TOLERATING OXYGEN EXPOSURE

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The fact that oxygen can be toxic is well known to divers, especially those practising the use of advanced techniques involving special breathing gases. Here oxygen tolerance techniques may be optimised in order to allow more efficient decompressions. Oxygen's toxicity is also a well recognised problem among the medical community, but in the latter case toxicity management techniques are not intended to be optimal or especially efficient; here the objective is to avoid making oxygen exposure, for the patient who needs it, become part of the problem.[1] This paper discusses some of the optimisation techniques.

The exact mechanisms of oxygen toxicity are gradually being worked out, but there is yet much to be learned.[2] We are notconcerned here with the mechanisms, because the methods of controlling oxygen exposure and of tolerating exposure to oxygen rely on empirical information rather than fundamental biochemistry or mathematical modelling. Although the mechanism at the cellular level is probably the same, we are concerned about two general manifestations of oxygen toxicity. For both of these categories, empirically derived procedures for use in managing exposure have been developed.

As this audience knows quite well the two categories of oxygen exposure are the toxicity that manifests itself in the central nervous system (CNS), and the whole-body or pulmonary toxicity. The two types of toxicity are distinct not only in their anatomical manifestations but also because of the "dose" of oxygen exposure required. CNS toxicity generally requires exposure to a level above about 1.6 bar (or atmospheres absolute) and may need only a few minutes exposure, while exposures for longer durations, hours or days, above about 0.5 bar may cause whole body toxicity. Management of both types of toxicity consists primarily of controlling the exposure and current procedures are entirely empirical. Other toxicities, such as to the eye, require longer and more intensive exposures than the two under consideration.

CNS toxicity

CNS oxygen toxicity may generally be seen as unconsciousness or incapacitation or may come on as a full blown epileptic-like convulsion. Lesser symptoms are important as warning signals but are not likely to be incapacitating. The convulsion itself is not particularly harmful, but the consequences of having a convulsion can be, especially for a diver in the water. People are occasionally injured when they convulse in a chamber. It is quite common to bite the tongue sometimes causing bleeding; this can be a misleading symptom in a rescue. In the case of a diver a convulsion underwater is extremely threatening because it can lead to drowning; one of the first reactions is an expulsive movement of the tongue, which will cause a mouthpiece to be spat out. For this reason divers pushing the oxygen exposure limits are well advised to wear a full-face mask or helmet to prevent loss of access to the breathing gas.

CNS toxicity requires a high level of oxygen exposure, and may occur after as little as a few minutes of exposure. Measured as partial pressure, the exposure level for CNS toxicity requires more than about 1.6 bars for a working diver, but a resting subject in a dry chamber may tolerate 2.5 or 3 bar for many minutes. Factors that increase susceptibility or reduce the tolerance threshold include exposure to an elevated carbon dioxide level, immersion, and both heat and cold.[3] An increase in brain blood flow could be a common element of all these factors. Exercise and breathing resistance due to equipment or dense gas all can cause CO_2 build up. Some individuals tolerate a higher level of CO_2 than normal and thus are at greater risk; these people are called "CO_2 retainers."

Pulmonary or whole body toxicity

The main manifestation of long term exposures to levels of oxygen not high enough to cause CNS toxicity is most commonly an effect on the lungs. This is marked by a substernal or chest pain and a feeling as if the lungs are burning (actually they are). There may be spontaneous coughing or difficulty in inspiring or exhaling a full breath without coughing. The symptoms become more severe with increasing exposure. From acute exposures this condition is regarded as being completely reversible, although from severe cases complete recovery can take a matter of months.[4] While the lung symptoms are the main focus and afford the method of monitoring this particular kind of toxicity, other symptoms are often seen that are not lung related. These are, in addition to the lung problems mentioned above, paraesthesias (especially numbness in fingertips and toes), headache, dizziness, nausea, effects on the eyes, and reduction of aerobic capacity. This has been described in detail by Sterk and Schrier.[5] Since this is more than a lung manifestation we feel that the term "whole body" is perhaps a better choice than just "pulmonary" toxicity[6] and "chronic" is not the right word here.

