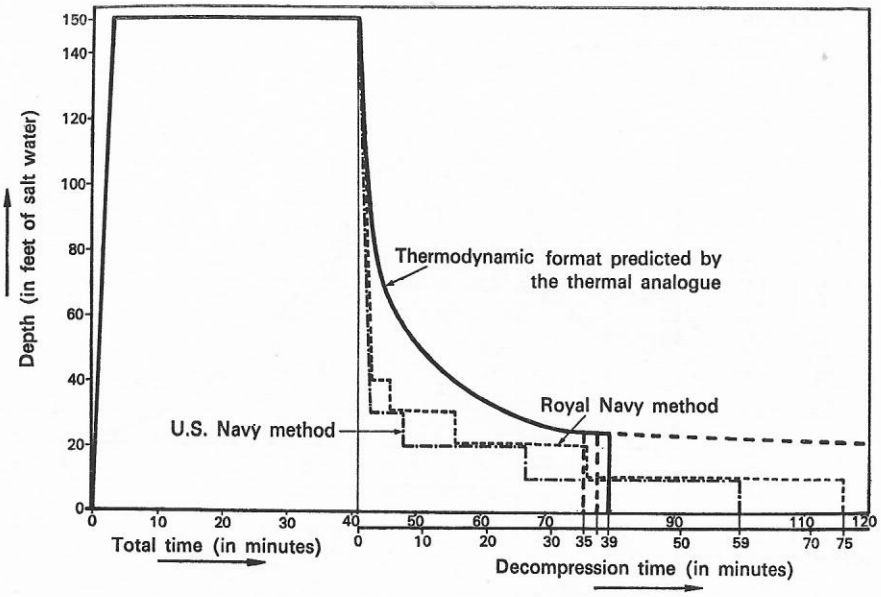

FIG. 20.9. The optimal deployment of decompression time as indicated by a thermal analogue based upon the zero supersaturation concept. Total decompression times indicated were those found by experimental 'titration' of large goats

to a thermal analogue to simulate the radial diffusion model (Hills 1967b). This has given the format shown in Fig. 20.9 which, when tested upon goats, showed an appreciable saving in total decompression time compared with the similar titration of the same animals upon the corresponding US Navy profiles.

It is particularly interesting to see the resemblance between this type of format and the purely empirical decompressions devised at the expense of many lives by Okinawan pearl divers operating in Australian coastal waters (LeMessurier & Hills 1965). These men also show substantial savings in total decompression time and feature both the same propensity for deep stops at the start of decompression and immediate surfacing upon reaching 22 to 35 feet. In terms of numbers of dives, the experience of these pearl divers must far outweigh that of all the navies combined.

However, the thermal analogue has the great disadvantage that it cannot allow for formation of the gaseous phase in tissue, a shortcoming also common to meters based upon the principle of critical supersaturation. These include the single air chamber fitted with a porous resistance plug made by S.O.S. (Italian patent 624174), the Canadian multi-chamber/orifice meter (Stubbs & Kidd 1965), the recent chamber/membrane meter (Borom & Johnson 1973) and several electrical analogues (Wittenborn 1963). All of these are essentially based upon equation (7) with no mechanism for reverting to equation (6) if the gas phase forms. Moreover, even if each were correct in the condition imposed for determining separation of the gas phase from solution, then any unheeded violation would cause the meter to register less gas remaining in the tissue and hence indicate even faster decompression—so exacerbating the initial error.

