

Work in Hypoxic Conditions-Consensus Statement of the Medical Commission of the Union Internationale des Associations d'Alpinisme (UIAA MedCom)

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Objectives: The Commission gives recommendations on how to provide health and safety for employees in different kinds of low oxygen atmospheres. So far, no recommendations exist that take into account the several factors we have outlined in this report.

Methods: The health and safety recommendations of several countries were analysed for their strength and deficiencies. The scientific literature was checked (Medline, etc.) and evaluated for relevance of the topic. Typical situations of work in hypoxia were defined and their specific risks described. Specific recommendations are provided for any of these situations.

Results: We defined four main groups with some subgroups (main risk in brackets): short exposure (pressure change), limited exposure (acute altitude disease), expatriates (chronic altitude disease), and high-altitude populations (re-entry pulmonary oedema). For healthy unacclimatized persons, an acute but limited exposure down to 13% O₂ does not cause a health risk. Employees should be advised to leave hypoxic areas for any break, if possible. Detailed advice is given for any other situation and pre-existing diseases.

Conclusions: If the specific risk of the respective type of hypoxia is taken into account, a pragmatic approach to provide health and safety for employees is possible. In contrast to other occupational exposures, a repeated exposure as often as possible is of benefit as it causes partial acclimatization. The consensus statement was approved by written consent in lieu of a meeting in July 2009.

Keywords: fire protection; high altitude; hypoxia; travel; Union Internationale des Associations d'Alpinisme

INTRODUCTION

The Union Internationale des Associations d'Alpinisme (UIAA) is the world umbrella organization

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for health and safety at altitude. Apart from pure technical aspects, expedition, doping, environmental protection, and others, which are all covered by specific commissions, the medical commission (UIAA MedCom) focuses on preventive aspects of high-altitude exposure. This traditionally includes the effects of hypoxia on humans. With more and more employees exposed to hypoxia in international business and others working in hypoxic rooms for fire protection or altitude training, the commission expanded its field to include occupational aspects of altitude or hypoxia exposure. In total, the UIAA represents 69 countries worldwide (delegates and corresponding members) with a total of 77 organizations, 37 of which have joined the medical commission (for details see www.theuiaa.org/organization.html). The recommendations given by UIAA MedCom are regularly updated and based on consensus from the entire commission.

The recommendations are based on intensive literature research which include the most important subject matter:

1. The guidelines of those European countries (and USA), where hypoxic chambers are in industrial use. The list of countries was obtained by the manufacturers of such equipment.
2. A detailed research of international medical databases (e.g. Medline) with the following keywords: hypobaric hypoxia, isobaric hypoxia, altitude, disorders, occupational safety, acute mountain sickness (AMS), occupational health, occupational medicine, and altitude training.

All previous recommendations conducted by the UIAA MedCom, which are relevant to this topic, have been referenced. These international recommendations are supported by a detailed literature research, which is therefore indirectly included in this report. The literature research was performed in international literature databases (e.g. PubMed, DIMDI, etc.) with an extensive list of keywords [e.g. altitude, hypoxia, isobaric hypoxia, occupational medicine, aviation, passengers, AMS), high-altitude diseases, high-altitude pulmonary oedema (HAPE), chronic mountain sickness (CMS), Monge's disease, several keywords for pre-existing diseases, and many others). For older literature, the reference list of the papers as well as the personal literature knowledge of the specialists were used. As there is a total of >1000 papers, which are potentially of interest for the topic, the consensus group had to select those which were considered to be most important for the actual recommendation. It must be pointed out that this is not a pure physiological paper: the multitude and variability of influencing factors

forces one to categorize these factors, which in consequence meant that not every detail can be discussed individually. Otherwise, the recommendation would be unmanageable. As most of the recent papers add only minimal and very detailed facts to older and well-established literature, the consensus group considered that it is fair to refer to the original (older) literature wherever possible. This also underscores that these respective statements are internationally well accepted.

There are no exact data available that how many employees are exposed to altitude or isobaric hypoxia, mainly because the group is extremely heterogeneous (mountain rescue, maintaining, service for tourists, mining, astronomers, mountain guides, pilots, people on business flights, coaches for altitude/hypoxia training, etc.). Küpper (2006) gives a survey of some data: there are ~10 000 members of the German mountain rescue organizations, their number in Europe exceeds 30 000. The alpine clubs of Europe operate >2100 huts in the Alps. With an estimated average of at least four employees per hut, this would result in ~9000 employees. Lufthansa, one of the biggest airlines in Europe, counts 3753 pilots and ~14 400 cabin crew members. In 2005, the World Travel Organization reported 16% of aircraft passengers being businessmen (800 million of the total of 5 billion passengers, but because the number of flights per individual is unknown, there is no exact number of persons exposed). In 1985, there were 27 000 mining workers in Bolivia. Thousands of soldiers are exposed to high altitude in Afghanistan (2500–5000 m), the astronomers of the European South Observatory are working at the Chajnantor plateau at 5320 m, and the athletes and crews of the rally Paris-Dakar, which took place in the Andes thrice, were racing and working up to 5300 m. Many other occupations expose people to hypoxia. Summarized Küpper estimated the total number of employees exposed to any kind of hypoxia exceeding 100 million per year (Küpper, 2006).

Note: From tradition, there are two different approaches to categorize the severity of hypoxia. While any situation at real altitude differentiates 'low altitude' (0–1500 m), 'moderate altitude' (1500–3500 m), 'high altitude' (3500–5300 m), and 'extreme altitude' (>5300 m), the isobaric hypoxia differs as follows (mainly for technical reasons in fire protection): 20.9–17.0% (corresponding to 0–1700 m), 16.9–14.8% (corresponding to 1700–2800 m), 14.7–13.0% (corresponding to 2800–3800 m), 12.9–10.7% (corresponding to 3800–5300 m), and <10.7% (corresponding to >5300 m). Because these systems are well established in the respective user groups, the commission decided to use both unchanged and refer to the

respective system when specific topics of one or the other are addressed.

OXYGEN, OXYGEN CONCENTRATION, AND OXYGEN PARTIAL PRESSURE—SIMILARITIES AND DIFFERENCES OF THEIR PHYSIOLOGICAL EFFECTS

While mountaineers traditionally use altitude above sea level as a term to describe the extent of hypoxia, technicians prefer %O₂ (which means oxygen concentration in ambient air at sea level pressure) and physiologists use oxygen partial pressure (pO₂). The latter is the most accurate term as pO₂ is the one and only parameter which is of interest within normal atmospheric conditions, as first explored by Bert (1878), Mosso (1899), and Zuntz *et al.* (1906) and in 1925, Barcroft for isobaric hypoxia (Barcroft, 1925), but both altitude and %O₂ are very closely related to pO₂. Although %O₂ and altitude are less exact than pO₂, the resulting errors are far too small to have any consequence for occupational medicine. There are some minor physiological differences between isobaric and hypobaric hypoxia [e.g. in pulse frequency and breathing frequency, reviewed in Savourey *et al.* (2003)], but again these differences are far too small for any clinical consequences. Therefore, the factors can be used equivalently.