Intermittent exposures

Before discussing specific algorithms for keeping track of oxygen exposure it is important to mention the technique that is overwhelmingly the most important one

for tolerating oxygen, intermittent exposure.[8,9] Tolerance to all types of oxygen toxicity is increased by interrupting the exposure with periods of breathing a low oxygen mix. This is manifested as "air breaks" in the hyperbaric oxygen treatment of decompression disorders.[10]

Managing whole body toxicity

The story of how the methods of managing whole body toxicity have been developed is a fine illustration of the empirical nature of this practice. Almost all of the early work on this particular type of oxygen toxicity was performed at the University of Pennsylvania by CJ Lambertsen and colleagues.[11] A fundamental contribution of this laboratory was the unit with which low level oxygen exposure is measured.[12]

The parameter monitored to assess lung toxicity is vital capacity. Vital capacity is the maximum amount of gas that an individual can expire after a maximal filling of the lungs; it is reduced by excessive oxygen exposure. A mathematical "curve fit" to empirical data on vital capacity changes as a result of oxygen exposure yielded an equation that can be used to calculate a "unit pulmonary toxicity dose" (UPTD). A unit dose is one minute of exposure to a PO_2 of one bar. The empirical curve (Equation 1) accounted for differences in effect on vital capacity of exposures above and below one bar. The threshold for exposure effects is 0.5 bar, since exposures below this level have no measurable effect on vital capacity. The cumulative pulmonary toxicity dose or CPTD is the sum of UPTDs. A somewhat less intimidating term for the unit dose coming into use is the oxygen tolerance unit, OTU, defined by the same empirical equation:

$$OTU = t \left\{ \frac{(PO_2 - 0.5)}{0.5} \right\}^{0.83} \quad (1)$$

where t is the exposure time and PO_2 is the oxygen partial pressure in bar.

The unit toxicity dose was developed as an empirical measure of changes in vital capacity as result of oxygen exposure. With trained investigators and subjects vital capacity measurements can be quite reproducible, but it is fraught with quantitative hazards and requires careful monitoring.[13]

The original development of the pulmonary tolerance unit used a change in vital capacity as a measure of whether or not the dose was acceptable. A single exposure of 615 units was found to cause a 4% decrement in vital capacity, and this was regarded as the maximum tolerable for an ordinary operational exposure.[14] There was no overt provision in the UPTD/CPTD approach for dealing with recovery; in due course this prompted further empirical investigations.[5]

A project designated Repex had a requirement to manage whole-body oxygen exposure over an operational exposure period of a few days.[15] This resulted in a management algorithm that considers total exposure over a number of days so in effect takes recovery into account over the exposure period. It had been observed that an operationally acceptable daily exposure for a "fresh" diver was 850 OTUs. This method also takes into account the additional tolerance on the first few days of exposure of an individual who has not recently been exposed. Total exposure doses for two, three, or several days were determined, again empirically. The average daily doses get smaller with time and level out at 300 OTU/day (Table 1). The resulting data were put together into an upper limit "Repex" curve for exposure durations of one to 14 or more days shown in Figure 1.[6,15]

TABLE 1

INCREASES IN TOTAL OTU OVER 15 DAYS SHOWING EARLY TOLERANCE

Days	Average daily dose	Increase in Total OTU	Total OTU
1	850	850	850
2	650	550	1400
3	600	460	1860
4	520	240	2100
5	450	200	2300
6	420	220	2520
7	400	140	2660
8	350	140	2800
9	330	170	2970
10	320	130	3100
11	300	200	3300
12	300	300	3600
13	300	300	3900
14	300	300	4200
15	300	300	4500

The degree of "intermittency" of the exposures contributing the data to the Repex curve was not controlled. Most exposures used as data were more or less intermittent, however.

The Repex method provides an empirical method of predicting tolerance. Another approach to empirical control of whole body toxicity is that of Harabin and colleagues.[16] They produced an empirical predictive equation based on a large data base that estimates the reduction in vital capacity as a result of oxygen exposure:

