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14

Thermodynamic Decompression: An Approach Based upon the Concept of Phase Equilibration in Tissue

B. A. HILLS

The ultimate goal of workers in the field of decompression sickness has been a realistic theory capable of mathematical expression in terms of the fundamental physiological parameters of the individual, and of those defining the pressure exposure to which he has been subjected. Once the system has been described in such a comprehensive quantitative form it should then be possible to devise the fastest, or safest, means of decompressing that individual under any conditions.

However, the mathematical description of the system can be no more realistic than the physics of the model upon which it is based. This poses many questions of which three of the most vital are:

(1) The number of tissue types involved in marginal cases of decompression sickness.

(2) Whether the separation of the gas phase from solution in tissue is:

(*a*) determined by critical supersaturation,

(*b*) rate-limited by the transfer of gas molecules across the gas-tissue interface,

(*c*) very rapid, the relevant thermodynamic condition being one of phase equilibration.

(3) Whether the rate-limiting process in the uptake of inert gas by tissue is blood perfusion, bulk diffusion, membrane permeation or a combination thereof.

Quantitatively, the first of these fixes the number of independent equations to be used, the second determines the driving force for gas exchange, while the third describes the transport model and hence the mode of resistance to such exchange.

The above list of vital issues provides a convenient basis for analysis of the fundamental approaches contained in the conventional quantitative theories. The latter have been tested mostly on dives the decompressions of which have been formulated upon similar assumptions. Even so, the deviation from experience becomes appreciable for long or deep exposures, Hempleman (1962) placing such limits in the region of 120 ft (4·6 ATA) and 60 min. However, such theories offer a very poor correlation with the incidence of decompression sickness in Okinawan pearl divers operating in Australian coastal waters (LeMessurier & Hills 1965). This is significant since their empirical methods vary greatly from the normal naval style of decompression and represent independent data which must be correlated equally well by any realistic theory. Therefore one is obliged to see what basic assumptions are contained in the conventional theories or may be implied by their mathematics.

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Number of tissue types involved

The conventional theories differ greatly upon this first vital issue. While the Haldane model (Boycott, Damant & Haldane 1908) requires at least

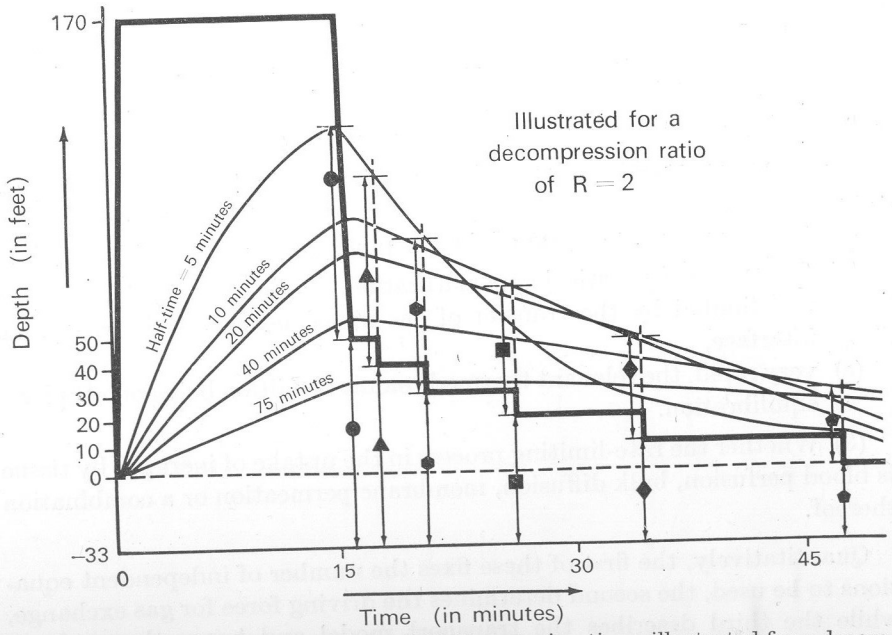

FIG. 14.1. The Haldane method of calculating staging times illustrated for a decompression ratio of 2:1

five tissue half-times to be considered, various combinations and total numbers have been used subsequently. Hawkins, Shilling and Hansen (1935), Yarbrough and Behnke (1939), Dwyer (1956) and many later U.S. Navy workers, have postulated a wide variety of tissue response times and decompression ratios with very moderate improvement. However, the advocates of such empirical approaches have never published any correlation between the theoretical tissue whose critical condition should have been exceeded and the type of symptom observed.

However, when Haldane employs one decompression ratio only, it may be said that his use of 5, 10, 20, 40 and 75 min half-times (Fig. 14.1) is a convenient approximation to estimating the response of a single tissue type in which there is a continuous spectrum of blood perfusion rates. If this were the case, then the envelope curve to the tissue responses should provide a better quantitative description. However, no improvement could be obtained in the correlation of practical data when implementing this concept by determining the worst possible time constant k for the exponential decay of tissue tension p, i.e.

$(\partial p/\partial k) = 0$ for which value of k:

$(\partial^2 p/\partial k^2) < 0$ for each critical stage of the particular decompression.

Single-tissue models have been proposed by Nims (1951), Bateman (1951), Hempleman (1952), Albano (1960) and Hills (1966).

It may be thought that the wealth of pathological data could be used to help reduce the extent of speculation upon this vital issue. The pathological approaches have been reviewed most comprehensively by Haymaker (1957), from which he admits that 'nothing really pertinent to establishing a model or mechanism can be extracted'.

Reverting to macro methods, an ingenious experiment has been designed by Rashbass (1954) to differentiate between the involvement of one or more tissue types. This is based upon the relationship between the titrated pressures of consecutive exposures, each of constant duration, and is thus independent of the transport model for comparative purposes. While its initial execution indicated a single-tissue model, later trials proved indecisive (Hempleman 1961).

Whenever one tissue type supersedes another as the closest to its respective threshold for provoking marginal symptoms, there should be a discontinuity in the parameters defining safe decompression limits. Selecting pressure and time as the two parameters most sensitive in determining proximity to marginal symptoms, no discontinuity could be detected in the plot of the limits of depth versus exposure time for safe no-stage

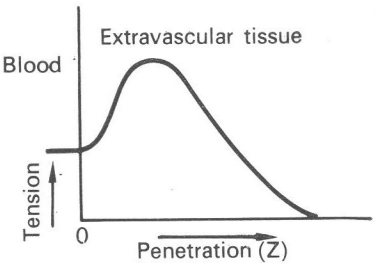

FIG. 14.2. A typical tension distribution within a homogeneous tissue whose boundary with blood is planar

decompressions. Such plots investigated include the diving data recorded by Van der Aue (1951) and Albano (1960) for air, and by Duffner, Van der Aue and Behnke (1946) for oxygen–helium mixtures.

In the apparent absence of any more convincing evidence to the contrary, it was therefore decided to adopt the concept of attributing marginal symptoms to the bubbles present in one tissue type only.

The histological site

If one postulates that diffusion makes a significant contribution towards limiting blood-tissue exchange, then the geometric location of potentially pain-provoking bubbles becomes important in calculating gas transport. Hence it is necessary to decide whether such bubbles are intravascular or not.

The vast mass of animal experimentation upon this issue seems to be influenced by the practical fact that it is far more simple to look for bubbles within the vascular system than elsewhere. However, in most instances where intravascular bubbles have been observed, the decompression has been severe and is in fact well in excess of that known to give marginal symptoms, e.g. Behnke and Shaw (1937) and many other cases summarized by Harvey (1951). Such experiments do not enable one to determine the site of origin of such bubbles, since large quantities of separated gas may cause vascular haemorrhage (Leyden 1879).

The theory of bubbles of extravascular origin appearing in intravascular sites by the laceration of capillary walls is certainly consistent with their decreased time of appearance with exercise (Blinks, Twitty & Whitaker 1951), and with any action likely to cause mechanical damage to the tissue. The latter cases have been well summarized by Harvey (1951).

More convincing evidence that the site of origin of bubbles responsible for marginal symptoms is extravascular has been presented by Ferris and Engel (1951) in their discussion of the aetiology of decompression sickness.

The single-tissue mathematical model thus progresses to one in which the bubbles provoking marginal symptoms are located in extravascular sites.

Single-tissue models

For dives of short or moderate duration, one of the best correlations of practical data is afforded by the model proposed by Hempleman (1952). His use of a $\sqrt{t}$ relationship for the uptake of gas, where t represents time, offers a very good prediction of no-stop dives whose durations do not exceed 20 min. The same model has been employed by Rashbass (1955) who applied the linear bulk diffusion equation, as first used in a biological context by Hill (1928).

However, the equations used by Hempleman and Rashbass are integral in nature, and thus express the net quantity of gas traversing a planar boundary between blood and tissue as illustrated in Fig. 14.2. Since both advocate supersaturation, it would seem more relevant to determine peak tensions, rather than mean extravascular tensions, in estimating the imminence of gas phase separation. However, the equations for such refinements (Hills 1966) afforded no better correlation of practical data; similar disappointment being experienced for a radial diffusion model.

It would therefore appear essential to take a further look at the one basic assumption common to all theories discussed so far. This is the implication that the relevant tissue is in a state of true supersaturation up to the point at which the particular criterion for safety is exceeded, whether such criteria are imposed in the form of decompression ratios (Haldane) or fixed tension differentials (Rashbass). This also applies to theories in which the incidence of symptoms is postulated as dependent upon the rate of gas transfer across the tissue-bubble interface (Nims 1951), or by this process in conjunction with the proliferation of nucleation (Bateman 1951).

However, the classical experimental work of Hempleman (1957) confirms the significance of a decompression ratio (P_1/P_2) or, at least, of a linear relationship between the bends-provoking pressure P_2 and that at which the subject had been living for an effectively infinite period immediately prior to decompression P_1. The significance of these findings is enhanced by their being independent of time, the interpretation of results avoiding the uncertainties associated with postulating any transport model. The question posed is whether the linear relationship between P_1 and P_2 is a manifestation of a critical limit to supersaturation or a fixed degree of embolism which the relevant tissue can tolerate. *The vital issue is thus whether there is a threshold to nucleation, i.e. is there a well-defined metastable limit to the formation of a stable gas phase in tissue by decompression?*

Suppressed transformation

The supersaturation of a tissue by a gas is just one example of a general phenomenon in nature known as 'suppressed transformation'. This is the suspended appearance of a new phase whose presence would enable the system to revert to a more stable thermodynamic state, the reluctance to undergo the change tending to be greater when a decrease of entropy is involved.

A general qualitative review of suppressed transformation (Hills 1966) has shown that, in all examples except decompression sickness, theoretical approaches have abandoned the concept of the metastable limit as originally proposed by Ostwald.