For the comparison of %O₂, which may be considered as 'simulated altitude at sea level' to that of 'real' altitude, the term 'corresponding altitude' should be used. The relationship between the parameters is illustrated in Fig. 1 and Table 1. Based on this relationship, the UIAA recommendation presented here provides altitude as the main parameter and %O₂ for isobaric conditions at sea level for technical applications. It should be noted that %O₂ refers to sea level conditions. If an oxygen-reduced atmosphere (isobaric conditions) is created at higher locations, a correction factor according to the respective altitude must be included. Table 1 provides the 'time of useful consciousness', which describes the period of time an unacclimatized person has at the respective oxygen conditions to 'escape' from hypoxia until severe impairment of consciousness or unconsciousness may occur.

It should be noted that there is no direct correlation between the decrease of inspired pO₂ and oxygen saturation (SaO₂). Several studies in the 'classic' area of high-altitude physiology have shown an increase of pulse rate and ventilation (frequency and volume) of ~6 to 8% at an altitude of ~2700 m (e.g. Glaisher, 1862; Bert, 1878; Viault, 1891; Miescher, 1893; Mosso, 1899; Jaquet, 1904; Zuntz *et al.*, 1906), but the sigmoidal form of the oxyhaemoglobin dissociation

curve and the later explored so-called 'Bohr effect' (left or right shift of this curve) cause a much lower decrease of SaO₂ at low or moderate altitude, where the ascent of the curve is low. Therefore, SaO₂ remains at >90% in healthy persons at ~3000 m (Fig. 2) (Küpper, 2006). This also remains constant at low workload (Küpper, 2006). Only if the person is loaded near his/her maximum workload does, pulmonary diffusion become a more important limiting factor, which can cause an additional decrease of SaO₂ (Küpper, 2006). For the recommendations presented here, the UIAA MedCom has defined the term 'mild hypoxia' as any kind of exposure where SaO₂ is ≥90%.

PATHOPHYSIOLOGICAL EFFECTS OF HYPOXIA

It should be emphasized that mild hypoxia is not normally a risk. For any risk estimation, at least a three-dimensional system should be taken into account, which includes independent variables such as altitude and the respective decrease of pO₂ and the duration of exposure and dependent variables such as an individual's own risk of symptoms. Several other variables have significant influence on the dependent variable, especially the acclimatization status of the individual. *Note:* All considerations given below focus on non-acclimatized persons. If a person is completely acclimatized to high altitude, there shouldn't be any risk even at altitude of ≥6000 m, if this person is exposed in isobaric conditions to an altitude or hypoxia corresponding to the altitude of acclimatization.

Extreme hypoxia (values >5000 m or well <11% O₂) may cause mental impairment up to unconsciousness within half an hour or less. While there is only marginal impairment at 5000 m, this problem increases significantly with increasing altitude as indicated by 'time of useful consciousness' in Table 1 (Amsler, 1971; Ernsting and King, 1994). On the other hand, these data suggest that this hazard does not exist if the person stays well <5000 m as most of employees do.

If non-acclimatized persons stay at altitude for several hours or days, altitude-related illnesses may arise. Because symptoms may only arise after 6–8 h at this altitude—often much later (>24 h)—most employees will be asymptomatic as they finish their daily work long before that may occur (Bartsch, 1990; Basnyat, 1993; Hackett and Roach, 2001; Maggiorini, 2001; Basnyat and Murdoch, 2003). Nevertheless, especially if sleep at altitude is necessary (e.g. businessmen at high-altitude destinations), this may happen. The risk increases with altitude. Above 2500–3000 m, AMS may occur, while high HAPE is very rare at this altitude [1:4000 nights at 3000 m (Hochstrasser

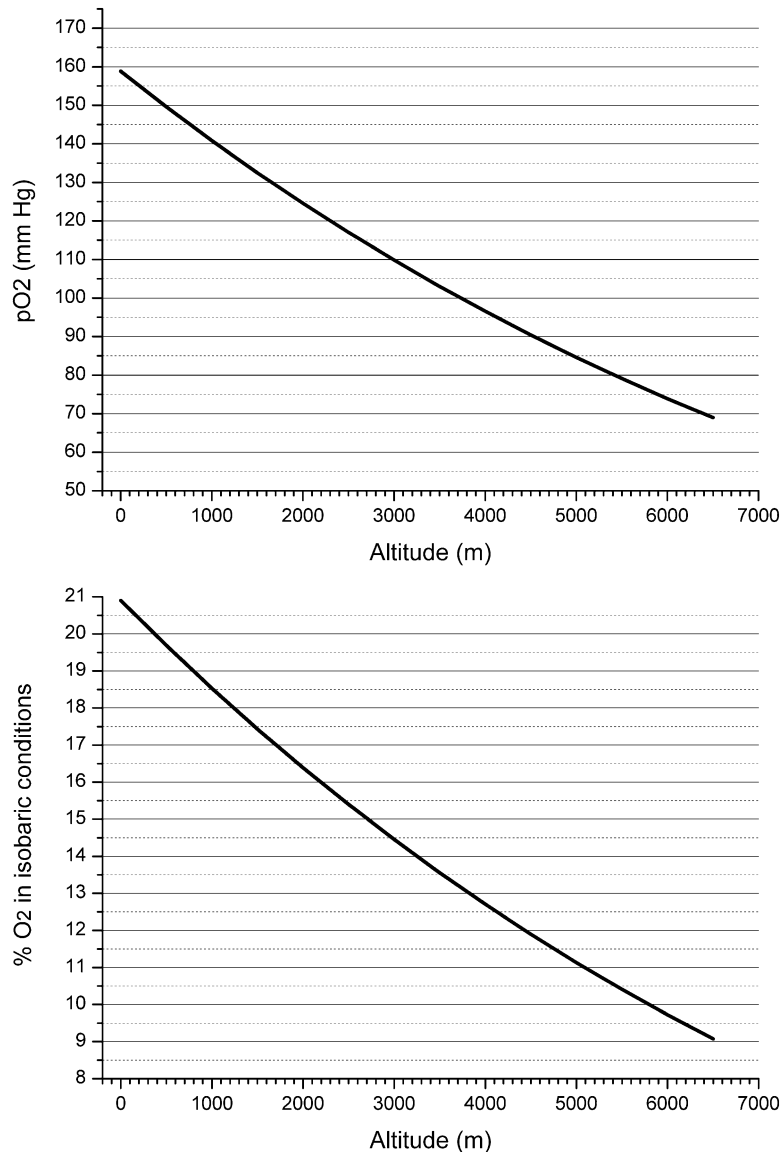


Fig. 1. pO₂ and isobaric %O₂ in relation to altitude. Graphs according to ICAO standard atmosphere as given by Ruff and Strughold (1944), Muller (1967), and Ernsting and King (1994) (see also Table 1).

et al., 1986)]. Normally, HAPE does not occur within <10–36 h of exposure and well >4000 m: if employees arrive by plane at 4500 m, the risk for severe HAPE increases to 1:600 (Hochstrasser *et al.*, 1986), and 30–57% will suffer from AMS (e.g. Maggiorini *et al.*, 1990; Basnyat *et al.*, 1999; Küpper and Classen, 2002; Savourey *et al.*, 2003; Küpper *et al.*, 2008c; Angelini and Giardini, 2009). On the other hand, these data suggest that some hours or even a night at 3000 m is relatively safe for unacclimatized but healthy persons. High-altitude cerebral oedema (HACE) happens

typically >5000 m and much later than AMS or HAPE (onset up to 72 h of exposure).

