EAD theory allows existing air decompression tables to be used with nitrogen–oxygen mixtures having elevated oxygen fractions.

The EAD is the depth of an imaginary air dive that would have the same nitrogen partial pressure as an actual dive with a gas having an oxygen fraction greater than air. EAD is given by

$$\text{EAD} = \frac{(1 - F_{IO2})\ (D + 10\,\text{m})}{0.79} - 10\,\text{m}$$

where D is the actual depth, and F_{IO2} is the inspired oxygen fraction. If the actual depth is 39 m (130 ft) and the F_{IO2} is 32%, for example, the EAD is 32 m (107 ft) and air decompression schedules for 33 m (110 ft) should be used.

The EAD theory should be reasonable at low inspired oxygen partial pressures (P_{IO2}'s) where the venous oxygen tension is relatively unchanged but might fail at high partial pressures if the metabolic requirements of tissue are met by oxygen dissolved in the blood. Weathersby *et al.* (1986b) tested the EAD theory during no-stop dives at various depths for bottom times of 30, 60 and 240 min and P_{IO2}'s of 0.21–1.3 ata (21–131 kPa). The mean incidences of decompression illness are shown in Fig. 14.18 at high and low P_{IO2}'s. Each point represents the average of 76–82 dives. The incidence of decompression illness increased slightly at the higher P_{IO2} for one dive series and decreased in two series. This could indicate either higher or lower risk at elevated P_{IO2}, but neither conclusion was supported statistically. A lower risk might be explained by decreased tissue perfusion and nitrogen uptake due to oxygen-induced vasoconstriction.

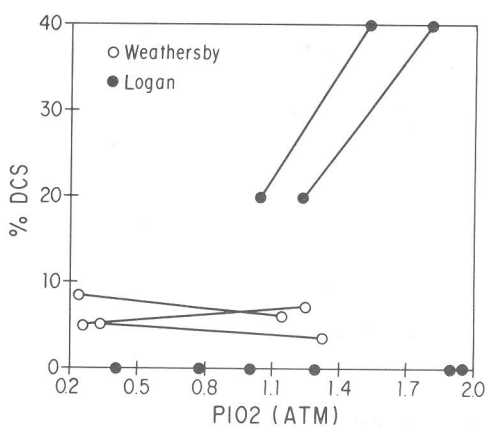

FIG. 14.18. The incidence of decompression illness as a function of P_{IO2} for humans from studies by Logan (1961) and Weathersby *et al.* (1986b)

Another study tested decompression dives with bottom times of 15, 30, 60 and 180 min at P_{IO2}'s of 1.0–1.8 ata (101–182 kPa; Logan 1961). The results of this study are also shown in Fig. 14.18. Three dive series were inconclusive as there was no decompression illness. During two series, one incident occurred in five trials at the lower P_{IO2} and two incidents in five trials at the higher P_{IO2}. These trials did not strictly test the EAD theory, however, as decompression took place with a higher P_{IO2} than in air. This would advantageously accelerate nitrogen elimination.

Logan (1961) concluded that oxygen partial pressures between 1.2 and 1.6 ata (121 and 162 kPa) make a small and statistically insignificant contribution to decompression risk and that this risk does not warrant abandoning the EAD theory. The results of Weathersby *et al.* (1986b) do not contest this conclusion, at least up to oxygen partial pressures of 1.3 ata (131 kPa). While the partial pressure at which the EAD theory begins to fail is unknown, oxygen partial pressures much higher than 1.3 ata (131 kPa) may not be altogether useful due to the increasing risk of central nervous system oxygen toxicity.

PROBABILISTIC MODELLING

A decompression model is a set of concepts which relates the occurrence or non-occurrence of decompression illness to changes in ambient pressure and breathing gas composition. The purpose of a model is to avoid an unacceptable incidence of decompression symptoms. A model may incorporate environmental or physiological factors such as exercise, temperature, body fat, etc., if sufficient data are available to justify their inclusion.

Models range from empirical mathematical functions with no physiological rationale to detailed descriptions of the biophysical processes believed to be relevant. The perfect model would predict the nature and onset time of every incident of decompression illness. Such a model does not yet exist and may never exist, but imperfect models have had reasonable success in computing useful decompression procedures (Chapter 13; Wienke 1991).

Deterministic and Probabilistic Models

Decompression models consist of two parts, gas kinetics and ascent criteria. The gas kinetics calculate a decompression 'dose' which accumulates and dissipates as the pressure varies over time, whereas the ascent criteria relate the dose to the occurrence of symptoms. Ascent criteria can be deterministic or probabilistic. Deterministic ascent criteria classify dives as 'safe' or 'unsafe' according to the magnitude of the dose. Probabilistic criteria compute the probability of decompression illness from the dose and ascend such that this probability does not exceed a level of risk previously judged to be acceptable.

Consider the inert gas exchange kinetics in a perfusion-limited tissue compartment in which the gas tension, $P(t)$, is defined by

$$P(t) = Pa + (P - Pa)e^{-kt} \quad (4)$$

where $Pa = (1 - F_{IO2})P_B$ and t, P, Pa, P_B and F_{IO2} are the time, initial inert gas tension in tissue, arterial inert gas tension, the barometric pressure and the inspired oxygen fraction. The rate constant, k, is an adjustable parameter used for finding the best description of empirical decompression data.

A deterministic ascent criterion might define the dose as the supersaturation ratio, $r(t)$:

$$r(t) < \frac{P(t) - P_B}{P_B} = \frac{Pa + (P - Pa)e^{-kt}}{P_B} - P_B \quad (5)$$

which is required not to exceed some maximum value. Should this criterion be violated, a diver would be subject to an excessive risk of decompression illness, but the extent of this risk and what could be done to recover from the violation could not be determined. Violation of ascent criteria is a particular problem when computing surface decompression schedules with deterministic models.

Probabilistic ascent criteria transform the dose into a decompression illness probability, $P(\text{DCI})$. One transformation method uses a sigmoidal dose–response function such as the Hill equation:

$$P(\text{DCI}) = \frac{r(t)^N}{r(t)^N + r_{50}{}^N} \quad (6)$$

where N and r_{50} are adjustable parameters, with r_{50} being the dose for $P(\text{DCI}) = 0.5$. A more formal approach uses a risk function described by:

$$P(\text{DCI})_{t_1,t_2} = 1 - \exp\left(-\int_{t_1}^{t_2} r(x)\cdot dx\right) \quad (7)$$

The supersaturation ratio, $r(t)$, is integrated over time from $t_1 = 0$, when it first becomes positive, to $t_2 = 24$ h, after which symptoms rarely occur. As risk cannot be negative, integration is stopped when $r(t)$ becomes negative and restarted when it is positive. The derivation of equation (7) is discussed in 'US Navy Models'. → p. 403

The probabilistic ascent criterion constrains $P(\text{DCI})$ to below an independently determined acceptable limit (see 'Acceptable Risk of Decompression Illness'). Unlike a deterministic model, however, this can be accomplished by an infinite number of profiles each having a different decompression time. The shortest profile is usually the most desirable, but determining which profile requires the least decompression time is computationally intensive (Weathersby *et al.* 1985a). Should a diver violate his prescribed profile, the risk of decompression illness accumulates in a quantifiable manner but can be decreased by prolonging the decompression. With a deterministic model, recovery from a violation of the ascent criterion is not possible.