Recent theories in all disciplines seem to adopt a statistical approach, postulating a finite probability of nucleation occurring for any conditions within the metastable zone. For the relevant case of solutions of gases in liquids, such theories have been expounded by Fürth (1941) and many subsequent workers in the field of gaseous cavitation induced by ultrasonic means.

Supersaturation of a liquid by a gas

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 14.1.

TABLE 14.1
Recorded 'tensile strengths' of various liquids

Tensile strength (atmospheres)	*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.

The variation of the values quoted in Table 14.1 needs no comment. However, most authors tend to emphasize their highest reading, often making no mention of other runs failing to reach the maximum. While this would seem quite acceptable in attempting to determine the 'fracture strengths' of liquids, such data would seem of limited value in deciding whether the metastable limit implied by most theories of decompression sickness exists or not. *Any estimate of the threshold for phase separation can be influenced greatly by the results which one is prepared to discard as affected by chance contamination and the whole study of suspended transformation suffers from the extreme disadvantage of never knowing with certainty when this has occurred.*

The random nature of nucleation by decompression is even more marked for 'gaseous' cavitation for which case Strasberg (1956) found it necessary to repeat each run 20 times to establish even the more obvious trends.

It would seem most significant that bubbles formed by simple decompression *in vitro* almost invariably appear at the walls of the container (Wismer 1922). Pease and Blinks (1947) found it impossible to initiate bubble growth in the bulk of the liquid, concluding that a solid surface is the separation point. Moreover Harvey (1951) commented that nucleation is more profuse when the solid surface is hydrophobic.

The foregoing discussion emphasizes the importance of phase interfaces present in the system and thus raises some apprehension about the relevance of quoting data collected *in vitro* to support theories of supersaturation *in vivo*.

Nucleation at liquid–liquid interfaces

Every tissue may be regarded as composed of two basic types of chemical solvent, one aqueous and the other lipid in nature. Even the predominantly aqueous tissue types have a finite lipid content (Widdowson, McCance & Spray 1951) which may have a very large boundary if membranes are built around a bimolecular layer of lipo-protein (Danielli 1935).

Other likely phase boundaries are afforded by the predominantly lipid myelin sheaths of 'encapsulated' nerve fibres. Haymaker (1957) has published photomicrographs of histological sections of decompressed animals which display fenestration in the myelin sheaths of the white matter in the central nervous system.

It is difficult to say whether a direct lipid-aqueous interface exists in the body or how it may be modified by the presence of so many compounds with surfactant properties. However, it is felt that many phase boundaries must exist with energy barriers to gas nucleation appreciably lower than those for the individual fluids isolated *in vitro*.

Fat is fluid at body temperature, the relevant phase boundary being a

liquid–liquid interface. A study of 580 decompressions of a hydrophobic phase in contact with various aqueous fluids (Hills 1967a) has shown that:

(1) Cavitation almost invariably occurs at the liquid–liquid interface, indicating that any lipid-aqueous boundary would present a site most conducive to initiation of the gas phase.

(2) Bubble formation is a random process, there appearing to be no metastable limit to supersaturation or, at least, nothing comparable to the 30 ft of sea water used by Rashbass or the pressure ratios of Haldane.

Fig. 14.3. shows the frequency of bubble formation plotted against the extent of decompression for a 'nucleus-free' liquid–liquid interface formed

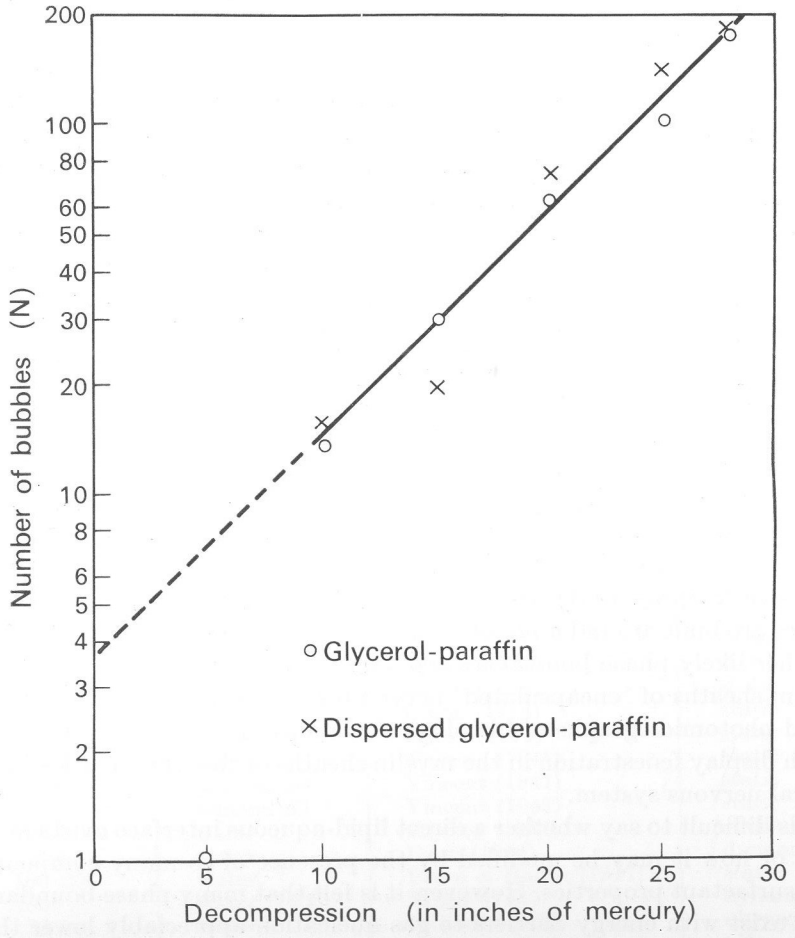

FIG. 14.3. The frequency of bubble formation at a hydrophobic–hydrophylic phase boundary in twenty runs for each extent of decompression (ΔP) from atmospheric

by the displacement of an oil by a denser aqueous fluid. These experiments were designed to avoid the presence of nuclei before decompression, Harvey (1951) having emphasized the role of gas pockets trapped in the micro-imperfections of solid–liquid boundaries in initiating cavitation at container walls.

While the preceding discussion would indicate that 'vaporous' and 'gaseous' cavitation at both solid–liquid and liquid–liquid interfaces is a random process, the ultimate tests must be performed *in vivo*.

Cavitation in vivo

Most experimenters have searched for bubbles in animals killed immediately before or after decompression between various combinations of initial and final absolute pressures.

One of the most comprehensive programmes in this field employed cats, the results being recorded in a series of joint papers (Harvey, Barnes, McElroy, Whiteley, Pease & Cooper 1944; Harvey, Whiteley, McElroy, Pease & Barnes 1944; Harvey, McElroy, Whiteley, Warren & Pease 1944; McElroy, Whiteley, Warren & Harvey 1944; McElroy, Whiteley, Cooper, Pease, Warren & Harvey 1944; Whiteley, McElroy, Warren & Harvey 1944). The results are summarized in Table 14.2, and would seem to offer convincing evidence that cavitation *in vivo* is a random process.

TABLE 14.2
Bubbles observed in resting cats

Time at pressure (P_1)	*Initial pressure (P_1) atmospheres absolute*	*Final pressure (P_2) atmospheres absolute*	*Number of cats in trial*	*Number displaying bubbles*
∞	1	0·14	37	4
∞	1		11	1 + 2?
2 to 5 hrs	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

The results in Table 14.2 are in quite good agreement with the general findings of Boycott *et al.* (1908) and Boycott and Damant (1908) using goats and guinea-pigs. The need to treat such experimental data upon a statistical basis is well illustrated by the use of the χ^2 significance test in extracting correlations (Harvey 1951).

Blinks, Twitty and Whitaker (1951) describe the work of Harris, Berg, Whitaker, Twitty and Blinks (1945) who have found bubbles in all of 31 bullfrogs exercised upon decompression to ambient following 1 hour at pressures ranging from 5 to 60 psi g (11 to 135 ft; 1·3 to 5·1 ATA). Inducing muscular activity in rats by 5 to 15 volt (60 cps) A.C. stimuli, they record a threshold pressure of 3 psi g (6 ft 8 in.; 1·2 ATA) at which two out of five animals gave bubbles just large enough to be observed.

This pressure differential is much smaller than any advocated in the semi-empirical methods conventionally employed for predicting marginal symptoms. Moreover, the random nature of detected bubble occurrence in both the resting and stimulated conditions would suggest that there is an appreciable probability of gas separating from solution in tissue whenever equilibrium concentrations are exceeded.

Supersaturation versus phase equilibration

The foregoing discussion would indicate that gas nucleation *in vivo* is basically no different from 'vaporous' or 'gaseous' cavitation at solid–liquid or liquid–solid interfaces, or from any other example of suppressed transformation, at least in so far as there is no true metastable limit to supersaturation. This implies that, for any given decompression beyond equilibrium conditions, it is impossible to predict with certainty whether nucleation of the gas phase will occur or not.

Is it therefore more realistic to programme a decompression, or to analyse a dive, according to the statistical average or according to the worst possible occurrence?

Before attempting to answer this vital question it would seem desirable to look at the possible mechanisms for the occurrence of pain and other symptoms. A realistic motivating force for distorting a nerve ending is provided by the pressure differential between the separated gas and surrounding tissue. If this differential pressure δ exceeds a critical threshold δ', then pain can occur if

$$\delta > \delta' \tag{1}$$

Experimental evidence for such a mechanical threshold has been provided by Inman (1944) and Saunders (1943). Inserting fine hypodermic needles into various tissues, they could induce pain by applying pressure differentials as low as 15 cm water gauge (0·015 ATS). These were transmitted by means of Ringer's solution, there being a definite threshold irrespective of the fluid flow required to maintain those differentials.

If one accepts the preceding emphasis upon pressure differential as a motivating force for bending nerve endings then one bubble, or one region of coalesced gas separated from solution, should suffice to cause pain.

Therefore it would seem more realistic to programme a decompression, or to analyse a dive, according to the 'worst possible' occurrence rather than according to the nucleation characteristics of the statistical average.

Such reasoning, in reply to the vital question terminating the discussion upon cavitation, represents a major departure from conventional theories of decompression sickness. However, the resulting thermodynamic approach (Hills 1966) is dependent upon the interpretation one places upon the 'worst possible' case. This has been taken as any 'fully nucleated' region where there is phase equilibration since this condition represents:

(1) Maximum separation of the gas phase from solution.
(2) Zero supersaturation, and hence the minimum driving force for elimination of the separated inert gas via the capillary.

