ORIGINAL ARTICLE

# TECHNOLOGIES FOR NORMOBARIC HYPOXIA AWARENESS TRAINING: WHAT AFFECTS THEIR ACCURACY OF PHYSIOLOGICAL ALTITUDE SIMULATION?


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## ABSTRACT

It has been suggested that alveolar $pH_2O$ introduced an error into normobaric altitude simulation. The reduced number of oxygen molecules entering a trainee's respiratory system with each inhalation determines the hypoxia level during altitude simulation. Therefore no special compensation for $pH_2O$ is required because all hypoxia demonstration systems in use, whether hypobaric chambers or normobaric hypoxicators, make measurements at *ambient temperature and pressure*. Other factors directly affect the accuracy of simulation. For example pressure in a hypobaric chamber is set using a standard altimeter without compensating for the extremely low temperature and humidity at real altitude compared with approximately room temperature inside the chamber. We conclude that the training results using normobaric hypoxicators or traditional hypobaric chambers are so similar that no urgency attaches to correcting the simulated altitude values used by either. However, of much higher importance and priority is the safety and educational impact of this relatively new technology.



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The present technical discussion was triggered by Conkin's[1] commentary whose worthwhile aim was to prompt manufacturers of normobaric hypoxia training devices to improve the accuracy of nominal chosen values for simulated altitude.

Manufacturers of normobaric hypoxia systems – hypoxicators – assume that 20.9% of oxygen (by volume) at barometric pressure of 760mmHg corresponds to a physiologic equivalent of "sea level". The reduced $p_iO_2$ arising from the reduced barometric pressure at altitude can be accurately reproduced by reducing the $F_iO_2$ at different atmospheric pressures[3]. As long as the person breathes air with reduced oxygen and the balance gases are inert and non-toxic e.g. nitrogen – this replicates the environment inside the hypobaric chamber. However, Table 1 lists a number of reasons why this only approximates the nominal altitude.

**Table 1. Comparison of the different methods for inducing hypoxia as part of hypoxia awareness training.**

| Method/ Parameter of Altitude Simulation | Classic hypobaric chamber | ROBD | GO2Altitude® Normobaric hypoxicator | ROBE |
|---|---|---|---|---|
| Technology used to induce hypoxic hypoxia | Ambient air pressure reduction by vacuum pumps | Industrial gas mixer of bottled gases: $N_2$, $O_2$, Air. | On-site semipermeable air-separation, medical grade hypoxic and hyperoxic gases | Filling a tent / chamber with hypoxic air or nitrogen-enriched air |
| Ambient Temperature (standard atmosphere at 25,000ft is -34.5°C) | Less than ambient room temperature unless controlled | Ambient room temperature | Ambient room temperature | Higher than ambient room temperature unless air-conditioned |
| Alveolar $pH_2O$ at body core temperature | 47mmHg | 47mmHg | 47mmHg | 47mmHg |
| Relative humidity in inspired air | If uncontrolled: 20–50% | 0–10% Ignoring oxygen mask dead space | 10–20% Ignoring oxygen mask dead space | 50–100% ($H_2O$ expired by subjects builds-up) |
| $FiCO_2$ | >0.0003 | <0.0003 | <0.0003 | 0.0003-0.01 |
| $P_iO_2$ during oxygen recovery | 282mmHg(*) | 760mmHg(**) | 300mmHg(*) | 760mmHg |

(*) +5 mmHg regulator safety pressure
(**) not accounting for military mask high inspiratory resistance

As a general comment, we believe that the class of devices for normobaric hypoxia training is best defined by the term "hypoxicator".[4,5] Hypoxicators are intended to *induce* hypoxia and limit oxygen supply to bodily organs and systems, producing detrimental but reversible effects on trainee physiology and cognitive function.

"Breathing device" is commonly used in context on any apparatus that *protects* against hypoxia, providing an adequate oxygen supply for humans in various harsh environments or medical emergency situations. Thus we believe the phrases "reduced oxygen" and "breathing device" are an oxymoron.

## TECHNOLOGIES CURRENTLY USED FOR HYPOXIA AWARENESS TRAINING

Since 1940-s the traditional hypobaric chamber has been and remains a de-facto standard for military aviation hypoxia training world-wide. Particularly over the last two decades, normobaric hypoxia training technologies have been introduced. Different practical systems are different in implementation, but they all aim to induce hypoxia in subjects and to demonstrate cognitive performance deterioration by some means.

In Table 1 we summarised parameters and principles of operation of the three types of normobaric hypoxicators mentioned by Conkin[1] and their specific differences. From the table we can describe these further.

