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THE PATHOPHYSIOLOGY RELATED TO THE TOXIC EFFECT OF OXYGEN. THE HAZARD OF CENTRAL OXYGEN TOXICITY PART 2

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ABSTRACT

The pathophysiology related to the toxic effect of oxygen is understood as an area dealing with an investigation of changes and disturbances in the functioning of cells, organs and body systems as a result of hyperbaric oxygen exposures.
Key words: oxygen toxicity, central nervous system oxygen toxicity, pulmonary oxygen toxicity, oxygen somatic toxicity, toxic effect of oxygen.

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CENTRAL NERVOUS SYSTEM OXYGEN TOXICITY

Oxygen is indispensable in the maintenance of homeostasis[1] in a human organism; however, under hyperbaric conditions it manifests toxicity in relation to the central nervous system and pulmonary tissues, a highly toxic effect on tissues as well as other adverse effec

Tab. 1

Allowable oxygen partial pressures and times of oxygen exposures according to the regulations of the Polish Navy.

Maximum oxygen partial pressure	Allowable exposure time
$[MPa]$	$[min]$
0.130	240
0.145	150
0.160	110
0.175	75
0.190	45
0.205	25
0.220	10

Until quite recently the Polish Navy acted accordingly to the effective regulations[2] regarding stay times and maximum oxygen partial pressures in the course of diving [1,2]. They corresponded to the regulations determined by the for the $USNavy$ 1960s – tab. 1 [3]. The manual published in 1981 by the Polish Ministry of National Defence already provided a distinction between routine and extraordinary exposures, with the specified threshold at the pressure value of $0.175MPa$ [4]. Currently, for dives performed with the use of close-circuit rebreathers with oxygen as a breathing mix, the Polish Navy applies the recommendations of the $USNavy$ [5].

According to some sources, there has been no significant progress in the knowledge regarding central nervous system oxygen toxicity $CNSyn$[3] [6]. Many researchers still refer to classical tests performed during World War Two by Kenneth Donald, which have recently been complemented with newer achievements and collectively published [7]. The most common scenarios of combat oxygen exposures were described in the 1980s [8,9,10].

The phenomenon of central nervous syndrome $CNSyn$ is difficult to investigate due to complicated interactions with numerous factors, including age, sex, individual predispositions or current psychophysical condition [7,11]. Toxicity is a phenomenon affecting numerous organs that play an important role in the preservation of homeostasis.

The explanation of the phenomena related to oxygen toxicity is often conducted on the basis of biochemical theory with the assumption of the adverse impact of free radicals[4] and other metabolites manifesting themselves as a result of occurrence of $CNSyn$ symptoms [12,13].

During oxygen exposures hydrogen peroxide H_2O_2 was observed in human blood and its impact on various regions of the brain were investigated [6]. It is postulated that oxygen exposures have an effect on various types of neuroreceptors[5], for instance $GABA$ [6] receptors, whereas the produced highly oxidised metabolic forms have a significant impact on the important enzymes of a human organism[7], for instance acetylcholine[8] [6].

Among the methods used in $CNSyn$ hazard reduction one may find the implementation of air breaks during oxygen decompression or hyperbaric treatment $HBOT$[9] [14].

It was observed that during oxygen exposures there is an initial constriction of brain blood vessels causing a decrease in the blood flow through the cerebral cortex [10], followed by their dilation. The time of occurrence of such a relaxation seems to constitute the $CNSyn$ threshold, which when exceeded causes the development of $CNSyn$ symptoms leading up to an attack of convulsions[11]. The substances reducing the blood flow through the cerebral cortex may inhibit the development of $CNSyn$ symptoms [12][6].

CNSYN MECHANISM

The phenomenon of $CNSyn$ shall be presented briefly on an example of a general biochemical theory concerned withoxygen toxicity.

Biochemical changes based on the use of oxygen constitute the source of energy for higher forms of life existing on Earth. The energy required to live is obtained through oxidation reactions occurring in cells. The energy of bonds released during the reaction of oxidation of carbohydrates, proteins and fats is stored in portions in phosphorous bonds GTP and ATP[13] [15]. Fig. 1 presents a simplified scheme related to GTP and ATP generation in a cell. The main part of ATP is received from the respiratory chain cycle[14]. In the respiratory chain combustion reactions of the hydrogen transported by such enzymes as nicotinamide-adenine dinucleotide NAD from the $Krebscycle$.

The oxygen is supplied to the respiratory chain with $hromes$[15]. They contain an iron atom capable of binding and returning oxygen. This is accompanied with a change in the iron valence and cytochromes' transformation from an oxidised to a reduced form and vice versa. In the reaction of oxygen with $NADH_2$ water is produced and the reaction energy stored in phophorous bonds $ATP$is released. This constitutes the primary pathway of ATPproduction, taking place in the cell[16] mitochondria [16].