The deterministic ascent criterion of equation (5) requires that the dose not exceed a *threshold* which, if violated, will result in an unacceptable but unkown risk of decompression illness. Figure 14.19 illustrates the threshold concept in a probabi-

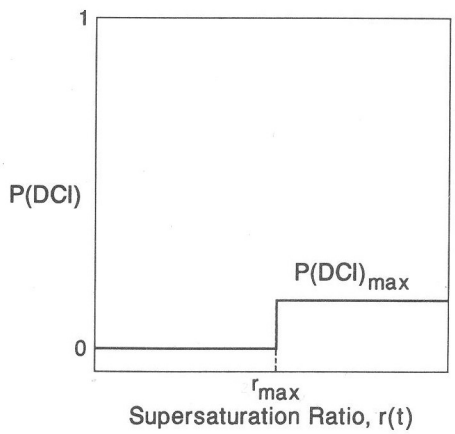

FIG. 14.19. A deterministic ascent criterion based upon a supersaturation threshold. When the supersaturation exceeds the threshold r_{max}, the population has a risk $P(\text{DCI})_{max}$.

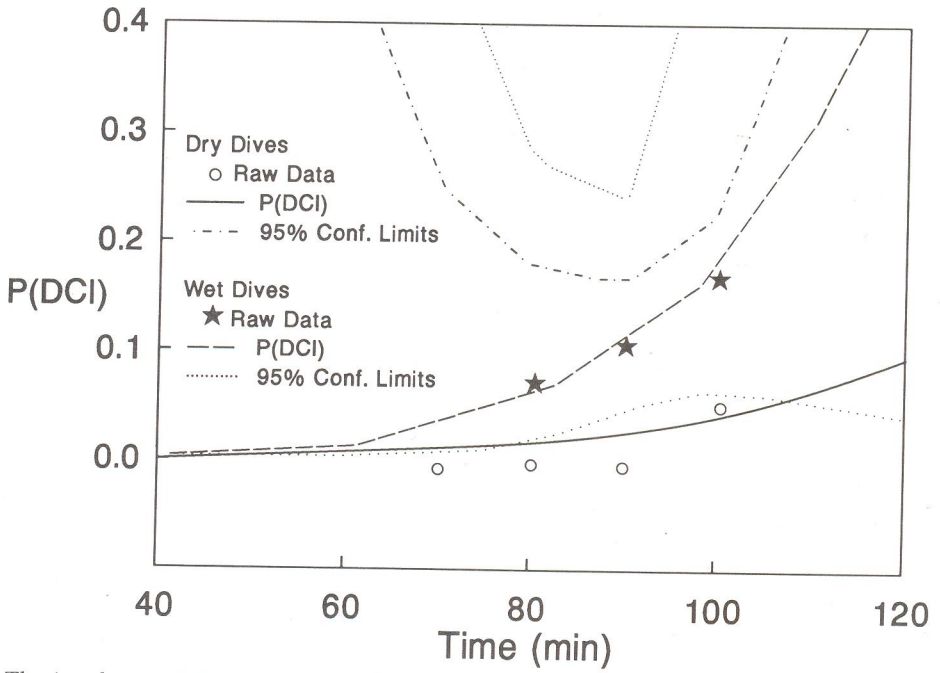

FIG. 14.20. The incidence of decompression illness as a function of bottom time for no-stop air dives at 18 m (60 ft) with a 18 m/min (60 ft/min) ascent rate. The wet divers exercised in cold water with the following bottom times and outcomes (DCI/Exposures): 80 min (1/14); 90 min (2/21); 100 min (2/13). Dry divers exercised at a similar workload in a room temperature chamber: 70 min (0/10); 90 min (0/20); 100 min (1/20). The 95% confidence intervals are shown (Thalmann *et al.* 1989)

listic context. The x axis represents the supersaturation, $r(t)$, and the y axis represents P(DCI), which lies between 0 and 1. When the threshold, r_{max}, is exceeded, P(DCI) makes an immediate transition from 0 (no-DCI) to $P(DCI)_{max}$, the unknown but acceptable incidence of decompression illness. This is tantamount to the entire population having the same risk.

While many useful decompression procedures have been developed with deterministic models, the concept of a population threshold is inconsistent with observation. Some divers develop decompression illness after innocuous dives, but others safely complete stressful dives. Decompression illness may be an all-or-none phenomenon for the individual, but only a fraction of a population sample may develop decompression illness for a given exposure. This has been demonstrated for both animals (Flynn & Lambertsen 1971; Berghage *et al.* 1974) and humans. Figure 14.20 shows the incidence of decompression illness as a function of no-stop bottom time for divers exposed to 20 m (60 ft) while breathing air (Thalmann *et al.* 1989). The divers exercised while dry or immersed in cold water. In both conditions, the incidence of decompression illness increased smoothly with the bottom time showing no evidence of a threshold. A Hill equation (Eq. 6) was fit to the raw data and 95% confidence limits were computed under the assumption that decompression illness is described by the binomial distribution (Berghage *et al.* 1974). The dry dives are just below the lower confidence limit of the wet dives, demonstrating greater risk for immersion in these no-stop exposures.

A diver with decompression illness—a P(DCI) of 1.0—derives little comfort from knowing his exposure had an exceedingly low probability of symptoms. The resolution of this apparent paradox may lie in the variability of susceptibility to decompression illness as a result of environmental factors, individual risk factors and factors that are unpredictable. Instead of a common threshold for the entire population as in Fig. 14.19, each diver may have a different threshold for every dive he makes (Vann *et al.* 1992). Susceptible divers would

have low thresholds and resistant divers high thresholds, but the threshold for a particular individual may be unpredictable.

This concept is illustrated in Fig. 14.21, where the maximum supersaturation threshold (r_{max}) that can be tolerated without symptoms is distributed over the population in a density function. Susceptible individuals fall in the region of low r_{max}, whereas resistant individuals fall in the region of high r_{max}.

The probability of decompression illness for a given dive is the fraction of the population for which the threshold is exceeded. In Fig. 14.21, for example, P(DCI) for a dive with a threshold r^*_{max} is the area under the density function (the integral) to the left of r^*_{max}. Figure 14.22 shows that this integral is a sigmoidal dose–response curve. Thus, P(DCI) does not refer to individual probability, but that fraction of the population that will develop symptoms.

In an alternative interpretation of probability, r_{max} is replaced by a time integral of an accumulating dose. In this case, the fraction of the *population* with symptoms will increase as the dose increases and can be predicted within certain confidence limits. Whether a *particular* individual develops symptoms, however, is a random event which cannot be predicted with certainty.