After several months of exposure, some people may develop chronic pulmonary hypertension and suffer from signs of insufficiency of the right ventricle (peripheral oedema, dyspnoea, cough, and angina pectoris), which is summarized as ‘high-altitude pulmonary hypertension,’ (HAPH), formerly called ‘subacute mountain sickness’. After years at altitude >3000 m, CMS (‘Monges Disease’) may arise (headache, poor concentration, dizziness, reduced work capacity,

Table 1. Atmospheric conditions according to ICAO standard atmosphere (Ruff and Strughold, 1944) and the time of useful consciousness for non-acclimatized persons (Amsler, 1971; Ernsting and King, 1994), which can be used to 'escape' from hypoxia if any health problem should arise. *Note:* There is no limitation of the time of useful consciousness up to 5000 m or 11.1% O₂, respectively. For corresponding O₂%, see also Fig. 1

(Corresponding) Altitude (m)	Atmospheric pressure (mm Hg)	pO ₂ (mm Hg)	%O ₂ , isobaric conditions, and sea level	Time of useful consciousness
0	760.0	158.8	20.9	No limitation
500	716.0	149.6	19.7	
1000	673.8	140.8	18.5	
1500	634.0	132.5	17.4	
2000	596.0	124.6	16.4	
2500	560.0	117.0	15.4	
3000	525.8	109.9	14.5	
3500	493.0	103.0	13.6	
4000	462.0	96.6	12.7	
4500	432.6	90.4	11.9	
5000	404.8	84.6	11.1	
5500	378.6	79.1	10.4	>30 min
6000	353.6	73.9	9.7	
6500	330.0	69.0	9.1	
7000	307.8	64.3	8.5	3–5 min
10 500	183.0	38.2	5.0	~1 min
12 900	123.5	25.8	3.4	15–30 s

cyanosis, clubbed/drumstick fingers, polycythaemia, and high haemoglobin concentration) (Monge *et al.*, 1992; Arregui *et al.*, 1994; Curran *et al.*, 1997; Moore *et al.*, 1998; Leon-Velarde and Reeves, 1999; Ge and Helun, 2001; Bernardi *et al.*, 2003). Retinal bleeding and other altitude-related problems occur at >7000 m only and therefore, these are normally not a topic of occupational medicine.

From several other fields of occupational medicine, it is proven that repeated exposures to moderate hypoxia do not have significant side effects. The biggest group of persons with such an exposure are pilots using small aircrafts without pressurized cabins or artificial oxygen. They are allowed to fly up to 4000 m and if they stay there as long as the range of the aircraft enables them, some of them complain about fatigue. All other complaints that may be triggered by hypoxia occur at extreme altitude and respective severe hypoxia only (e.g. Küpper and Classen, 2002; Küpper *et al.*, 2008c; Milledge and Küpper, 2008; Angelini and Giardini, 2009).

TYPICAL RISKS OF OCCUPATIONAL EXPOSURE TO HYPOXIC CONDITIONS

Based on the kinetics of altitude-related symptoms as described above, people at risk can be grouped into

four characteristic types of exposure (Fig. 3, Table 2). To do so, five important factors must be taken into account to differentiate the risk profile of exposure to hypoxia:

- Altitude (metre) or equivalent altitude (% O₂), respectively
- Duration of exposure
- Altitude profile/acclimatization (intermittent hypoxia included)
- Workload in hypoxic condition
- Native highlanders versus native lowlanders

Individual risks caused by pre-existing conditions will be discussed later [but we also refer to Milledge and Küpper (2008)]. With the five major points given above, at least four kinds of exposure groups can be established (Fig. 3), each with a completely different risk profile.

Extreme short exposure

Extreme short exposure normally takes place at altitude between 1800 and 2500 m and for a period of minutes to some hours. The most important kind of occupational exposure is business trips by car (mountain pass) or aircraft but also maintenance work at cable cars, service of ski slopes, or the associated infrastructure like restaurants, etc. Recently, isobaric

hypoxia of ~ 17 to 14.8% O_2 (± 0.2) is used more and more for the fire prevention of rooms; this exposes another group of personnel to hypoxic conditions corresponding to an altitude of ~ 1700 – 2700 m [based on International Civil Aviation Organization (ICAO) standard atmosphere, Fig. 1]. The duration of exposure here is defined by risk: taking the three-dimensional approach of the risk factors as described above, it is defined as a period which is known to be free of AMS symptoms. As most of the employees are ex-

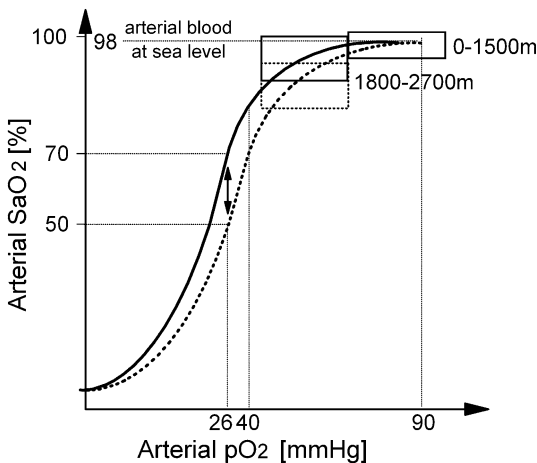


Fig. 2. SaO_2 with Bohr effect included: caused by an increase of 2,3-diphosphoglycerate and respiratory alkalosis SaO_2 at 2600 m does not drop to $\sim 85\%$ as expected without Bohr effect (dotted curve) but only to ~ 90 – 95% (solid curve). At higher altitude with pO_2 at ~ 40 mmHg, this effect becomes more important and at extreme altitude, it is the basic principle for survival as it shifts SaO_2 from ~ 50 to $\sim 70\%$ [double arrow; data from Hultgren (1997) and Küpper (2006)].

posed to a maximum of 2700 m or a respective 14.8% O_2 , the period of risk is proven to be much >4 h and therefore, any employee who spends his/her lunch break in normoxia will not develop AMS (e.g. Bartsch, 1990; Rabold, 1992; Basnyat, 1993; Bartsch, 1999; Hackett and Roach, 2001; Maggiorini, 2001; Basnyat and Murdoch, 2003; Küpper, 2006).

A total of ~ 4 billion aircraft passengers or billions of smokers worldwide, who easily show CO-haemoglobin levels of 10%, are exposed annually to such an extent of hypoxia. This is well within the range of the so-called 'threshold altitude', which is the (corresponding) altitude, where the body shows the first responses to hypoxia. Depending on the system observed, the threshold altitude varies between 1500 (slight increase in pulse rate at rest) to 2400 m (increase of erythropoietin serum concentration) (Gunga *et al.*, 1994; Sakata *et al.*, 2000). In conclusion, altitudes around the threshold do not cause any risk for healthy people by hypoxia, but they cause a physiological response on the body. It also does not cause risk for people with chronic diseases of moderate severity (Milledge and Küpper, 2008). Severely ill people will be discussed later. The threshold for altitude disease is somewhere >2500 m depending on the kind of disease, individual factors, and the duration of exposure. The latter is usually much longer than some hours; therefore, altitude disease should be extraordinary rare in this group of exposure (in contrast to the group of limited exposure, see below).

