Tolerating Exposure to High Oxygen Levels: Repex and Other Methods

R.W. Hamilton

Hamilton Research, Ltd.
Tarrytown, New York

ABSTRACT
Exposure to high oxygen levels occurs in diving and other situations; oxygen poisoning can be avoided by controlling the exposure dose. A number of methods of accounting for dose and for setting limits have been developed, including the unit pulmonary toxicity dose oxygen “unit” (UPTD; when “cumulative” it is called CPTD), which we call the oxygen toxicity unit (OTU). Methods that set exposure limits based on PO₂ and duration are appropriate for avoiding central nervous system (CNS) toxicity, but these are not usually optimal for the general “whole body” symptoms, which in this approach also includes lung symptoms. The Repex method developed for habitat saturation-excursion diving is appropriate for a variety of exposures. CNS toxicity is avoided by staying below 1.5 bars PO₂ except for short excursions. Whole body toxicity is managed on a multiday basis by staying below an empirical limit that depends on the number of days of exposure as well as the daily dose. This method accounts for variable daily exposure and recovery during periods of exposure to lower oxygen levels, and it allows a diver’s reserve capacity to be used if exposure is for only a few days.


INTRODUCTION: THE NEED FOR OXYGEN TOLERANCE
A number of activities result in the exposure of humans to oxygen levels greater than normal. The area of primary interest here is diving, but astronauts, tunnel or caisson workers, and medical personnel may also take advantage of the benefits of oxygen breathing — the objective in these cases is to improve decompression. Certain patients may also benefit from oxygen breathing under pressure. Among the few options available for improving the efficiency and reliability of decompression procedures, creative management of oxygen offers overwhelmingly the best opportunity. Oxygen not only speeds up decompression, it can make the resulting decompression tables or procedures more reliable as well. There are, of course, other situations where elevated levels of oxygen are breathed, but our interest here is for its benefit to decompression or the treatment of decompression sickness.

Although oxygen is beneficial, too much can be toxic. This paper deals with oxygen tolerance, i.e., methods of using oxygen that avoid the development of oxygen poisoning. Oxygen poisoning is avoided primarily by controlling exposure — by making it intermittent and by limiting the overall dose. This requires monitoring of oxygen exposure doses and controlling exposure based on the doses.

The main theme of this paper is a method for managing oxygen exposure developed for a specialized diving situation but that can easily be adapted for general use where operational exposure to high oxygen levels is required. The method is from a project known as Repex, sponsored by the Office of Undersea Research, National Oceanic and Atmspheric Administration (NOAA), U.S. Department of Commerce, and carried out by Hamilton Research, Ltd. of Tarrytown, New York (Hamilton, Kenyon, and Peterson 1988; Hamilton, Kenyon, Peterson, Butler, and Beers 1988). The Repex method of oxygen exposure management is reviewed and presented here, along with a review of other methods.

NATURE OF OXYGEN POISONING
Consider first the oxygen toxicity problem itself. To help in oxygen management, but not as a strict physiological classification, we consider two "types" or levels of oxygen toxicity. These are the classic central nervous system (CNS) toxicity and a more slowly developing syndrome sometimes referred to as "pulmonary" oxygen toxicity, which affects primarily the lungs but can also affect the whole person in a variety of ways (Clark and Lambertsen 1971; Clark 1982).

CNS Oxygen Toxicity
CNS toxicity (the "Paul Bert effect") acts at higher PO₂ levels after short exposures. It may develop within a few to many minutes on exposure to levels of oxygen above about 1.8 bars and may have as an end result an epileptic-like convulsion that is not dangerous in itself (under normal circumstances) but that will be quite disruptive in any case and can result in drowning or physical injury. Susceptibility to CNS toxicity is exacerbated by other factors, particularly those that cause an increase in internal PCO₂ such as exercise and breathing dense gas, breathing against a resistance, and by other physiological factors such as high body temperature or hypothyroidism.
General Somatic Oxygen Toxicity

As mentioned, to manage long range exposure to elevated oxygen we can group the familiar pulmonary toxicity with a more general, whole body category.