General analogue

An attempt to overcome these shortcomings has been made (Hills 1967c) by permitting each chamber of a 27-compartment pneumatic analogue to expand wherever the simulated total gas tension exceeds the absolute pressure ($P+b$). Thus the driving force is reduced in accordance with equation (6) (Fig. 20.10) while the total expansion must be proportional to the volume of tissue gas since Boyle's Law is applied automatically

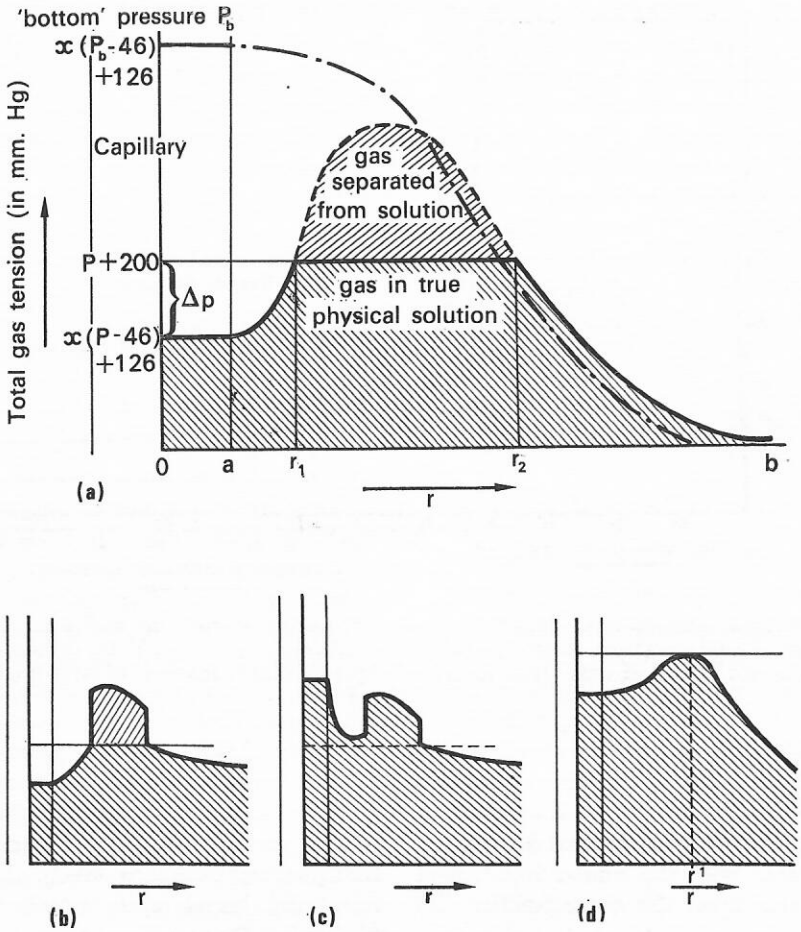

FIG. 20.10. Radial tension and separated gas distributions illustrated for phase equilibration at various stages of decompression and recompression. The inherent unsaturation (ΔP) is shown as the driving force for diffusion (1) —·—·— before decompression, and (2) ——— immediately after decompression to pressure, P

(Fig. 20.11). While this very large analogue (Fig. 20.12) has correlated the incidence of bends from decompressions based upon very different approaches, it has now been reduced to a small liquid-filled 6-chamber version for use as a meter (Hills 1973a) for optimizing on the zero supersaturation principle and capable of rescheduling following a diver mistake and gas phase formation.

OTHER BIOPHYSICAL ASPECTS

There are a number of interesting biophysical phenomena which have been reported recently. These include several facets of dysbaric osteonecrosis, gas-induced osmosis, collision fission of microbubbles and counter-diffusion supersaturation. The latter is an ingenious concept (Graves et al. 1973) which is described in another chapter (21) and could well explain hyperbaric urticaria (no-decompression skin bends), as observed by Blenkarn et al. (1971).

