# CENTRAL NERVOUS SYSTEM OXYGEN TOXICITY

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Central nervous system (CNS) toxicity is the most common and most serious oxygen toxicity risk in technical diving. Pulmonary toxicity (14) and ocular toxicity (vision changes) (9) can occur with long exposures but are not addressed here.

## Biochemistry of Oxygen Toxicity

Digestion breaks food into simple sugars which react with oxygen to produce high energy molecules that are used to do physical work, build or repair tissue, and maintain physiological homeostasis such as body temperature and oxygen ($O_2$) and carbon dioxide ($CO_2$) levels (Fig. 1).

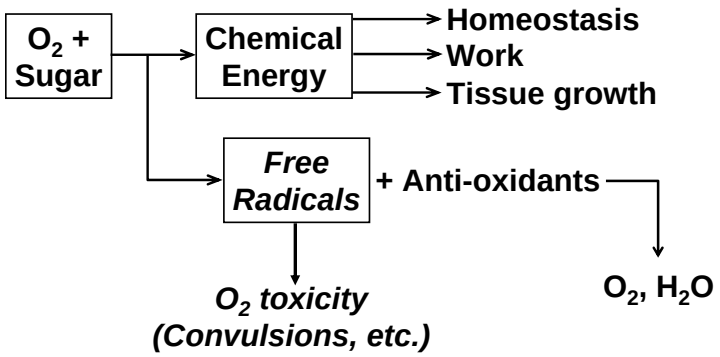



**Figure 1. The biochemistry of oxygen toxicity.**

As a normal part of oxygen metabolism, a small fraction of the chemical energy escapes from the proper pathways to form "free radicals" that are chemically unstable and can cause tissue damage or interfere with normal tissue function (14). Fortunately, anti-oxidant defenses have evolved that scavenge the free radicals and re-convert them into water and oxygen.

A diver who breathes elevated oxygen partial pressures, however, generates more free radicals than the anti-oxidants can deactivate. If enough free radicals accumulate, they can interfere with normal brain function and cause the signs and symptoms of $O_2$ toxicity such as seizures.

**Physiology of Oxygen Toxicity**

Cerebral blood flow (CBF) controls the rate of oxygen delivery to the brain. If CBF is high, free radicals accumulate rapidly, and oxygen toxicity occurs sooner. If CBF is low, free radicals accumulate more slowly, and oxygen toxicity is delayed. Arterial carbon dioxide is important in controlling CBF. CBF increases when the arterial $CO_2$ is high and decreases when the $CO_2$ is low. The arterial $CO_2$ is controlled by ventilation.

Carbon dioxide is eliminated by ventilation that reaches the alveoli. This is the alveolar ventilation. Every breath cycles one tidal volume into and out of the respiratory system (Fig. 2). The total ventilation is the breathing frequency times the tidal volume. Part of the tidal volume is trapped in the airway dead space, however, and never reaches the alveoli. Thus, the alveolar ventilation is the tidal volume minus the dead-space volume times the breathing frequency.

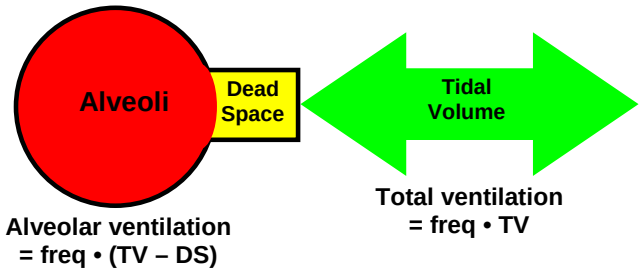



**Figure 2. Total and alveolar ventilation.**

Hyperventilation occurs when the alveolar ventilation is excessive and removes too much $CO_2$ from the alveoli so that the arterial $CO_2$ partial pressure falls below its normal homeostatic level of about 38 mmHg or 5 kPa.[1] Abnormally low alveolar $CO_2$ is known as hypocapnia and may cause numbness and tingling. Hyperventilation and hypocapnia are unusual during diving, however, because of increased breathing resistance. They are more common at sea level, particularly during anxiety, and divers who become anxious after surfacing sometimes hyperventilate leading to symptoms that can be mistaken for decompression sickness.

[1] One Pascal (Pa) is a unit of pressure equal to 1 Newton/$m^2$=$10^{-3}$ kPa (kilopascal). A $CO_2$ partial pressure of 6 kPa is also a Surface Equivalent Value (SEV) of 6% since 100 kPa = 1 bar = 10 msw = 0.987 atmospheres.

Hypoventilation is a greater problem in diving than is hyperventilation. During hypoventilation, the alveolar ventilation is too low so that not enough $CO_2$ is removed from the alveoli, and the arterial $CO_2$ rises above its normal homeostatic level. This is hypercapnia. Hypoventilation can occur if the tidal volume is too small, the total dead space (including airways and breathing apparatus) is too large, or the breathing frequency is too low (Fig. 3). In any of these cases, the alveolar ventilation is insufficient to eliminate enough $CO_2$, and hypercapnia occurs even though the total ventilation may appear high. Thus, even though a diver seems to be breathing excessively, he or she is hypoventilating if the gas does not reach the alveoli. It is important to remember that the term hypoventilation really means alveolar hypoventilation.


**Figure 3. Causes of alveolar hypoventilation.**

## $CO_2$ Retainers

While arterial $CO_2$ is a powerful ventilatory stimulus, not everyone has an equally strong ventilatory drive when presented with an increase in $CO_2$. Those who have relatively small increases in ventilation when $CO_2$ rises are called $CO_2$ retainers and might be susceptible to $O_2$ toxicity as a result of higher cerebral blood flow.

Dr. Karl Schaefer worked in submarine medicine for the German Navy during World War II, and, after the war, he did similar work for the U.S. Navy. Schaefer investigated the ventilatory response of seven breath-hold who were U.S. Navy submarine escape instructors (30). Schafer measured the ventilation of these divers before, during, and after breathing air containing 5% $CO_2$ (Fig. 4). The y-axis in Fig. 4 is ventilation in liters per min. The x-axis shows 15 min of ventilation on air followed by 15 min on 5% $CO_2$ and 15 min on air. The lower line is the increase in ventilation that occurs during $CO_2$ breathing during a period of intense breath-hold diving activity. The upper line represents the same seven divers after a 3-month layoff during which their sensitivity to $CO_2$ increased by 25% as indicated by the rise in ventilation. The point is that a $CO_2$ retainer today may not be a $CO_2$ retainer tomorrow. Variability in $CO_2$ response is another source of uncertainty that makes susceptibility to oxygen toxicity difficult to predict.