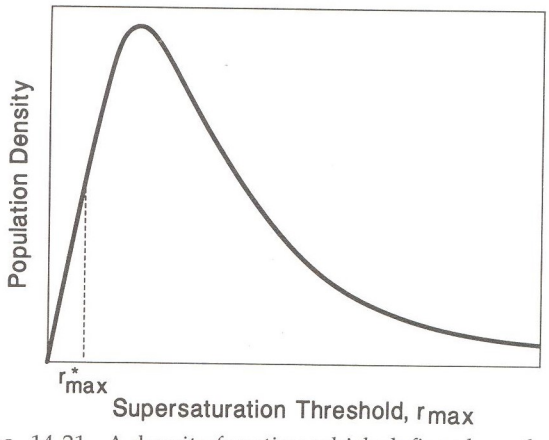

FIG. 14.21. A density function which defines how the supersaturation threshold for decompression illness is distributed across the population. The largest part of the population develops decompression illness at intermediate thresholds. Smaller fractions have low thresholds and are susceptible or high thresholds and are resistant. P(DCI) for a dive with a threshold r^*_{max} is the fraction of the population having thresholds of less than r^*_{max}

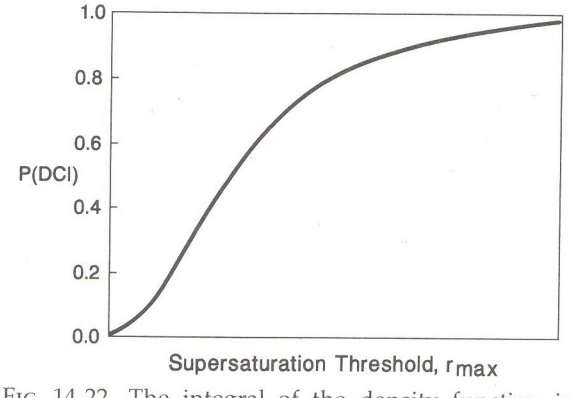

FIG. 14.22. The integral of the density function in Fig. 14.21 is a dose–response curve which defines how P(DCI) varies with supersaturation threshold. P(DCI) is the fraction of the population which develops decompression illness

Primary and Secondary Data

The probability of decompression illness usually cannot be defined for the entire population of dives or divers but only for a small sample of that population. This estimate of 'true' probability is more certain if the dive profiles in the population sample are precisely defined to within a metre and a few minutes. Other essential information which increases the estimate precision includes descriptions of symptoms (should they occur), their onset time, treatment and treatment outcome. All dives must be reported, including those which are safe. The dive circumstances and diver characteristics are also important. This information is referred to as *primary* data to indicate it is the primary standard for deriving probability estimates from decompression models (Weathersby & Survanshi 1990). Primary data are usually developed in expensive laboratory trials, but accurate depth–time recorders and medical evaluations of all divers may someday make primary data available from selected open-water dives (see 'Dive Computers').

The nature of the primary data affects the accuracy and uncertainty of the P(DCI) estimates. The most useful databases are large and diverse with dives distributed over a range of decompression illness probabilities. A well-documented database used by the US Navy for model comparisons, for example, has 921 man-dives with a mean incidence of decompression illness of 5.6% (Weathersby *et al.*

1992). These data were derived primarily from laboratory trials in which high incidences of decompression illness, while statistically desirable, would be unacceptable by modern standards.

At present, all symptoms (i.e. pain, neurological, etc.) are assumed to have an equal probability of occurrence and are equally weighted. This is the only alternative until sufficient data are available to allow individual symptoms to be differentiated through modelling. Symptoms must be accurately described, however, and while the Type I (minor) and Type II (serious) classifications of Golding *et al.* (1960) are helpful in selecting therapy, they are non-specific and are often applied inconsistently (Kemper *et al.* 1992). A recently proposed classification system based upon objective description may help provide the needed information (Francis & Smith 1991).

Secondary data are derived from exposures where the conditions are not documented with the accuracy of primary data and may be influenced by procedural (inaccurate time keeping, calculation error, non-reporting of symptoms, etc.), environmental (cold, rough water, current, etc.) and physiological factors (work, dehydration, injury, etc.). Secondary data are usually from open-water exposures where variations from planned profiles or multi-level profiles are not recorded, and dives are specified only by table or maximum depth and total time. Secondary data are mainly used to monitor the incidence of decompression illness in operational settings (Shields & Lee 1986), but have also been employed to guide model development as in the 1986 Comex Air Tables (see 'In-Water Decompression with Air'). Published decompression tables are neither primary nor secondary data, but with well-documented statistics concerning their use, can be useful benchmarks for comparison with other tables.

Primary and secondary databases are maintained by many individuals and organizations, but there is little agreement as to what should be their structure and content (Sterk & Hamilton 1991). These issues will be resolved as databases are developed and shared.

Parameter Estimation and Maximum Likelihood

Whether deterministic or probabilistic, all models have certain parameters (e.g. blood flow, tissue half-time, supersaturation, etc.) for which numerical values must be found such that the model predictions conform reasonably well to empirical data. For deterministic models, profiles are analysed for some measure of decompression dose which violates a threshold (e.g. a compartment gas loading; Freitag & Hamilton 1974), and the model parameters are adjusted such that violations occur mostly on unsafe rather than on safe dives. This is more successful for data with many replicated trials of a few profiles, which provide measures of decompression illness risk, rather than for few trials of many profiles. Estimating deterministic parameters is a subjective process, but one which has provided useful decompression procedures over many years (Dwyer 1956; Thalmann 1984, 1985, 1986; Boni *et al.* 1976).

Parameter estimation for probabilistic models also begins with a decompression dose, such as defined by equation (5), which is used to compute a $P(\text{DCI})$ for every dive in the database. Each dive will have one of two outcomes—decompression illness or no decompression illness—with corresponding probabilities, $P(\text{DCI})$ and $1 - P(\text{DCI})$. $P(\text{DCI})$ is computed from a decompression model described by relationships such as equation (6) or equation (7). The probability of the observed outcome is defined as the *likelihood*, L. If decompression illness has occurred, $L = P(\text{DCI})$; if not, $L = [1 - P(\text{DCI})]$.

For a database with three dives, two of which result in decompression illness, the likelihood is:

$$L_{\text{database}} = P_1(\text{DCI}) \cdot P_2(\text{DCI}) \cdot [1 - P_3(\text{DCI})]$$

analogous to the joint probability for coin tosses. The likelihood of a database is the computed probability of all the observed outcomes.

For a dive profile i which is tested k times with j incidents of decompression illness, the likelihood is:

$$L_i = P_i(\text{DCI})^j \cdot [1 - P_i(\text{DCI})]^{k-j}$$

The likelihood of an entire database with n profiles is the product of the likelihoods for each individual profile:

$$L_{\text{database}} = L_1 \cdot L_2 \cdot \ldots \cdot L_i \cdot \ldots \cdot L_n \qquad (8)$$

The value of L_{database} changes as the parameters in the model are varied. When the parameter values are found that maximize L_{database}, the *maximum likelihood* has been determined, and the optimal parameter values have been estimated. These parameter estimates define the best description of the database by the model, and are objective with

accuracy and uncertainty which depend only on the model and data (Weathersby *et al.* 1984). Probabilistic models do not require replicated dives as is desirable for deterministic models. A thousand different profiles with one exposure each are handled just as a single profile with a thousand exposures. Since multiplying probabilities results in a small number, the natural logarithm of the likelihood is reported and appears as a negative quantity called the log likelihood (*LL*).