Equilibrium phase distribution at an arbitrary stage in decompression is shown in Fig. 14.4. This is illustrated for a transport model in which radial bulk diffusion has been taken as the process limiting the rate of blood-tissue exchange, although the same basic argument would apply to one in which perfusion was rate-controlling.

In postulating phase equilibration, supersaturation can no longer be invoked to provide the driving force for tissue desaturation which has proved so convenient in conventional theories. However, it is well known that mild bends pain may eventually disappear and that gas injected into animals will be completely absorbed by the tissues in time (Campbell 1924). One is therefore faced with the problem of ascertaining the true driving force for elimination of inert gas from tissue via capillary blood after separation of the gas phase from solution.

The driving force for inert gas elimination during decompression

In most conventional theories it is assumed that the inhaled gas behaves as though it were entirely inert gas. In others the same implication is made when no independent terms are introduced into their quantitative expressions to describe the tensions of metabolic gases present. It is therefore felt that all volatile substances must be considered individually.

The driving force for the elimination of separated inert gas from tissue must be the differential Δp between its tension in capillary blood Pc and that in separated gas, p, i.e.

$$\Delta p = p - \mathrm{Pc} \tag{2}$$

The separated gas must be in both mechanical and chemical equilibrium with the tissue immediately adjacent to it. Thus for marginal symptoms

$$p + p_{CO_2} + p_{O_2} + p_{H_2O} = P + 2\gamma/y + \delta' \tag{3}$$

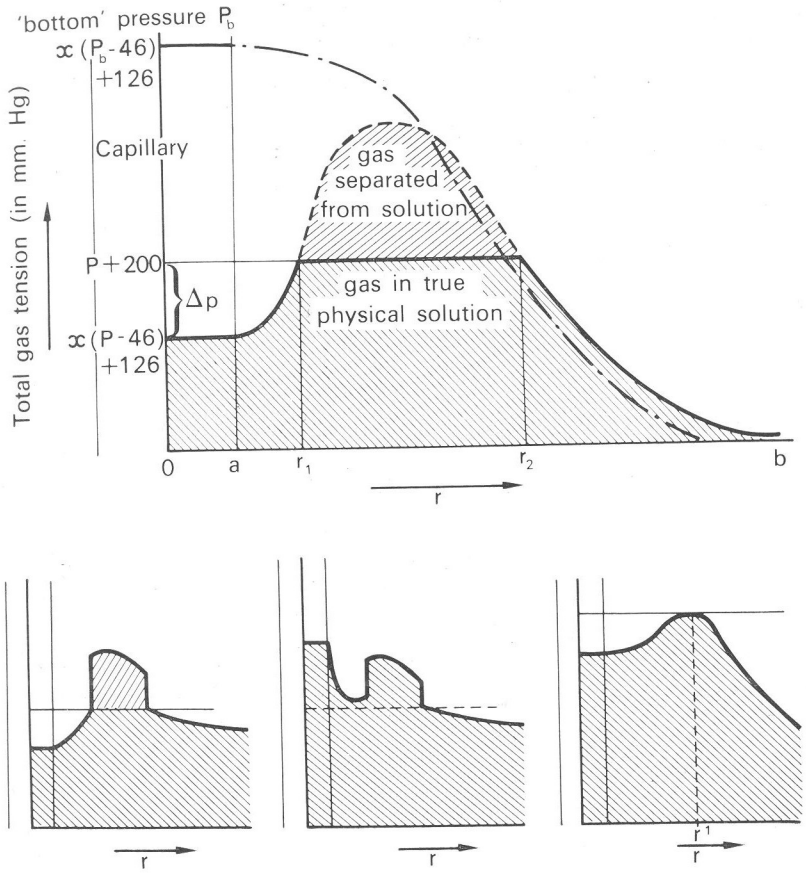

FIG. 14.4. Radial tension and separated gas distributions illustrated for phase equilibration at various stages of decompression and recompression. The inherent unsaturation (Δp) is shown as the driving force for diffusion (1) —·—·— before decompression, and (2) ——— immediately after decompression to pressure, P.

where $p\mathrm{CO}_2$, $p\mathrm{O}_2$ and $p\mathrm{H}_2\mathrm{O}$ are the respective mean extravascular tensions of carbon dioxide, oxygen and water in the critical tissue type. γ is the surface tension and y is the bubble radius giving the critical tissue deformation pressure (δ').

Substituting for p in equation (2)

$$\Delta p = \Delta p^* + 2\gamma/y + \delta' \qquad (4)$$

where

$$\Delta p^* = P - \mathrm{Pc} - p\mathrm{O}_2 - p\mathrm{CO}_2 - p\mathrm{H}_2\mathrm{O}$$

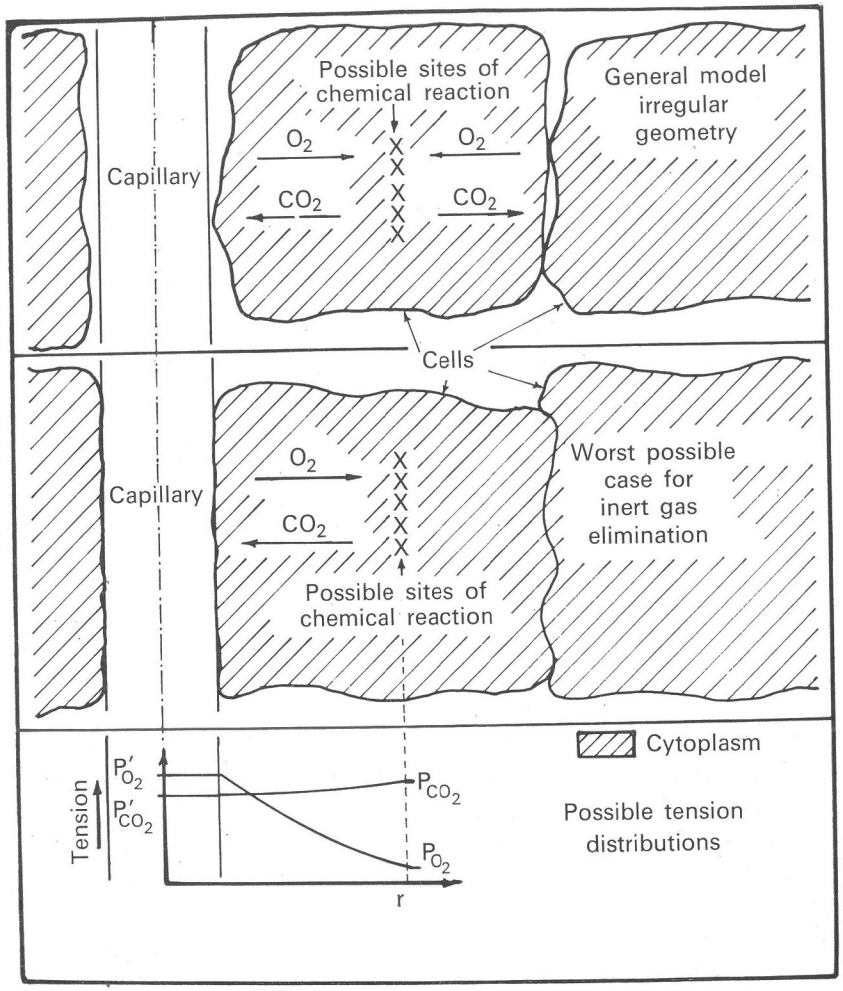

FIG. 14.5. Model used for estimating the tension distribution of the metabolizable gases by a physico-chemical analysis of the system

i.e. Δp^* is an unsaturation inherent in all living tissue under normal steady state conditions.

Considerations of surface tension and elastic deformation, plus a physico-chemical analysis of metabolism according to the model shown in Fig. 14.5 (Hills 1966) gives

$$2\gamma/y + \delta' = 200 \text{ mm Hg} \qquad (5)$$

and

$$(1 - x)P + 47x - 92 \geqslant \Delta p^* \geqslant (1 - x)P + 47x - 132 \text{ mm Hg} \quad (6)$$

the limits being necessary to allow for any variation in the metabolic rate.

However, for normal resting conditions relevant during decompression

$$p_{O_2} + p_{CO_2} + p_{H_2O} = 126 \text{ mm Hg} \quad (7)$$

when equations (3) and (5) give

$$p = P + 74 \text{ mm Hg} \quad (8)$$

and equation (6) reduces to

$$\Delta p^* = (1 - x)P + 47x - 126 \text{ mm Hg} \quad (9)$$

when equations (4) and (5) give the maximum driving force for the elimination of separated inert gas from tissue as

$$\Delta p = (1 - x)P + 47x + 74 \text{ mm Hg} \quad (10)$$

The inherent unsaturation

For depths in excess of 30 ft (1·9 ATA), equations (5) and (9) would indicate that the major contribution to Δp should be provided by the inherent unsaturation. This may be attributed to two sources:

(1) Metabolism, which can be regarded as a very complex series of chemical reactions in which one gaseous reagent, oxygen, is converted into a comparable number of molecules of one gaseous product, carbon dioxide, respiratory quotients varying from 0·71 to 1. However, the solubility of carbon dioxide in water is some twenty-six times that of oxygen in water. Hence there should be a net drop in the sum ($p_{CO_2} + p_{O_2}$) as reaction proceeds since

$$\text{(tension)} = \text{(concentration)/(solubility)}$$

where solubility is expressed as a Henry's law constant.

(2) The physical chemistry of the oxygen-haemoglobin and oxyhaemoglobin system. This is illustrated in Fig. 14.6 where widely different arterial oxygen tensions A_1 and A_2 should result in similar venous tensions v_1 and v_2 for blood supplying a constant metabolic demand for oxygen ΔQ to the tissue.

The expression describing the overall system (equation 6) is considered most significant since it predicts that the unsaturation Δp^*, and hence the driving force Δp, will increase linearly with respect to

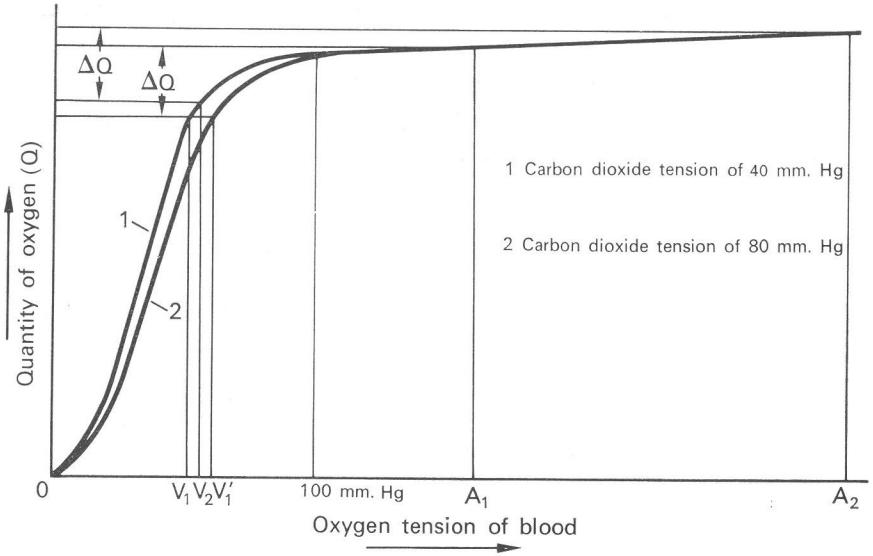

FIG. 14.6. The variation of the oxygen capacity of blood with oxygen tension

(1) decrease of mole fraction of inert gas x in the inspired atmosphere, and

(2) increase in absolute pressure P.