Pulmonary or Lung Oxygen Toxicity

Another classical symptom of oxygen poisoning in addition to those of CNS is pulmonary, oxygen’s effect on the lung (the “Lorrain Smith effect”). This takes hours or longer to develop from exposure levels that may be lower than those that cause CNS symptoms; it is seen as substernal (chest) pain or discomfort, coughing, inability to take a deep breath without pain or coughing, a development of fluid in the lungs, and a reduction in vital capacity.

For practical purposes the pulmonary oxygen poisoning encountered in diving or in relation to decompression is, in time, fully reversible and leaves no long term effects. A different hospital-related “chronic lung toxicity” may lead to lung fibrosis after very long exposures, but this type is not of concern here.

Whole Body Oxygen Toxicity

Another “category” of oxygen poisoning that develops after hours to days of exposure has been widely observed but is not prominently mentioned in the classical literature. We prefer to call it “whole-body” or “somatic” oxygen toxicity. Its effects are a collection of symptoms in addition to the lung problems mentioned above that include paresthesias (especially numbness in fingertips and toes), headache, dizziness, nausea, effects on the eyes, and reduction of aerobic capacity. It has been described in detail recently by Sterk (1986; 1987), who has called it “chronic” oxygen toxicity (at the risk of confusion with the fibrotic condition just mentioned).

Also, after many days of exposure to increased oxygen, a reduction of hemoglobin and red blood cells has been noted in some divers; this is a normal adaptive response, the converse of the acclimation to high altitude. Because management of the general whole body syndrome also takes care of pulmonary symptoms, we include both types together in the “whole body” category. All forms of oxygen toxicity show highly variable effects on different individuals and even significant differences in the same individual at different times.

MEASURING THE OXYGEN EXPOSURE DOSE

Oxygen poisoning is the effect of a drug, and the degree of exposure is a dose. Some methods of measuring or estimating the dose of oxygen exposure are given here.

Partial Pressure Versus Time

A simple but meaningful method of measuring exposure to oxygen is to consider the inspired PO₂ (the oxygen partial pressure) and the duration of the exposure. In this approach the dose is the integral (or product) of the PO₂ over time. Limits are expressed as the time limit that a given inspired PO₂ may be tolerated.

Oxygen Tolerance Units, OTUs

Traditional Pulmonary Toxicity Units, UPTD and CPTD

With regard to pulmonary oxygen toxicity, a method of computing the dose of an exposure was developed some years ago at the University of Pennsylvania, the unit pulmonary toxicity dose or UPTD (when “cumulative” it is called CPTD). A unit dose is 1 min of exposure at 1 bar or atm PO₂, and the effect of the dose is a reduction in lung vital capacity. Vital capacity is chosen as the affected parameter because it is one of the most prominent subjective symptoms, and because it can be measured non-invasively, albeit with careful techniques on trained subjects. The method uses a curve that has been fitted to the available vital capacity data and described by an exponential equation.

Whole Body Units, OTU

The Pennsylvania unit (UPTD or CPTD) has served well and is based on empirical data; it is the basic unit used in the Repex method. For two reasons, however, we prefer to use an alternative term, OTU or “oxygen tolerance unit.” First, since we are dealing with operational physiology in managing exposure to oxygen in diving we prefer to refer to these as techniques for “tolerance” of oxygen exposure, rather than for avoiding oxygen “toxicity.” They are the same thing, but we feel it offers a more positive approach. Second, there has been some confusion between the acronyms UPTD and CPTD, although there is really only one “unit.”