### Reduced-oxygen breathing device – ROBD®

The Reduced-Oxygen Breathing Device – ROBD® (Environics) is an operator-controlled industrial gas mixer of non-medical grade bottled gases: $N_2$, $O_2$ and compressed air.[3] The operator selects a level of hypoxia and observes subject arterial oxygen saturation ($SpO_2$) and Heart Rate (HR) using a stand-alone pulse oximeter. The trainee must increase inspiratory effort to compensate for high resistance of non-rebreathing valves in the military oxygen mask. ROBD® produces dry hypoxic air by mixing bottled nitrogen and bottled air (both compressed bottled gases contain a negligible amount of water vapour); the compressed oxygen is used for recovery only.

### GO2Altitude® aviation training system

The GO2Altitude® aviation training system uses a semipermeable air-separation nanotechnology to produce the required medical-grade hypoxic and hyperoxic gases on site.[6] The gases are then remixed by a microprocessor-controlled


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desktop hypoxicator that is part of the computer-controlled system coordinating the delivery of the required simulated altitude flight profile and hyperoxic recovery.

Vital signs of arterial oxygen saturation ($SpO_2$), (HR), and ventilatory frequency (Vf) are collected by the hypoxicator itself and stored for printout reports and research purposes, as well as being continuously displayed for the safety monitor. Continuous video of the trainee is automatically recorded. Hypoxia is automatically cut-off and hyperoxic air (typically $F_iO_2 \leq 0.40$) is supplied via the same breathing circuit if either vital sign reaches a pre-set critical threshold. Training for civil aircrew comprises a hand-held mask with a set of ultra-low resistance (<1cm $H_2O$) non-rebreathing valves. Training for military aircrew uses a military oxygen mask attached to a pressure-demand valve i.e. hypoxic or hyperoxic air supply is triggered by inhalation beginning. High airflow of the gases (35-45 LPM) ensures minimal inspiratory resistance. The gases produced by the GO2Altitude® hypoxic air generator are dry because it employs molecular sieve air-separation technology that dehumidifies the air as the gases are separated.

## REDUCED-OXYGEN BREATHING ENVIRONMENT – ROBE.

Reduced-oxygen breathing environments comprise a chamber, or air-tight room or tent that is filled with an oxygen-depleted gas mix. The hypoxic gas mix can be sourced from bottled compressed nitrogen or on-site air-separation generator(s). The hypoxia training paradigm is the same as in hypobaric chambers: students take their mask off to experience hypoxia, and put their mask back on for recovery. Normally air content inside the gas tent is not ventilated at the same rate as the traditional hypobaric chamber due to the high cost of producing hypoxic air. Therefore, in such an enclosed system the humidity builds-up from the subjects' exhaled water vapour. Relative humidity of the air inside can be anywhere between 40% and 100%.[7]

From Table 1 we can see that both ROBD® and GO2Altitude® hypoxicators deliver hypocapnic air. On the other hand, ROBEs have the potential to expose trainees to a higher $FiCO^2$, and therefore special precautions need to be taken to prevent this from happening.[7] Further investigation needs to be made on the possible effect of hypercapnia on hypoxia awareness training.

## INFLUENCE OF ALVEOLAR WATER VAPOUR ON $F_iO_2$

Alveolar air is fully saturated with water vapour.[2] The $PH_2O$ in the alveolar space is approximately 47 mmHg at 37°C, and this remains constant at different altitudes. This condition is called body *temperature and pressure saturated with water vapour* (BTPS).

It is important to consider the influence of water vapour for spirometer measurements or when *exhaled* gases are bag-collected; these conditions of measurement are called *ambient temperature and pressure saturated with water vapour* (ATPS).[2] However for the purpose of inducing and demonstrating hypoxia, the oxygen partial pressure in the *inspired* air is the most important factor. In this case measurements are said to be at *ambient temperature and pressure* (ATP).[2]

In hypobaric chambers, hypoxia is produced by reducing the ambient pressure in order to reduce the $P_AO_2$. The target simulated altitude is set by using an altimeter (manometer) in accordance with the standard atmosphere barometric pressure table. It is our understanding that there is no special compensation for $P_AH_2O$, and most importantly for the ambient temperature, made during hypobaric chamber training.

In normobaric hypoxia, the same physiological effect (reduced bioavailability of oxygen) is achieved by reducing the inspired fraction of oxygen ($F_iO_2$) at a ground-level pressure.

Dalton's Law states that the pressure exerted by a gas mixture equals the sum of pressures that each would exert if it alone occupied the space filled by the mixture.[2]

Therefore earth air composition can be expressed mathematically

$$Pt = PO_2 + PN_2 + PAr + PTG$$

where $P_t$ is the total pressure of the mixture, and $PO_2$, $PN_2$, PAr, PTG (trace gases and water vapours) are the partial pressures of each component.