Both correlations have been verified experimentally *in vivo* (Hills 1966) using constant volume gas cavities and both are in direct agreement with the observations of Van Liew et al. (1965) who used subcutaneous gas pockets at constant pressure.

The second relationship is particularly significant since it implies that the rate of elimination of gas from tissue should be greater at greater pressure whenever the gas phase is present. This is the exact converse of conventional reasoning from which the navies have adopted the practice of giving their diver a large and rapid initial decompression in the belief that they are obtaining the maximum excess of mean tissue over blood tension.

Thus if the 'worst possible' is the relevant case, and no supersaturation can be guaranteed, then *equation (10) would suggest more effective decompression by keeping the dive much deeper—particularly during the initial stages.* This is in qualitative agreement with the format derived empirically by native pearl divers over almost a century. These men surface regularly in times far shorter than any predicted by conventional supersaturation theories for long deep dives, e.g. up to 300 ft (10 ATA) for 1 hour, sometimes twice a day working 6 days per week. Some of their deep dives were recorded by LeMessurier in 1959 and have been published with their technique for shallower repetitive diving (LeMessurier & Hills 1965).

The foregoing discussion has outlined the mechanism whereby an inherent unsaturation arising by virtue of metabolism can become a driving force for eliminating gas separated from solution in tissue. However, before exploiting this concept for devising the optimal deployment of decompression time, it is necessary to ascertain the relevant transport model.

TRANSPORT

Inert gas exchange

In deriving quantitative expressions for the kinetics of inert gas transfer within any organ, it is imperative to establish the relative contributions of diffusion and circulation in controlling blood-tissue exchange. Blood perfusion has been widely accepted as the process limiting the uptake or elimination of inert substances in tissue, most advocates quoting the work of Kety (1949, 1951), Jones (1951) or Kety and Schmidt (1945). If this assumption is made, then the following expression can be derived to relate the mean tension of inert gas $\bar{p}$ to the blood perfusion rate Q:

$$\bar{p} = P_a . \exp(-\lambda Q t) \qquad (11)$$

for a step in arterial tension p_a defined by $p_a = P_a$ for $t \leqslant 0$ to $p_a = 0$ for $t > 0$, where t represents time. λ is the blood to tissue partition coefficient for the inert gas and P_a is constant. Equation (11) has been used widely for estimating local blood perfusion rates (Kety 1949) and is based upon a model comprising a 'fully-stirred' tank whose venous 'overflow' leaves in equilibrium with the tissue.

Equation (11) forms the basis of the argument of Jones in favour of a circulation-controlled system, on the grounds that very similar time constants k should be obtained for the 'wash-out' of different inert gases from the same tissue. In fact they should be identical if the tissue has no lipid content, $\lambda = 1$, when $k = \lambda Q = Q$, the blood perfusion rate Q being the same for both gases. Thus the major evidence which Jones (1951) offers in support of advocating circulation as the process limiting the rate of blood-tissue exchange is the similarity of his experimental time constants obtained for two inert gases simultaneously eliminated from the body by oxygen 'wash-out'. He measured exhaled nitrogen together with either helium, krypton or radioactive xenon.

However, in his comparison of values, the method of Jones of enumerating exponential terms would seem to be purely arbitrary, there being no apparent reason why k_1 should be assigned the largest value, k_2 the second largest, etc. On the other hand there would seem to be several reasons for adopting the reverse order, i.e. k_1 is the smallest, k_2 the next smallest, etc. These include

(1) From experience it is impossible to isolate the very 'fast' components by backward projection. It is therefore difficult to see how anyone can say which is the first component according to this method of enumeration. For small values of time a $\sqrt{t}$ relationship would seem most realistic for total elimination (Eggleton, Elsden, Fegler & Hebb 1945). On the other hand, the reverse order to that of Jones avoids any ambiguity however the values are interpreted.

(2) If diffusion is rate-contributing, the solutions to all bulk diffusion equations can be expressed as Fourier series in which the first time constant k_1 is the smallest (Hills 1967b).

A comparison of the values of Jones for different gases is made by both methods of enumeration in Table 14.3.

TABLE 14.3
Analysis of inert gas elimination from man (data from Jones 1951)

Gas	*Method of enumeration (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}.

It can be seen from Table 14.3 that his method of enumeration would indicate that the rate-limiting process is blood perfusion, but the reverse order would suggest diffusion. Hence there would seem to be little justification for the popular reference to this data in dismissing diffusion as making no significant contribution to controlling blood-tissue exchange.

Both the perfusion and diffusion models offer reasonable explanations for most other facets of blood-tissue exchange. The remarkable parallelism of the arguments has been traced and leads to the alternatives of postulating that the rate-limiting process is either two-phase diffusion or blood perfusion in which parallel arteriovenous pathways accommodate discrepancies from a simple exponential response (equation 11), although the latter would seem unlikely (Hills 1967e, 1968).

Diffusion times

The vital factor in differentiating between the validity of the two models is the diffusion time of the solute in the tissue. Hence one of the major arguments put forward by advocates of blood perfusion for the rate-limiting process is their estimation that mean extravascular tension should

attain 95% of the asymptote within 1 sec of a step in blood tension of the same solute. Thus Kety (1951), Thompson, Cavert and Lifson (1958) and Roughton (1952), using the same transient equation, have concluded that radial diffusion from a capillary should make an insignificant contribution to controlling blood-tissue exchange.

In their calculations, the above authors have used values of diffusion coefficients which are either those for the same solute in water or those determined from excised tissue sections by steady-state methods, often those of Krogh (1918). However, the use of steady-state values in transient equations only retains any physical meaning if the extravascular region can be regarded as a homogeneous diffusion medium. If values of diffusion coefficients in cellular material are several orders less than those in water or in interstitial fluid, then solute molecules would mostly by-pass cells in traversing a tissue section under the constant concentration gradients employed by steady-state methods.

It is interesting to note that Krogh (1918) obtained values for diffusion coefficients for various gases which were one-third to one-fifth of those for the corresponding solutes in water. However, this is of the order of magnitude to be anticipated for the fraction of cross-sectional area of tissue occupied by extracellular fluid.

The justification for the relatively small contribution which Forster (1963) attributes to diffusion in controlling blood-tissue exchange is thus dependent upon the relative diffusion coefficients of extracellular and cellular material.

Diffusion coefficients

Very few values of diffusion coefficients could be found which had been determined by truly transient methods. Dick (1959) quotes a range of $1{\cdot}5 \times 10^{-8}$ to $5{\cdot}0 \times 10^{-10}$ cm^2/sec for water in cytoplasm compared with 10^{-5} cm^2/sec for the self-diffusion coefficient of water. Fenichel and Horowitz (1963) quote values ranging from 3×10^{-8} to 3×10^{-10} cm^2/sec for ten polar compounds in the isolated fibres of frog sartorius muscle. These include urea for which Perry (1950) quotes $1{\cdot}4 \times 10^{-5}$ cm^2/sec as the diffusion coefficient in water.

Reverting to inert non-polar gases, relevant to decompression sickness, Hills (1967b) has obtained a value of $2{\cdot}3 \times 10^{-10}$ cm^2/sec for the diffusion coefficient of acetylene in the cellular material of undisturbed skeletal rabbit muscle. Acetylene has a molecular weight of 26 while that of nitrogen is 28. Justification for the mathematics used in determining the diffusion coefficient in cytoplasm is provided by the fact that very similar values were obtained for this and several other basic parameters of the same model from data collected when

(1) the uptake of gas was effected by blood perfusion, and
(2) an excised section of the same tissue was exposed to the gas.

Thus the diffusion coefficients derived by truly transient analysis indicate that skeletal muscle is very heterogeneous in its permeability to inert substances. While the size and macro-uniformity of muscle has attracted much attention experimentally, the above conclusions probably apply to other tissues—particularly those closely associated with the locomotor system as we know is the case with decompression sickness (Ferris & Engel 1951).

Model relevant to decompression sickness

The foregoing discussion would indicate that it is a gross assumption to regard normal tissue as anything less complex than a three-dimensional structure in which the two most prominent phases are

(1) A continuous extracellular phase comprising plasma and pericapillary filtrate of diffusion coefficient comparable with that of the same solute in water and, in part at least, hydrodynamically perfused by solvent when the circulation is functioning.

(2) Cellular material of uniform yet far lower permeability to inert non-polar solutes, the cells being irregularly distributed and of irregular profile.

If the concept of irregular cellular boundaries is accepted, then the worst cases for desaturation must occur in the few random instances where two or more cells completely envelope a capillary. While these may represent no more than several occurrences in several million possible sites, such locations would retain the largest quantities of separated gas if nucleated during decompression.

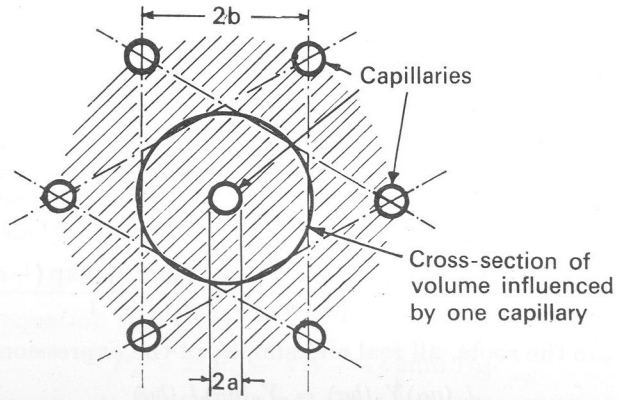

FIG. 14.7. The mathematical model corresponding to the 'worst possible' case, i.e. radial diffusion from blood directly into cellular material

Thus, to be consistent with the policy of programming a decompression according to the worst possible occurrence, the relevant case is one of radial diffusion from a capillary into cytoplasm. The corresponding mathematical model is shown in Fig. 14.7. This is consistent with that used to illustrate separated gas distribution (Fig. 14.4) and to estimate the extravascular tensions of the metabolic gases (Fig. 14.5).