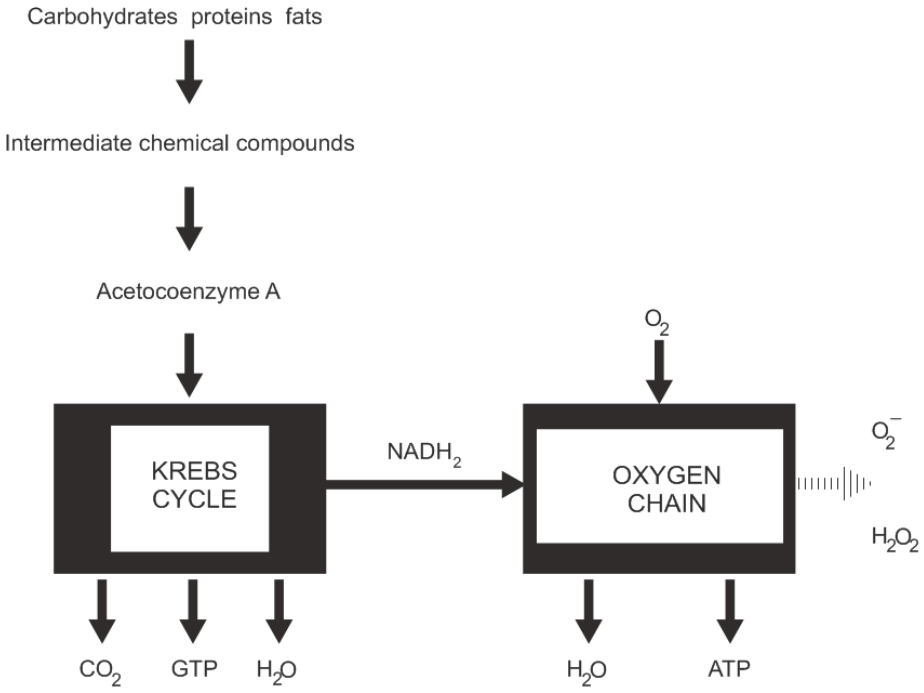

Fig. 1. General scheme of ATP and GTP production.

Tab. 2

Oxygen toxicity symptoms [17].

Hazard degree	Symptoms	Number of cases of
	Nausea	75
	agitation, breathlessness, sleeplessness, depression	12
	Headache	5
	numbness, burning sensation	13
	Dizziness	63
	Cramps	335
	hearing impairment	7
	visual impairment	17
	loss of consciousness, speech disorder	16
	Convulsions	91
	Total	**634**

In the case when oxygen pressure in tissues is large, it may enter the respiratory chain in large quantities. At that point biochemical reactions also lead to the emergence of free radicals and hydrogen peroxide - . The responsible enzymes are the accelerating reactions[17] . The produced free radicals and are potentially toxic for the cell [18]; however, under normal conditions they should be deactivated [19] [13,18]. In the situation of a significant increase in the oxygen pressure, the rate of generation of toxic compounds is increased and the biochemical protective system is not capable of deactivating all of them, which results in certain biochemical and physiological changes in the functioning of an organism.

They manifest themselves in the form of $CNSyn$symptoms[20].

Such symptoms have never been observed to occur immediately following an organism's exposure to the activity of oxygen[21]. The state of toxicity is known to present the $CNSyn$–specific symptoms preceding an attack of convulsions, such as: anxiety, paleness in the face, trembling of the lips and eyelids, nausea, cramping, dizziness, lack of coordination, visual and

auditory hallucinations, reduced vision[22]or speech impairment tab. 2. The above symptoms are rarely noticeable before the occurrence of convulsions[23] [19,20].

An onset of a generalised seizure is sudden. The attack begins with a tonic phase commonly lasting 30 s, during which a diver experiences a loss of consciousness and respiratory arrest. It is then followed by a clonic phase consisting in uncoordinated movements of the entire body. The attack usually lasts approximately $2min$. After a longer period of breathing with oxygen in a hyperbaric chamber where it is possible to replace oxygen with air, it is allowable that the period of apnea in the affected person lasts up to $5-8min$ [24] [14]. The sensitivity to $CNSyn$symptoms is raised by factors inducing an increased cerebral blood flow, including: immersion, undercooling, workload, an elevated level of Carbon dioxide CO_2 concentration, etc. [21]. CO_2 may be present in the exhaled breathing mix or come from the so-called dead spaces[24]. Through the CO_2 concentration receptors an organism increases the intensity of ventilation.