The OTU and its predecessors — the oxygen toxicity unit — are calculated by the following expression:

\[ OTU = t (\text{PO}_2 - 0.5)0.83 \]

where t is the duration of the exposure in minutes and PO₂ is the oxygen partial pressure in bars or atm. The 0.5 bar is the “threshold” below which no significant symptoms develop (Bardin and Lamberts 1970; Wright 1972; for a review and look-up charts see the Underwater Handbook, Shilling et al. 1976, p. 154); even oxygen-injured lungs can recover below this level (Eckhoff et al. 1987). The exponent 0.83 was determined to give the best fit to the data on reduction of vital capacity as a function of oxygen exposure. The resulting dose tends to give added effect to doses above a PO₂ of 1.0 bar and less to those lower than 1.0 bar. An important benefit to this method is that the units are additive, and the net result of multiple short exposures can be totalled.

Computers and hand calculators that can perform this calculation are readily available, but the values can also be taken from a chart such as those in the Underwater Handbook (Shilling et al. 1976) or the one included as Table 1.
Table 1
Chart of OTU dose by PO2 and air depths. The values in the table from left are the PO2, the depth in msw or fsw diving with air to give that PO2, and the number of OTU per minute at the indicated PO2 level. To calculate a dose multiply the value in the chart for the exposure PO2 by the number of minutes of the exposure. For exposures at different PO2's calculate the dose in OTU for each exposure period at a given PO2 and sum the OTUs to get the total exposure.

<table>
<thead>
<tr>
<th>PO2 atm or bar</th>
<th>fsw Depth</th>
<th>msw Depth</th>
<th>OTU/ min</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.50</td>
<td>45.6</td>
<td>13.8</td>
<td>0</td>
</tr>
<tr>
<td>0.55</td>
<td>53.4</td>
<td>16.2</td>
<td>0.15</td>
</tr>
<tr>
<td>0.60</td>
<td>61.3</td>
<td>18.6</td>
<td>0.27</td>
</tr>
<tr>
<td>0.65</td>
<td>69.1</td>
<td>21.0</td>
<td>0.37</td>
</tr>
<tr>
<td>0.70</td>
<td>77.0</td>
<td>23.3</td>
<td>0.47</td>
</tr>
<tr>
<td>0.75</td>
<td>84.9</td>
<td>25.7</td>
<td>0.56</td>
</tr>
<tr>
<td>0.80</td>
<td>92.7</td>
<td>28.1</td>
<td>0.65</td>
</tr>
<tr>
<td>0.85</td>
<td>100.6</td>
<td>30.5</td>
<td>0.74</td>
</tr>
<tr>
<td>0.90</td>
<td>108.4</td>
<td>32.9</td>
<td>0.83</td>
</tr>
<tr>
<td>0.95</td>
<td>116.3</td>
<td>35.2</td>
<td>0.92</td>
</tr>
<tr>
<td>1.00</td>
<td>124.4</td>
<td>37.6</td>
<td>1.00</td>
</tr>
<tr>
<td>1.05</td>
<td>132.0</td>
<td>40.0</td>
<td>1.08</td>
</tr>
<tr>
<td>1.10</td>
<td>139.9</td>
<td>42.4</td>
<td>1.16</td>
</tr>
<tr>
<td>1.15</td>
<td>147.7</td>
<td>44.8</td>
<td>1.24</td>
</tr>
<tr>
<td>1.20</td>
<td>155.6</td>
<td>47.1</td>
<td>1.32</td>
</tr>
<tr>
<td>1.25</td>
<td>163.4</td>
<td>49.5</td>
<td>1.40</td>
</tr>
<tr>
<td>1.30</td>
<td>171.3</td>
<td>51.9</td>
<td>1.48</td>
</tr>
<tr>
<td>1.35</td>
<td>179.1</td>
<td>54.3</td>
<td>1.55</td>
</tr>
<tr>
<td>1.40</td>
<td>187.0</td>
<td>56.7</td>
<td>1.63</td>
</tr>
<tr>
<td>1.45</td>
<td>194.9</td>
<td>59.1</td>
<td>1.70</td>
</tr>
<tr>
<td>1.50</td>
<td>202.7</td>
<td>61.4</td>
<td>1.78</td>
</tr>
<tr>
<td>1.55</td>
<td>210.6</td>
<td>63.8</td>
<td>1.85</td>
</tr>
<tr>
<td>1.60</td>
<td>218.4</td>
<td>66.2</td>
<td>1.92</td>
</tr>
<tr>
<td>1.65</td>
<td>226.3</td>
<td>68.6</td>
<td>2.05</td>
</tr>
<tr>
<td>1.70</td>
<td>234.1</td>
<td>71.0</td>
<td>2.07</td>
</tr>
<tr>
<td>1.75</td>
<td>242.0</td>
<td>73.3</td>
<td>2.14</td>
</tr>
<tr>
<td>1.80</td>
<td>249.9</td>
<td>75.7</td>
<td>2.21</td>
</tr>
<tr>
<td>1.85</td>
<td>257.7</td>
<td>78.1</td>
<td>2.28</td>
</tr>
<tr>
<td>1.90</td>
<td>265.6</td>
<td>80.5</td>
<td>2.35</td>
</tr>
<tr>
<td>1.95</td>
<td>273.4</td>
<td>82.8</td>
<td>2.42</td>
</tr>
<tr>
<td>2.00</td>
<td>281.3</td>
<td>85.2</td>
<td>2.49</td>
</tr>
</tbody>
</table>