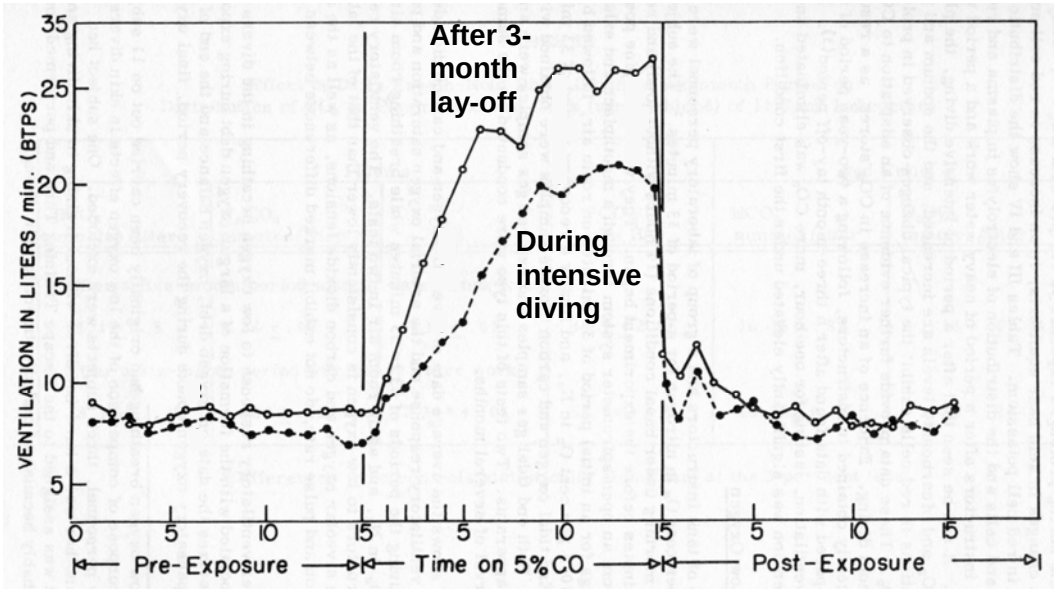
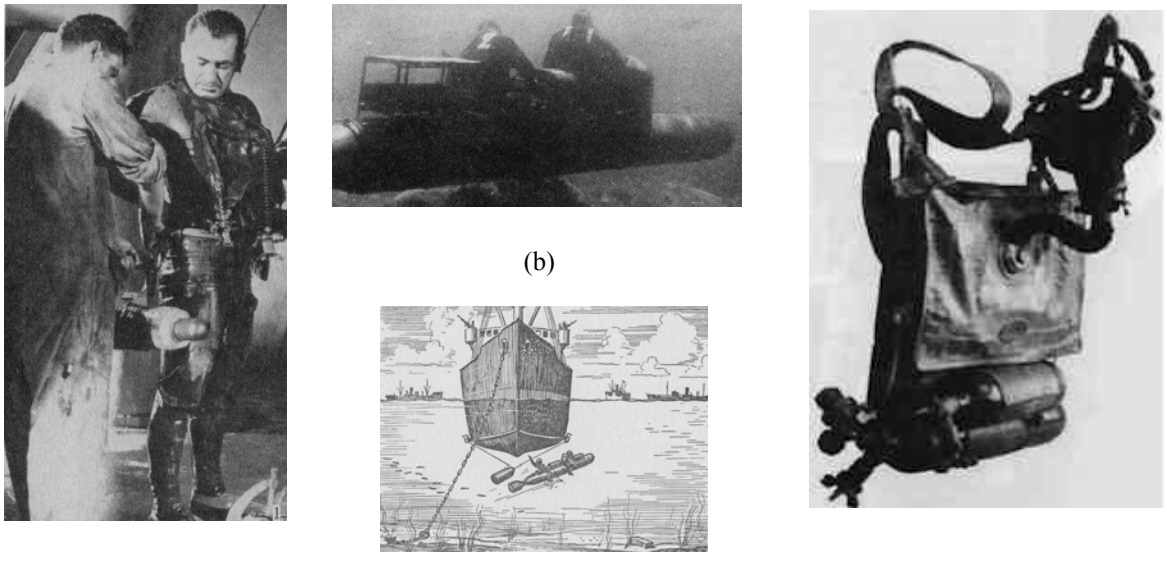



**Figure 4. Ventilation while breathing 5% $CO_2$ during a period of intensive breath-hold diving activity and after a three month period of no diving (30).**

## Operational Oxygen Toxicity

The problem of operational CNS $O_2$ toxicity first became apparent during the Second World War. The 10th Light Flotilla of the Italian Navy used oxygen divers to sink or disable some 30 British and allied ships in the Mediterranean (8). An Italian combat diver might surface swim to within a hundred yards of a target ship before submerging for the final attack and placing a limpet mine on the bilge keel (Fig. 5a). The Human Torpedo was another method of attack for distances greater than a man could swim (Fig. 5b). Piloted by two divers, this vehicle had a large warhead that could be fastened under the target ship's hull (5c).



(a) (b) (c) (d)

**Figure 5. The 10th Light Flotilla of the Italian Navy. (a) Combat diver preparing to attack a British ship in Gibraltar harbor (31). (b) "Human torpedo" piloted by two divers used for longer range attacks from outside harbors and launched from a submarine (31). (c) Placing a warhead underneath a target ship (37). (d) Closed-circuit pendulum oxygen rebreather used by 10th Light Flotilla divers (http://regiamarina.net/xa_mas/history/origin_us.htm).**

The divers breathed oxygen from a pendulum rebreather (Fig. 5d) and, on occasion, would become unconscious and be lost. There was a rare story from a diver who survived an apparent episode of oxygen toxicity during an attack in Gibraltar harbor (8) (pg. 94).

"… the torpedo … began to sink at a great rate … I felt … a strange sensation of well-being, with red, yellow, and blue sparks before my eyes … more than 30 meters down and … still sinking … I felt that the strange sensation of well-being was about to turn to loss of consciousness. … I had to … swim as hard as I could … at last I reached the surface."

In the U.S., Dr. Chris Lambertsen developed an oxygen rebreather for the Office of Strategic Services (OSS; (33)). Lambertsen spent many hours in the Caribbean instructing the OSS swimmers in oxygen diving. The oxygen exposure limits at the time were 30 min at 90 fsw or 120 min at 50 fsw (18), and Lambertsen would occasionally feel signs of toxicity such as twitching and fluttering of the diaphragm. These signs resolved if he hyperventilated. At the University of Pennsylvania after the war, he confirmed the influence of ventilation, $CO_2$, and cerebral blood flow on $O_2$ toxicity (33).

**Figure 6. OSS Operational Swimmer training with the Lambertsen Amphibious Respiratory Unit (LARU; CJL photo).**

Figure 7 shows two World War II combat divers wearing oxygen rebreathers that pass the exhaled gas through an absorbent canister to remove $CO_2$. The device on the right is a British pendulum unit in which the diver inhales and exhales through the same hose into the $CO_2$ scrubber. The pendulum system is simple and requires no one-way valves, but $CO_2$ is retained in the hose, and this dead-space increases as the absorbent bed is exhausted. The device on the left (the LARU) is Lambertsen's recirculating unit in which the diver inhales from the $CO_2$ scrubber through one hose and exhales into the scrubber through another hose. One-way valves ensure unidirectional gas flow, but breathing resistance in the hoses and scrubber can restrict the increase in ventilation that would occur at sea level with elevated $CO_2$. This becomes a greater problem as depth increases.

**Figure 7. The LARU-X and the Amphibian Mark II (CJL photo).**

The Lambertsen unit also used a full facemask. After the War while demonstrating it to the U.S. Coast Guard, Lambertsen inadvertently found himself at a depth of 100 fsw, alone, and on the verge of oxygen toxicity. Just prior to onset of a convulsion, he inflated his

counterlungs to increase his buoyancy and rose to the surface, unconscious, but where he was rescued (33). Because unconsciousness, particularly due to hypoxia or oxygen toxicity, appears common in rebreather fatalities (34), a full facemask and a nearby dive buddy might significantly improve the safety of rebreather diving.

Increased breathing resistance is a threat to adequate ventilation, particularly during exercise. This is illustrated by the effect of depth on the Maximum Voluntary Ventilation (MVV), which is the highest ventilation sustainable for 15 sec (Fig. 8). As depth increases, so does resistance to gas flow in the airways causing increased work of breathing (10). At 100 fsw, for example, the MVV is only about half of what it was on the surface. The greater work of breathing in the airways and breathing apparatus can cause respiratory muscles to fatigue sooner than they would on dry land.

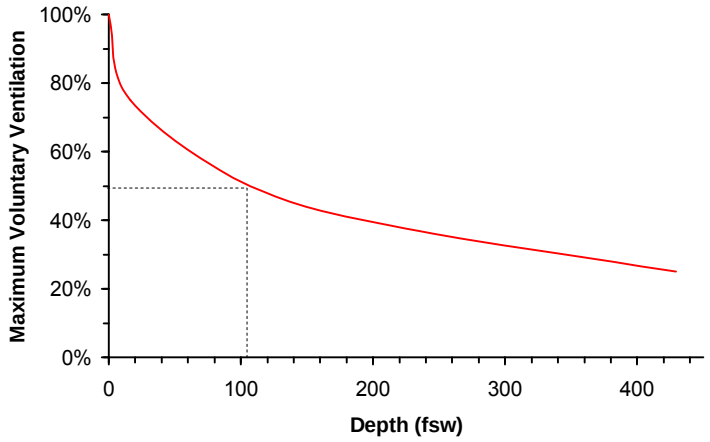



**Figure 8. Maximum Voluntary Ventilation (MVV) (10).**

## Kenneth Donald and Oxygen Diving during World War II

The British Navy developed its own underwater attack capability during World War II including a "Human Chariot" (Fig. 9) that was modeled on captured Italian equipment (37). With U.S. Navy oxygen exposure limits of 50 fsw for 120 min and 90 fsw for 30 min, divers began to "flake out" in training and after one died, formal scientific investigation began (18).