An increased intensity of ventilation is also accompanied by an increased density in the inhaled breathing mix, breathing resistance, etc. In normobaric conditions the occurring CO_2 excess could be more efficiently evacuated as compared with hyperbaric conditions. Usually, an elevated pressure leads to an accumulation of CO_2 in an organism. Initial hyperventilation leads to hypocapnia[26] causing an observable reduction in the respiratory activity during oxygen exposures.

The defence mechanism causing constriction of the blood vessels of the brain leads to increasing CO_2 concentrations in cerebral vessels in relation to peripheral vessels. Hence, the CO_2 receptors are incapable of increasing ventilation in the initial phase. However, such a defence mechanism has its flaws, as an increased CO_2 concentration in cerebral vessels leads to a raised concentration of hydronium ions H_3O^+, due to which the haemoglobin loses oxygen more quickly, thus increasing its pressure in the plasma[27]. Thanks to this, cerebral tissue is exposed to greater pressures of oxygen π_{O_2}. It seems, however, that an organism makes attempts to compensate such effects with enzymes deactivating the emerged free radicals.

In the performance of work the emission of CO_2 from tissues into the peripheral blood may cause: an increased ventilation, vasoconstriction at the periphery thus elevating the blood pressure and dilating cerebral blood vessels. This may increase cerebral blood flow resulting in a potential increase in the O_2 stream flowing through the brain.

ANTIOXIDANTS

As already mentioned, a rise in the pressure of oxygen π_{O_2} in tissues may involve its increased presence in the respiratory chain, resulting in the production of free radicals and superoxides. It is assumed that in normal conditions they are deactivated by antioxidants.

An effective antioxidant is melatonin[28], the effect of which has been widely discussed. Nonetheless, the activity of melatonin is distributed over time and

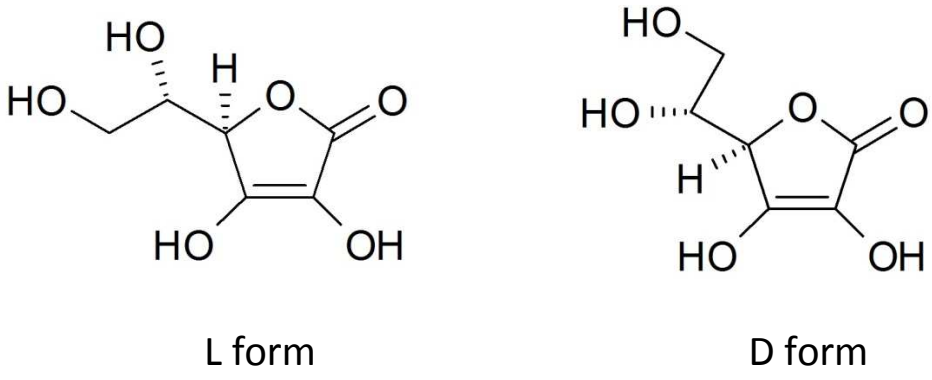

Fig. 2. Optical isomers of ascorbic acid.

does not cause shifting of the threshold regarding the occurrence of $CNSyn$ symptoms [22]. Additional intake of melatonin causes drowsiness, hence its use is limited only for the planned time of rest.

The evaluation of efficiency of antioxidants depends on the applied research method. For example, studies conducted on healthy men exposed to hyperbaric oxygen, whose diet was enriched with vitamins C and E failed to confirm any significant antioxidant capabilities of those vitamins [23]. The previous research conducted on mice infected with malaria[29]indicated a significant antioxidant activity of isoascorbic acid[30] being an isomer of Lascorbic acid[31] [24] - fig. 2.

The difference between the effectiveness of optical isomers[32] of ascorbic acid was examined and proved to be significant; however, it was not considered in more recent studies [23].

OXYGEN EXPOSURES

It is assumed that O_2 exhibits no toxic effect on the central nervous system with its partial pressure p_{O_2} equal to or lower than

Tab. 3

Allowable oxygen partial pressure values and oxygen exposure times as approved by $USNavy$ in early 1990s [25].

Oxygen partial pressure	Standard exposures	Extraordinary exposures
$[MPa]$	$[min]$	$[min]$
0.10	240	*
0.11	120	*
0.12	80	*
0.13	60	240
0.14	50	180
0.15	40	120
0.16	30	100
0.17	**	80
0.18	**	60
0.19	**	40
0.20	**	30

*–times limited only due to L.Smith effect
**–exposures prohibited during standard dives

$p_{O_2} \leq 0.1MPa$[33] [26]. During combat dives, oxygen partial pressures p_{O_2} often exceed the presented limit[34].