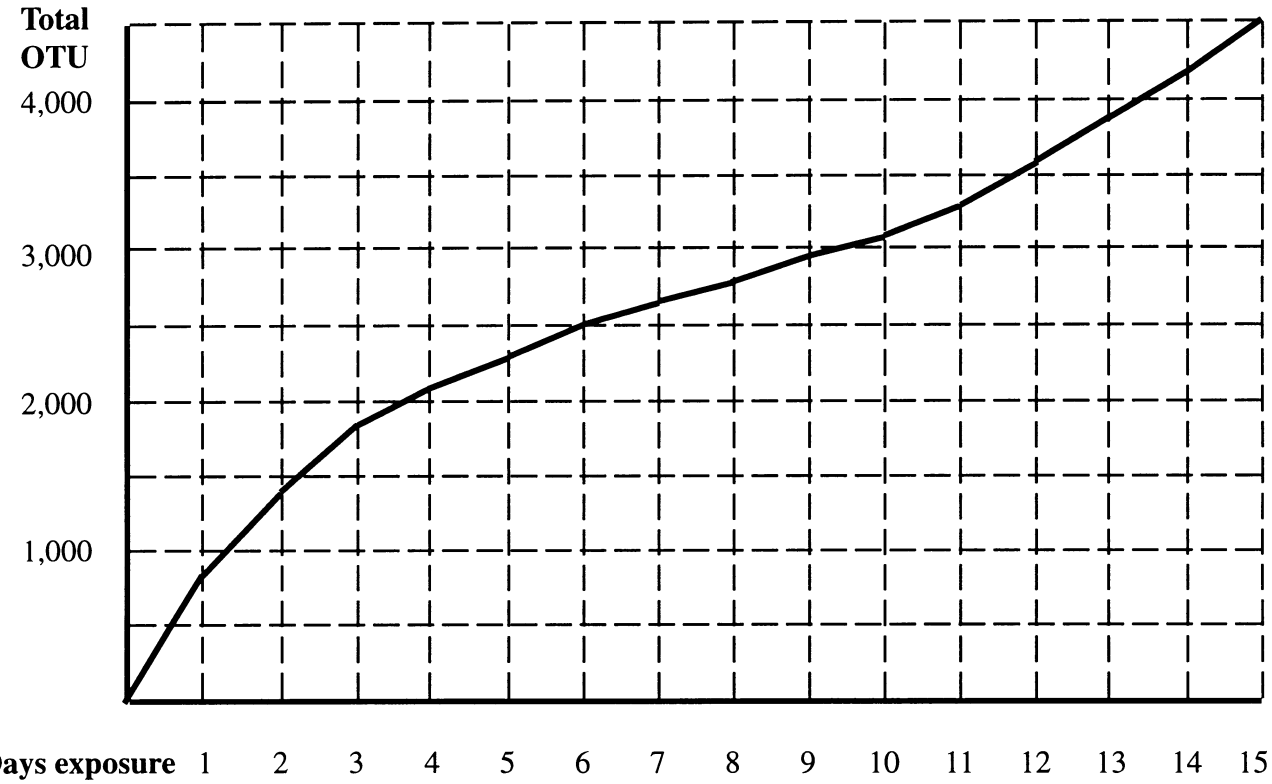

Figure 1. The allowable cumulative oxygen dose for daily exposures up to 15 days. The average daily doses are shown in Table 1. except for the first day and after day 11 the increment in total dosage is less than the daily dose due to tolerance which steadily decreases.

% VC drop = -0.011 (PO_2 - 0.5) t (2)
where t is time in minutes of the exposure, and PO_2 is the exposure level in bar.

The Harabin equation offers an attractive alternative if only vital capacity decrease is to be estimated. Because it is based on data from a wide range of exposures including some very long ones it thus takes recovery into account. A more complex exponential equation based on the same vital capacity data set has been derived recently by Arieli and associates; according to their analyses it gives a better fit.[17]

Managing CNS toxicity

Descriptions of the mechanism of CNS oxygen toxicity are not yet precise enough to permit predictive modelling or development of a "first principles" algorithm for managing exposure. Toxicity appears to be dose related, such that both level and duration of exposure are involved. A high degree of variability between individuals and even at different times in the same individual makes modelling CNS toxicity an imprecise art. Donald recently reviewed a lifetime of his work on CNS toxicity, and one major conclusion is that it is hard to predict.[3] Virtually all of Donald's data was from exposures where the individual was breathing pure oxygen, usually from a rebreather.

For many years there was only one recognised guideline on avoiding CNS toxicity during mixed gas diving (oxygen diving uses more liberal limits). This was a table from the US Navy Diving Manual.[18] This USN Oxygen Partial Pressure Limits Table has been widely reproduced and even incorporated into national law in some places. The table consists of a set of time limits, which are "allowable" exposure limits for various oxygen partial pressures. The values in the table are not expressly physiological, but are appropriate for the allowable exposure time of 30 min at 1.6 bar PO_2; they become excessively conservative for the next few exposure levels lower than 1.6 bar. There are a couple of other things wrong with this table as the sole means of managing CNS toxicity. It does not tell the user what to do if the exposure is not exactly on one of these PO_2 limits, and does not say what to do if part of the exposure is at one O_2 level and part in another. Nor does it provide a method of dealing with recovery e.g. after how much time and in what recovery situation can the exposure begin again.