In some special circumstances, there are some employees exposed to equivalent altitudes between 2700 and 3800 m in rooms for fire protection. This

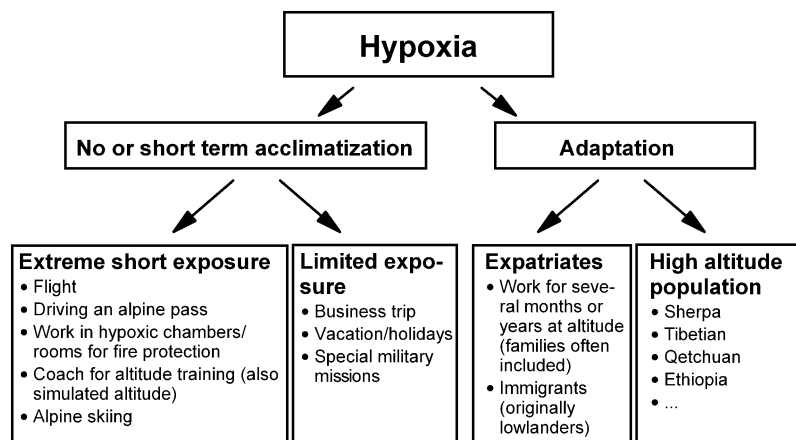


Fig. 3. Different types of occupational exposure to hypoxic conditions (see also Table 2). *Note:* Because of a multitude of influencing factors (individual, environmental, and work-related), there would be no advantage for occupational medicine if the classification of the types of exposure would be described in more detail or based on individual physiological data.

Table 2. Characteristics of the types of altitude or hypoxia exposure

Group	Typical (equivalent) altitude and % O ₂ (isobaric conditions)	Typical duration of exposure	Typical risk
Extreme short exposure (aircrafts, cable cars, skiing, road traffic, and fire protection rooms)	1800–2600 m, 18–15%	Minutes to some hours	Pressure changes (persons with infection of the upper airways) No risk by hypoxia for any person who does not have severe cardiopulmonary illness
	2600–3800 m, 15–13%		No risk for healthy persons
Limited exposure	2000–3000 m	Days to weeks	AMS if the unacclimatized person sleeps at this altitude Beside AMS, there is normally no risk to any person who does not have severe cardiopulmonary illness (HAPE is extremely rare at this altitude)
Expatriates	3000–4500 m	Years	HAPH Insufficiency of the right ventricle CMS (Monge's Disease)
Altitude populations	>3000 m	Several generations	CMS (see above) Re-entry pulmonary oedema

situation is limited by the duration of exposure to a maximum of a few hours, often for <60 min. As for any room equipped with hypoxia systems for fire protection, these employees can leave immediately at any time and with plenty of time (see Table 1) if they do not feel well. Nevertheless, any break should be spent outside of the hypoxic area (e.g. lunch).

Some common activities expose people to even higher altitude, e.g. skiing at 3800–4000 m or road or railroad traffic [\sim 3000 m (Europe), \sim 4000 m (USA and Tibet), and >5000 m (South America)]. Here, the main problem may be the change of pressure, especially for children or persons suffering from an infection of the upper airways.

The longest exposure of this type (extreme short exposure) is long distance flights, which could also be classified as 'limited exposure'. Data exist that some airlines operate at an even higher cabin altitude than the limit of 2400 m, which is given by the ICAO regulations, especially when using modern aircraft (Cottrell, 1988).

There is one other small subgroup of people who are a special case: Persons who coach people, normally mountaineers, who pre-acclimatize for extreme altitude expeditions. This is increasingly used, often in facilities that offer isobaric hypoxia. This may expose participants to an altitude of \geq 5300 m. In most cases, the exposure of employees is limited for some minutes to up to half an hour. With the special advantage of isobaric hypoxia that these employees can easily escape to normal atmospheric conditions at any time if they should feel unwell. People with pre-existing conditions may suffer from severe problems at this altitude

while healthy persons should tolerate this exposure well: The duration of exposure is too short to develop AMS and it is also well below the limits of the period after which significant neurological risks may arise (Table 1).

As stated above, the exposure time normally does not exceed a few hours. Up to 3000 m (and even higher), there is no risk in developing any altitude disease during this period (Rabold, 1992; Basnyat, 1993; Hackett and Roach, 2001; Basnyat and Murdoch, 2003). The main problem for this group may be the acute change of pressure, especially if a person is suffering from the common cold. Normally, everybody—including pregnant women (Jean *et al.*, 2005, 2008) and children (Meijer and Jean, 2008)—will feel well at these altitudes. Exceptions are people with severe pre-existing diseases (see specific paragraph below and Table 3).

With increasing altitude, the maximal workload decreases from -10 to -15% per 1000 m of altitude (beginning at 1500 m above sea level) with highly trained people losing the most power (Fig. 4) (Kuhne, 1877; Bert, 1878; Loeb, 1896; Zuntz *et al.*, 1906; Buskirk *et al.*, 1966, 1967; Jackson and Sharkey, 1988; West, 1990; Küpper, 2006). Since most work performed at altitude is of limited load on the human body [estimated 0.5 – 1.0 W kg⁻¹ body weight, (Küpper, 2006)], this effect does not limit most of the previously described activities at altitude. During very demanding or exhausting work at >3000 m, O₂ diffusion and reduced contact time of the erythrocytes in the pulmonary capillaries create more limiting factors for people doing intense work as they

cannot stabilize their SaO₂ at a level which can be expected for the respective altitude (Küpper, 2006). As a result, their SaO₂ will decrease. Working conditions like these are exclusively for healthy people (Küpper, 2006) and even then the limited (decreased) workload must be taken into account when the required activity and the resources are planned (Fig. 4). If possible, only well acclimatized persons should perform such a work.

Limited exposure

The typical exposure of the 'limited exposure group' is 2000–3000 m for a few days or weeks.

Table 3. Examples for permanent or temporary contraindications for altitude sojourns of the 'extreme short exposure group' or 'limited exposure group' as defined above (Milledge and Küpper, 2008) [according to the recommendations for aircraft travellers (Siedenburg, 2009)]

Diagnosis	Period for which altitude/hypoxia should be avoided
Stroke	3 months
Myocardial infarction	6 weeks, if no complications 10 weeks (or more) in the case of complications (e.g. significant arrhythmia)
Aortocoronary bypass operation	2–3 weeks
Percutaneous transluminal coronary angioplasty	3 days
Stent	3–10 days
Pace maker implantation	After a check for correct function is ok
Acute broncho-pulmonary infections	No exposure until recovery
Asthma (stress induced)	No exposure, if not sufficiently treated

At some places, these people will be exposed to even higher conditions of 4000–5000 m, e.g. at Colorado or South America. Examples of locations for businessmen or normal travellers (not mountaineers) are given in Fig. 5.

In contrast to the 'extreme short exposure group', the combination of altitude and duration of exposure can potentially cause altitude-related diseases (AMS). An increase of the pulse rate for ~12 to 14% should be expected at 2500–3000 m (e.g. Glaisher, 1862; Muller, 1967). A comparable increase of minute ventilation and breathing frequency will occur (Rupwate *et al.*, 1990). Oxygen saturation will decrease only for ~6 to 8% of the saturation measured at sea level and be stable at 90–94% (Horii *et al.*, 1994; Cottrell *et al.*, 1995). A slight decrease of aerobic performance (without significant effect on performance at work) must be expected at 3000 m (Fig. 4), but no significant effect on psychomotoric functions (Tune, 1964; Waanders and Riedmann, 1994). There are some data, which indicate a slight impairment in the coordination of complex movements, especially when they have to be performed very quickly.