**Figure 9. British Navy Human Chariot (37; pg. 81).**

Surgeon LT Kenneth Donald volunteered for 'special service' to study the problem of oxygen toxicity. With no research background and little hyperbaric experience, Donald found himself in charge of an experimental program that ran from 1942-45 and was the largest study of oxygen toxicity conducted to that time. Much of this work remained confidential until his 1992 book, *Oxygen and the Diver* (18).

Figure 10 is the wetpot where Donald conducted his studies. A test diver in the water was tended by a safety diver above him. Sidney Woollcott, a Human Chariot diver who won the Distinguished Service Medal for sinking the Italian liner *Sumatra* at Phuket, described his experience as an experimental subject (37) (Chapter 3).

"I had been down about 20 min (at 50 feet) when I felt the first twitching of the lips. I exercised my lips around the mouthpiece, and the twitching went off… (At 30 min,) I suddenly felt a violent twitching of my lips. I tried to wriggle them around the mouthpiece again, my mouth was blown out like a balloon … The twitching of my lips increased, and I felt a terrific tingling sensation at the side of my mouth, as if someone were touching it with a live wire. This … became a definite pain, and my lips became so distorted … as if my mouth were stretched to … near my right ear. I tried to climb the ladder, but … my whole body was convulsing … I tried to shout to the attendant to grab me before I fell back. Although my lips formed words, no sound came … blackness closed in on me – I was out."

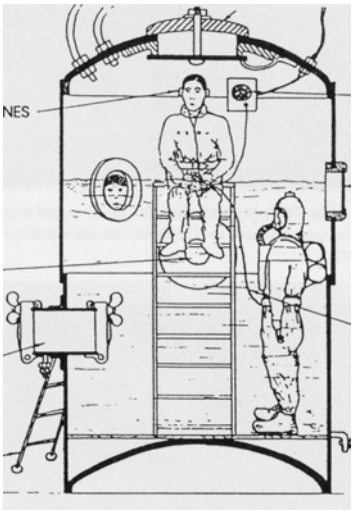


**Figure 10. Admiralty Experimental Diving Unit chamber (37) (Chapter 3).**

Sidney Woollcott's experiment was more spectacular than most but, otherwise, it was typical. For each depth tested, a diver would breathe oxygen until he developed signs or symptoms. Figure 11 summarizes 1,212 $O_2$ toxicity symptoms reported in 2,170 exposures by the U.S and British navies (21). Over half were muscular twitching, sometimes occurring several times in one exposure. Nausea was next most common followed by dizziness and vertigo, and convulsions, all at about 10%. Half the convulsions appeared to occur without premonitory symptoms (21).

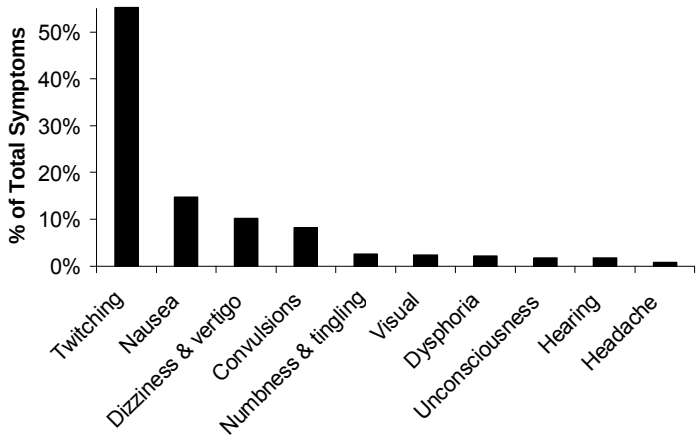



**Figure 11. Reported signs and symptoms believed to have been associated with CNS oxygen toxicity (21).**

After enough dives were conducted, Donald constructed a "survival curve" as shown in Fig. 12a where the percentage of divers who "survived" (did not develop symptoms) to a given time was presented as a function of time. The y-axis in Fig. 12a is the percentage of divers who developed symptoms, and the x-axis is the exposure time in minutes. In Fig. 12a, 37 dry, resting divers were exposed to 90 fsw of oxygen, and 50% developed symptoms by 22 min.

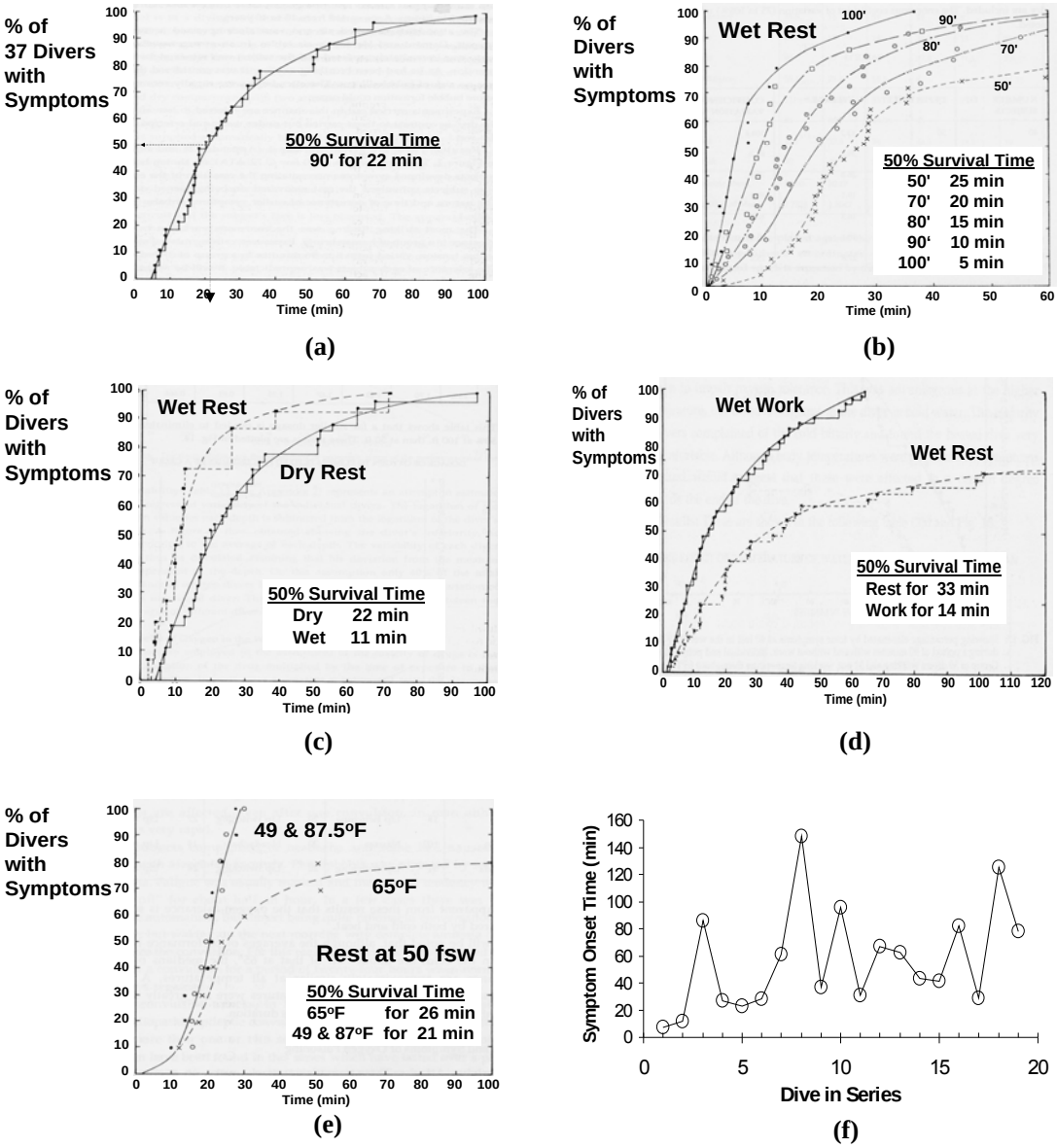



**Figure 12. CNS oxygen toxicity "survival" (18).**
**(a) Survival curve at 90 fsw for dry, resting divers.**
**(b) Survival curves for 50, 70, 80, 90, and 100 fsw for wet, resting divers.**
**(c) Survival curves at 90 fsw for wet and dry divers at rest.**
**(d) Survival curves at 50 fsw for wet divers at work or at rest.**
**(e) Survival curves for resting divers at 65°F and at 49 or 87°F.**
**(f) Symptom onset time for multiple exposures of a single diver.**