The maximum likelihood is determined by iterative adjustment of the model parameters through non-linear regression. Weathersby *et al.* (1984) used an optimization procedure based on the Marquardt (1963) algorithm, which computes standard errors on the parameter estimates (Bailey & Homer 1976). The standard errors reflect the inherent uncertainty of statistical modelling and are expressed as upper and lower 95% confidence limits on estimated probabilities of decompression illness (Weathersby 1990). Confidence intervals for dives which are well-represented in a database are smaller than for poorly represented dives. Large confidence intervals indicate dives for which more testing may be desirable. Interpolation between profiles that are well-represented in the database is warranted with the expectation that the risk of decompression illness will not differ significantly from the risks of nearby profiles. Extrapolation to dives outside the range of the data requires cautious testing as actual and estimated risks may be substantially different (Weathersby *et al.* 1984).

Maximum likelihood methods can estimate the parameter values which best describe the data for any model, but they do not eliminate the judgement necessary to construct good models. Of two models, the one with the greater maximum likelihood (least negative *LL*) is a better description of the data, but tests to determine if a difference between likelihoods is statistically significant are available only for general and restricted models. A general model has many parameters. A restricted model is a subset of a general model derived by setting one or more parameters of the general model to zero. General and restricted models can be compared using the likelihood ratio test (Weathersby *et al.* 1984) to determine if parameters in the general model are statistically justified. The likelihood ratio test can also be used to determine if the same model describes two different data sets equally well or if two different sets of parameter values provide equivalent fits to the data. The likelihood ratio test is inappropriate for comparing models based on different premises, however, such as models with tissue compartments in parallel and in series. Comparisons of this nature require absolute goodness-of-fit criteria which have not yet been firmly established.

Acceptable Risk of Decompression Illness

An acceptable risk of decompression illness is the incidence that would be tolerable during operational use if a procedure or algorithm were followed exactly to its limits for an infinite number of exposures. Acceptable risk may be different from the incidence observed in operational use, in which procedures are usually not followed to their limits and often followed incorrectly. Most useful procedures appear to have a finite risk of decompression illness. The choice of acceptable risk is a matter of judgement, circumstance and field of work. The factors affecting acceptable risk include the likelihood of those exposed to admit symptoms, their reliability in following procedures, their ability to recognize and not deny symptoms, the simplicity of the procedures, the presence of supplemental risks, the availability of recompression facilities and medical personnel, the importance of the task, the effect of decompression illness on confidence and morale, the potential organizational or legal consequences, and the possibility of permanent injury.

Compressed air workers, for whom decompression procedures are generally considered inadequate, have a history of tolerating decompression illness as an occupational hazard (Kindwall 1989). Recreational divers frequently deny or do not recognize their symptoms. Other risks such as hypothermia and oxygen toxicity must be considered as well as the risk of decompression illness (see 'Decompression Practice'). Neurological symptoms are generally considered less acceptable than pain-only symptoms, and their occurrence can lead to recommendations for significant curtailment of diving practice even when the overall incidence of decompression illness may be less than 0.5% (Shields & Lee 1986).

A survey concerning acceptable operational risk indicated a wide range of opinion concerning decompression illness pain while generally agreeing that neurological symptoms were unacceptable although perhaps not altogether avoidable (Fig. 14.23; Vann 1991). Based upon ground-based

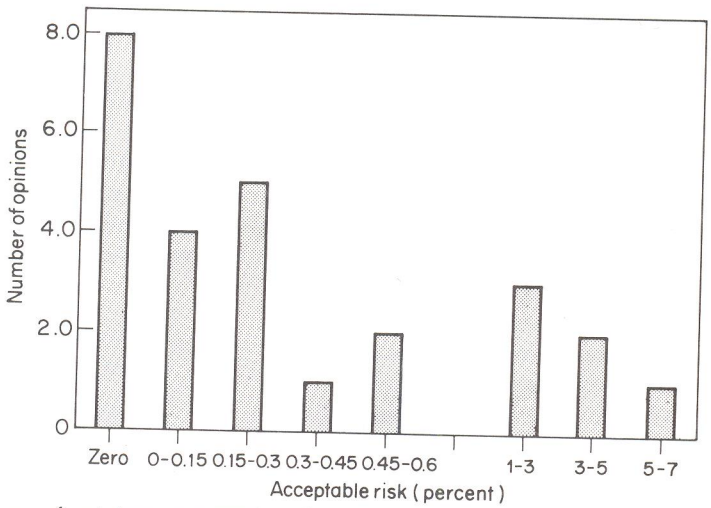

FIG. 14.23. A survey of opinions concerning the acceptable risk of decompression illness (Vann 1991)

studies, acceptable risk was proposed for Space Shuttle operations at 6% moderate pain (Waligora (1986). Neurological decompression illness was rare in these studies, and decompression illness has not been reported during extravehicular activity by in-flight space crew. For crew aboard the less accessible Space Station, acceptable risk was proposed at 1%.

Within the hyperbaric community, the US Navy would accept decompression procedures with an upper 95% confidence limit of 3–4% based on several hundred dive trials and the expectation of a lower operational incidence (Thalmann 1989a). A 2% incidence was considered acceptable for caisson workers (Paton 1967). Commercial diving companies would accept an incidence of 0.1–0.5%, while scientific and recreational divers desired zero incidence (Vann 1991; Lang & Vann 1992). The selection of a low acceptable risk must be weighed against increased decompression time and restricted no-stop limits. This choice will vary between diving communities.

During laboratory trials, supplemental risks are minimized (see 'Decompression Practice'), protocols are critiqued by Institutional Review Boards, and experimental subjects give informed consent. Lanphier (1989) reviewed the ethical and institutional aspects of experimental trials. Trials with a wide range of risks for decompression illness may be desirable to verify the accuracy of model risk estimates. Some of these trials may exceed operationally acceptable risk, but the likelihood of injury is generally less than in the field as medical personnel and treatment facilities are immediately available. Acceptable risk during trials depends upon the nature of the expected symptoms and their response to treatment. Neurological symptoms and residua are more frequent in diving than in altitude exposures, for example, where symptoms usually resolve during descent to ground level (Waligora 1986). This permits altitude trials with an incidence of decompression illness of up to 50–90% (Balldin 1973b; Vann *et al.* 1989b).

There is a movement towards increased safety in diving. During the 1970s, there was competitive emphasis on rapid decompression in commercial diving (Hamilton 1976), but the recent trend has been towards industry cooperation, low-risk procedures, and fast, aggressive treatment of incidents of decompression illness (Galerne 1989; Beyerstein 1992). When many dives are conducted, however, even a low incidence of decompression illness can result in an unacceptable number of cases, particularly if a substantial fraction are neurological (Shields & Lee 1986). It may be difficult, therefore, to achieve an acceptably low risk with decompression times that are not unreasonably long (see 'In-Water Decompression with Air'). The goal of statistical modelling is to provide the tool to permit rationale choices between risk and time in the water.

US Navy Models

The first probabilistic model of decompression data applied a dose–response analysis to no-stop

upward excursion dive trials from helium–oxygen saturation (Weathersby *et al.* 1984). This simple approach defined the decompression dose as the supersaturation ratio (Eq. 5), which was transformed into a P(DCI) occurrence using a Hill equation (Eq. 6) as a dose–response function. The resulting expression for probability was applied to the experimental data through the likelihood equation (Eq. 8), and the model parameters were estimated.

The next approach was to treat decompression illness as a systems failure in which a system (diver) exposed to a stress (dive) has a finite probability of failure (DCI). The mathematics of this approach have been developed in failure time analysis (Kalbfleish & Prentice 1980) and survival analysis (Elandt-Johnson & Johnson 1980).