Collision fission of bubbles

Recent experiments in the author's laboratory have shown that microbubbles formed by air injection (Fig. 20.13) into human plasma in vitro

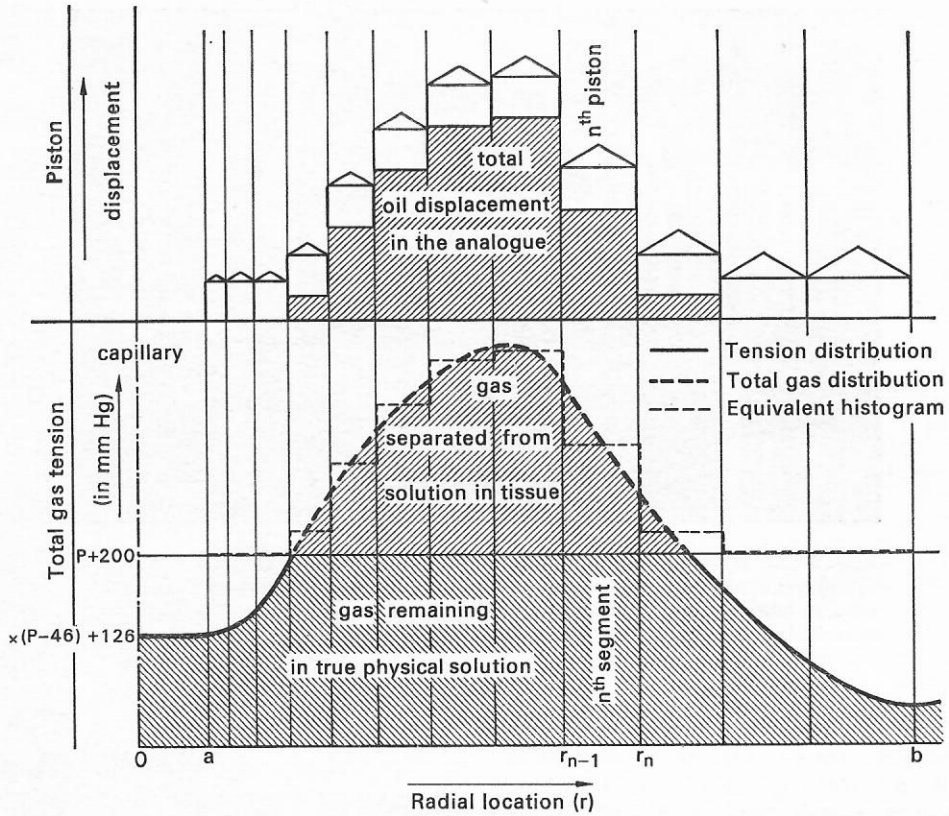

FIG. 20.11. Each radial segment around a cylindrical capillary is represented by a chamber of fixed minimum volume (see Fig. 20.12) but sealed by a moveable piston to ensure that its internal pressure does not exceed ambient. This simulates the 'cut-off' in driving force for gas elimination imposed by phase separation, limiting it to the inherent unsaturation (equation 6). Since Boyle's Law is applied to chamber gas, the piston displacements represent a histogram of the volume distribution of separated gas illustrated in Fig. 20.10

burst into many small bubbles upon collision. It is surprising that this only occurs if the diameter of the progenitors is less than 200 to 250 μm, while their size seems to have a negligible effect upon that of the progeny (about 40 to 50 μm diameter). This phenomenon could represent a protective mechanism of the body in minimizing the pathological effects of air emboli by reducing their size, although increasing their number.

It was found that the progeny of collisions would dissolve, even in air-saturated fluids, so supersaturating plasma!

Gas-induced osmosis

It has been demonstrated, by a transient technique, that nitrous oxide can induce osmosis across a synthetic membrane specifically formulated to be impermeable to that gas relative to water (Kylstra, Longmuir & Grace 1968). Moreover, it has now been shown that the phenomenon applies to biological membranes, since several gases have been shown to induce osmosis across various excised tissue sections under steady state conditions and in vivo (Hills 1971a). More significant to diving, perhaps, is the observation that nitrogen can 'pull' water away from helium if high pressure is used to emphasize the physical differences in these gases (Hills 1971b).