Figure 12b shows the results for wet resting exposures at 50-100 fsw. The 50% survival times were short, ranging from 25 min at 50 fsw to 5 min at 100 fsw. The 50% survival time decreased by about 5 min for each 10 fsw increase in depth.

The effect of immersion on symptom onset time is shown in Fig. 12c for resting divers exposed dry and wet at 90 fsw. A wet diver survived only about half as long as a dry diver. The 50% percent survival times were 22 min dry and 11 min wet.

The difference between work and rest is shown in Fig. 12d for divers who were immersed at 50 fsw. Exercise reduced the 50% survival time from 33 to 14 min.

Water temperatures of 49, 65, 87.5$^{o}$F were tested at 50 fsw with resting divers (Fig. 12e). Forty-nine and 87.5$^{o}$ F seemed to have the same effect and decreased the 50% survival time from 26 to 21 min. The differences were greater at longer times. Since the divers were thermally comfortable when the exposures began, the absence of a larger effect at the short times probably reflected the time necessary for the divers to heat or cool.

One of the most striking observations was the wide range of variability within individual divers. Figure 12f shows the onset times for one diver who made 19 resting dives to 70 fsw at two dives per week. The day in the dive series is shown on the x-axis and the symptom onset time on the y-axis. Similar variability in susceptibility from day to day was typical for most divers.

Donald conducted 611 individual exposures at depths of 25 to 100 fsw. Immersion decreased the 50% survival time by half, from 22 to 11 min, for resting divers at 90 fsw. The mechanism responsible for this decrease is uncertain although the diving response as a result of facial immersion has been observed to cause increased cerebral blood volume (29). Exercise decreased survival time by 58%, from 33 to 14 min, for wet divers at 50 fsw. Although exercise with air at sea level typically decreases arterial $CO_2$, experiments with graded exercise while breathing oxygen at 2 ata have found a progressive increase in arterial $CO_2$ (13). Temperatures above and below 65$^{o}$F caused a 19% decrease in survival time from 26 to 21 min for divers resting at 50 fsw. This effect was probably underestimated due to beginning from a pre-dive thermoneutral state. No human studies have investigated possible causes of the temperature effects. The 50% survival time at 50 fsw for wet resting divers was about 25 min and each additional 10 fsw decreased this about 5 min. Perhaps the most surprising finding was the extreme variability of symptom onset times, one diver having a range of onsets of 7–148 min with a mean of 57 min. No convulsions occurred, and the distribution of symptom onset times was otherwise similar to observations for other divers.

Donald concluded (pg. 78) (18),

"The variation of tolerance between individuals, the variation of tolerance of each individual, the impairment of tolerance with work and under water, all make diving on pure oxygen below 25 fsw a hazardous gamble… the complete absence of symptoms before convulsions constitute a grave menace to the independent oxygen diver."

These conclusions were based on extensive data and do not seem unreasonable. The final conclusion was more speculative, however, as it extrapolated beyond the available information.

"… exclud(ing) covert military diving … 15 fsw would now be an appropriate limit." (Pg. 100-101)

Donald's work has been criticized due to a rumor that his divers feigned symptoms to reduce their risk of oxygen convulsions. Although he denied this with vigor (pg. 195-196) (18), it has cast unfortunate uncertainty over a unique body of work that was executed in difficult times with great effort and dedication.

**U.S. Navy Oxygen Exposure Trials**

There are independent data from U.S. Navy studies from which quantitative risk estimations can be made. These included 773 single and multilevel working dives at 20-50 fsw in which the $O_2$ percentage was controlled to over 99%. Manifestations of $O_2$ toxicity were described as 11 convulsions, 33 definite symptoms, and 37 probable symptoms (32).

The Navy data can be modeled statistically (20, 21, 32). Suppose $O_2$ toxicity were caused by a toxic substance "X" as suggested by the biochemistry of free radicals reviewed earlier. High oxygen partial pressures might generate more "X." Some "X" might be deactivated by protective agents. The probability of $O_2$ toxicity might be modeled to increase with the concentration of "X."

A simple statistical model fit to the Navy data estimated the probability of convulsions during square dives (32). In Fig. 13, the oxygen exposure time is on the x-axis, and the dive depth is on the y-axis. The model predicted the rectangular hyperbolas that have traditionally been used to represent the relationship between time and the occurrence of oxygen toxicity (11, 12). Figure 13a shows the probability of convulsions in increments of 1% from a threshold of 0% at 19 fsw to 8% at the top of the figure. The points marked by "X" represent seven convulsions. For example, one convulsion occurred after 31 min at 40

fsw for which the estimated risk was slightly less than 2%. Four other convulsions occurred on multilevel dives and are not shown.

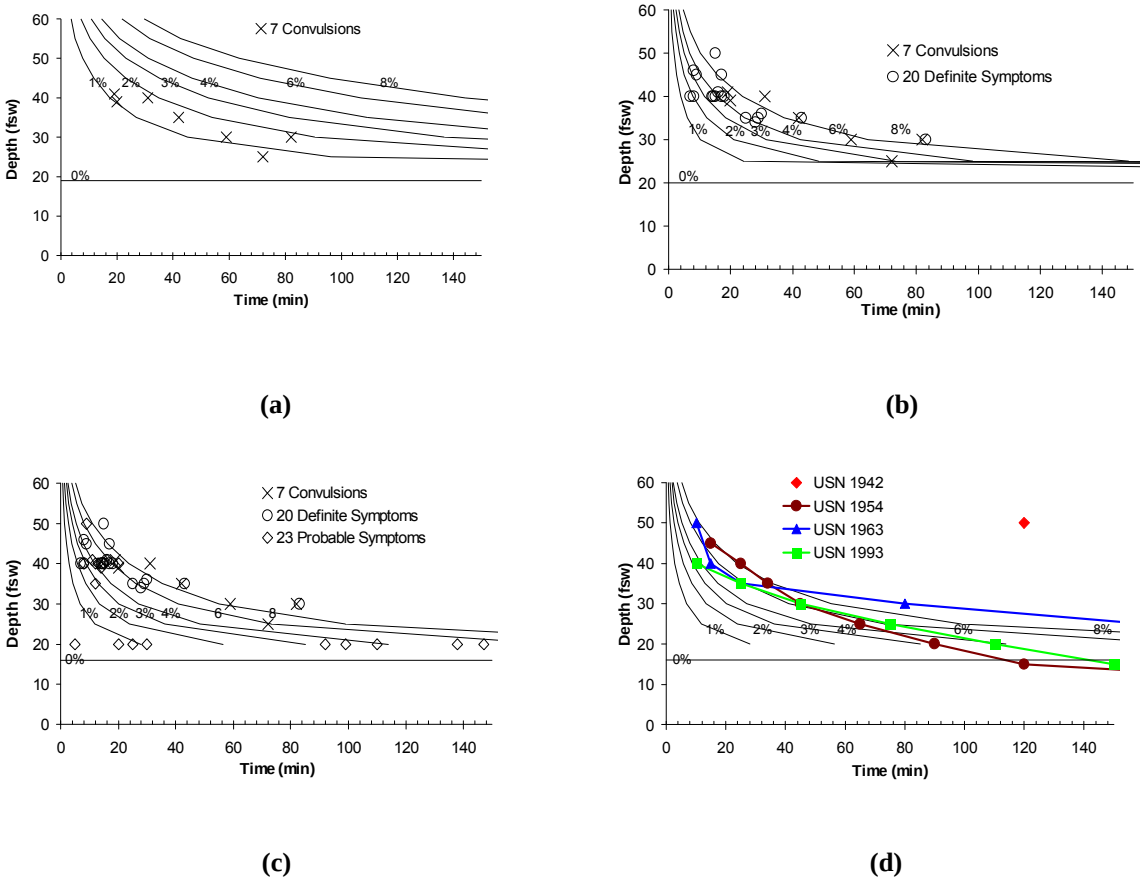



**Figure 13. Statistical models of CNS oxygen toxicity (32). (a) Convulsions only. (b) Convulsions and definite symptoms. (c) Convulsions, definite, and probable symptoms. (d) U.S. Navy oxygen exposure limits, 1942 to 1993 (18).**