The main risk for the limited exposure group is the development of altitude diseases, most often AMS. HAPE is extremely rare at this altitude [1:4000 nights at 3000 m (Hochstrasser *et al.*, 1986)] as it normally occurs >4000 m. A significantly increased risk exists for any person who had a rapid ascent profile, e.g. businessmen arriving by aircraft at high-altitude destinations like La Paz. If the arrival destination is ~4500 m, the risk for HAPE with severe symptoms increases to 1:600 (Hochstrasser *et al.*, 1986) [signs for HAPE in X-ray up to 31.7% (Bircher *et al.*, 1994)] and 30–57% will suffer from AMS (Hackett

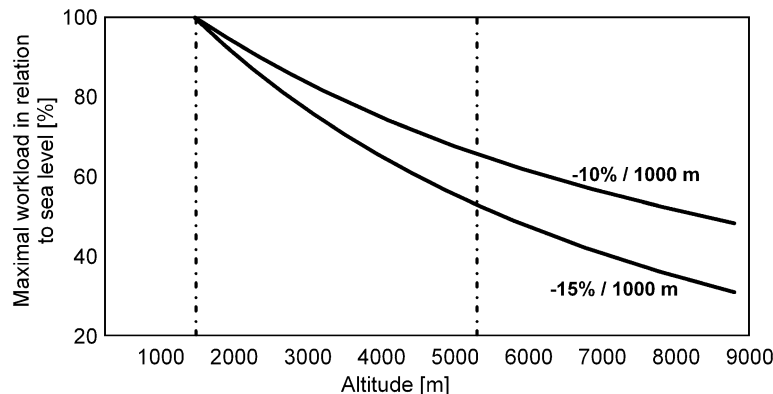


Fig. 4. Decrease in maximal workload at altitude (Buskirk *et al.*, 1966; Buskirk *et al.*, 1967; Jackson and Sharkey, 1988; West, 1990; Küpper, 2006). At above ~7500 m, the maximal workload is decreased in such an extent that rescue of a stranded person is impossible in most cases. 1500 m: 'threshold altitude'; 5300 m: limit of complete acclimatization/permanent stay.

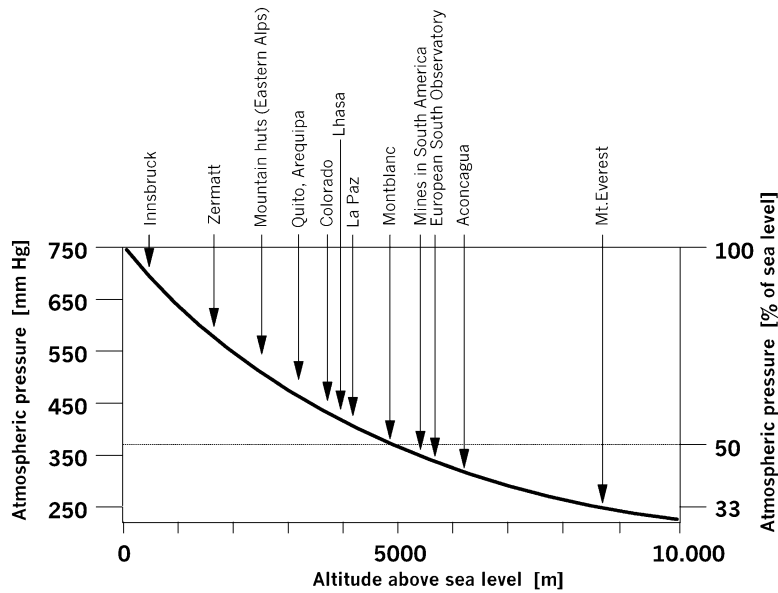


Fig. 5. Examples for destinations of businessmen or normal travellers. *Note:* Some working places e.g. at mines in South America are higher than the highest mountains in the European Alps.

and Rennie, 1979; Maggiorini *et al.*, 1990; Basnyat, 1993; Basnyat *et al.*, 1999; Schneider *et al.*, 2002). On the other hand, these data indicate that some hours or even a night at 3000 m is relatively safe, at least for healthy people. Some people with pre-existing diseases may be at specific risk (Milledge and Küpper, 2008). Nevertheless, any strategy for occupational health and safety for the limited exposure group has to focus on AMS.

Expatriates and immigrants

Expatriates and immigrants in this paper are defined as persons who migrate as lowlanders to high-altitude regions, normally >3000 m. Some of them are living >4500 m. The duration may be for several months but is frequently for years. Normally, this group will not suffer from acute altitude diseases as they are acclimatized completely except during the first day after arrival if the arrival was characterized by 'too fast too high'.

In many cases, the employees are attended by their families. As a consequence, pregnancy may be a problem (Jean *et al.*, 2008) and more often children of different age will be exposed to high altitude. After a while they may suffer from specific diseases of the cardiopulmonary system: HAPH (formerly called subacute mountain sickness) with acute bouts of high blood pressure in the pulmonary vessels (Sui *et al.*, 1988) and high-altitude heart disease. For details, see Meijer and Jean (2008).

After some months at high-altitude, adults may develop the symptoms of subacute mountain sickness. Caused by chronic pulmonary hypertension, these patients suffer from signs of insufficiency of the right ventricle (peripheral oedema, dyspnoea, cough, and angina pectoris). After years at altitude, CMS (Monge's Disease) may arise (headache, poor concentration, dizziness, reduced work capacity, cyanosis, clubbed/drumstick fingers, polycythaemia, and high haemoglobin concentration) (Monge *et al.*, 1992; Arregui *et al.*, 1994; Curran *et al.*, 1997; Moore *et al.*, 1998; Leon-Velarde and Reeves, 1999; Ge and Helun, 2001; Bernardi *et al.*, 2003).

Altitude populations

Altitude populations are defined as populations living for several generations (some for >30 000 years) at altitude >3000 m. These people show long-term and genetic adaptations. Most health problems are not altitude related but caused by socio-economic factors [e.g. chronic bronchitis, Kangri carcinoma (skin cancer in cicatrice caused by multiple burning either by carrying a small oven heated with charcoal (kang) under the coat or by sleeping around a fire and burning the belly when the person turns around during sleep) etc.]. While altitude-related health disorders are very uncommon in Tibetans and occupational medicine is not yet established in Ethiopia, South American highlanders—many of them working in mines—have been studied and are of special interest here. Some

of them may develop CMS (see above). Another specific problem is re-entry pulmonary oedema where highlanders and also expatriates or immigrants who visit friends or relatives near sea level are of special risk when they return home at high altitude. The symptoms are the same as that for HAPE.

Note: In contrast to the belief of most Westerners, many porters in the Himalayans are not true Sherpas anymore and are immigrant or expatriate lowlanders! They may suffer from the same altitude-related risks as any other visitor (Basnyat and Litch, 1997).