In any hyperbaric exposure this phenomenon has two potential components: a transient

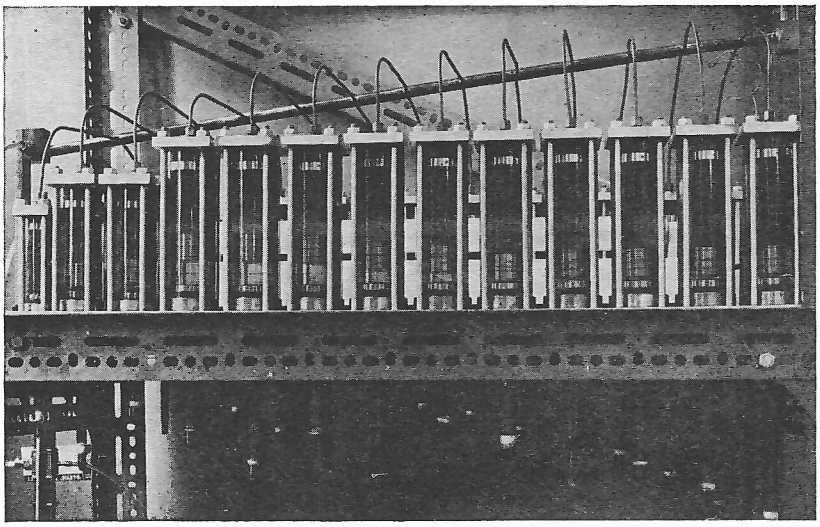

FIG. 20.12. A pneumatic analogue capable of simulating radial diffusion and the phase change indicated in Figs 20.9 and 20.10. The instrument has been used to analyse data irrespective of the rationale underlying the decompression design

contributed by the inert gas until it equilibrates throughout the tissue (see Fig. 20.14) and a change in the steady state effect of the permanent gradients of the metabolic gases, O_2 and CO_2. The former offers a convenient explanation for the time-dependent aspects of hyperbaric arthralgia, the high pressure nervous syndrome, minor changes in narcosis, vestibular problems, etc.

The steady state contributions suggest a possible involvement of osmosis in neurological oxygen toxicity (Hills 1972c) while it has implications in pulmonary O_2 poisoning, i.e. the effect of Lorraine Smith [1902]. This is based upon the observation that a lung selectively ventilated with 80% N_2O +20% O_2 accumulates more extravascular fluid than a control ventilated with air in the same animal (Hills 1972a).

Longmuir and Grace (1969) have shown transient changes in the volume of red cells when suddenly exposed to nitrous oxide solutions, the effect indicating an osmotic mechanism. The subject of gas-induced osmosis has been recently reviewed (Hills 1972b) with the conclusion that the osmotic potency of gases is simply an extrapolation from those of non-volatile solutes (Fig. 20.15).

Dysbaric osteonecrosis

The thermodynamic approach to decompression sickness would seem particularly compatible with the clinical data which shows no correlation between the incidence of bends and bone lesions in non-experimental divers and caisson workers, in so far as its calculation method predicts the formation of the gaseous phase, and hence 'silent bubbles', in the bends-free diver. It should thus be possible to avoid these 'silent bubbles' to which bone lesions are widely attributed (James 1945; McCallum & Walder 1966) by continuing the gradual ascent to the surface without the 'drop out' from 25 ft (1·7 ATA) now advocated. Support for this approach was provided by Doppler monitoring (Vann et al. 1973) when it was found that intravascular bubbles were not detected upon 'thermodynamic' profiles until the 'drop out' (Fig. 20.16).