Tab. 4

Allowable exposure times and oxygen partial pressures in Nx as approved by $NOAA$ [27].

Standard exposures				
Oxygen partial pressure	Allowable exposure time		Maximum exposure time for the period of $24hours$	
$[MPa]$	$[min]$	$[hour]$	$[min]$	$[hour]$
0.16	45	0.75	150	2.5
0.15	120	2.0	180	3.0
0.14	150	2.5	180	3.0
0.13	180	3.0	210	3.5
0.12	210	3.5	240	4.0
0.11	240	4.0	270	4.5
0.10	300	5.0	300	5.0
0.09	360	6.0	360	6.0
0.08	450	7.5	450	7.5
0.07	570	9.5	570	9.5
0.06	720	12.0	720	12.0
Extraordinary exposures				
0.20	*30*	*0.50*		
0.19	*45*	*0.75*		
0.18	*60*	*1.00*		
0.17	*75*	*1.25*		
0.16	*120*	*2.0*		
0.15	*150*	*2.5*		
0.14	*180*	*3.0*		
0.13	*240*	*4.0*		

Tab. 4 cont.

Allowable exposure times and oxygen partial pressures in Nx as approved by $NOAA$ [27].

NOTE !
- Should one of the dives involve complete usage of the time or exceeding of the allowable exposure time, the diver will be required to take a rest at the surface for at least $2hours$ before further exposures.
- If one or numerous dives carried out within $24hours$, thus leading to complete usage or exceeding of the maximum exposure time by $24hours$, the diver will be required to take a rest at the surface lasting at least $12hours$ before further exposures [28].

In the 1970s, the $USNavy$ introduced modification in the standards concerned with oxygen exposures due to the risk of occurrence of $CNSyn$ symptoms. The changes involved a reduction in the allowable partial pressures to $p_{O_2} \leq 0.20MPa$, a division into standard and extraordinary exposures, and a reduction in the allowable stay times for particular exposures. Tab. 3 presents the specification of oxygen exposures in dives with the use of oxygen effective until the early 1990s [25]. In the 1990s, the $USNavy$ modified the allowable oxygen exposure times for $CCR-SCUBA$[35] with the purpose of ensuring greater flexibility of diving operations [5]. In 1991 the $NOAA$[36] changed the regulations concerning allowable oxygen partial pressures during nitrox exposures[37] Nx [27]. The amendment involved the approval of longer stay times with the preservation of allowable oxygen partial pressures in Nx, as well as setting the maximum exposure time within a 24-hour period - tab. 4.

In deep dives, breathing resistance increases due to an increased density of the breathing mix. This may be accompanied with an increased accumulation of CO_2 in a diver's organism due to previously described reasons. With an increased distance from the surface, the possibility to provide help or to self-rescue by divers of whom one or several experience oxygen toxicity becomes complicated. Hence, the maximum permitted oxygen partial pressures in deep dives should be reduced[38].

Similarly, during cave or wreck diving, due to a limited access to the surface, the same principles as those related to deep dives should be applied. The division into standard and extraordinary oxygen exposures is connected with diving conditions. Extraordinary exposures may be applied only with the purpose of rescuing a human life or under other important circumstances.

PULMONARY TOXICITY

Oxygen reveals its toxic effect on the respiratory system. This was observed for the first time during prolonged[39] respiration with pure oxygen at atmospheric pressure and is sometimes referred to as the $LorrainSmitheffect$ after the pathologist who first observed it, or pulmonary oxygen toxicity [29]. The symptoms of pulmonary oxygen toxicity are very similar to pneumonia[40]. During dives beyond the saturation zone, the effect plays a less significant role as compared to the $PaulBerteffect$; however, its monitoring is recommended in oxygen dives.

Pulmonary toxicity units

At the end of the 1960s, the dose $UPTD$[41] of pulmonary oxygen toxicity Q was determined as being equivalent to one-minute exposure with the oxygen partial pressure of $p_{O_2} = 0.1MPa$ (30).

Repex

The most commonly applied system of protection against pulmonary toxicity consists in a method validated during the $Repex$ programme [31,32]. However, there are numerous different models described in the available literature [33]. An intense research conducted in this area is related to the development of technical dives and the medical use of O_2; however, there are also studies on military applications [34].

Tab. 5

Values of a minute dose $UTPD \cdot min^{-1}$ $of oxygen pulmonary toxicity$ $\dot{Q}$, in the function of oxygen partial pressure p_{O_2} [35].