A more conservative approach in Fig. 13b modeled the probability of either convulsions or definite symptoms (32). The circles in the figure represent 20 definite symptoms. The probability curves are shifted downwards to shallower depths, and the 0% symptom threshold was 20 fsw.

A still more conservative approach results from including convulsions, definite, or probable symptoms. The diamonds in Fig. 13c represent 23 probable symptoms. The probability curves are shifted further downwards indicating higher predicted risk as shallow depths. The 0% threshold for symptoms is 16 fsw, near Donald's recommendation of 15 fsw. Because of the unpredictable nature of $O_2$ toxicity, the most conservative model of convulsions, definite or probable symptoms is used in the subsequent discussion.

Figure 13d shows model predictions for convulsions, definite, and probable symptoms in comparison with the U.S. Navy $O_2$ Exposure Limits from 1942 to 1993 (18). The 1942 limit of 50 fsw for 120 min has an estimated risk well above 8%. The largest decrease in the limits occurred from 1942 to 1954. For the short, deep exposures, the estimated risks were about 8% and fell to below zero by 120 min. The 1963 limits were 7-8% for the short, deep dives and even higher for longer dives. The 1993 limits were more conservative than the 1963 limits but had estimated risks starting at 6% deep and falling to below threshold at shallow depths.

The finite, non-zero risks of the 1993 limits for 100% oxygen were also estimated by Navy models (20, 21, 24), but for operational diving with closed-circuit oxygen, procedures for purging the breathing apparatus counterlung are such that dives begin with about 75% oxygen rather than pure oxygen (3) which results in estimated risks of less than 1% (20, 21, 24).

Donald had reported that some divers seemed more susceptible to oxygen toxicity that others. The U.S. Navy searched for evidence of differing susceptibility among divers in their oxygen trials, but there were too few toxicity episodes to show this statistically (23).

**Mixed Gas Oxygen Exposure Limits**

Donald also had the task of developing equipment and diving procedures for use by Port Clearance divers (Fig. 14) whose job was to sweep European harbors of mines and booby traps after the Allied invasion in Normandy in 1945 (18). (Today, these are called explosive ordinance disposal (EOD) divers.) Because the harbor depths were too great for pure oxygen, Port Clearance Divers used semi-closed breathing apparatus as indicated by the stream of bubbles from the diver in Fig. 14. Donald believed the exposure limits were the same for pure oxygen and for oxygen in mixed gas. However, he recognized that the risk of $CO_2$ retention was greater at the deeper depths with mixed gases, and this might increase the $O_2$ toxicity risk.

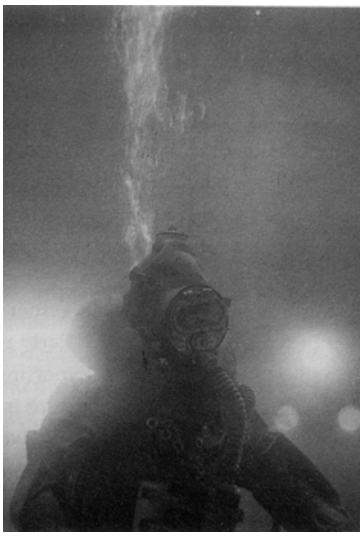


**Figure 14. Port Clearance diver with a semi-closed circuit rebreather (18).**

Figure 15 shows risk estimates for mixed gas diving using the same values as in Fig. 13 but expressed in terms of $O_2$ partial pressure in atmospheres rather than in fsw. The 0% threshold is at 1.5 atm. Figure 15 also shows the 1959 U.S. Navy (1) and 1991 NOAA (2) mixed-gas limits for comparison. For short, Navy exceptional exposure limits, estimated risks are on the order of 4-6% and decrease to 0% at 1.5 atm for longer exposures. For normal limits, the maximum risk is 1% and below the 0% Navy threshold at 60 min. The 1991 NOAA exceptional exposure limits are similar to the 1959 USN Exceptional Exposure limits while the normal exposure limits decrease from 2% to below the 0% threshold.

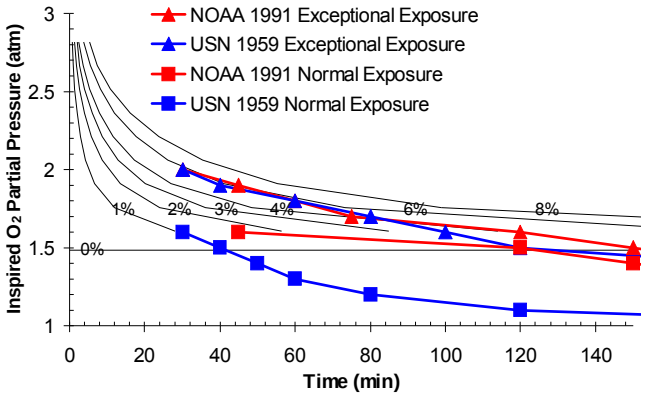



**Figure 15. Statistical model of the probability of convulsions, definite symptoms, and probable symptoms expressed in terms of oxygen partial pressure rather than depth (32).**

The constant risk isopleths for the Duke model are about 2% lower than for the Navy model, but the 0% risk isopleth of 1.5 atm for the Duke model is greater than the 0% risk isopleth of 1.3 atm for the Navy model (24). This was the basis on which the Navy selected a maximum $O_2$ partial pressure setpoint of 1.3 atm for closed-circuit mixed gas diving, but the Navy also imposed an arbitrary time limit of 240 min at 1.3 atm because of potential onset of pulmonary oxygen toxicity (personal communication, CAPT E.T. Flynn, MC, USN (ret)).

Both the Duke and Navy models were calibrated with dives of 20 fsw (1.6 atm) or deeper, and there was only one probable, dive-stopping event in 93 dives at 20 fsw (20). With one event in 93 exposures, the 95% binomial confidence interval includes all incidences of oxygen toxicity between 0.03% and 5.8%. Thus, while oxygen toxicity models are useful for illustrating principles, predictions for partial pressures of 1.6 atm or less are unreliable at best. For this reason, we shift our attention to observational studies and case reports, which although more ambiguous and less desirable than controlled trials, are the only other sources of information bearing on the problem of CNS toxicity at low oxygen partial pressures.

**Observational Studies**

Leitch reviewed 1,301 dives conducted at the British Navy Deep Trials Unit to investigate why exposures below 155 fsw (46.5 msw) were aborted (26). Incidents leading to dive termination included respiratory distress, disturbed consciousness, panic, nausea, malaise, mood or sensory disturbances. When categorized by $O_2$ partial pressure, there were 0% incidents in 319 dives at partial pressures of 0.9-1.2 atm, 2% in 299 dives at 1.3 atm, 8% in 155 dives at 1.4-1.6 atm, and 5% in 530 dives at 1.7-2 atm (Fig. 16). These findings do not address oxygen toxicity directly, but the absence of incidents below partial pressures of 1.3 atm was consistent with a threshold for oxygen-related problems of 1.2-1.3 atm.