The partial pressure of any gas in a mixture is given by the relationship:

$$P_x = F_x \times P_t$$

where $P_x$ is the partial pressure of gas 'x', $F_x$ is the fractional concentration of gas x in the mixture and $P_t$ is the total pressure exerted by the gases.[2]

Thus the partial pressure of oxygen ($PO_2$) in the dry atmosphere at mean sea-level pressure is:

$$PO_2 = \frac{20.94}{100} \times 760 = 159 mmHg$$

At altitude of 25,000ft:

$$PO_2 = \frac{20.94}{100} \times 282 = 59 mmHg$$

Therefore $PO_2$ is 2.7 times higher (159÷59=2.7) at sea level than at 25,000 ft.

From this, if we lower the $F_iO_2$ in a normobaric gas mix in the same proportion – with a gas that has $F_iO_2$ 7.6% (20.95÷2.7=7.76) – we produce at ground level a normobaric oxygen equivalent to the traditional chamber. This calculation does not consider differences between ambient temperatures at sea level and at real altitude, nor does it examine the alveolar $PO_2$, which is lower than $P_iO_2$ in both these situations. The contribution of $PaCO_2$ depends upon the degree of alveolar hyperventilation.

The alveolar $PH_2O$ is 47 mmHg because of the warming and humidification of inspired air. The upper respiratory tract warms and humidifies inspired air regardless of its origin – whether it is air breathed at 'real' altitude, in a hypobaric chamber, or gases produced by a normobaric hypoxicator. Alveolar water vapour influences $P_AO_2$ as part of normal respiratory physiology.[2] However, these two physical facts are separate: a) the value of $PH_2O$ in alveolar air and b) how many oxygen molecules enter a trainee's respiratory system with each inhalation.

We believe that no special compensation for $PH_2O$ is required when using a normobaric hypoxicator to induce hypoxia because the alveoli are always fully saturated with water vapour. This is irrelevant to achieving the hypoxia training aims. We therefore disagree with Conkin[1] that the alveolar $PH_2O$ and the accuracy of physiological simulation should be linked. The same question has not been posed to the accuracy of hypobaric chamber calibration concept which has satisfactorily met the altitude simulation aims for >70 years.

## STANDARD ATMOSPHERE TEMPERATURE

Drafting these notes required review of basic altitude physiology and the way altitude was simulated for physiological training since 1940-s. It is clear that temperature, is potentially another important source of error that was overlooked, contributing to inaccuracy of physiological simulation.

Ambient temperature does have a direct impact on the altitude prediction and the accuracy of physiological simulation. The relation between pressure and altitude is defined by the ICAO standard atmosphere and based upon several important assumptions, amongst which are: the air is dry, mean sea level pressure is 760 mmHg, and *mean* temperature lapse rate is +1.98°C per 1,000 ft. Given the standard temperature lapse rate, the estimated ambient temperature at 25,000 ft ambient temperature would be -34.5°C, within a great variation between approx. -15°C – 50°C.[2]

To our knowledge the hypobaric chamber altimeter is initially calibrated to zero altitude at room air conditions and then is used to "measure" the simulated altitude inside the chamber, which is cooler than room air temperature but does not reach -35°C. If the temperature in the hypobaric chamber at simulated altitude of 25,000 ft is +16°C, this is 50°C higher than the expected temperature at real altitude (-35°C). That must contribute to a significant error!

Charles' law states that at constant pressure, the volume of the gas is directly proportional to its absolute temperature.

$$\frac{V1}{V2} = \frac{T1}{T2} = \frac{(t1 + 273)}{(t2 + 273)}$$

where V is volume, and T is the absolute temperature (in degrees Kelvin).

From this law follows that the difference of volumes is proportional to their temperatures and in our case it is: (-35 + 273) / (16 + 273) = 238 / 289 = 0.82. This reduction of 18% means that cold air outside an unpressurised aircraft at an altitude of 25,000 ft is *18% thicker* than the warmer air inside. The same argument applies to the whole spectrum of hypobaric or normobaric simulation. There is a discrepancy in the calculations when simulating a 25,000 ft altitude in a hypobaric chamber at close-to-room air temperature whilst setting the pressure-altitude by selecting a pressure value of the standard atmosphere that assumes completely different ambient temperatures.

If chamber pressure is set to 282 mmHg at 16°C, the reduction in barometric pressure by the factor of 0.82 increases the volume of air by 18%. Because the same number of gas molecules are distributed over a larger volume, this means that the subject receives fewer oxygen molecules with each inhalation. In fact, an ambient pressure of 282 mmHg, the further reduction in pressure arising from the temperature discrepancy (282 mmHg x 0.82 = 231 mmHg) equates to a simulated altitude of approximately 29,500 ft instead of the targeted 25,000 ft.