Consider the large population of divers in Fig. 14.24 who have been exposed to various decompression stresses. Decompression incidents begin to occur some time after the dive and accumulate with time to a maximum number. If the curve in Fig. 14.24 is divided by the total number of divers, the resulting function approximates the *failure distribution*, $F(t)$, which is the cumulative P(DCI) over time. The probability of surviving past a particular time, t, is the *survivor function*:

$$S(t) = 1 - F(t)$$

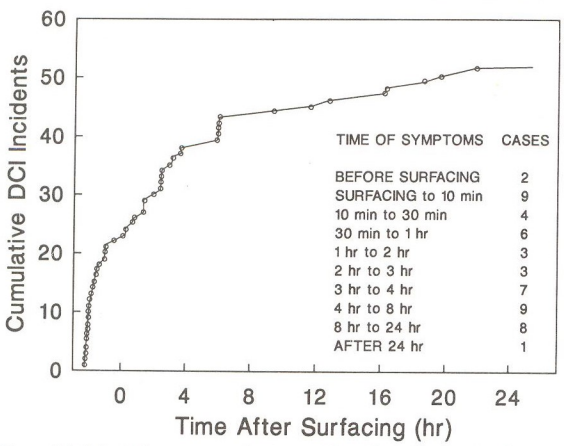

FIG. 14.24. The cumulative distribution of decompression illness onset times from a primary database (Weathersby *et al.* 1992). When divided by the total number of dives in the database, this curve approximates the *failure distribution* which is the cumulative P(DCI) over time

The derivative of $F(t)$ is the *probability density function*:

$$f(t) = \frac{d}{dt}F(t) = -\frac{d}{dt}S(t)$$

which is the instantaneous rate at which symptoms occur for the entire population. The ratio of the probability density function and the survivor function is the *hazard* or *instantaneous risk function*, $r(t)$:

$$r(t) = \frac{f(t)}{S(t)} = -\frac{1}{S(t)} \cdot \frac{d}{dt}S(t) \qquad (9)$$

which is the relative failure rate or the instantaneous rate at which symptoms occur among survivors, i.e. those not yet having developed symptoms. Solving equation (9) for $S(t)$ by integration gives

$$S(t) = \exp\left(-\int_0^t r(x)\cdot dx\right)$$

The probability of not developing symptoms between t_1 and t_2 is:

$$P(\text{no-DCI})_{t_1,t_2} = S(t_1,t_2) = \exp\left(-\int_{t_1}^{t_2} r(x)\cdot dx\right) \qquad (10)$$

while the probability that symptoms will develop is:

$$P(\text{DCI})_{t_1,t_2} = F(t_1,t_2) = 1 - \exp\left(-\int_{t_1}^{t_2} r(x)\cdot dx\right) \qquad (11)$$

In applying failure time analysis, the US Navy used instantaneous risk functions based on the supersaturation ratio (Eq. 5). The initial application only considered the occurrence of decompression illness and not the onset time (Weathersby *et al.* 1985b). This was achieved by setting $t_1 = 0$ and $t_2 = 24$ h, beyond which decompression illness was unlikely. To use symptom onset time, the time up to which a diver was symptom-free, t_1, must be known as well as the time, t_2, at which he reported symptoms. Although t_2 is usually known with some precision, t_1 may be more difficult to establish. The interval from t_1 to t_2 is the period of uncertainty. For a diver who reports symptoms 10 min after a symptom-free examination, this interval is 10 min, but for the diver who goes to bed symptom-free and awakens with symptoms, the interval is the time he was asleep. Rules have been suggested for estimating t_1 from t_2 when t_1 is unknown (Weathersby *et al.* 1992).

When decompression illness does not occur, the outcome probability is computed by the integration of equation (10) with $t_1 = 0$ and $t_2 = 24$ h. When decompression illness does occur and the onset time is known, the probability of the observed outcome is now the joint probability of no decompression illness before t_1 and decompression illness in the interval from t_1 to t_2. This joint probability is the product of equations (10) and (11):

$$P(\text{DCI})_{0,t_2} = P(\text{no-DCI})_{0,t_1} \times P(\text{DCI})_{t_1,t_2}$$

$$= \left(\exp\left(-\int_0^{t_1} r(x)\cdot dx\right)\right) \times \left(1 - \exp\left(-\int_{t_1}^{t_2} r(x)\cdot dx\right)\right) \quad (12)$$

Symptom onset time was implemented through two definitions of instantaneous risk, which are illustrated in Fig. 14.25 (Weathersby *et al.* 1992). Figure 14.25 (top) shows a no-stop dive to a pressure P_{AMB} and the corresponding inert gas tension, P_{TIS}, described by equation (4). In Fig. 14.25 (bottom), r_1 is the instantaneous risk defined by a supersaturation ratio (Eq. 5). The maximum post-dive risk of decompression illness occurs immediately upon surfacing, implying early symptom onset. The second definition of instantaneous risk, r_2, integrates the supersaturation ratio over time (Fig. 14.25, bottom). This delays the maximum risk well into the post-dive period.

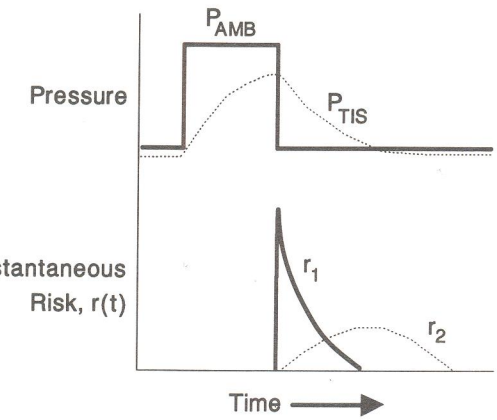

FIG. 14.25. The top figure shows a no-stop dive to a pressure P_{AMB}. The exponential response of the tissue inert gas tension (Eq. 4) is P_{TIS}. The bottom figure shows the response of the instantaneous risk, $r(t)$. For r_1, the instantaneous risk is proportional to the supersaturation ratio (Eq. 5). For r_2, it is proportional to the time integral of the supersaturation ratio. The total P(DCI) is a function of the area under each instantaneous risk curve. (Reproduced with permission from Weathersby *et al.* 1992)

Both representations of instantaneous risk were applied to experimental data using maximum likelihood, and both described the data equally well when only the occurrence of decompression illness was considered (Weathersby *et al.* 1992). With the inclusion of symptom onset time, however, r_1 failed to describe the data, while a greater maximum likelihood indicated an improved description for r_2. Thus, the power of the parameter estimation process to discriminate between poor and good models on the basis of their maximum likelihoods was enhanced by including symptom onset time.

Probabilistic decompression modelling by failure time analysis has been used to: estimate the risks of the USN Standard Air Tables (Weathersby *et al.* 1985b), air saturation tables (Hays *et al.* 1986), repetitive nitrox dives (Albin & Weathersby 1991) and air and He–O_2 dives (Tikuisis *et al.* 1991); compare USN, Canadian and British air tables (Weathersby *et al.* 1986c); and compute iso-risk (equal probability) air tables (Weathersby *et al.* 1985a). Probabilistic models could be used to develop low-risk no-stop tables for recreational divers for whom treatment is not readily available and higher risk tables for commercial or military diving where longer bottom times without excessive in-water decompression time might be desirable. Surface decompression procedures can be computed by probabilistic models without violating the ascent criterion during the surface interval. Computational complexity is the main drawback of probabilistic models.