To its credit, the USN did some additional targeted research and was able to replace this table in the 1991 issue of the US Navy Diving Manual.[10] As before, the new procedures allow somewhat more time for shallow water oxygen divers than for mixed gas divers. For mixed gas diving the Navy takes a fresh approach by setting a flat upper PO_2 limit of 1.3 bar; below this level there are no

time limits, and above this level emergency limits are set out in a chart that allows 30 min at 1.6 bar just as before and goes to a PO_2 level of 1.8 bar where 15 min are allowed; approval by the Chief of Naval Operations is needed for mixed gas diving at a PO_2 of greater than 1.3 bar.

In many situations there is nothing wrong with limitations that are more conservative than they need to be, but in some operational situations such limits can be a considerable handicap. One of these was the situation in undersea habitats. In normal surface-oriented diving with air it is almost impossible to get in a situation that will lead to central nervous system toxicity because of decompression limitations. However, when divers live in a habitat and make excursions with air as the breathing gas the bottom time can be more or less unrestricted; in such cases oxygen exposure while breathing air can become quite significant. This is true of both whole body and CNS toxicity. With the older USN chart as the only thing to go on, oxygen limits became somewhat frustrating for many of the scientists wanting to do extensive work from undersea habitats.

In an attempt to resolve this question NOAA sought the advice of a leading expert on oxygen tolerance, Dr C J Lambertsen. Lambertsen, in collaboration with others familiar with this problem, came up with a new set of oxygen limits. These are in Table 15-1 of the NOAA Diving Manual which came out in 1991, about the same time as the newer USN limits (Table 2). Recovery information is factored in by providing a 24 hour exposure limit as well as single exposure durations for specific oxygen partial pressures. The all-day limits take into consideration whole body exposure as well.

Normal exposures are those involved in standard diving operations. A series of repetitive dives may be accumulated within a single limit. If the single limit is exceeded wait for 2 hours before diving again. If the day limit is exceeded wait for 12 hours.

The new NOAA limits were welcomed by habitat divers but especially by the technical diving community, divers whose decompression is limited in a major way by oxygen exposure. In retrospect, because there have been some oxygen toxicity incidents within the limits of this table,[19] it is best to use these limits conservatively and regard them as applying to a diver performing light work with little or no breathing resistance and thus a normal threshold to CNS toxicity. Many incidences of divers being affected within the limits of this table appear to be related to high workloads or breathing resistance or the like. The NOAA table is not based on a specific set of experiments but rather on the accumulated wisdom of experts in this field.

The structure of this table is just like the old Navy one in that there are limits specified as the number of minutes allowed given oxygen partial pressures. Again there is no provision for intermediate levels or multilevel diving, nor is there an algorithm for recovery.

TABLE 2

NOAA OXYGEN PARTIAL PRESSURE AND EXPOSURE TIME LIMITS
(from Table 15-1, NOAA Diving Manual 1991)

Oxygen partial pressure (PO_2) in bar	Maximum single exposure in minutes	Daily limit: Maximum total duration for any 24-hour day in minutes
1.6	45	150
1.5	120	180
1.4	150	180
1.3	180	210
1.2	210	240
1.1	240	270
1.0	300	300
0.9	360	360
0.8	450	450
0.7	570	570
0.6	720	720

The matter of operating at several PO_2s during an exposure or at values between these stated limits has been dealt with by a simple matter of lineal extrapolation. There is no specific physiological basis for this but likewise there is no meaningful physiological argument against it. All of these limits are empirical operational guidelines and they imply no particular physiology. A first approach was a computational method proposed by Kenyon and Hamilton[20] which called for a linear interpolation between exposure levels and limits, such that, for example, half the exposure time at a given limit would use up half the tolerance and the other half could be used some other way. This same approach was arrived at independently by a group of operationally oriented technical divers, which increments an “oxygen clock” as tolerance time is used up. These unpublished methods have worked well in practice.

Another somewhat arbitrary method of accounting for recovery has been proposed for dive computers.[21] This uses an arbitrary but quite conservative “decay” of the accumulated “oxygen clock” when oxygen exposure is low. This allows computation of decompressions over extended periods and multiple dives.

Harabin and colleagues at the U.S. Navy Medical Research Institute, using survival and likelihood statistics, have a mathematical model that predicts the benefit of intermittency when exposure is above a critical PO_2

threshold,[22] but it does not yet account for immersion and exercise.

Conclusion

Exposure to oxygen can be managed to minimise the operational cost of both of the major toxicities. In both cases it is a matter of staying below reasonably sound empirical limits. For CNS toxicity the limits can be interpolated, allowing oxygen to be used effectively for decompression. For whole body toxicity taking advantage of the initial tolerance at the beginning of an exposure can have equally beneficial effects for the kinds of operation that encounter this problem. For all exposures, tolerance can be increased substantially by keeping the exposures intermittent.

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