PROBLEMS WITH PRESENT GUIDANCE

Up until now, there was no single guidance worldwide which took into account the multidimensional specificities of hypoxia exposure. Some papers are based on guidelines established for mining or work in storage tanks, silos, reaction vessels, enclosed drains, or sewers, for fire or explosions (e.g. HSE, 2005). These papers assume that the 'lack of oxygen' causes danger. All guidelines ignore that there is no risk for altitude disease when the duration of exposure is limited for some minutes or hours (e.g. FPA, 2005; HSE, 2005; Bilzon and Stokes, 2008) and most workers have finished their work long before this may happen (Bartsch, 1990; Basnyat, 1993; Hackett and Roach, 2001; Maggiorini, 2001; Basnyat and Murdoch, 2003). Things become critical when the science is misinterpreted within these papers: concentration of oxygen <16% does not lead to unconsciousness and death (HSENI, 1999). This may be true for extreme hypoxia well <10.5% or 5500 m but not for 16% as stated in HSENI (1999) (see also Table 2).

Some recommendations state that HAPE or HACE 'could be particularly problematic' (Bilzon and Stokes, 2008), which >140 years of altitude research proves to be incorrect. Interestingly, the same report includes the statement that '... it is unlikely that working in conditions of 13–15% oxygen represents a meaningful risk' [chapter 2.6.6 in Bilzon and Stokes (2008)]. The recommendation to use self-containing breathing apparatuses at oxygen concentrations of 13–15% would result in nearly exact the amount of additional oxygen which is needed to carry the 16.8 kg equipment and to breath through its mask. A medical examination is suggested to exclude pre-existing diseases and special investigations are recommended if pathologies were found in the screening. Although not referenced, the latter mainly follow international guidelines, such as Milledge and Küpper (2008). It is interesting, that the authors also mention possible health benefits of long-term work in hypoxic conditions as some recent papers about hypoxia training indicate (e.g. Boyer and Blume,

1984; Rose *et al.*, 1988; Kayser, 1992, 1994; Armellini *et al.*, 1997; Schobersberger *et al.*, 2003; Haufe *et al.*, 2008; Netzer *et al.*, 2008).

Other reports clearly state that there is no increased risk for employees in a 17–15% low oxygen atmosphere environment (FPA, 2005). Consequently, it is recommended to perform health assessments only for individuals who will be working and performing full time strenuous work in a 15% low oxygen atmosphere environment and full time work in a 13% low oxygen atmosphere environment. The health assessment is not necessary if the oxygen concentration will be 17%, where the exposure will be <2 h day⁻¹ (FPA, 2005).

The Austrian and German Governments (Huke *et al.*, 2005) require a medical check for any person working at <17%, while the Swiss regulations do so at <18% (SUVA, 2009). Analysed in detail, the German regulation (Huke *et al.*, 2005) is not an official recommendation (just an internal letter for the ministry) and shows lack of knowledge about the physiology of hypoxia. Therefore, some recommendations derived from Huke *et al.* (2005), such as Angerer and Nowak (2003), include the same problems. From the viewpoint of physiology, the U.S. recommendations given by OSHA, which apply for confined spaces and not just for hypoxia, have strange implications. If any atmosphere with <19% O₂ is life threatening, as stated in these papers, humans could not live in many parts of the USA and American businessmen visiting Europe should do so by ship, because they would not survive the flight (OSHA, 1993a, b).

There is no guidance worldwide, which takes into account whether a person is able to 'escape' from hypoxia at any time or not for the risk assessment. With this aspect, a businessperson arriving at a high-altitude destination like La Paz is significantly more at risk than a maintenance worker in a room with hypoxia for fire protection.

It is surprising that nobody brought to the attention of the authors when the several national guidelines were established that high performance tasks like piloting an aircraft is allowed up to 4000 m (13 000 ft, equivalent to 97 mm Hg of pO₂ or 12.5% O₂) without a pressurized cabin or supplemental oxygen in most countries of the world (in some of them even higher, e.g. South America). The whole discussion is dominated by (fictive) risk assumptions, while some data suggest that intermittent hypoxia of moderate degree also has some benefit instead of risk for persons who are regular exposed as there are an amelioration of the lipid profile, insulin resistance, leptin, body weight, and others (e.g. Boyer and Blume, 1984; Azevedo

et al., 1995; Armellini *et al.*, 1997; Grosfeld *et al.*, 2002; Schobersberger *et al.*, 2003; Simler *et al.*, 2006; Yingzhong *et al.*, 2006; Netzer *et al.*, 2008). In conclusion, a more detailed specialized analysis of the individual exposure is necessary to provide adequate advice for health and safety.

ASPECTS OF OCCUPATIONAL SAFETY AND HEALTH

In contrast to any other occupational exposure where less exposure normally means less risk, employees at altitude benefit if they are exposed as often as possible to hypoxia because a partial adaptation can be expected, although scientific data about intermittent hypoxia are limited (Richalet *et al.*, 1992; Beidleman *et al.*, 2004; Jones *et al.*, 2006; Muza *et al.*, 2006). Comparisons between the several studies are also limited because of the altitude profiles; the duration of exposure and the normoxic phases between exposures are different; and the studies prove that repetitive exposure to hypoxia increases acclimatization and decreases the risk for AMS. In most cases, the hypoxic exposure was equivalent to an altitude of 4000 m, but the duration per day and the total period of exposure were very different (≥ 3 h day⁻¹ for 6–20 days) (Levine *et al.*, 1992; Richalet *et al.*, 1992; Beidleman *et al.*, 2004; Jones *et al.*, 2006; Muza *et al.*, 2006; Katayama *et al.*, 2007). Even short exposures 2–4 h are expected to have some effect on acclimatization (Burtscher *et al.*, 2008). This corresponds to findings in physiology and molecular biology which proved effects of intermittent hypoxia with simulated altitude for hypoxic ventilatory drive, hyperventilation, and arterial oxygen saturation (Levine *et al.*, 1992; Richalet *et al.*, 1992; Garcia *et al.*, 2000a; Garcia *et al.*, 2000b; Bernardi *et al.*, 2001a; Bernardi *et al.*, 2001b; Beidleman *et al.*, 2004; Jones *et al.*, 2006; Lusina *et al.*, 2006; Muza *et al.*, 2006) or for hypoxia inducible factor alpha (HIF-1 α), 2,3-diphosphoglycerate, and others (Chilov *et al.*, 1999; Richard *et al.*, 1999; Hofer *et al.*, 2001; Heinicke *et al.*, 2002) during several hours. A detailed survey about this topic is given in (Küpper and Schoffl, 2009).

All persons working at altitude or in hypoxic conditions should be advised to drink enough to keep their fluid balance stable. *Note:* In contrast to common medical thinking, it is not the heart, which carries the greatest risk for people at altitude. While the myocardium is able to handle astonishing degrees of hypoxia, the lung may be the limiting factor in the case of a pre-existing disease (Milledge and Küpper, 2008).

Extreme short exposure

As mentioned above, the situation for this group may be best illustrated by the situation inside an aircraft's cabin (this excludes very high workload subjects and coaching of athletes who acclimatize to extreme altitudes, see below). In this

• Vital capacity	• 3 l
• FEV1	• 70%
• SaO ₂	• 85%
• pO ₂ art	• 70 mmHg

well-studied situation, there are the following minimum requirements given by aviation medicine (values for sea level in adults) (Siedenburg, 2009):

Haemoglobin should be >10 g dl⁻¹ and erythrocyte count >3 million μ l⁻¹ (Siedenburg, 2009), but strictly spoken, this focuses an acute loss of blood while both are relative contraindications in the case of a chronically anaemic fully compensated patient who may be completely adapted.