CONTROLLING OXYGEN EXPOSURE

Once an exposure dose is determined it is then necessary to assign some limits relevant to the dose that will protect the diver from excessive exposure. Approaches to this have generally been based on either the duration of a specific exposure to a given PO2 or on a dose of oxygen. The former usually does not deal explicitly with partial exposures nor does it account for recovery, and the dose-related method accounts for partial exposures but may not consider recovery. The dose-based Repex method considers recovery by adjusting exposure to fit the overall mission duration.

Intermittency

Before discussing limits it is relevant to mention a well-established technique for reducing or postponing CNS oxygen poisoning. This is the method of intermittent exposure. If "breaks" of a period of lower oxygen are taken during oxygen breathing, the tolerance is greatly improved. This is demonstrated, for example, in the U.S. Navy (USN) tables for treatment of decompression sickness using oxygen, where breaks of five minutes of air breathing are taken every twenty or thirty minutes of oxygen breathing. This has been demonstrated to avoid oxygen convulsions in all but very rare cases (Lambertsen 1988; Butler and Thalmann 1984) and to postpone pulmonary toxicity at high PO2's (Hendricks 1977).

In practice, oxygen or high oxygen mixtures are usually breathed in cycles. A "cycle" is a period on oxygen followed by a period off oxygen breathing air or the chamber atmosphere. Typical cycles are twenty minutes on O2 followed by five minutes off, or twenty-five minutes on followed by five off. A longer cycle of thirty minutes on, ten minutes off has also been used.

The relation of intermittent breathing to oxygen tolerance limits is not always clear. Usually, it is not practical or even possible for a diver to switch gases during the work period or early stages of decompression, thus the PO2-based CNS limits are generally for continuous exposure. Pulmonary tolerance is also improved by breaks, but in the long run of several days the overall average is probably the dominant factor (Lambertsen 1988; Clark 1989).

Direct Partial Pressure Limits

The classical set of limits for oxygen exposure is that of the U.S. Navy Diving Manual (1981) for mixed gas diving (Table 2). This chart of allowable exposure times for different PO2's has been widely reproduced and its values picked up by many standards. It has been criticized as being too conservative, but more cogent criticisms are that it is designed for CNS toxicity but goes well beyond the range where CNS toxicity is likely, that it covers short duration exposures only, that it does not consider work level, and that it does not include stated algorithms for dealing with recovery or partial exposures. The USN chart represents an operational decision, not research results. Indeed, USN is working to prepare limits that are more physiologically realistic and operationally workable (Butler and Thalmann 1984).