Oxygen partial pressure p_{O_2}	The dose of oxygen pulmonary toxicity per minute $\dot{Q}$	Oxygen partial pressure p_{O_2}	The dose of oxygen pulmonary toxicity per minute $\dot{Q}$
$[MPa]$	$[UTPD \cdot min^{-1}]$	$[MPa]$	$[UTPD \cdot min^{-1}]$
0.05	0.000	0.16	1.92
0.06	0.265	0.17	2.01
0.07	0.490	0.18	2.20
0.08	0.656	0.19	2.34
0.09	0.831	0.20	2.48
1.00	1.00	0.21	2.61
0.11	1.16	0.22	2.74
0.12	1.32	0.23	2.88
0.13	1.47	0.24	3.00
0.14	1.62	0.25	3.14
0.15	1.77		

Tab. 6

Allowable dosage of $oxygen pulmonary toxicity$ Q during an oxygen exposure lasting for many days.

Exposure time	Allowable daily dose of pulmonary oxygen toxicity Q	Allowable total dose of pulmonary oxygen toxicity Q
$[days]$	$[UPTD]$	$[UPTD]$
1	850	850
2	700	1400
3	620	1860
4	525	2100
5	460	2300
6	420	2520
7	380	2660
8	350	2800
9	330	2970
10	310	3100
11	300	3300
12-30	300	

Tab. 7

The decrease in the vital capacity of lungs following an oxygen exposure and the required rest to level the effect.

Maximum absorbed dose of pulmonary oxygen toxicity Q	Decrease in the vital capacity of lungs	Minimum required time between oxygen exposures
$[UPTD]$	[]	$[hour]$
615	2	2
825	4	4
1035	6	6
1230	8	8
1425	10	10-12
1815	15	13
2190	20	20

In The $Repex$ system it is assumed that O_2 begins to be toxic in relation to the pulmonary tissue when its partial pressure exceeds $p_{O_2} > 0.05MPa$. The calculations on pulmonary oxygen toxicity Q may be carried out on

the basis of tab. 5, which specifies the values of $\dot{\varrho}$ dose per minute in the function of oxygen partial pressure p_{O_2}. For instance, breathing with pure O_2 for the period of $t = 30min$ under the pressure of $p_{O_2} = 0.15MPa$ causes diver's exposure to a pulmonary toxicity dose ϱ of ca. $\varrho = \dot{\varrho} \cdot \tau = 1.77UTPD \cdot min^{-1} \cdot 30min \cong 53UPTD$, where: $\dot{\varrho}$ – pulmonary toxicity dose per minute from tab. 5, τ – exposure time. For the same purpose we may use the following function relation [33,35]:

$$\varrho = t \cdot \left(\frac{p_{O_2} - p_{O_2 max}}{p_{O_2 max}}\right)^{\frac{5}{8}} \quad (1)$$

where:

ϱ – pulmonary toxicity dose,

p_{O_2} – oxygen partial pressure [MPa],

t – time [min],

$p_{O_2 max}$ - pressure below which pulmonary toxicity symptoms are not observed [MPa], $p_{O_2 max} = 0.05MPa$,

$\frac{5}{8}$ – exponent for the best model to approximate the experimental data.

Maximum safe doses of *oxygen pulmonary toxicity* ϱ depend on exposure time tab. 6. Tab. 7 presents average values related to the reduction of vital capacity of the lungs resulting from an oxygen exposure and the average required time of rest levelling that effect.

SOMATIC TOXICITY AND OTHER HAZARDS

Oxygen is used at a wide range of partial pressure values - tab. 8. The issues related to hypoxia constitute the domain of aerospace medicine. They are also important for survival on high mountains. With regard to diving, this phenomenon is significant in relation to bodies of water situated on high mountains. The acclimatisation performed before diving and the decompression problems are in such conditions caused not only by a lower ambient pressure but also due to a decreased oxygen content C_{O_2}. Sometimes the oxygen content C_{O_2} is deliberately decreased, as it is the case in fire extinguishing procedures with such mixes as *INERGEN*[42] - tab. 8.

Tab. 8

The important applied ranges of oxygen partial pressures.

Oxygen partial pressure [*MPa*]	Specification
0.010	fire-extinguishing gases $INERGEN$[43] - safe to breathe over a limited period of time with the mix of nitrogen, argon, CO_2 and oxygen, in which oxygen partial pressure drops to $0.008\ MPa$, on condition that the partial pressure of CO_2 will reach $0.005\ MPa$ [36]
0.012	lower security limit due to hypoxia
0.016	first symptoms of hypoxia
0.021	regular oxygen partial pressure in atmospheric air
0.035-0.040	typical saturated exposures
0.050	maximum oxygen partial pressure during saturation dives and an onset of pulmonary oxygen toxicity[44]
0.10	breathing with pure oxygen on the surface
0.16	most commonly adopted upper security limit for nitrox dives beyond the saturation zone [27,35]
0.20	treatment table $CX–30$[45] prepared by COMEX in 1986. [37]
0.24	proposal to use nitrox $Nx\ 0{,}4$ with the pressure of $0{,}6\ MPa$ in treating diving diseases [28]
0.25	upper limit of allowable combat dives with the use of oxygen[46] [10]
0.28	$20\ min$ oxygen tolerance text [27] and oxygen treatment tables[47]
0.30	proposal to use nitrox $Nx\ 0{,}5$ with the pressure of $0.6\ MPa$ in treating diving diseases [48] [28]