Other Models

Deterministic models can be made probabilistic by transforming the dose into a probability using a dose–response function such as the Hill equation (Eq. 6). Haldanian models have been converted in this manner (Vann 1987) and were used to develop the 1986 Comex air tables (Imbert 1991), but Haldanian models were not as successful as the US Navy implementation of failure time analysis in describing databases of dissimilar dives (Parsons *et al.* 1989).

While the US Navy used supersaturation as the basis for instantaneous risk, bubbles are another logical choice given their suspected role in decom-

pression illness. Various bubble simulations have been used to develop deterministic decompression procedures (Vann 1982a; Hennessy & Hempleman 1977; Thalmann 1984, 1985, 1986; Gernhardt *et al.* 1992). A bubble model might be a suitable instantaneous risk function for failure time analysis but has yet to be implemented. Current probabilistic bubble models use dose–response functions to convert the bubble-dose into *P*(DCI) (Vann 1986, 1987).

Figure 14.26 shows three parallel tissues, each containing a bubble which grows or shrinks according to the difference between the internal nitrogen partial pressure and the nitrogen tension in tissue (Fawcett *et al.* 1992). These bubbles are surrounded by diffusion barriers which make their growth a gradual process consistent with delayed symptom onset. Nitrogen exchange between blood and tissue is perfusion-limited as in a Haldane tissue compartment.

Upon arrival at the surface after a dive, the bubble in each tissue grows gradually, passes through a maximum, and resolves. The greatest risk of decompression illness is assumed to occur when the largest of the bubbles reaches its maximum volume. The maximum volume is transformed into a *P*(DCI) by a Hill equation. Figure 14.27 illustrates the time course of the risk of decompression illness during a series of no-stop repetitive dives (Gerth *et al.* 1992).

Many simulations of bubble kinetics are possible. The implementation of Fig. 14.26 treated bubbles as flat sheets of gas with constant surface areas subject to a constant tissue elastic pressure and unaffected by surface tension. This approach seems roughly consistent with radiographic studies of altitude decompression illness (Fig. 14.1) and allowed an analytical solution of the first-order differential equation describing bubble growth for a step change in pressure or gas composition. When spherical bubbles and surface tension are included, bubble resolution is accelerated and decompression time reduced for small radii (Gernhardt *et al.* 1992).

Diving procedures were developed by probabilistic bubble models for nitrogen–oxygen saturation decompression (Vann 1986), in-water oxygen decompression during repetitive air diving (Fife *et al.* 1992) and surface interval oxygen during repetitive nitrox diving (Fawcett *et al.* 1992; Vann *et al.* 1992). These procedures have worked reasonably well in preliminary trials.

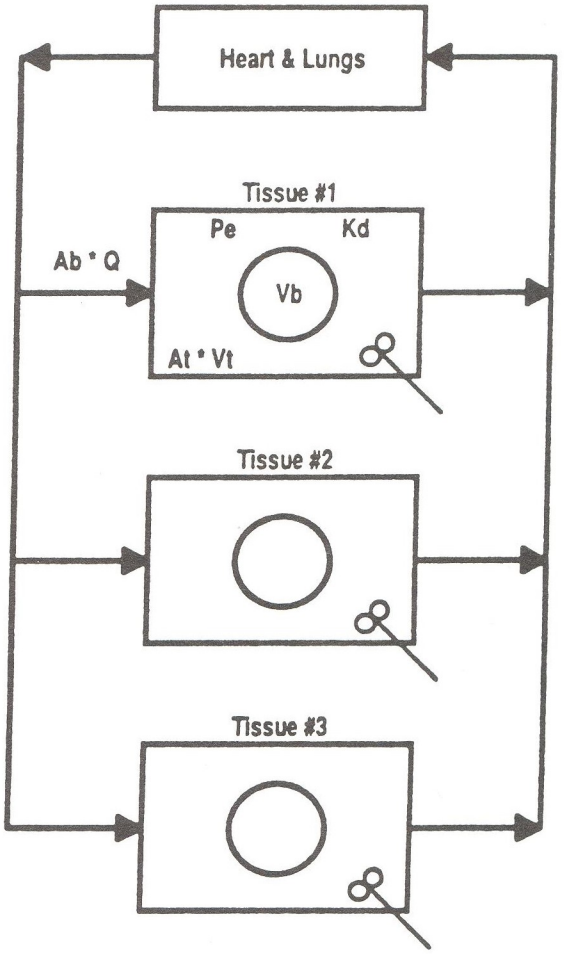

FIG. 14.26. A three-tissue bubble model. Inert gas exchange in tissue is perfusion-limited, while gas exchange between a bubble and tissue is diffusion-limited. Gas must diffuse across a barrier to enter or leave a tissue. V_b is the bubble volume, P_e is the pressure due to tissue elasticity, K_d is the diffusion barrier permeability, $A_b \times Q$ is blood inert gas solubility times blood flow, and $A_t \times V_t$ is tissue inert gas solubility times tissue volume. *P*(DCI) at any given time is a function of the largest bubble volume (Fawcett *et al.* 1992)

Decompression Trials

The statistical methodology used in probabilistic decompression modelling is not new, but its application to decompression is recent and rapidly evolving. Estimates of the risk of decompression illness often have a wide range of uncertainty as indicated by their confidence limits. While the precision of risk estimation will improve as primary data accumulate, the estimates discussed in this

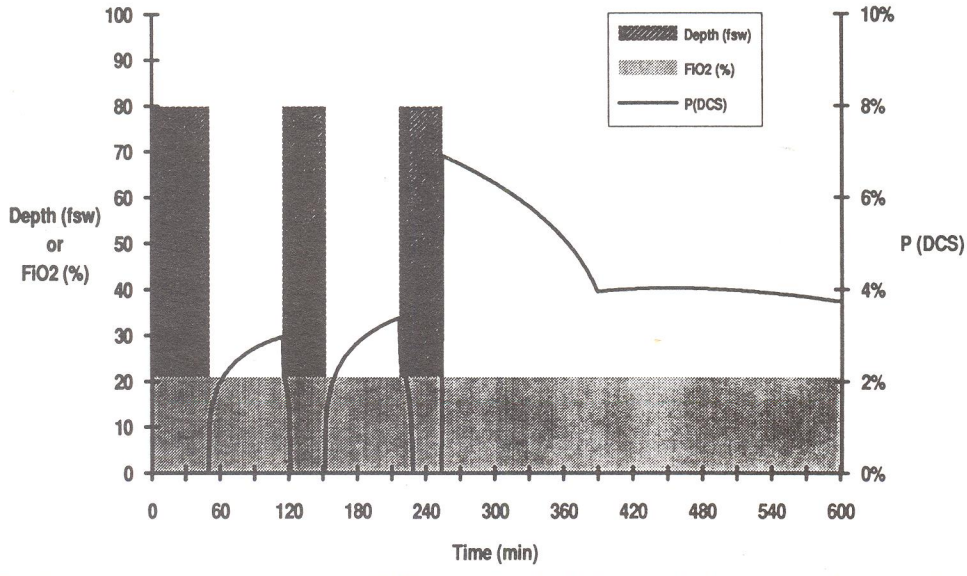

FIG. 14.27. The time course of estimated P(DCI) in a two-bubble model during repetitive air diving to 24 m (80 ft). Bubble growth and risk are delayed by diffusion (Gerth *et al.* 1992)

chapter should be viewed as 'indices' of risk which are useful for ranking decompression procedures but do not necessarily represent their true values. One of the primary objectives of decompression trials is to assess the accuracy of risk estimation.