The USN values for "exceptional exposures" are probably not conservative enough for general use but, in any event, could not properly be used for routine diving if the Navy's definition of an exceptional exposure is followed (Table 2).

A set of limits drawing on recent data (such as the Predictive Study V program at the University of Pennsylvania, Lambertsen et al. 1987) and intended to be more realistic than the USN chart has been proposed for use in the Third Edition of the NOAA Diving Manual now in preparation (due early 1990). These limits are presented in a somewhat the same style as the USN chart, but in addition to single-exposure CNS PO2-time limits, they also include limits for the maximum exposure in a 24-hr day; they thus combine CNS and whole-body limits. See
limits should have low resistance breathing equipment and should avoid heavy exercise, any buildup of CO₂, and extremes of temperature.

The Pennsylvania UPTD-CPTD Method

This empirical method is based only on observed changes in lung vital capacity. The method for determining the dose is given above. Although widely used as a dose measure, the method does not specify limits for different situations, and it lacks an algorithm for dealing with recovery and multiday exposures; one guideline “limit” is that 615 units accumulated in a relatively short time (hours) predicts a vital capacity reduction of 4 percent, and this is considered operationally acceptable (Wright 1972). As will be seen later, 615 units per day on a continuous basis is far too much oxygen.

Harabin’s Vital Capacity Decrease

A recent reexamination of these data and more that have accumulated since the CPTD method was proposed has been performed by Harabin and colleagues at the Navy Medical Research Institute (1987). This is not a dose measure but rather goes directly from the data to a vital capacity drop. This group took another look at the data originally used by Lambertsen and colleagues at Pennsylvania and added some more data not available earlier. They derived a linear equation that gives the best estimated prediction of the drop in vital capacity:

\[
\text{% VC drop} = -0.011 \text{ (PO}_2 - 0.5\text{)} \times t
\]

where \( t \) is time in minutes of the exposure, and \( \text{PO}_2 \) is the exposure level in bars or atm.

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 in Israel, and according to their analyses, has a better fit (Arieli et al. 1989).

Hills’ Cumulative Oxygen Toxicity Index (COTI)

Another approach to CNS oxygen toxicity management has been proposed by Hills (1976). Its concept is to use the mathematical principle of “superposition” to reduce the influence of each minute of exposure as it recedes into the past, thus accounting for recovery. Hills performed limited tests with rats, but in the analysis of the SHAD and Nisat dives it did not appear to be a good predictor of pulmonary toxicity (Hamilton et al. 1982).

The Repex Approach

Another totally empirical approach developed for managing oxygen tolerance in air excursions from a seafloor habitat is the Repex algorithm (Hamilton, Kenyon, and Peterson 1988; Hamilton, Kenyon, Peterson, Butler, and Beers 1988). This was developed as a means...
of dealing with daily hyperoxic exposures over a mission duration of several days or longer. It picks a CNS "threshold" level (1.5 bar) and allows only fixed short exposures beyond this limit; all other dives are limited by "whole body" criteria (which are presumed to take care of pulmonary problems), and the daily limit depends on the exposure to that point. The method is based on empirical data, uses familiar units, accounts for recovery, takes multiday exposures into account, and allows use of a person's initial reserve.

Background of the Repex Method

This method grew out of a need for managing daily high oxygen doses on a multiday basis over the duration of a mission. The classic oxygen exposure unit, which we call OTU, was chosen because it allowed an integration over time of exposures to different oxygen levels. We looked for practical experience in order to set limits. A recent and relevant series of studies are those by Sterk and colleagues. These were performed on divers doing diving work and stressed the levels most relevant to the Repex project (Sterk and Shrier 1984; 1985; Sterk 1986; 1987). Another recent notable study is Predictive Studies V (Lambertsen et al. 1987). Still another source of information is a substantial amount of undocumented laboratory and commercial diving experience (by the Ocean Systems/Union Carbide Laboratories at Tonawanda and Tarrytown, New York). Long duration experience was from the SHAD-Nisat project (Hamilton et al. 1982).