During slow cabin depressurization, ambient temperature will not drop as far as it would in explosive decompression; therefore, this artifact introduced by the temperature discrepancy is of academic interest, but it doesn't undermine the realism of the hypobaric chamber training.

## INSTRUMENTAL FACTORS AFFECTING THE ACCURACY OF PHYSIOLOGICAL SIMULATION

In order to verify the $F_iO_2$ in the product gas, hypoxicators incorporate an oxygen analyser into their design. Oxygen analysers use an electro-galvanic oxygen sensor to measure the $F_iO_2$. These oxygen sensors are typically calibrated for normal-humidity room air. Accuracy of these commonly used oxygen sensors and analyzers can be only guaranteed within certain tolerance specified by their manufacturers and also contribute to overall inaccuracy of simulation. For instance, one manufacturer (http://www.maxtecinc.com/products/analyzers.php) provides the following specifications for the accuracy of the oxygen measurement – accuracy of ±1% *at constant temperature, relative humidity, and pressure* when calibrated; accuracy of ±3% over full operating temperature range.

However, when used in hypoxia training, oxygen sensors that have been calibrated for use at room humidity are used to measure either the $F_iO_2$ of dry gases (as in the ROBD® and GO2Altitude® hypoxicators) or hypoxic air of variable humidity present in a reduced-oxygen breathing environment. This introduces the possibility of another confounder into comparisons between the physiological equivalence of hypobaric and normobaric methods of inducing hypoxia.

## OTHER FACTORS INFLUENCING THE FIDELITY OF HYPOXIA TRAINING

Even more controversial is the decision of what $P_iO_2$ should be used for oxygen recovery after hypoxia exposure. In hypobaric chambers, 100% oxygen is routinely used for recovery after hypoxia demonstration. At an altitude of 25,000 ft, 100% oxygen delivered via mask provides $P_TO_2$ of 235 mmHg (tracheal $PO_2$ = 282 mmHg – 47 mmHg = 235 mmHg).

The US Navy uses 100% oxygen recovery at ground level after inducing hypoxia with the ROBD®.[3] At sea level, 100% oxygen provides a $P_TO_2$ of 760 mmHg. This has been presented as an advance in training methodology, but unfortunately no rationale for providing oxygen at $P_TO_2$ 760 mmHg during recovery has been given. This is a radical change to the accepted practice of giving oxygen at $P_TO_2$ 235 mmHg during recovery, a practice that has been well-proven over many decades in hypobaric chambers. The good intention for quicker recovery at near sea level may possibly hide new hazards. For example a severe adverse effect of clonic- tonic seizures has been reported.[8] Unfortunately, no corrective action was suggested by the authors.

We hypothesize that the oxygen paradox phenomenon is artificially and significantly amplified by supplying recovery oxygen at $P_TO_2$ 760 mmHg to a subject who is profoundly hypoxic. At $P_TO_2$ 760mmHg, oxygen causes a pulmonary vascular vasodilatation via autonomic nervous system controlled mechanisms without any brain feedback control. This consequential chain of events can lead to the hypoxic brain rapidly becoming anoxic, disconnected from the proper respiratory function control, and with various negative outcomes, demonstrated in detail in the adverse effect report.[8]

We believe that recovery action using normal room air, or air that is slightly enriched with oxygen, after severe hypoxia exposure at ground level better matches what happens in the alveoli when recovering on 100% oxygen during hypoxia demonstrations in a hypobaric chamber. Recovery on 100% oxygen at 25,000 ft (ambient pressure 282 mmHg) provides $P_TO_2$ 235 mmHg; recovery with 33% oxygen at ground level (ambient pressure 760 mmHg) provides $P_TO_2$ 235 mmHg.

## CONCLUSION

Hypoxicators are intended to provide a physiological simulation in order to educate aircrew about the insidious nature hypoxia and demonstrate each trainee's personal symptoms. Our experience is that the GO2Altitude® hypoxicator system[6] and other hypoxicators produce symptoms with a range and incidence that is comparable to symptoms of hypoxia reported for traditional hypobaric chambers.[9] In this respect, hypoxicators provide a training environment equivalent to traditional hypobaric chambers.

With the increasing use of hypoxicators to provide hypoxia awareness training to military and civil aviators around the world, it is important to establish the safety of these relatively new technologies[8] rather than focus on small and trivial differences in alveolar physiology, especially where these don't affect the training benefit of normobaric hypoxicators. We agree with Stepanek[10] that as hypoxicators are now available "outside of the lab" their practicality and safe use is a critical issue of interest. In a separate communication we intend to present a formal evaluation report on hypoxicator-specific risks.

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