For exposure up to 2700 m or 14.8% O₂, a check-up by occupational medicine is considered to be necessary only in cases, if the worker is obviously unfit. Only very severe cardiopulmonary diseases [New York Heart Association (NYHA) stages III–IV, (N.N., 1994)] would exclude the person from occupational exposure to hypoxia (Milledge and Küpper, 2008) and this situation is easily identifiable by others as these patients will suffer from significant shortness of breath after climbing one floor and normally they appear unfit for any work. If in doubt, the person who supervises the respective work and the employee may send the unfit person to occupational medicine before he or she enters a hypoxic environment. This also includes business people who are due to visit high-altitude destinations.

On the other hand, if the employee performs any aerobic endurance sport regularly and without problems, there is no doubt—without any other medical investigation—that there is no risk if this person is exposed within the conditions as described for the 'extreme short exposure group' up to 2700 m or ~ 15 to 14.8% O₂. Laboratory or technical investigations by occupational medicine are only required in

cases, which are not completely clear as described above. These should include:

- Significant anaemia: blood status
 - exclude sickle cell anaemia if the person belongs to a group where this is endemic
- Pulmonary hypertension: echocardiography
- Pulmonary disease: spirometry and ergometry
- Cardiac disease: ergometry, (stress) echocardiography

If a person is not perfectly fit, this does not necessarily exclude this employee from work in hypoxia, but then a more careful fitness check should be performed and the expected workload estimated, e.g. according to (Spitzer *et al.*, 1982). For employees with a body mass index within normal range, a minimum fitness of 75 W is considered to be sufficient for any work without additional workload, e.g. pure supervising, while a minimum of 125 W is recommended for low intensity activity and 200 W for high intensity work (e.g. carrying heavy loads) [Spitzer *et al.*, 1982; Küpper *et al.*, 2009]. For standardized environmental conditions like hypoxic rooms, the procedure for occupational health and safety as given in Fig. 6 can be simplified to the flowchart given in Fig. 7.

If employees are exposed to equivalent altitudes of 2700–3800 m (14.8–13% O₂, respectively), a consultation with a physician for occupational medicine and with experience or training in hypoxia or altitude medicine is mandatory (Küpper *et al.*, 2009, 2010). The medical check should include:

- The employee's medical history:
 - Any indicators for cardiopulmonary diseases or for significant limitations of maximum workload? (Sports?)
 - Any significant disease or surgery in the last year?
 - Any problems during altitude sojourns in the past?
 - High or extreme workload at altitude expected?
- Red blood cell count
- Ergometry
- Spirometry

As VO₂max is the limiting factor at high altitude, ergometry and spirometry may be combined as spi-roergometry. Due to the loss of work capacity at altitude (e.g. in isobaric hypoxia), a higher minimum fitness is necessary at sea level. A total of 100 W are considered to be sufficient for supervising or similar activities, 150 W for low intensity, and 200 W for high intensity work (Spitzer *et al.*, 1982; Küpper *et al.*, 2009, 2010). For employees working with no or low workloads in isobaric environment, a break

of 15 min every 2 h in a normoxic environment is recommended (which, of course, is impossible for work at real altitude). For high intensity activities, there should be a break in normoxic conditions for 30 min every 2 h (Küpper *et al.*, 2009, 2010).

Employees who go >3800 m (respectively work at <13.8% O₂) should be checked as mentioned in the previous section. For 3800–5300 m, the minimal workload at sea level should be 125 W for supervision or similar tasks and 200 W for low intensive work (Spitzer *et al.*, 1982; Küpper *et al.*, 2009). High intensive work is for fully trained and acclimatized people only and without any cardiopulmonary disease (Küpper *et al.*, 2009, 2010). For supervision, a break of 15 min every 2 h in normoxic conditions is sufficient, but for any higher workload, it should be extended to 30 min (Küpper *et al.*, 2009, 2010).

Any exposure >5300 m or at <10.7% O₂ requires completely acclimatized and fully trained employees without any cardiopulmonary disease for any expected workload. The significant decrease of work capacity (~50% compared to normoxia or respective sea level!) should be taken into account when planning such tasks. At altitudes, which are normally visited for extreme short duration (1500–3000 m), the maximal workload is only marginal impaired (Fig. 4). Therefore, the recommendations given for demanding work (e.g. in Spitzer *et al.*, 1982) can be used without modification. Above that the reduction of 10% workload per each 1000 m, above 1500 m should be added to the minimal requirements, e.g.:

If a minimal requirement for a certain work at sea level is estimated as 2 W kg⁻¹ body weight and this work shall be done at 4000 m, the estimation is as follows:

$$(4000 - 1500)/1000 = 2.5; 2.5 * 10\% = 25\%;$$

$$2 \text{ W/kg} + 25\% = 2.5 \text{ W/kg}.$$

At sea level, this employee must be able to provide at least 2.5 W kg⁻¹ to be able to do the respective work at 4000 m.

Since hypoxic chambers are increasingly available (e.g. rooms or training centres for hypoxia training), employees who shall be exposed to <12.9% or >3800 m should be exposed to well-controlled hypoxia once before their exposure at work. The exposure must take into account the kind of work and the expected duration and especially the (equivalent) altitude (pO₂) of the exposure during work: for a task to be