We noted first that for a single exposure lasting only one day about 850 OTU was a tolerable dose. For two days the dose was less, but still high, about 700 OTU per day. For long missions (multiday exposures) of about ten days the level had to be reduced to about 300 to 350 OTU per day. These data are compiled in a chart showing the daily allowable for up to fourteen days (Figure 1). Note the "bulge" in the curve that represents the "initial reserve" of tolerance at the beginning of an exposure. This curve is still in the process of being defined and, in fact, eventually may become a family of curves in order to deal with operational experience or desired conservatism.

![Figure 1. Repex oxygen exposure limits. The line shows the total allowable oxygen exposure in OTUs as of each day in a multiday exposure ("mission"). The lower line shows average daily limit to yield the curve. The chart contains the same values (from Hamilton, Kenyon, Peterson, Butler, Beers 1988).](image-url)
The daily limits are intended to be operational limits. At any time a diver should be able to tolerate a USN Table 6 treatment (about 600 units) with only mild lung irritation and, perhaps, other minor symptoms.

Using the Repex Limits

Using the Repex limits is simple. First, determine the daily dose in OTU of the oxygen exposures in question. This may be included as part of a decompression table calculation or may be determined from a chart such as Table 1. Next, determine how this exposure fits into the overall pattern of predicted exposures in Figure 1. For a given mission the diver is within limits if his total at the end of each mission day does not go above the line in Figure 1 or exceed the level on the included table. Small excursions above the line are tolerable if later recovery is ensured.

In planning an exposure it is important to ensure that a diver starting out has not had appreciable exposure to elevated PO2 for several days before the new accounting. If there has been an exposure, it should be included in the accounting. Likewise, a diver should have several days off after a mission or exposure before starting again. Five days a week of exposure with weekends off should be considered as continuous long term exposure in relation to Figure 1.

The column of average daily doses does not mean that an individual can have 850 units the first day, 700 the second, and so on. If a mission or exposure has to be extended, say from eight to nine days, the difference between the totals, here 170 units, is the correct dose for the ninth day (assuming the diver is at the full maximum of 2,800 units at the end of the eighth day).

Because of the nature of the Repex operation its algorithm does not devote much attention to acute CNS oxygen toxicity specifically. It is intended that divers just stay out of the CNS toxicity zone by staying below 1.5 bars PO2. In the Repex decompression procedures CNS toxicity is avoided by setting a limit such that if the limit is not exceeded, CNS toxicity is not at all likely. Divers that do not exceed this limit are restricted only by the whole body criteria of Figure 1. Divers that exceed the limit are limited in duration according to depth, staying within the USN criteria (Table 3). This limit is considered to be 1.5 atm or bars PO2 or an air dive limit of 60 msw (200 fsw).

The oxygen exposure limits given here are ones that have been selected for specific operational situations. Individuals vary greatly in their susceptibility to oxygen toxicity, and there is no guarantee or implication that these values will be suitable for everyone. One comforting factor is that pulmonary and whole-body toxicity usually come on gradually and an exposure can be stopped or the PO2 reduced before symptoms get serious. Evaluation of the operational situation is an important factor in avoiding CNS toxicity and helps determine the limits selected. For example, in cave diving where a convulsion is almost certainly fatal, the limit should be lower than for experimental diving or treatment in a dry chamber.

REFERENCES


Figure 1. Repex oxygen exposure limits. The solid line shows the total allowable OTU count for each day in the mission (from Hamilton, Kenyon, Peterson, Butler, and Beers, 1988). This figure shows the curve beyond about 8 days more clearly.