Having derived a transport model, it is now possible to determine the optimal deployment of decompression time according to the principle of phase equilibration advanced earlier. However, before expressing this quantitatively, it is necessary to obtain expressions for inert gas distribution before the phase change.

Radial diffusion

Let us consider the critical tissue type of a diver who normally lives at atmospheric pressure P_0, and who has just completed an exposure time τ at a 'bottom' depth corresponding to an absolute pressure P_b. In going to depth rapidly there should be an effective step change in the inert gas tension of capillary blood p_c defined by $p_c = x(P_0 - 47)$ mm Hg for $t \leqslant 0$ to $p_c = x(P_b - 47)$ mm Hg for $t > 0$, after allowing for alveolar dilution by water vapour. This is the boundary condition for $0 \leqslant r \leqslant a$, where r is radial distance from the axis of a cylindrical capillary of radius a as shown in the transport model (Fig. 14.7). If the volume of tissue receiving gas from one capillary has a radius b, then there can be no transfer at $r = b$, i.e. $(\partial p/\partial r) = 0$.

Applying the above boundary conditions to the general solution of the Fick–Fourier equation for transient radial diffusion (Carslaw & Jaeger 1959) as

$$\frac{\partial^2 p}{\partial r^2} + \frac{1}{r}\cdot\frac{\partial p}{\partial r} = \frac{1}{D}\cdot\frac{\partial p}{\partial t}$$

the above boundary conditions give (Hills 1966) the inert gas tension p, at a general radial location r and time t, as

$$p = x(P_0 - 47) + x(P_b - P_0).\Phi(r\,;t) \qquad (12)$$

where

$$\Phi(r\,;t) = 1 - \pi\sum_{n=1}^{\infty}\left[\frac{\{J_0(r\alpha_n)Y_0(a\alpha_n) - Y_0(r\alpha_n)J_0(a\alpha_n)\}.\exp(-\alpha_n{}^2Dt)}{\{J_0(a\alpha_n)/J_1(b\alpha_n)\}^2 - 1}\right] \qquad (13)$$

where $\pm\alpha_n$ are the roots, all real and simple, of the expression:

$$J_0(a\alpha)Y_1(b\alpha) = Y_0(a\alpha)J_1(b\alpha) \qquad (14)$$

J and Y signify Bessel and Neumann functions respectively according to the nomenclature defined by Watson (1944).

Equations (7) and (12) now enable the total gas tension $\sum p$ at any point in the tissue to be described quantitatively. Upon completion of the exposure time τ at P_b, this would be

$$\begin{aligned}\sum p &= p + p_{O_2} + p_{CO_2} + p_{H_2O}\\ &= x(P_b - P_0).\Phi(r\,;\tau) + x(P_0 - 47) + 126 \text{ mm Hg}\end{aligned} \qquad (15)$$

Thermodynamic optimization

According to the thermodynamic hypothesis, staging is advocated following any dive from which immediate decompression to atmospheric pressure P_0 could cause a volume of gas to separate from solution which is in excess of that required to produce the critical deformation pressure necessary to provoke marginal symptoms. The object in finding the optimum is therefore to remove this excess in the minimum time. To achieve this, each portion must be eliminated from tissue under conditions such that the driving force for desaturation is maintained at a maximum. However, this driving force should be a maximum for the greatest pressures if the gas phase is present (equation 10), but for the lowest pressures if it is not.

Thus, for the 'worst possible' case, the fastest elimination of the excess gas should be effected by adjusting the pressure of the diver continuously such that his critical tissue type is maintained just on the brink of a phase change. After each move towards the surface the 'inherent unsaturation' will be rapidly re-established in capillary blood to correspond to the new pressure P in equation (6), and so provide a driving force for desaturation which will decrease as the diver approaches the surface.

According to the foregoing reasoning, the thermodynamic approach would predict the shortest overall decompression time for a diver to return safely to the surface by adhering to the following sequence:

(1) A very rapid initial decompression from the bottom pressure P_b to an 'equilibrium' pressure P_e beyond which any further rapid rise towards the surface could cause gas phase separation. This move is designed to 'take up' the inherent unsaturation at the bottom pressure which should determine the total gas tension in at least those tissue layers immediately adjacent to the capillary, i.e.

$$P_e = P_b - (\Delta p)_{P=P_b}$$

from which equation (10) gives

$$P_e = x(P_b - 47) - 74 \text{ mm Hg}$$

(2) A continuous decompression from P_e maintaining the system just on the brink of gas phase separation at the radial distance r' where total tension is a maximum. Such a condition is illustrated in Fig. 14.4 (graph 5).

The gradual raising of the diver is continued by this format until a pressure P_s is reached from which he can surface directly with the separation of a sub-critical volume of gas from solution. The condition for the continuous decompression is thus

$$p' + 126 = P \text{ mm Hg} \tag{16}$$

where p' can be estimated from equation (12) in which r' is the value of r for which p is a maximum, i.e.

$$(\partial p/\partial r) = 0 \tag{17}$$

for which value of r', $(\partial^2 p/\partial r^2) < 0$.

(3) Rapid decompression from P_s to atmospheric pressure P_0. P is a function of the extent of gas phase separation and the tolerance of the individual. The latter can be conveniently described quantitatively by the minimum bends pressure of a man P_∞ from which immediate decompression to P_0, after an effectively infinite exposure, just gives marginal symptoms, i.e.

$$P_s \geqslant P_\infty - (\Delta p)_{P=P_\infty}$$

from which equation (10) gives

$$P_s \geqslant xP_\infty - 47x - 74 \text{ mm Hg}$$

P_s is difficult to estimate exactly but, for most individuals, it lies within the range 1220 to 1560 mm Hg. This corresponds to direct surfacing from depths of 20 to 35 ft (1·6 to 2·2 ATA).

Automatic optimization

The continuous application of equation (17) to equation (12) is complicated by the fact that the point tension p must be modified during decompression to account for the superposed effects of n stagings. If the mth stage consists of time τ_m spent at pressure P_m

$$p = x(P_0 - 47) + x(P_b - P_0).\Phi(r;\tau) + x.\sum_{m=1}^{n}(P_m - P_{m-1}).\Phi(r;t-\tau-\Sigma\tau_m)$$

When the equilibrium condition, equation (3), is applied to the above expression to determine the optimal pressure P at time t, the necessary analysis is exceedingly complex. This arises since P, r' and t are mutually dependent variables.

However, such mathematical complexity can be circumvented by use of a thermal analogue (Hills 1967c) in which the conduction of heat simulates the diffusion of gas. An asbestos block used to preserve the geometric

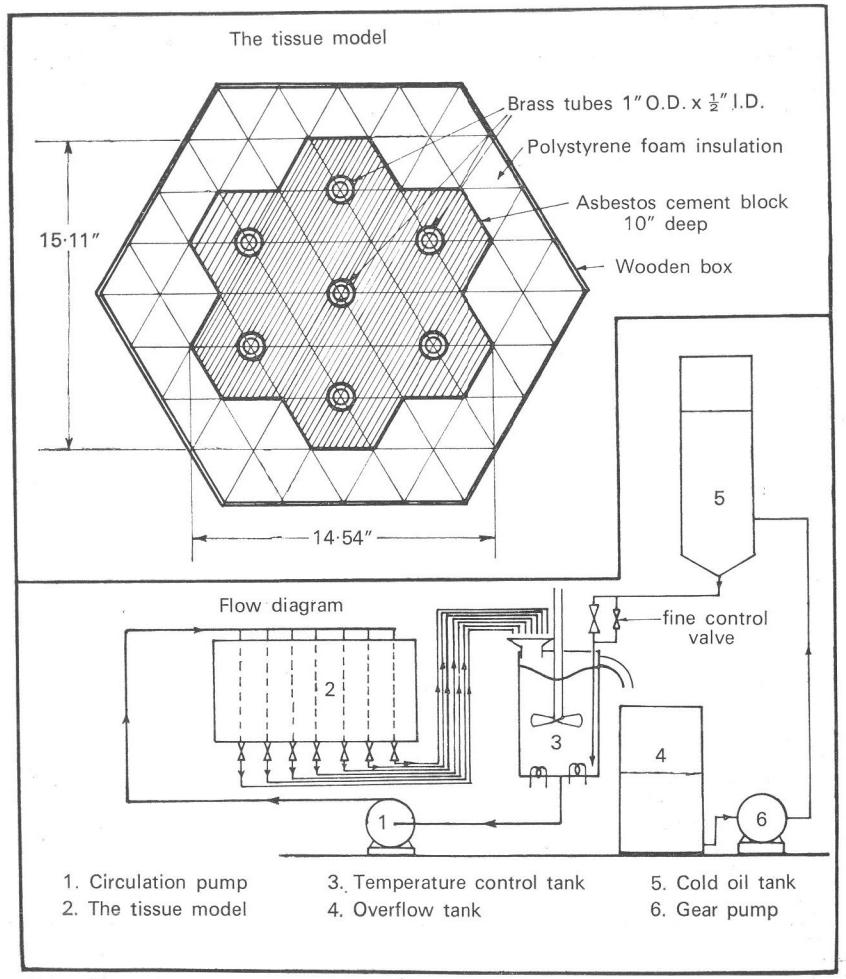

FIG. 14.8. Drawing of an asbestos block in which the conduction of heat simulates the diffusion of inert gas

similarity to the transport model (Fig. 14.7) is shown in Fig. 14.8. This analogue embodies all the foregoing mathematics and enables one to locate peak temperatures instantaneously, so indicating any immediate adjustment to the pressure P of the diver necessary for it to comply with the equilibrium condition expressed by equation (3).