However, if silent bubbles, thrombi or fat emboli were responsible for dysbaric osteonecrosis, one could expect a much shorter time course for the disease than the clinical evidence seems to indicate. This is discussed in detail in another chapter (27) but, if these doubts are well founded,

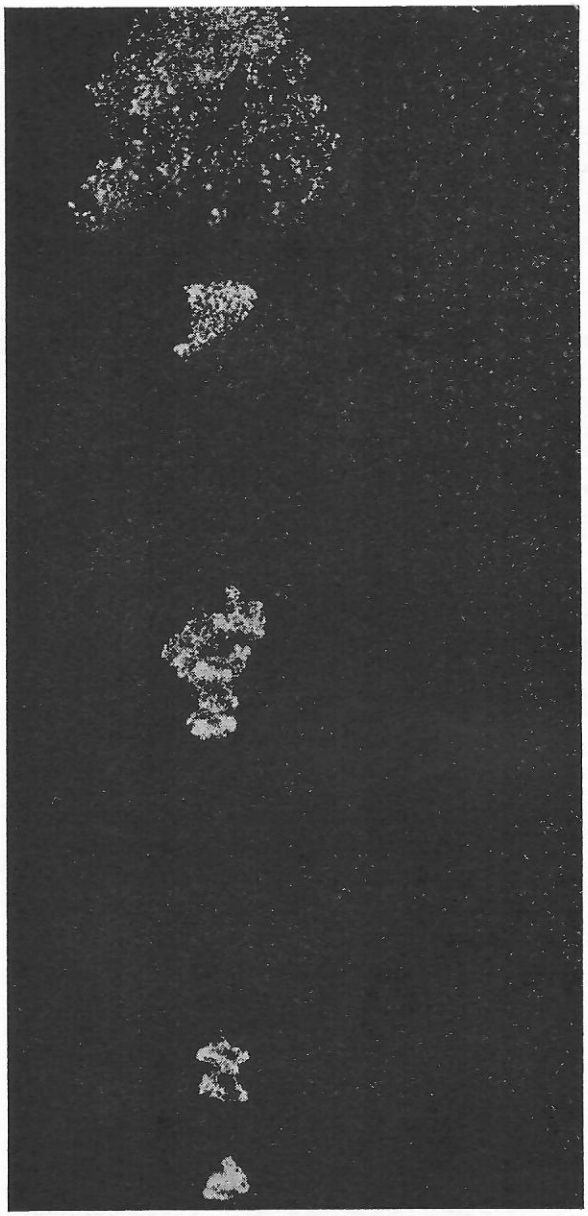

FIG. 20.13. The disintegration of successive complexes, each formed by the collision of two microbubbles of less than 200 μm diameter in plasma (from Hills 1974)

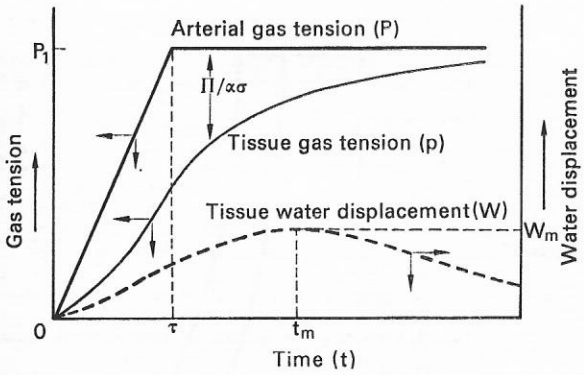

FIG. 20.14. The predicted transient displacement of fluid induced osmotically across a blood–tissue barrier by compression, at a uniform rate, to a 'bottom' pressure which is then held constant