The carcinogenic effect of O_2 accompanies not only diving activity, but the sole nature of the O_2 effect on the human organism [13]. A theory is postulated saying that the O_2 contained in the air and its long-term carcinogenic effect is largely correspondent to the effects of ageing[49].

Undoubtedly, hyperoxia and hypoxia are connected with a direct threat to health and life.

Chronic oxygen toxicity

A generally poisonous effect of O_2, also referred to as somatic toxicity[50] are chronic[l] effects related to breathing with a mix of an increased oxygen partial pressure p_{O_2}. One of the described effects consists in an observed reversible reduction in the content of haemoglobin and the number of red cells in saturated divers, as well as an occurrence of their increased quantity after long-term acclimatisation to hypoxia. Such effects are reversible in healthy persons; however, they should be considered in planning dives and the periods of rest that follow them.

Another, more dangerous effect is paraesthesia[51] and avascular necrosis, although their indirect connection to diving may be difficult to demonstrate [35].

Oxygen chemisorption in the middle ear

An unpleasant effect observed after oxygen dives may be a collapse of an eardrum as a result of O_2 chemisorption from middle ear cavity.

During depth changes, a diver is forced to level the pressure in the middle ear cavity through the Eustachian tube. After repetitive depth changes during oxygen dives a significant increase in O_2 concentration in the gas space of the middle ear is possible. Already minor symptoms of a common cold cause the canal of the ear trumpet to reduce its patency and even the best-trained divers[52] need to perform forceful *Valsalva manoeuvres*[53]. The O_2 trapped in the auditory canal is subject to diffusion through the membrane of the oval window into the inner ear, where it is absorbed and consumed[54] thus causing a pressure decrease in the middle ear and tension on the eardrum from the outside. If this phenomenon is allowed during the sleep, the diver will wake up experiencing a headache resulting from an excessive strain on the eardrum. The usual symptoms include plethora of the eardrum, exudate both into the external ear and the middle ear, as well as an increased production of cerumen in the external ear. This is accompanied with an irritating reduction in the auditory sensitivity. Commonly there is no perforation of the eardrum unless it is due to previous injuries resulting in its reduced elasticity or cicatrization.

What may be hazardous is an excessive accumulation of dissolved oxygen in the perilymph[55] which may cause its dislocation, thus inducing symptoms resembling neurological disorders occurring in decompression sickness [38]. There have been reported cases of labirynth irritation leading to its intensified activity during oxygen decompression of hyperbaric oxygen treatment. The effect was combined with the dislocation of the lymph due to pressure differences of the gases dissolved in it. Such cases were rarely encountered during domestic diving operations, nonetheless there are credible descriptions concerned with these issues in foreign literature [39].

Oxygen blindness

The vasoconstriction of cerebral blood vessels, as a physiological defence effect related to the exposure of the brain tissue to high oxygen partial pressures, may pose a particular threat to the organ of vision.

In the course of hyperbaric oxygenation procedures[56], $HBOT$, cases of the stenosis of the artery of the retina $CRAO$[57], progressed on to complete blindness[58]. Quick restoration of circulation resulted in restored vision [40].

Also, another observation concerned a disturbing percentage of neonates irreversibly losing sight after being kept over a long period of time in incubators with an atmosphere enriched in O_2 [13]. For this reason, presently the incubators are supplied only with air.

Visual disturbances connected with exposures to high oxygen partial pressures have been investigated since the very beginning of a scientific attempt at performing dives with its use [41]. The adverse effect resulting from oxygen applied at a high partial pressures was observed on the organ of vision on numerous occasions [14].

Oxygen blackout

There is vast available literature on the phenomenon of oxygen deficiency related blackout in apnea dives. The issue concerned with the genesis of hypoxia during the return to the surface in these types of dives will not be discussed here.

The term oxygen blackout with regard to oxygen
combat dives will be understood as a loss of consciousness of a combat diver after switching from breathing oxygen to the air at the atmospheric pressure upon completion of a combat operation. One of the reasons may lie in the already mentioned physiological defence reaction of an organism consisting in the constriction of cerebral blood vessels leading to a reduced cerebral blood flow.