Decompression trials can have a number of goals: to *investigate* the effects of risk factors; to *validate* the acceptability of dive profiles; and to *verify* the predictions of decompression models. The overall objective is to measure the incidence of decompression illness with the greatest possible certainty and ensure the most efficient use of resources.

Laboratory trials for investigating a risk factor would test a group of subjects twice, with and without the risk factor, to determine if it were associated with a significant change in the incidence of decompression illness. A two-tail, chi-square test with Yates correction for small sample size (Mode 1961) and statistical significance set at $P < 0.05$ reveals the following requirements: (1) there must be at least 5–6 incidents of decompression illness in one test if there are no incidents in the other; (2) there must be at least 7–8 incidents in one test if there is one incident in the other. These estimates are nearly independent of the total number of trials. While this comparison will indicate if a risk factor is significant, quantitating the risk is a more difficult proposition (Weathersby 1989).

Five incidents of decompression illness represent an observed incidence of 50% in 10 trials or 5% in 100 trials. Whether five incidents or a 50% incidence is acceptable depends on the nature of the expected symptoms, the simplicity and effectiveness of treatment, and the Institutional Review Board which must approve the trials (see 'Acceptable Risk of Decompression Illness'). Altitude studies with an incidence of decompression illness of 50–90% have been conducted because symptoms were minor joint pain with a low risk for permanent injury when treated promptly. Serious symptoms are more common in diving studies, and few are tolerated on any one test profile. An unacceptable incidence of serious symptoms is usually avoided if test profiles do not exceed decompression incidences of 5–7% (Thalmann 1989a).

Berghage *et al.* (1974) proposed, and provided supporting evidence from animal experiments, that the statistical uncertainty of decompression trials could be described by the binomial distribution. The binomial distribution has been tabulated in publications which list the number of trials, the number of successes (incidents of decompression illness) and the upper and lower limits for 95 and 99% confidence around the observed incidence (Diem 1962). In the discussion below, attention is focused on the upper 95% confidence limit as an index of decompression 'safety'

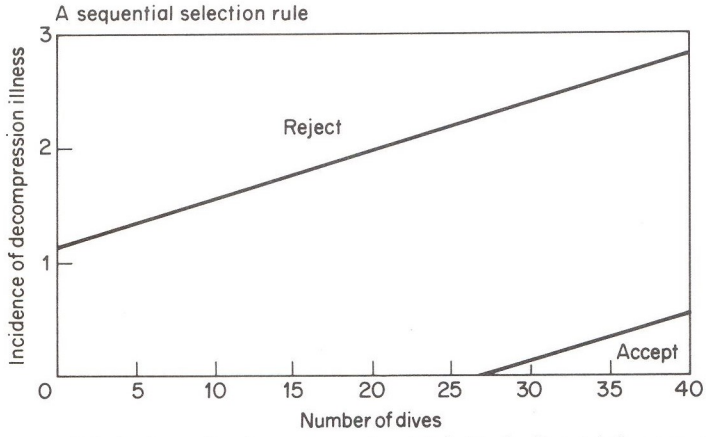

FIG. 14.28. An open sequential design of a decompression trial. Each dive trial represents a step to the right and each incident of decompression illness a step up. A trial ends when either the upper or lower bound is crossed. Profiles are rejected early in a test series if there are early incidents of decompression illness. Profiles are accepted before reaching the end of the series if no incidents occur. This strategy reduces the number of required tests. (Reproduced with permission from Homer & Weathersby 1985)

where 95% (or $P < 0.05$) is the lowest commonly accepted level of statistical significance.

Reference to binomial tables indicates that 35 trials with a zero incidence of decompression illness have an upper 95% confidence limit of 10%. Should one incident occur (a 2% incidence), 54 trials are necessary for a 10% confidence limit. Acceptable risk for operational procedures is probably less than 10%. To achieve an upper 95% confidence limit of 1%, 370 incident-free trials are required. With one incident (a 0.2% incidence), 600 trials are needed.

While the acceptable risk of decompression illness is closer to 1% than 10%, resource limitations usually make verification of acceptable risk practically unachievable in a single dive series even at minimal statistical significance. Haldane, for example, conducted the first decompression trials with two tests per profile which served only to rule out catastrophic failures (Boycott *et al.* 1908). Schedules in the USN Standard Air Table were accepted after four incident-free trials (Des Granges 1957a) with an upper 95% confidence limit of 60%. In the 1970s, decompression procedures were accepted after 12 incident-free trials with an upper limit of 27% (Hamilton 1976). More recently, procedures have been accepted with not more than one incident in 30 trials for each tested profile (an upper limit of 22%) and an overall incidence of 4% for all profiles tested (Thalmann 1984, 1985, 1986, 1989a).

Decompression trials can only conduct a finite number of dives. While the number of dives and incidents of decompression illness are desired to be low and the results to be statistically certain, all three conditions cannot be met simultaneously (Survanshi *et al.* 1992). If the trial size and number of incidents are minimized, the answers will be uncertain. If certain answers and a minimum number of incidents are required, the trial size will be large. Efficient trial designs are essential to achieve the greatest certainty, but even so, enough trials usually cannot be conducted to make the results statistically defendable at desired levels of acceptable risk.

The simplest decompression trial, the *fixed design*, tests a profile a fixed number of times and accepts it if the number of incidents of decompression illness do not exceed a number judged to be acceptable. Should this number be exceeded, the profile is rejected, and the model or acceptable risk is adjusted to make decompression illness less probable. A more efficient *sequential design* (Fig. 14.28) accepts profiles as low risk before reaching the maximum number of trials if no incidents have occurred, while profiles are rejected as high risk after a few trials if incidents occur early in the series (Homer & Weathersby 1985).

The statistical characteristics of fixed and sequential designs are described by *power curves* (Fig. 14.29) in which the x axis is the true (but unknown) P(DCI) of a profile, and the y axis is the probability of accepting that profile. The results of every trial design are represented by a different