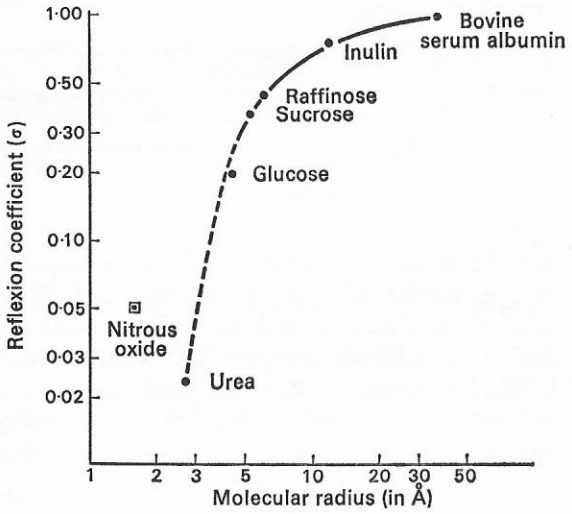

FIG. 20.15. The osmotic potency of a gas (nitrous oxide) is shown to be roughly predictable from an extrapolation of data for non-volatile solutes on the basis of the reflexion coefficient (σ). This is proportional to the number of solute molecules which are reflected rather than transmitted upon collision with the membrane.

then it would appear that a much more subtle form of insult to the bone occurs upon hyperbaric exposure, to become manifest much later as the ischemia leading to necrosis. A process which could continue slowly with no further exposure is the deposition of bone mineral in unwanted sites due to the known permanent supersaturation of hydroxyapatite in body fluids. This has led to two mechanisms to be proposed for dysbaric osteonecrosis based upon uncontrolled mineral precipation. Sobell (1971) has shown changes in colla-

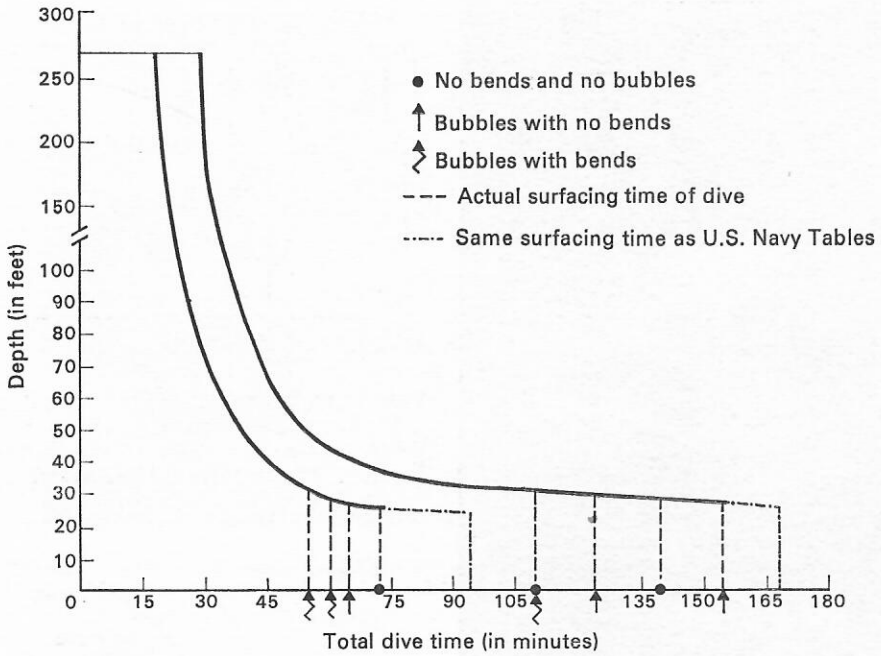

FIG. 20.16. Two decompressions optimized on the 'thermodynamic' principle, showing that bubbles were not detected by a Doppler ultrasonic meter until after the final 'drop out' from about 25 ft (1·7 ATA) (after Vann et al. 1973)

gen following quite small increases in inspired oxygen partial pressure, implicating that these sites of chemical cross-linking could be more inducive to mineral precipitation. Hills (1970a; 1972b) has shown that bones are good osmometers and that articular cartilage is an effective osmotic membrane for gases. Thus, if the ions do not move as easily as the water, there could be further local supersaturation resulting in spontaneous formation of nuclei, whose growth to sizes of clinical significance could take months or years. This hypothesis (Hills 1970a) would implicate any rapid change of pressure—either rapid decompression to the first stop or compression!

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