A decompression format predicted by the analogue for a dive of 40 min at 150 ft (5·5 ATA) is shown in Fig. 14.9. This has been compared experimentally with the corresponding U.S. Navy (1964) schedule by cutting time from both until goats developed symptoms (Hills 1966). The pressure

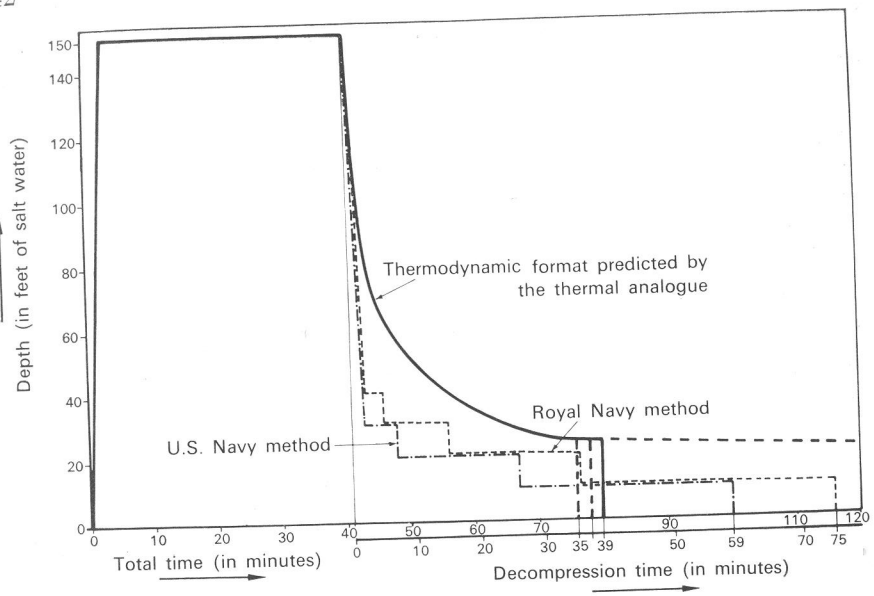

FIG. 14.9. The optimal deployment of decompression time as indicated by the thermal analogue for a dive of 40 min at 150 ft (5·5 ATA)

chamber and control system were found to be perfectly satisfactory for the task, guaranteeing a continuous replacement of warm dry air in the tank and a fidelity of ± 1% to any decompression format which had been previously fed to the automatic programmer. The results of 25 goat exposures (Table 14.4) indicate that the standard 59 min total decompression time advocated by the U.S. Navy tables is equivalent, following the thermodynamic format, to 36 ± 1 min. However, many more trials are needed to confirm the apparent advantages of the latter, and these are now under way.

Viewed from the 'thermodynamic' standpoint, the conventional tables are safe but far from optimal. *They would represent a therapeutic treatment for a large molar quantity of gas separated from solution by virtue of the first*

TABLE 14.4
Summary of goat trials

Decompression format	*Total decompression time (min)*	*Runs*			*Number of symptoms*	*Total animal decompressions*	*% with symptoms*
		Total	*Safe*	*% Safe*			
Thermodynamic	35	1	0	0	1	1	(100)
Thermodynamic	37	4	2	50	2	6	33
Thermodynamic	39	4	4	100	0	8	0
U.S. Navy	59	4	0	0	6	8	75
Royal Navy	75	1	1	(100)	0	2	0

long decompression, symptoms not becoming manifest by virtue of the Boyle's law effect. The basic difference is that gas in excess of the minimum required to give pain is eliminated at much shallower depths if one follows the format of any theory invoking supersaturation. However, this is the region of lowest driving force if the 'worst possible' is the relevant case for predicting symptoms.

Although the foregoing discussion suggests that supersaturation schedules are far from optimal, it is important to show that the vast wealth of recorded experimental data upon dives programmed according to such premises can be correlated by the 'thermodynamic' approach. This requires a quantitative method of analysis which can allow for a phase change.

QUANTITATIVE ANALYSIS

The phase change

The type of analogue shown in Fig. 14.8 cannot be used to analyse the conventional type of dive since it cannot simulate a phase change. However, this problem has been overcome in the case of a pneumatic analogue (Hills 1967d) in which the transport system is allowed to expand at any point where total gas tension exceeds the absolute pressure of the diver (plus allowances for surface tension and elastic deformation). This analogue (Fig. 14.10) has produced a correlation of both conventional decompressions and those of native pearl divers.

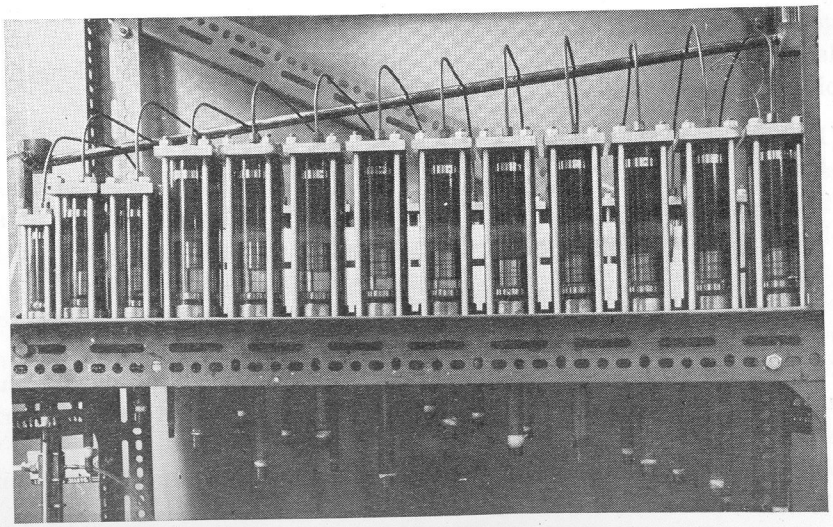

FIG. 14.10. A pneumatic analogue capable of simulating radial diffusion and the phase change illustrated in Fig. 14.4. This instrument can be used to analyse any diving data according to the hypothesis proposed

However, even with such 'tools', it is desirable to have a means of mathematical analysis.

Quantitative derivation

If K is the bulk modulus for *expansion* of the tissue, the deformation pressure is given by

$$\delta = Kv$$

where v is the volume of gas separated from unit volume of tissue. Hence equation (1) indicates that pain can occur if

$$Kv > \delta' \tag{18}$$

If the partial volume of inert gas separated from solution in unit volume of tissue is u, then:

$$v = u(P + 200)/(P + 74) \tag{19}$$

since the total pressure of separated gas is $(P + 200)$ mm Hg (equation 5) and the partial pressure of gas is $(P + 74)$ mm Hg (equation 8).

Several workers have shown that transfer of the inert gas determines the rate of absorption of any gas pocket in tissue (Campbell 1924; Coryllos & Birnbaum 1932; Rahn 1961; Van Liew 1962; Van Liew et al. 1965). After any change of hydrostatic pressure, oxygen, carbon dioxide and water tensions rapidly revert to values conforming to equation (7).

Hence the parameter u will determine v at any stage of decompression in accordance with equation (19). Now u may be estimated from a mass balance for inert gas in the tissue volume influenced by unit length of capillary where

(1) Inert gas in unit volume of tissue before dive $= S$ (initial capillary tension) $= xS(P_0 - 47)$ allowing for alveolar dilution by water vapour.

(2) Inert gas *in true physical solution* in unit volume of tissue at an arbitrary stage (pressure P) of decompression = S (inert gas tension in solution) $= S$ (inert gas tension in separated gas) $= Sp$, since there is phase equilibration. Substituting $p = (P + 74)$ according to equation (8), inert gas remaining in solution $= S(P + 74)$.

(3) Let GS be the quantity of inert gas taken up by unit volume of tissue at maximum depth P_b, expressed as a volume reduced to atmospheric pressure P_0 and body temperature.

(4) Let $G'S$ be defined, on the same basis, as the gas eliminated from unit volume of tissue during decompression.

To maintain uniform dimensions, S is the Henry's constant or solubility of inert gas in extravascular tissue expressed as the volume of gas, reduced

to P_0 and body temperature, per unit volume of tissue and per mm Hg partial pressure of that gas.

Thus the volume of gas, reduced to pressure P_0 and body temperature, separated from solution at pressure P

$$= xS(P_0 - 47) + SG - S(P + 74) - SG'$$
$$= S(G - G' - P - 74 + xP_0 - 47x)$$

Hence the partial volume of this gas u at the total pressure of separated gas $(P + 200)$ mm Hg for the ambient external pressure P, is given by Boyle's law as

$$u = (G - G' - P - 74 + xP_0 - 47x)SP_0/(P + 200)$$

Substituting this expression for u, equation (19) gives the total volume of gas separated at the ambient pressure as

$$v = (G - G' - P - 74 + xP_0 - 47x)SP_0/(P + 74)$$

Substitution for v in equation (18) indicates that pain can occur if

$$f = \frac{(G - G' - P - 74 + xP_0 - 47x)}{(P + 74)} > \frac{\delta'}{KSP_0} = f_c \tag{20}$$

where f is a convenient dimensionless parameter for estimating the proximity to symptoms, the critical value being f_c, i.e. possible pain if $f > f_c$.

The functions to be determined are now G and G'.

Inert gas uptake at depth (GS)

At maximum depth there can be no gas phase present and hence G may be determined by applying Fick's law to the capillary wall, i.e.

$$\frac{d(GS)}{dt} = -\left(\frac{\text{volume}}{\text{surface area}}\right) \cdot SD \left(\frac{\partial p}{\partial r}\right)_{r=a}$$

or

$$\frac{dG}{dt} = -\frac{(b^2 - a^2)D}{2a} \cdot \left(\frac{\partial p}{\partial r}\right)_{r=a}$$

Applying this expression to the equations for inert gas tension distribution (equations 12 and 13), and integrating with respect to time following a step change in pressure of $P = P_0$ for $t \leqslant 0$ to $P = P_b$ for $t > 0$:

$$G = x(P_b - P_0).\psi(t) \tag{21}$$

where

$$\psi(t) = 1 - \frac{4}{[(b/a)^2 - 1]} \cdot \sum_{n=1}^{\infty} \left[\frac{\exp(-a_n^2 Dt)}{(a\alpha_n)^2[\{J_0(a\alpha_n)/J_1(b\alpha_n)\}^2 - 1]}\right] \tag{22}$$

Thus, upon completion of the exposure time τ at maximum depth:

$$G = x(P_b - P_0).\psi(\tau) \tag{23}$$

In equation (22), α_n is still the nth root of equation (14) for which solutions are given in Fig. 14.11 as the plot of two dimensionless parameters: $a\alpha_n$ against b/a. The latter is the ratio of intercapillary distance to capillary diameter and thus provides a convenient index of vascularity. This has proven particularly expedient in allowing for the vasodilatation associated with exercise (Hills 1966).