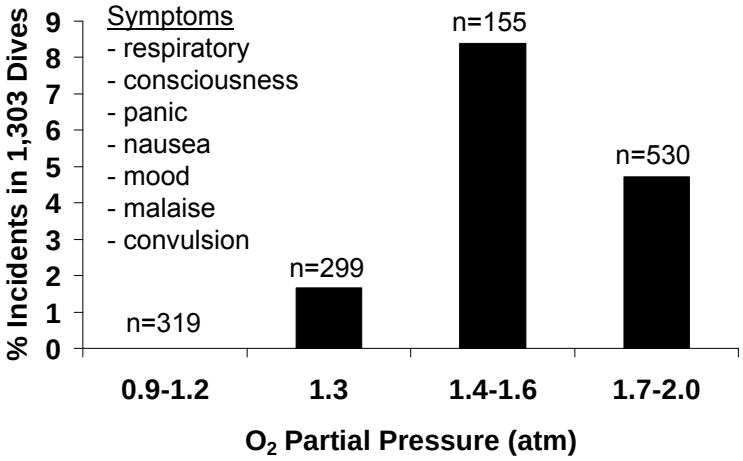



**Figure 16. Inspired oxygen partial pressures in effect during dives that were aborted (26).**

In 2006, Arieli and coworkers reported on signs and symptoms in 2,527 closed-circuit oxygen training dives by 473 Israel Navy combat swimmers (6). The mean $O_2$ fraction was 91±5% so the actual $O_2$ exposure was less than indicated by the dive depth. No symptoms were reported at 7 fsw (2 msw) or less in 61 dives, 2.7% of 711 dives had symptoms at 10 fsw (3 msw), 3.3% of 269 dives had symptoms at 13 fsw, 3.9% of 1108 dives had symptoms at 17 fsw (5 msw), and 6% of 164 dives had symptoms at 20 fsw (6 msw). Eight divers (0.4% of 2,500 dives) lost consciousness after 3-4 hrs although the depths were not specified.

While the Arieli paper refers to CNS oxygen toxicity (6), the most common signs and symptoms (e.g., 4.5% headache, 2.6% hyperventilation, 2.4% heavy breathing) were attributable to $CO_2$ retention while signs and symptoms attributable to oxygen poisoning (e.g., 2.6% nausea, 1.6% dizziness, 0.9% tinnitus, 0.6% disorientation, 0.4% tingling, 0.4% hearing disturbances, 0.32% loss of consciousness) were less common and might also reflect $CO_2$ retention. Indeed, loss of consciousness after 3-4 hrs was consistent with the breakthrough of a depleted $CO_2$ scrubber, and the increase in symptom incidence with depth could reflect $CO_2$ retention due to increased gas density.

In a second publication, the same authors investigated the relationship of inspired $CO_2$ to unconsciousness (5). $CO_2$ scrubber performance was tested in 18 of 36 divers who developed symptoms. Only rebreathers that had remained sealed after the incident were tested. The divers peddled a bicycle ergometer for 10 minutes while the inspired $CO_2$ was monitored. When the results were categorized as high or low inspired $CO_2$, 11 divers in the high $CO_2$ group had a mean 4.2% surface equivalent value (SEV), and four of these (36%)

had become unconscious. Seven divers in the low $CO_2$ group had a mean 0.2% SEV, but none of these divers lost consciousness. The causes of the high $CO_2$ were poor canister packing, strenuous activity, or water leaking into the canister. A study in 2008 found that both under and over-packing a canister with absorbent reduced the duration to effectively remove $CO_2$ (7).

While unconsciousness due to $CO_2$ poisoning is no less hazardous that from $O_2$ poisoning, differentiating between the two based only on signs and symptoms may not always be obvious, and of course, $CO_2$ retention also potentiates oxygen toxicity.

**"Shallow Water Blackout"**

During his oxygen toxicity investigations, Donald identified a phenomenon he called "shallow water blackout (SWBO)" in which closed-circuit oxygen divers became unconsciousness at depths of less than 20 fsw (17, 18). (Donald's shallow water blackout was different from, and predated, the shallow water blackout associated with breath-hold diving today.) Symptoms reported by SWBO survivors included feeling "muzzy, hazy, confused, distant, out of touch, and everything went in waves." During recovery, the divers often had marked tremor.

Two groups of divers were at risk for SWBO: (a) "Human Chariot" pilots whose risk was associated with inspired $CO_2$ due to faulty scrubbers (Fig. 9). (b) Landing Craft Obstruction Clearance Divers, a secret unit that cleared obstacles from Sword and Gold beaches prior to the D-Day invasion in Normandy (Fig. 17). Their risk was associated with $CO_2$ retention during bouts of extreme anaerobic exercise (17, 18).

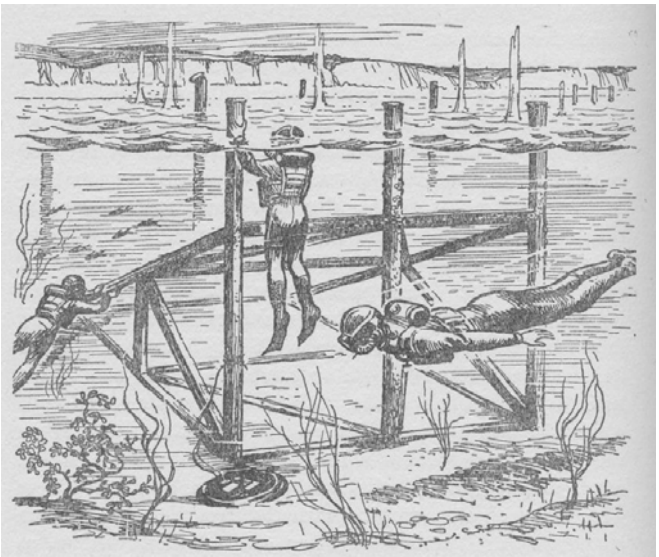


**Figure 17. Landing Craft Obstruction Clearance Divers, pg. 116 (37).**

Donald ruled out CNS oxygen toxicity because he had not observed it at less than 25 fsw. $CO_2$ retention seemed a possible candidate, but the respiratory distress associated with $CO_2$ was uncommon even though the $CO_2$ levels were high. Donald's investigations led him to conclude that the normal ventilatory response to $CO_2$ was diminished in hyperoxia thus allowing arterial $CO_2$ to rise to narcotic levels without stimulating the usual respiratory symptoms.

The signs and symptoms reported by Arieli in the Israeli combat divers also occurred at depths too shallow for CNS oxygen toxicity, and excess $CO_2$ was also implicated (5, 6). There is certainly no question that $CO_2$ narcosis is a significant hazard to divers. Whether $CO_2$ narcosis is a greater risk with hyperoxic gases and whether Arieli's divers were affected by SWBO remain to be determined.

Modern technical divers commonly breathe inspired oxygen partial pressures of 1.3-1.6 kPa, can have physiological $CO_2$-retention due to breathing resistance, and sometimes use closed-circuit mixed gas breathing apparatus with the potential for inspired $CO_2$ from faulty scrubbers. These divers are occasionally subject to a phenomenon called "deep water blackout," which appears similar to Donald's observations at shallow depth (28). Whether the mechanisms of the two phenomena are similar also remains to be determined.

**Case Reports**

Case 1. A DAN member reported a series of dives including the profile shown in Fig. 18 which was for about 27 min to 200 fsw on trimix 18/45 (18% oxygen, 45% helium). At 120 fsw, he shifted to trimix 35/25, and at 80 fsw, he took a low $PO_2$ break on 18/45 trimix before switching to 50% nitrox at 70 fsw. After another low $PO_2$ break at 30 fsw on 35/25 trimix, he switched to 100% $O_2$ at 20 fsw. After about 7 min at 20 fsw, he noted involuntary contractions of his diaphragm and switched to 18/45 trimix. The contractions lasted for less than 1 min, and he completed the dive on 50% nitrox without further incident. Having made many dives with these gases, he passed this off as an interesting experience and continued using the same procedures until similar episodes of diaphragmatic contractions at 20 fsw and 70 fsw on 50% nitrox (both with 1.6 atm $PO_2$) got his attention. He has since switched to a rebreather and uses a constant 1.25 atm $PO_2$ setpoint to avoid the oxygen partial pressure spikes that occur when switching open-circuit gas mixes. A comparison between oxygen partial pressures for open-circuit and rebreather diving is presented in Assessing the Risk of Decompression Sickness (35) relative to the balance between the risks of decompression sickness and CNS oxygen toxicity.