This is often accompanied by dilation of peripheral vessels that may lead to hypothermia caused by the cooling effect of the aquatic environment. In hyperbaric conditions, the oxygen pressure in the peripheral blood occurs at a higher

level, hence the oxygen receptors in the carotid body cause slowing down of the respiratory activity and a decreased blood flow. A sudden switch to breathing air containing less O_2, usually combined with the necessity to perform work[60] before relaxation of the cerebral vessels and an increase of the cerebral blood flow may induce the phenomenon of hypoxia. Additionally, a decrease in the pressure connected to the immersion is accompanied with a decrease in the CO_2 partial pressure thus reducing respiratory stimulation, similarly as it is after performing hyperventilation. If the effect occurs in water there is a risk of a diver's choking or drowning; however, in the majority of cases it only leads to temporary disorientation and loss of concentration [42].

There are postulated hypotheses on the toxic properties of an observed increased pressure of CO_2 in cerebral vessels; however, in the light of the in $vivo$ studies it appears that the impact of hypercapnia on oxygen blackout is limited, as the observed increase in the CO_2 pressure is in normal conditions well tolerated and symptomless [43]. Although an increase in the CO_2 pressure in cerebral vessels has a significant impact on O_2 loss by haemoglobin, this effect has no significance for the occurrence of oxygen blackout, but rather for the previously described toxic effect of O_2 on the cerebral tissue. It seems that the mechanism of oxygen blackout during an oxygen mission may rather be related to a decrease in O_2 pressure in peripheral vessels causing a lack of sufficient stimulation of the respiratory center[61].

Bends

Research on animals showed that there is a possible occurrence of symptoms of decompression sickness DCS[62] induced by compression with the use of pure oxygen, followed by quick decompression [44,45].

However, the course of the thus induced $bends$ would be milder [7]. The DCS induced this way usually does not require hyperbaric treatment being subject to intrinsic compression over time [46]. Although the phenomenon of $bends$ is possible, it does not pose a significant threat during typical diving operations with the use of O_2 as a breathing mix. It may have an unfavourable impact on diver transportation by air following an oxygen exposure, for instance during the recover of a group/special section.

CONCLUSIONS

It is true that oxygen manifests its toxicity towards the human organism; however, during oxygen dives and in the majority of combat dives the most important role is played by its central form – $CNSyn$ The article described a biochemical approach to $CNSyn$ connected to the emergence of free radicals and forms of a higher oxygenation level, which may be potentially toxic for the man. Moreover, it mentioned biochemical protection mechanisms against those harmful products, which, however, ensure only minimal security against $CNSyn$.

The procedure of pre-selection of persons sensitive to $CNSyn$ within the Polish armed forces was enhanced with an oxygen tolerance test [47]. The procedure was outlined within the targeted project No. 148-101/C-T00/96 entitled Technology of Oxygen Combat Diving implemented in the years 1996-1998 by the Polish Naval Academy.

This article is second in a series of articles containing the results of studies conducted in the Naval Academy of Gdynia and financed from educational funds in the years 2009 – 2011 within a developmental research project No. O R00 0001 08 entitled: Designing decompression in combat missions.