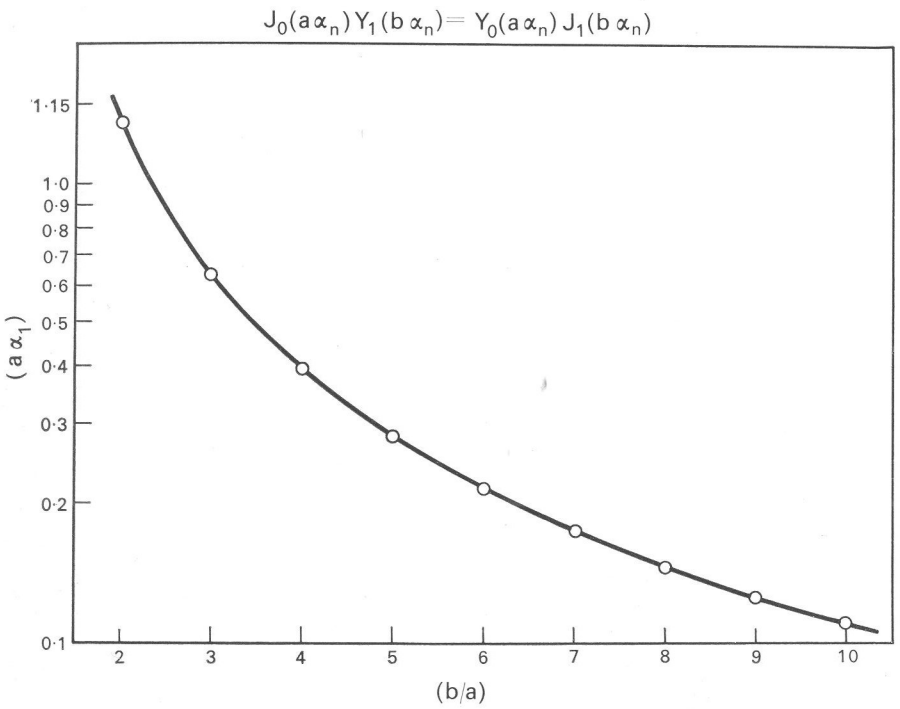

FIG. 14.11. The first root of equation (14) expressed graphically according to the solutions of Jahnke *et al.* (1960)

Substituting for G according to equation (23), where pressures are expressed in mm Hg, equation (20), gives the condition for possible symptoms as

$$f = \frac{[x(P_b - P_0)\psi(\tau) - G' - P - 74 + x(P_0 - 47)]}{(P + 74)} > f_c \qquad (24)$$

This expression (24) is the culmination of the analysis.

The mathematical complexity indicated by equation (22) can be avoided once the function $\psi(t)$ has been calculated and presented in a general form. The solution is plotted in Fig. 14.12 as two dimensionless groups—$\psi(t)$ against Dt/a^2. These have been computed for three exercise

levels for which the corresponding degrees of vasodilatation have been determined from dive analysis (Hills 1966) as

$b/a = 5{\cdot}29$ resting
$b/a = 4{\cdot}91$ for moderate work
$b/a = 4{\cdot}73$ for hard work.

D/a^2 was found to be $0{\cdot}129\ \text{min}^{-1}$ for nitrogen and the application of Graham's law gave a value of $D/a^2 = 0{\cdot}129\sqrt{28/4}\ \text{min}^{-1}$ which enabled helium results to be correlated by the same function.

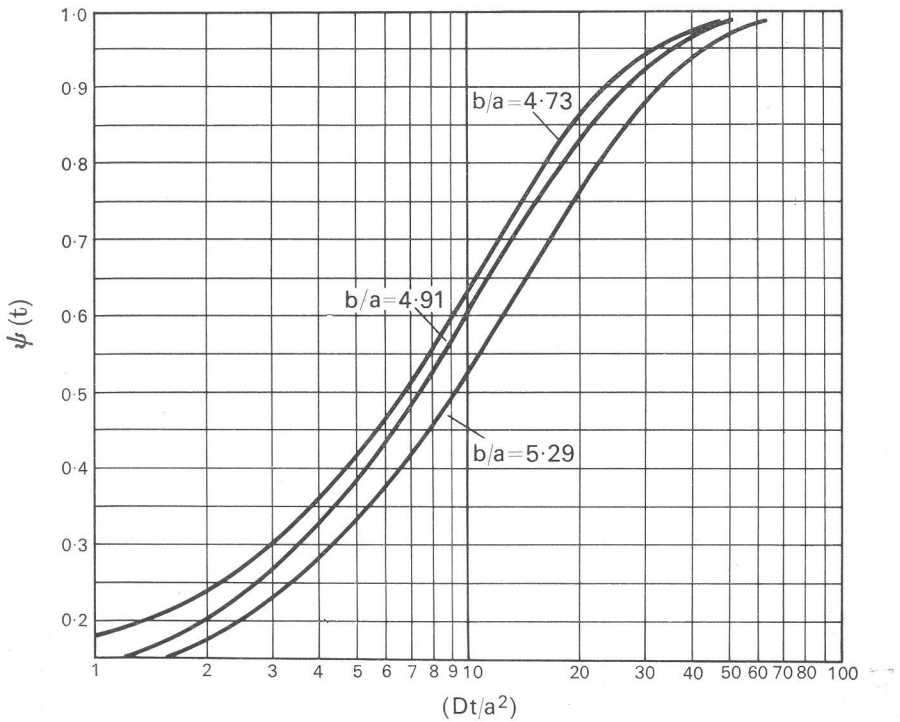

FIG. 14.12. The uptake of inert gas expressed as a function of time by plotting dimensionless groups. The functions are plotted for three exercise levels and are the same for all inert gases

Elimination of gas

Following a phase change equation (21) cannot be used to describe inert gas transport since the physics of the whole system are now different. *Only gas in true physical solution can contribute to a driving force for diffusion.* For a conventional decompression the reservoir of separated gas should be so large that its elimination should approximate to a steady-state process, i.e.

$$G' \approx \Lambda \sum \tau_m . (\Delta p)_m$$

Where τ_m is the time spent at the mth stage (pressure P_m) for which the

TABLE 14.5

Titrated 'bounce' dives, moderately working divers (data from Albano 1962)

Titration no.	*Bottom depth (H_b) in ft*	*Duration of dive (τ) in min*	$D\tau/a^2 = 0{\cdot}129\tau$	$\psi(\tau)$ *(Fig. 14.12)*	$H_b\psi(\tau)$ *in ft*	f *(eqn. 14.24)*	*Practical result*
1	213·4	10	1·29	0·155	32·9	0·411	safe
	213·4	10·5	1·35	0·161	34·2	0·439	unsafe
2	197	11·5	1·48	0·167	32·9	0·411	safe
	197	12	1·55	0·171	33·7	0·428	unsafe
3	180·5	12·5	1·61	0·177	31·9	0·389	safe
	180·5	13	1·68	0·183	33·0	0·413	unsafe
4	164	14·5	1·87	0·196	32·1	0·393	safe
	164	15	1·94	0·202	33·1	0·415	unsafe
5	148	17	2·19	0·221	32·7	0·406	safe
	148	17·5	2·26	0·224	33·2	0·417	unsafe
6	133	20	2·58	0·246	32·7	0·406	safe
	133	21	2·71	0·254	33·8	0·430	unsafe
7	115	24	3·10	0·277	31·9	0·389	safe
	115	25	3·23	0·287	33·0	0·413	unsafe
8	98·6	31	4·00	0·330	32·5	0·401	safe
	98·6	32	4·13	0·336	33·1	0·415	unsafe
9	82	42	5·42	0·402	33·0	0·413	safe
	82	43	5·55	0·414	33·9	0·432	unsafe

$(b/a) = 4{\cdot}91$. The practical results can be correlated for a critical value of f given by $f_c = 0{\cdot}413$.

TABLE

Analysis of working dives—standard

Series no.	*Dives*	*Cases*	*Duration of dive (τ) (min)*	*Bottom depth (Hb) (ft) (swg)*	*Atmospheres absolute*	*Gas intake*			*First stage*		
						$D\tau/a^2 = 0{\cdot}129\tau$	$\psi(\tau)$ *(Fig. 14.12)*	$H_b\psi(\tau)$	*Depth (H_1) (ft)*	*Time (τ_1) (min)*	$H_1\tau_1$
1	1	0	85	50	2·6	11·0	0·660	33·0	—	—	—
	18	0	60	60	2·8	7·74	0·543	32·6	—	—	—
2	2	0	20	100	4·0	2·58	0·278	27·8	—	—	—
	8	0	17	110	4·3	2·19	0·250	27·5	—	—	—
	10	0	14	120	4·6	1·81	0·227	27·3	—	—	—
3	10	0	11	130	4·9	1·42	0·205	26·6	—	—	—
	10	0	9	140	5·2	1·61	0·189	26·5	—	—	—
	1	0	8	150	5·5	1·03	0·181	27·2	—	—	—
4	17	0	20	120	4·6	2·58	0·278	33·4	10	3	30
5	25	2	30	120	4·6	3·87	0·360	43·2	20	3	60
	2	0	25	130	4·9	3·23	0·321	41·7	20	3	60
6	8	0	40	120	4·6	5·16	0·424	50·9	30	3	90
	2	0	35	130	4·5	4·52	0·391	50·8	30	3	90
7	9	0	10	140	5·2	1·29	0·196	27·4	10	2	20
	2	0	10	150	5·5	1·29	0·196	29·4	10	2	20
8	4	0	20	140	5·2	2·58	0·278	38·9	20	3	60
	2	1	15	150	5·5	1·94	0·233	35·0	20	2	40
	1	0	15	160	5·8	1·94	0·233	37·3	20	2	40
9	15	3	25	150	5·5	3·23	0·321	48·2	30	3	90
10	4	0	10	160	5·8	1·29	0·196	31·4	10	2	20
	6	0	10	170	6·1	1·29	0·196	33·3	20	2	40
11	11	2	20	160	5·8	2·58	0·278	44·5	30	2	60
	6	0	20	170	6·1	2·58	0·278	47·25	30	2	60
12	10	3	25	160	5·8	3·23	0·321	51·4	30	2	60
13	10	0	10	180	6·4	1·29	0·196	35·3	20	2	40
	1	0	10	190	6·7	1·29	0·196	37·2	20	2	40
14	7	0	15	180	6·4	1·94	0·233	41·9	30	2	60
	1	0	15	190	6·7	1·94	0·233	44·3	30	2	60
15	10	0	20	180	6·4	2·58	0·278	50·0	30	2	60
16	9	0	10	200	7·0	1·29	0·196	39·2	20	2	40
17	10	0	15	200	7·0	1·94	0·233	46·6	30	2	60

For working dives $b/a = 4{\cdot}75$.

driving force is $(\Delta p)_m$. The minimum value for the latter is (Δp^*), i.e. before coalescence of gas films to give a bubble, mechanical effects may be smaller than indicated by equation (5). Thus, for the 'worst possible' case

$$G' \approx \Lambda \sum \tau_m (\Delta p^*)_m$$

Substituting for $(\Delta p^*)_m$ according to equation (9) (pressures in mm Hg)

$$G' \approx \Lambda.[(1 - x) \sum P_m \tau_m - (126 - 47x) \sum \tau_m] \qquad (25)$$

Λ is a constant which has been estimated empirically as $0{\cdot}0241\ \text{min}^{-1}$. Equation (25) is simple to apply since $\sum P_m \tau_m$ is the area under the pressure-time curve for a decompression and $\sum \tau_m$ is the total staging time.