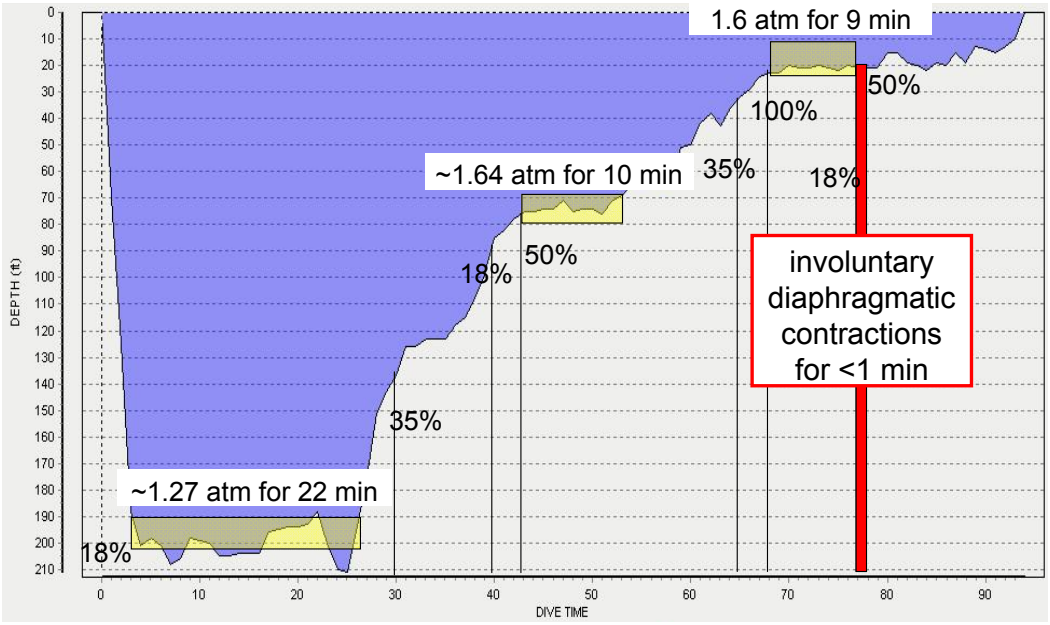



**Figure 18. Apparent CNS oxygen toxicity reported to DAN by a diver who frequently changed gases using open-circuit breathing apparatus.**

Case 2. Another report to DAN concerned a diver using a rebreather with a 1.3 atm oxygen setpoint had made a 247 fsw dive and was finishing his 40 fsw decompression stop when he noted diaphragmatic contractions that began like cold shivers and strengthened over 30-60 sec before ending as a convulsion. (His 'CNS $O_2$ clock' – see below – was less than 50%. During a dive 28 hrs earlier, his 'clock' had reached nearly 100%.) He had enough time to close his mouthpiece valve and was preparing to breathe 50% nitrox by open circuit when the convulsion occurred. An attentive dive buddy took charge and returned him to the surface where he was recompressed despite the absence of DCS symptoms. While breathing oxygen during recompression, diaphragmatic contractions occurred 6-7 times suggesting continued sensitivity to oxygen, but he breathed air to avoid convulsions.

Cases 1 and 2 are important anecdotes regarding CNS oxygen toxicity but would have been more useful had they been accompanied by computer-recorded depth, gas switch, and time profiles (Case 1) and $O_2$ sensor and time recordings from the rebreather "black-box" (Case 2). For the future, divers are encouraged to send full recordings and symptom descriptions to DAN for analysis. Problem-free dives are just as important as dives on which problems occur.

Case 3. This case occurred in the Duke wetpot with a Mk 15 rebreather, an air diluent, and 1.6 atm $O_2$ setpoint (36). A Navy diver had a seizure after 40 min of heavy work at

100 fsw (30 msw). The original Scott mouthpiece in the Mk 15 was found to be a major source of breathing resistance and was replaced with a low resistance design. After reducing the setpoint to 1.4 atm, 156 dives were completed without further oxygen incident.

Case 4. This was a fatal dive to 180 fsw on air with an oxygen partial pressure ($PO_2$) of 1.36 atm. Decompression was conducted at 20 fsw and 10 fsw on 100% $O_2$ where a seizure was witnessed. The diver was reported to have been taking multiple medications including epinepherine, darvocet, ventolin inhaler, lomotil, marax, transdermscop, decongestants, mylanta, tylanol, and sudafed.

Case 5. This was a fatal cave dive to 95 fsw on 39% nitrox with a $PO_2$ of 1.51 atm. The diver was witnessed to have a seizure and was later reported to have been taking pseudoephedrine, phenylpropanolamine and antihistamine.

Case 6. This was a fatal open-circuit cave dive on 24.3/26 trimix with a $PO_2$ of 1.4 atm. The diver appeared uncertain after 25 min at 156 fsw and aborted the dive. At 147 fsw, she fell sideways and convulsed. She dropped her regulator which could not be reinserted as her jaws were locked. A post-dive investigation found no problems with her equipment and gas. She had taken a decongestant and birth control medication.

Case 7. This was a non-fatal training dive for 15 min at 90 fsw on air (0.8 atm $PO_2$). The diver made a 10 min safety stop at 20 fsw on 82% $O_2$ (1.3 atm $PO_2$). On ascending from 20 fsw, his visual field became orange, and he had two violent spasms during which his back arched and head snapped rearwards. Upon reaching the surface, he had 10-15 additional spasms on the swim platform but remained conscious. There were no further symptoms.

This case occurred after a short exposure to a low $O_2$ partial pressure. The case was remarkable in that the diver had recently taken Cialis whose active ingredient, tadalifil, is known to increase blood flow. We tested the hypothesis that tadalifil might increase susceptibility to oxygen toxicity in rats (16). Tadalafil caused no change in cerebral blood flow (CBF) in air at 1 ata, but CBF increased at 6 ata of oxygen through nitric oxide dependent pathways, and the onset of $O_2$ toxicity was accelerated. These experiments do not prove that tadalafil will accelerate $O_2$ toxicity in humans, but they suggest caution. Moreover, Cases 4-6 involved other medications and occurred at apparently low $O_2$ partial pressures suggesting further investigation of other medications is warranted.

**The "$O_2$ Clock"**

In the 1980s, the National Oceanic and Atmospheric Administration (NOAA) found that the existing oxygen exposure limits did not address the oxygen exposures in its undersea habitat program where divers might be saturated on nitrogen-based atmospheres at depths of 30 to 100 fsw and make long excursions to depths as great as 300 fsw on air. The Navy oxygen limits of Fig. 13 were easily exceeded during these excursions. NOAA asked Dr. Lambertsen if he would develop exposure limits that might be more appropriate for habitat excursion diving.

Table 1 shows the Lambertsen limits that were published in the 1991 NOAA Diving Manual (2). These limits were based on best judgment from extensive experience, not on the statistical analysis of quantitative data. Indeed, the NOAA limits apply not just to CNS oxygen toxicity but also to pulmonary toxicity and to symptoms such as finger numbness that have been described as "whole-body" oxygen toxicity (19, 25).