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[1]a living organism's capability to maintain a relatively permanent state of balance, e.g. in blood composition, temperature, through proper coordination and regulation of life processes,
[2]the diving regulations were withdrawn due to a legal defect related to their implementation [2],
[3]the toxic effect of oxygen on the central nervous system is called $Paul\ Bert's\ effect$ or the acronym CNS – $Central\ Nervous\ Syndrome$ is used; for the purposes of this paper, we shall apply the acronym $CNSyn$ in order to distinguish it from the acronym CNS applied in relation to the nervous system ($Central\ Nervous\ System$),
[4]a group of atoms, usually incapable of durable individual existence, with unpaired electrons - free valencies,
[5]neural receptor,
[6]there are two types of $GABA$ receptors binding γ-aminobutyric acid:
- $GABA_A$ receptor regulates the inflow of chloride ions into cells, inhibiting the firing of new action potentials responsible for transmitting information in the nervous system
- $GABA_B$ receptor regulates the inflow of potassium and calcium ions neutralising the impact of chloride ions and regulating neurotransmitter release,
[7]mainly protein, high polymer chemical compounds regulating life processes,
[8]a neurotransmitter replacing an electrical signal with a chemical signal in a synapse, playing an essential role in a quick transmission of nerve signals,
[9]known as Hyperbaric Oxygen Therapy; also in an abbreviated form HBO,
[10]an observed defence reaction to the growth in oxygen partial pressure,
[11]spasms,
[12]caffeine is an example of such inhibitors,
[13]e.g. adenosine triphosphate – ATP, guanosine triphosphate - GTP,
[14]electron transportation,
[15]*cytochromes* are proteins occurring in the cell mitochondria demonstrating the properties of biocatalysts participating in electron transportation,
[16]a structure surrounded with a membrane occurring in the plasma of most cells with a nucleus, being a place where as a result of the cellular respiration process the majority of cell ATP is produced,
[17]oxidant–antioxidant,
[18]e.g. cause deactivation of numerous enzymes,
[19]e.g. through: vitamin E, catalases, peroxidases, etc.,
[20]convulsions are the most often mentioned symptoms,
[21]this is an indirect evidence of the above mechanism,
[22]the so-called tunnel vision,
[23]however, it is recommended to make the divers acquainted with them, as sometimes trained divers were able to notice the onset of oxygen toxicity faster, thus preventing the occurrence of severe $CNSyn$ symptoms [17],
[24]due to good oxygenation of an organism,
[25] e.g. spaces of a diving apparatus with a limited gas exchange,
[26]hypcapnia, also hypcarbia, is a condition of a reduced partial pressure of CO_2 in the blood below the specified norm,
[27]an increase in the pH value causes an increase in the haemoglobin's binding capability of oxygen– $Bohr\ effect$,
[28]a hormone regulating circadian rhythms, for instance of sleep and awakeness,
[29]an infection causes a significant production of oxidants by malaria protozoans,
[30]an allowable antioxidant used in food industry in prevention of undesired oxidation processes, extending the durability of foodstuffs $E-315$,
[31]constituting vitamin C,
[32]an observed common occurrence of differences in biochemical activity of optical isomers ,
[33]in $NOAA$ tables the threshold of $0.06\ MPa$ was adopted,
[34]an additional complication lies in the fact that oxygen partial pressure may be subject to significant changes in the course of diving,
[35]a closed circuit re-breather for oxygen as a breathing mix – Self Contained Breathing Apparatus,
[36]$National\ Oceanic\ and\ Atmospheric\ Administration$,
[37]the said changes were preceded with medical examinations conducted during dives over ten-years with the use of nitrox mixes and the $Repex$ programme [31,32,35],
[38]in such operations there is a tendency to neglect the aspect of stress, which may significantly increase cerebral blood flow to a similar extent as other enumerated factors,
[39]more than $24\ hours$,
[40]the symptoms include: dry cough, increased respiratory resistances, problem to perform full inhalations, etc.,
[41]unit of pulmonary toxic dose – $UPTD$, cumulative pulmonary toxic dose – $CPTD$, oxygen tolerance unit – *out,*
[42]what should be noted is a fact of partial mutual cancellation of hypoxia and hypercapnia in the atmosphere of $INERGEN$,
[43]a mix of argon, carbon dioxide and nitrogen with air [36],
[44]$Lorrain\ Smith$ effect,
[45]the use of heliox $Hx\ 0.5$ at the pressure of $0.4MPa$ [37],
[46]short exposures,
[47]optimal conditions to "ventilate" the system of nitrogen,
[48]an effective reduction of gas bubbles in decompression sickness,
[49]e.g. the carcinogenic effect of oxygen occurring during numerous and long oxygen exposures [49],
[50]Somatic, i.e. concerning the body; bodily, physical,
[51]chronic ,
[52]an impairment in the reception of tactile sensations consisting in an erroneous localisation of stimuli and a distorted experience of numbness, stiffening, tingling, etc.,

[53]those who do not have a problem with equalising pressure by swallowing saliva or making movements with lower jaw,
[54]blowing a breathing mix from the lungs into the nose while the mouth is closed and the alae of the nose are pinched,
[55]physical absorption combined with a chemical reaction is referred to as chemisorption,
[56]or perilympha, a liquid filling the bony labirynth in the inner ear,
[57]treatment applied frequently for general and local oxygenation of tissues against anaerobes, following respiratory poisoning, to secure transplants, frostbites, burns, post-radiation damage, osteoarthritis, osteomyelitis, secure slow-healing wounds, sudden deafness, etc.,
[58]known as **C**entral **R**etinal **A**rtery **O**cclusion – $CRAO$,
[59]the blindness concerns more often only the part of the main artery supplying the retina and may be observed as a partial problem with acuity, with similar effects provided by numerous diseases of the circulatory system, including system hypertension, inflammatory states of arteries or such diseases as syphilis,
[60]e.g. connected with the necessity to maintain position on the surface of the water , go ashore, swim away from the area, counteract waves, etc.,
[61]any lack of stimulation of the nervous system results in perturbations in signal transmission, with the most common consequence being control deactivation leading to respiratory arrest,
[62]decompression sickness.