Fourteen different sets of decompressions have been correlated quantitatively by equation (24) (Hills 1966) including those with and without staging, for air and helium and aerial decompressions. The expression would predict that a diver with a minimum bends depth of 33 ft (2 ATA) is of equal tolerance to a pilot of minimum bends altitude 21,000 to 22,000 ft (0·45 to 0·42 ATA) ($f_c = 0{\cdot}413$ in equation (24). Examples of analyses are given in Table 14.5 and 6 for equation (24) converted to depth ($H = P - 33$) and pressure units of feet (water gauge).

14.6

exercise (data from Crocker 1957)

Second stage			*Third stage*			*Gas elimination (G)*					*Net gas uptake*		*Practical result*
Depth (H_2) (ft)	*Time (τ_2) (min)*	$H_2\tau_2$	*Depth (H_3) (ft)*	*Time (τ_3) (min)*	$H_3\tau_3$	*Total time* $\sum \tau_m$	$12{\cdot}6 \sum \tau_m$	$\sum H_m\tau_m$	$12{\cdot}6 \sum \tau_m$ $\sum H_m\tau_m$ *(A)*	$G' = 0{\cdot}0241\ A$	$= H_b\ \psi(\tau) - 0{\cdot}0241\ A$	f *(eqn. 14.24)*	
—	—	—	—	—	—	—	—	—	—	0	33·0	0·413	
—	—	—	—	—	—	—	—	—	—	0	32·6	0·404	
—	—	—	—	—	—	—	—	—	—	0	27·8	0·298	
—	—	—	—	—	—	—	—	—	—	0	28·5	0·291	
—	—	—	—	—	—	—	—	—	—	0	27·3	0·287	
—	—	—	—	—	—	—	—	—	—	0	26·6	0·271	
—	—	—	—	—	—	—	—	—	—	0	26·5	0·269	
—	—	—	—	—	—	—	—	—	—	0	27·2	0·285	
—	—	—	—	—	—	3	38	30	68	1·6	31·8	0·386	
10	10	100	—	—	—	13	164	160	324	7·8	35·4	0·466	Bends
10	10	100	—	—	—	13	164	160	324	7·8	33·9	0·432	
20	5	100	10	20	200	28	353	390	743	17·9	33·0	0·413	
20	5	100	10	20	200	28	353	390	743	17·9	32·9	0·411	
—	—	—	—	—	—	2	25	20	45	1·1	26·3	0·265	
—	—	—	—	—	—	2	25	20	45	1·1	28·3	0·309	
10	10	100	—	—	—	13	164	160	324	7·8	31·1	0·371	
10	5	50	—	—	—	7	88	90	178	4·3	30·7	0·362	Itching
10	10	100	—	—	—	12	151	140	291	7·0	30·3	0·353	
20	5	100	10	15	150	23	289	340	629	15·1	33·1	0·415	
—	—	—	—	—	—	2	25	20	45	1·1	30·3	0·353	Bends
10	5	50	—	—	—	7	88	90	178	4·3	29·0	0·325	
20	5	100	10	10	100	17	214	260	474	11·4	33·1	0·415	Bends
20	5	100	10	15	150	22	277	310	587	14·15	33·1	0·415	
20	10	200	10	15	150	27	340	410	750	18·1	33·3	0·419	Bends
10	5	50	—	—	—	7	88	90	178	4·3	31·0	0·369	
10	5	50	—	—	—	7	88	90	178	4·3	32·9	0·411	
20	5	100	10	10	100	17	214	260	474	11·4	30·5	0·358	
20	5	100	10	10	100	17	214	260	474	11·4	32·9	0·411	
20	10	200	10	15	150	27	340	410	750	18·1	31·9	0·389	
10	10	100	—	—	—	12	151	140	291	7·0	32·2	0·395	
20	5	100	10	15	150	22	277	310	587	14·1	32·5	0·405	

A correlation of all except series 8 for $f_c = 0{\cdot}415$. Series 8 was a case of itching.

Fundamental constants

The constants required for the foregoing correlations (e.g. $D/a^2 = 0{\cdot}129\ \text{min}^{-1}$) can be reduced to give numerical values for the following fundamental physiological parameters

(1) Capillary diameter of 5·9 to 8·0 μ depending upon what value one takes for the intercapillary distance (2b).

(2) Diffusion coefficient for nitrogen in cytoplasm of

$$D = 2{\cdot}2 \times 10^{-10}\ \text{cm}^2\ \text{sec}^{-1}$$

which is in good agreement with the value of $2{\cdot}3 \times 10^{-10}\ \text{cm}^2\ \text{sec}^{-1}$ for acetylene in the fibres of skeletal rabbit muscle (Hills 1967b).

(3) A Young's modulus for the critical tissue type of $7{\cdot}6 \times 10^6$ compared with 8×10^6 dyne cm^{-2} for smooth muscle (Abbot & Lowy 1958).

PRACTICAL ASPECTS

In addition to offering a quantitative correlation of bends cases in many sets of published data, any comprehensive theory must be compatible with a number of different qualitative aspects of decompression sickness. The more important of these may be grouped as follows:

Random occurrences

The random occurrence of symptoms following a potentially dangerous decompression would seem more compatible with an hypothesis postulating random nucleation than with any based upon critical supersaturation. Moreover the random onset time of symptoms would seem more consistent with the random nature of coalescence, or of any other mode of congregating the gas initially deposited from solution as films at lipid-aqueous interfaces, so producing a local mechanical stress capable of bending a nerve ending beyond its threshold for pain. Variable onset time is a major feature of decompression sickness (Levy 1922; Thorne 1941), yet one receiving little attention by most advocates of conventional theories.

Exercise

The effects of exercise *at depth*, or *during pre-oxygenation* of a pilot are compatible with all theories. Increased inert gas transport can be accredited to increased blood perfusion rate on the conventional approach or to increased vasodilatation according to a diffusion-limited transport model. The same parallel explanations may be offered for the effects of *temperature*. Exercise *following* decompression should provide the ideal mechanical action for hastening coalescence and so reducing the onset time of symptoms, practical evidence being summarized by Cook (1951).

Exercise *during* decompression is, however, particularly interesting since coalescence and vasodilator effects should be opposed, supremacy depending upon the quantity of gas separated from solution. Thus it would seem most significant that the U.S. Navy (1943), with their first decompression presumably forming much gas, do not advocate exercise during staging. On the other hand Japp (1909), using much higher staging pressures, found no deleterious effect in letting his caisson workers walk through a tunnel during decompression.

Metabolic gases

The negligible change in bends incidence upon substituting carbon dioxide for inert gas in the inhaled atmosphere (Cook 1951) is compatible with the derivation of equation (24).

The advantages of substituting oxygen for inert gas in the breathing mixture are compatible with all theories which do not presume that the inhaled atmosphere is effectively 100% inert gas. Practical applications include the improved treatment of symptoms upon recompression (Goodman & Workman 1966), increase in the minimum bends depth of a diver (Pellegrini 1962) and the protection afforded pilots by pre-oxygenation. The latter is well described by Bateman (1951).

The interesting case is the decreased advantage of pre-oxygenation if undertaken at altitudes above 10,000 ft (0·69 ATA) (Gray 1944). According to the 'thermodynamic' hypothesis this observation is compatible with a lower value of Δp in equation (10), or driving force for inert gas elimination, for a smaller value of P. This phenomenon is difficult to explain by any supersaturation theory since the tension differential providing the driving force for inert gas 'washout' by 100% oxygen should be the same for any external pressure. The only explanation, on such a basis, would seem to be one of vasoconstriction at greater altitude—an effect which seems unlikely for lower alveolar oxygen tension.

Tissue constitution

Higher lipid content of tissue is likely to increase susceptibility to decompression sickness according to any theory. Indications of this include obesity (Vernon 1907) and a higher natural water turnover (Cook et al. 1944), although the latter can be interpreted in terms of decreased surface tension of plasma (Walder 1948).

A phenomenon avoided by most advocates of quantitative theories is the effect of age, Gray (1951) showing a linear variation with susceptibility. This relationship can be predicted from equation (20) if the bulk modulus K for the critical tissue type increases in the same linear manner as the Young's modulus versus age relationship found by Hallock and Benson (1937) for the threshold deformation stress δ' in the aorta.

Another phenomenon which may be attributed to variation in modulus by the 'thermodynamic' approach is acclimatization (Paton & Walder 1954). Tissue, as a plastic, should display considerable mechanical hysteresis, the same strain producing less stress with successive deformations. Moreover recent experiments by the writer indicate that the relaxation time of cartilage and tendon corresponds to the 3 to 5 days required to halve the number of symptoms following a return to work by caisson workers (Walder 1966).

Evidence of a phase change

The vital issue between equilibrium and supersaturation concepts is whether the gas phase is formed for decompressions well below the metastable limits indicated by conventional decompression ratios (≈ 2).

X-ray evidence, summarized by Ferris and Engel (1951), indicates the onset of a phase change upon reaching an altitude of 10,000 to 12,000 ft (0·69 to 0·63 ATA). Moreover, manometers connected to the spinal columns of men and goats showed transition points in the increase of cerebrospinal fluid volume with decompression at equivalent altitudes of 10,500 ft (0·67 ATA; 512 mm Hg) to 12,000 ft (0·63 ATA; 483 mm Hg) (Walsh 1941; Boothby, Lovelace & Benson 1940).

Equation (10) would predict a phase change at a pressure $P' = P - (\Delta p)$ for $P = 760$ mm Hg and $x = 0{\cdot}8$ (air), giving $P' = 497$ mm Hg. This is well within the range of 0·63 to 0·67 ATA (483 to 512 mm Hg) indicated by the above evidence as the decompression threshold for a phase change after breathing air at ground level. If the above evidence is correctly interpreted there would seem little doubt that a stable gas phase can be established in tissue without giving pain.

Surface decompression

Surface decompression is the name given to the process whereby a diver may be rapidly brought to the surface, immediately recompressed on deck, and then decompressed as though still at depth (Behnke 1951).

The fact that the same decompression format may be used is exactly contrary to all theories postulating a critical degree of supersaturation, since the system must have been nucleated during the initial 'pull' to the surface. On the other hand, adherence to the concept of thermodynamic equilibrium implies that the large initial phase separation would greatly reduce the driving force for inert gas redistribution during ascent to the chamber on deck. Provided the divers were recompressed before appreciable coalescence of the separated gas could occur, the inert gas distribution should be little different when maximum pressure is re-attained (e.g. Fig. 14.4, graph 4). Hence the same subsequent decompression procedure should hold.

In conclusion it may be said that the 'thermodynamic approach', and conventional theories of limited supersaturation, represent the two extreme cases for the separation of the gas phase from solution in tissue.

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