**Table 1. NOAA oxygen partial pressure and exposure time limits (2).**

| Oxygen partial pressure (atm) | Normal exposure mits (min) | Exceptional exposure limits (min) |
|---|---|---|
| 2.0 | -- | 30 |
| 1.9 | -- | 45 |
| 1.8 | -- | 60 |
| 1.7 | -- | 75 |
| 1.6 | 45 | 120 |
| 1.5 | 120 | 150 |
| 1.4 | 150 | 180 |
| 1.3 | 180 | 240 |
| 1.2 | 210 | -- |
| 1.1 | 240 | -- |
| 1.0 | 300 | -- |
| 0.9 | 360 | -- |
| 0.8 | 450 | -- |
| 0.7 | 570 | -- |
| 0.6 | 720 | -- |

Figure 15 showed the limits of Table 1 in the context of a model of CNS oxygen toxicity that suggested the NOAA normal exposure limits were between zero and 1%. Because the data on which the model was based were practically non-existent at these low partial pressures, all that can be stated about the limits of Table 1 is that the risks of CNS toxicity are probably small. The risks of pulmonary or "whole-body" toxicities were not examined here.

The time limit for each oxygen partial pressure in Table 1 assumes a "square" dive, i.e., the partial pressure is constant throughout the exposure. Technical dives, however, typically change gas mixes multiple times (Fig. 18) to keep the oxygen partial pressure as high as possible in order to reduce decompression time.

The purpose of "$O_2$ clock" was to track oxygen exposure using the NOAA limits through a series of gas mixes. (The term "O2 clock" appears to have been initiated by Dick Rutkowski (personal communication). See http://www.iantd.com/articles/95-2gurr.html for a more complete discussion.) The concept associates a percentage of the allowable oxygen exposures in the NOAA table with each minute of exposure time (%CNS/min). For example, 45 minutes at 1.6 atm is equivalent to 2.22% per minute (100%/45 min), and 180 min at 1.3 atm is equivalent to 0.56% per minute (100%/180 min). The total $O_2$ clock percentage is found by multiplying the %CNS/min by time for the partial pressure of each mix and summing these products for all mixes. A diver who breathes 1.3 atm for 60 min accumulates 33% of his or her $O_2$ clock. An additional 80 min at 1.5 atm is 67%, which would bring the total to 100%, and in theory, further oxygen exposure would be unsafe.

Another concept sometimes used in $O_2$ clock calculations holds that the CNS $O_2$ risk can be reduced by breathing low oxygen partial pressures. This is the principle of "intermittency" is used in the U.S. Navy Oxygen Treatment Tables 5 and 6 by alternating between oxygen (2.82 atm) and air (0.59 atm) at 60 fsw. Intermittency has been demonstrated experimentally for pulmonary oxygen toxicity in animals and humans, but little work has tested its validity for CNS toxicity (15, 22).

Applying the $O_2$ clock to the dive of Fig. 18 (Case 1 of the Case Reports) suggests that the diver reached approximately 80% of his allowable CNS exposure, but this does not include the 3 min periods on 18% (about 0.6 atm) and 35% (about 0.7 atm) oxygen which by intermittency theory, should allow some reduction of risk. Nonetheless, the diver developed definite signs of CNS oxygen toxicity. The diver of case 2 appeared to have an oxygen convulsion at 50% of his $O_2$ clock.

The $O_2$ clock is a logical tool for applying square dive exposure limits to multilevel exposures, but its foundation is uncertain, and as indicated by cases 1 and 2 above, obeying its principles it does not guarantee freedom from CNS toxicity. The value of the $O_2$ clock as a predictor of CNS toxicity probability might be better assessed if technical divers recorded their depth, time, and $O_2$ partial pressure profiles and sent them to DAN (with medical outcomes) for analysis.

## CNS Oxygen Toxicity Safety

Safety is acceptable risk where risk depends on the probability and severity of injury (27). If the injury is mild, the acceptable probability might be higher. If the injury is serious, the acceptable probability should be lower. If the probability is unpredictable as in CNS oxygen toxicity, the acceptable probability should be lower still.

What oxygen partial pressures are safe? The question does not have an unequivocal answer. The Navy is responsible for the safety of Navy divers and publishes its safety guidelines in the U.S. Navy Diving Manual (4). DAN attempts to provide the best information available and offers to assist the diving community in formulating its own safety guidelines. At present, the available information seems sufficient to say that the risk of oxygen may be worrisome at or above 1.3 to 1.6 atm, but even this non-specific conclusion is tempered by the possibility that intra- and inter-individual variability, environmental effects, pharmaceutical influences and $O_2$-$CO_2$ interactions could reduce the threshold to less than 1.3 atm.

If the technical diving community wants more specific answers, technical divers should contribute specific information about their practices and experience. Contact DAN for details.

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**Discussion**

SIMON MITCHELL: A comment to make sure none of you are confused between my message and the message we've just heard about hyperventilating to lower $CO_2$. That will work when you're near the surface and your gas isn't dense. It may not work if you're down on the bottom and your gas is more dense.

BILL HAMILTON: Especially if you're in the effort independent zone.

SIMON MITCHELL: That's right. In addition I thought Bill raised an important point about diver rescue. I completely agree with Bill. This idea that during the clonic phase of a convulsion (alternate contractions and relaxations), your airway is spasmed shut is not correct, or only partially so. The airway is not spasmed shut, as has been demonstrated in animal studies. So I agree that the risk of embolism is very small. If you hold an unconscious diver under water, the risk of drowning is very high.

PETER BENNETT: It's a comment about the symptoms. I've seen a lot of oxygen convulsions in the chamber in front of me. I didn't see anything happen first; they just went very pale and they convulsed right in front of my face. With regard to premonitory facial twitching, a lot of that came out of Donald's work. Recruitment of divers was on the basis of "you, you and you," and when Jim sat there he was told you're going to get lip twitching before you convulse. And he sat there, and poor old Joe convulsed in front of him so he started his lips twitching. He didn't want to convulse, so he started lips twitching. He was then pulled back to the surface for having a symptom. And that was the talk in all the pubs. Donald would say that's not quite true, you know, Peter, but, in fact, the sailors said it was true.

DICK VANN: Twitching was observed in the U.S. Navy studies as well.

JEFF BOZANIC: Several people have recommended the use of an antioxidant regime to reduce the problems that we talked about with free radicals. Is that effective or likely to be effective in diving scenarios?

DICK VANN: That's been looked at. And some were shown not to be effective. There are some potential drugs that might be useful, and I think that work may still be ongoing. Jake, can you comment on that?

JAKE FREIBERGER: There's work ongoing, but no, antioxidants have not helped with pulmonary toxicity.

HAL WATTS: I'd like to see a show of hands on how many divers in here has had a symptom of $O_2$ hit. (Editor's note: many hands.) That's pretty interesting, isn't it?

SIMON MITCHELL: We've got to stop. There's a lot of technical divers in here who have spent a lot of time sitting at their last decompression stop, 10 feet, three meters, breathing 100 percent oxygen and the oxygen clock is way up over 100 percent. What should they do to reduce their risks of a seizure?

BILL HAMILTON: If you can switch periodically to bottom mix, switch off the pure oxygen every 20, 25 minutes for 5 minutes, that will allow you to go all day. The hyperventilation business is a quick and immediate thing, and you pointed out that it doesn't always work. But the intermittency is something that you'll find in Lambertsen's work and it seems always reliable.

DICK VANN: How do you know?

BILL HAMILTON: That's what's in the literature.

SIMON MITCHELL: If I had to pick the question that most of the technical divers had brought to this session today, that's the one because it really worries them to do these calculations and sit there at that last deco stop with the oxygen clock way up over 100 percent.

JEFF BOZANIC: The question is if you're going to be intermittent and switch to a lower $PO_2$ how low is effective?

BILL HAMILTON: The conventional wisdom is below 0.5 atmospheres of oxygen is what it will take. To get below 1 or anything like that will be helpful if you're up at 1.6 the rest of the time.

BILL HAMILTON: Now, if you do have to rescue, there's one last point here, and that is if a diver needs to be rescued, you may not be able to replace the mouthpiece. You may be able to hold it in if it's still in his mouth, but if it's not, the conventional wisdom is not to try to put it in. If the diver doesn't have an airway, get him out of the water, because there's nothing else you can do. There's a small, very small chance of embolism. We heard a good lecture on that in the workshop on breath-hold diving a year or so ago. You're not likely to have embolism, but if you stay in the water trying to breathe the water, you're going to drown, that's for certain, for sure. So this is what you have to do if you've got to rescue someone, get them out of the water.