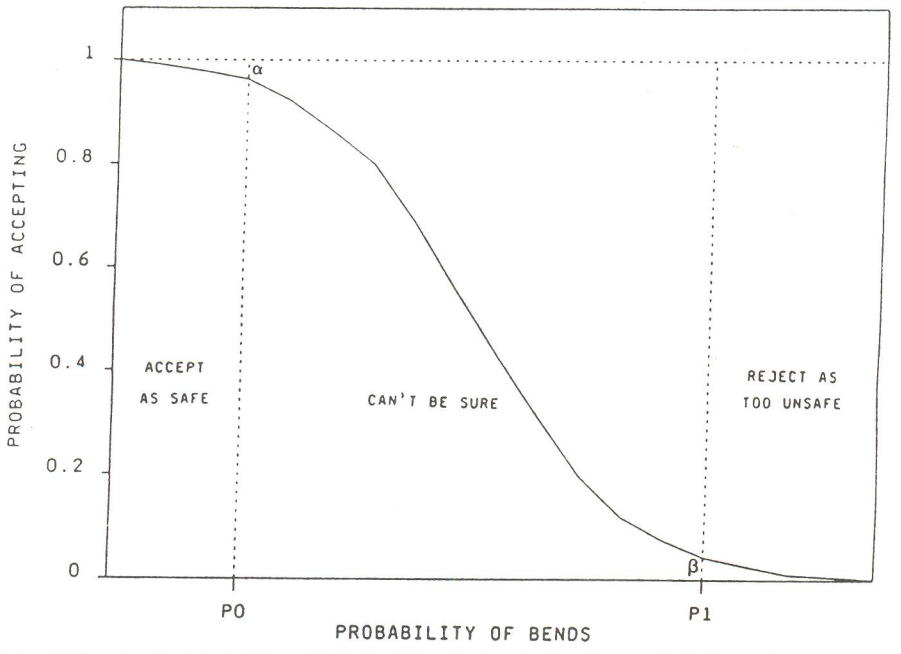

FIG. 14.29. A typical power curve for a trial design shows how the probability of accepting or rejecting a profile varies with the true *P*(DCI). There is a different power curve for every trial design. Alpha is the probability of rejecting a 'safe' profile and beta is the probability of accepting an 'unsafe' profile. (Survanshi *et al.* 1992)

power curve. If the true *P*(DCI) in Fig. 14.29 were P_0, for example, the probability of accepting the profile would be good, and the type I statistical error of rejecting a satisfactory profile (indicated by alpha) would be low. If the true probability were P_1, the probability of rejecting the profile would also be good, and the type II error of accepting an unsatisfactory profile (indicated by beta) would be low. The region between P_0 and P_1 is the *zone of indifference*, which is small for statistically certain results.

Power curves are helpful for accepting or rejecting test profiles. Large trials have steep power curves and small zones of indifference, but most trials are small with indifferent outcomes. Figure 14.30 shows power curves for the outcomes of three fixed trial designs, all having raw decompression illness incidences of 5%. A fixed rule of two incidents in 40 dives has an 80% chance of rejecting profiles with true risks of 8% or more. Changing the rejection rule to 15 incidents in 300 dives rejects profiles with risks of 6% or more, but the difference between 6 and 8% profiles may be too small to justify the large increase in the number of dives per profile since fewer profiles can be tested. A similar analysis for sequential trial designs shows that they provide the same information as fixed designs but require fewer dives (Homer & Weathersby 1985; Survanshi *et al.* 1992).

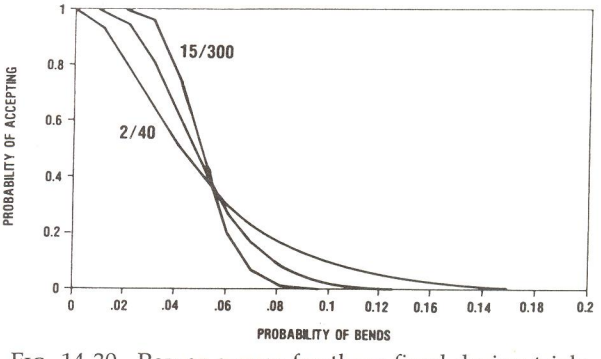

FIG. 14.30. Power curves for three fixed design trials each with a raw incidence of decompression illness of 5%. The three rejection criteria are: 2/40, 5/100 and 15/300 incidents/dive trials. The probability of accepting a profile is shown against the true *P*(DCI). (Reproduced with permission from Homer & Weathersby 1985; Survanshi *et al.* 1992)

Validation trials seek to ensure that profiles do not exceed some maximum acceptable incidence of decompression illness. A validation trial can be successful even if the validated profiles are overly

conservative, and the number of observed incidents is less than expected. *Verification trials*, on the other hand, test the accuracy of estimated risk and require trials of profiles that may exceed operationally acceptable risk. This avoids overly conservative procedures and improves risk estimate precision but results in more incidents during testing than would be acceptable in the field. While validation trials might take place under closely controlled open-water conditions, verification trials can only be conducted safely under laboratory conditions with rigorous medical supervision.

Having selected a trial design, test profiles and criteria for changing these profiles must be chosen. Profile changes are made by adjusting the model parameters as a result of an unacceptable number of profile failures or serious incidents of decompression illness. Profile change criteria are established before testing begins and are a matter of judgement. When the profiles are recomputed after a change, those which are judged more conservative (i.e. lower risk) than previously accepted profiles are usually not retested.

Test profile selection depends upon the type of diving. For single dive schedules, no-stop times, maximum bottom times and one intermediate time might be chosen at representative operational depths (Thalmann 1984, 1985, 1986, 1989a). For repetitive diving, a factorial design of depth, bottom time and surface interval might be used (Fawcett *et al.* 1992). Another approach is to choose dives for which there is little experience in the primary data. For dives which extrapolate beyond the range or mode of the primary data, cautious testing is warranted.

For decompression procedures that are new, are of uncertain risk, or are significantly different from established procedures, controlled chamber trials must be conducted before open-water trials are possible. Controlled field trials of new procedures are justified without previous chamber trials, however, if they represent minor modifications to existing procedures or when sufficient data exist to establish reasonable certainty of a low risk of decompression illness. Schreiner and Hamilton (1989) discussed decision guidelines for decompression procedure development in a workshop on procedure validation.

Two approaches to testing operational conditions are possible. In the first, chamber dives or closely controlled open-water dives attempt to reproduce the operational workload and water temperature. The second approach conducts tests under conditions believed to impose near-maximum decompression stress. The evidence concerning what constitutes maximum stress is mixed, however, one study finding a large difference between dry, resting and wet, working divers (Vann 1982a) and another study finding little difference between dry and immersed exposures (Weathersby *et al.* 1990). While recognizing these uncertainties, US Navy decompression trials are conducted with immersed divers who perform mild exercise at depth and rest during decompression (Thalmann 1984, 1985, 1986, 1989a). The water temperature is adjusted to produce the maximum expected operational cold stress, while the inspired oxygen partial pressure is maintained at its lowest expected level.

Ideally, profiles are tested exactly as they are computed, but ear clearing and chamber operations cause occasional unplanned deviations. The uncertainty this introduces is eliminated by computing profiles in real-time according to the algorithm being tested (Thalmann 1983, 1984, 1986). This provides a record of the exact test profiles for subsequent use as primary data. Diver-worn computers in which depth is adjusted according to the algorithm while simultaneously recording the depth–time profile may eventually allow open-water trials to be used as primary data.

When a dive series is finished, the depth–time domain over which the tables will be used is defined by acceptable risk at maximum reasonable dive times. For procedures computed by deterministic models, every profile must be treated independently, and the uncertainty of the overall incidence of decompression illness is similar to the uncertainties of the individual profiles. For procedures computed by probabilistic models, on the other hand, estimation of an overall risk for the entire trial is justified when the profiles are iso-risk and quantitatively derived from empirical data. Thus probabilistic models provide a more accurate estimate of overall risk of decompression illness for a given trial size than do deterministic models. Several iterations of trials may be necessary before a set of procedures is judged to be ready for field use (Hamilton & Schreiner 1989).