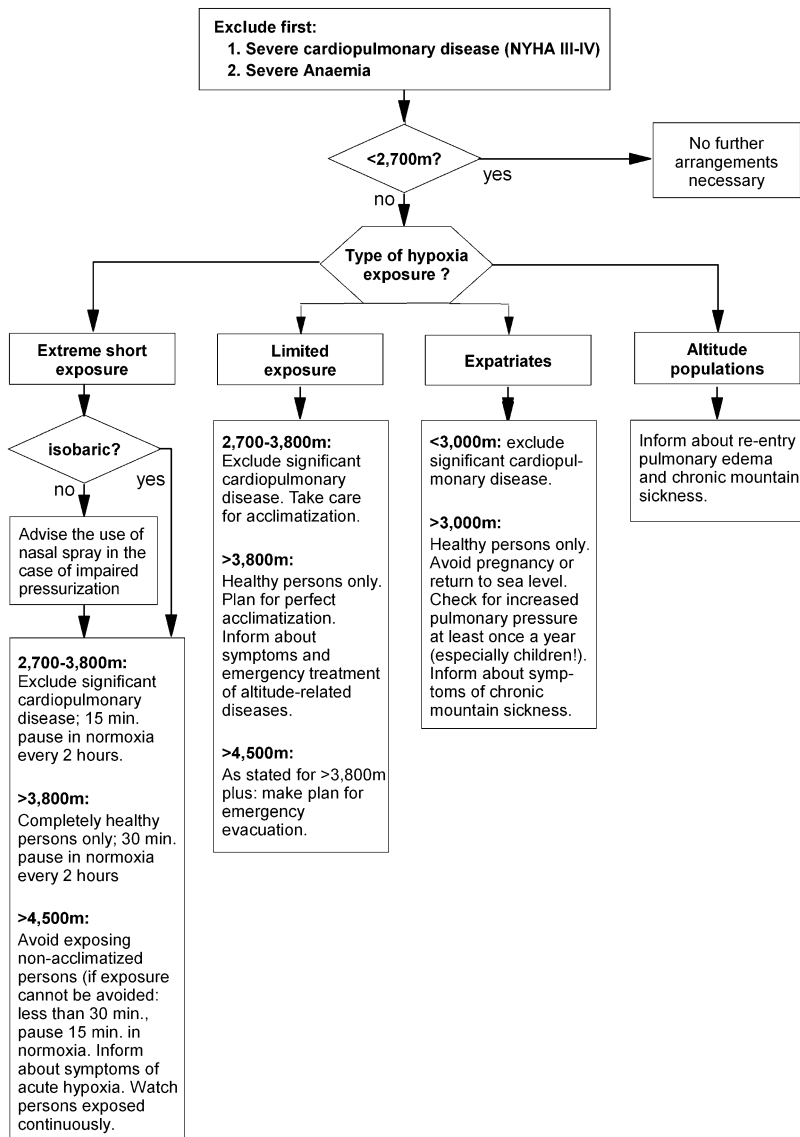


Fig. 6. Occupational health and safety for work in hypoxia.

performed in a controlled environment (hypoxic rooms) for a limited duration, an acute exposure for 1–2 h at the (equivalent) altitude where the work will be performed later should be sufficient. During exposure, the person should be monitored for SaO_2 , pulse rate, and altitude-related symptoms by persons with adequate skills in altitude medicine and supervised by a physician. Persons with cardiopulmonary diseases >NYHA I, anaemic or pregnant persons should not be chosen for work at high altitude or hypoxia which corresponds to >3800 m or <13% O_2 (Küpper, 2005; Jean *et al.*, 2008; Milledge and Küpper, 2008).

Any employee should be advised to leave hypoxic areas if he/she feels unwell. Retreating to a normoxic area as soon as possible is the most effective therapy in such a situation. As altitude-related diseases never start suddenly, any employee will have plenty of time to leave hypoxia (see also Table 2). It is not necessary to have a stand-by 'rescue team'. If the symptoms recover completely after $\frac{1}{4}$ – $\frac{1}{2}$ h, the person can re-enter, if necessary. If the subject does not recover within $\frac{1}{2}$ h, he/she should be advised to consult a physician who is a specialist in altitude medicine and occupational medicine before the next exposure.

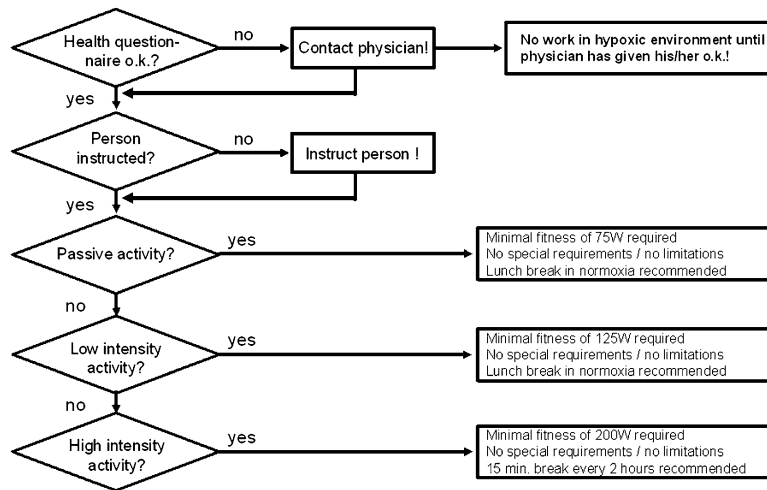


Fig. 7. Flowchart for occupational health and safety for standardized conditions at 16.9–14.8% O₂ or 1700–2700 above sea level [Küpper *et al.*, 2009].

If the employee cannot escape for any reason at >3800 m (e.g. work in remote regions at high altitude or overnight stay of unacclimatized businessmen at high destinations), an oxygen bottle and a mask with reservoir balloon (e.g. Venturi mask) may be added to the first aid equipment and at least one person of the team must get the instructions on how to use this equipment. A device for immediate and easy communication with a doctor or rescue team (radio, mobile phone, etc.) is recommended.

People with fairly advanced pre-existing conditions need detailed analysis of their actual health status before entering hypoxic environments. Those with cardiopulmonary diseases are of special interest. According to stages specified by the Criteria Committee of the NYHA, the following limitations for any exposure should be considered (NYHA, 1928, 1994; Miller-Davis *et al.*, 2006):

- NYHA I (no symptoms): no limitations at altitude, except high intensive activity at high altitude (>3800 m)
- NYHA II (symptoms during moderate workload): no limitations at altitude for activities of minor workload, take caution at >3800 m or <13% O₂.
- NYHA III–IV (symptoms during minimal workload or at rest): contraindication for altitude. Diagnoses and situations, which are a permanent or temporary contraindication, are given in Table 2. We also refer to the recommendations given in (Milledge and Küpper, 2008).

Persons with pulmonary hypertension should avoid altitude or hypoxia, at least for overnight stays. Table 3 gives an overview about some important permanent or temporary contraindications for hypoxia exposure. For details about several other pre-existing conditions and individual risks (diseases, pregnancy, children, etc.) at altitude, see also Jean *et al.* (2005, 2008), Meijer and Jean (2008), Milledge and Küpper (2008), and Angelini and Giardini (2009).

Facilities for training and acclimatization, which typically expose employees (and clients) to >4500 m should consider a safety concept during construction. At extreme altitude or severe hypoxia, the persons exposed should be observed for safety by a ‘rescue person’ who is outside the isobaric hypoxia but in permanent contact to the person(s) inside. For optimum supervision rooms, isobaric hypoxia should be constructed with a big window to the next room. Above 4500 m, safety may be further increased if an oxygen bottle and a mask is available. Above 4500 m, a specialized high-altitude physician should be on call. Above 5000 m, he/she should be on scene.

Employees working in extreme conditions need to be educated about symptoms and management of acute hypoxia. Again, if they work regularly in such conditions (e.g. every day 2–3× for 15–60 min or even more) a benefit by partial acclimatization can be expected (although data are not yet sufficient to recommend details).

Limited exposure

As this group goes to comparable altitude as the ‘extreme short exposure group’, the minimal

requirements of the cardiopulmonary system and the exclusion criteria (Table 3) are the same (Milledge and Küpper, 2008). Special attention should be paid to persons who might be suspected for obstructive sleep apnoea as this is often combined with pulmonary hypertension. The later will increase significantly at altitude. As mentioned above, AMS is a risk for this group, which cannot yet be predicted sufficiently by any medical investigation. Here, preventive occupational medicine includes detailed advice about the symptoms of AMS and how to treat them (Küpper *et al.*, 2008a). If possible, those persons who are responsible for the management of the specific work should be contacted to provide such information and an adequate ascent profile should be included in the plans. This may include an extra day on arrival and an overnight stay at intermediate altitude. If an immediate ascent and overnight stay >2500 m cannot be avoided, prophylaxis with drugs may be considered [acetazolamide 125 mg bid (Basnyat *et al.*, 2003; Bartsch *et al.*, 2004; Küpper *et al.*, 2008a)].

It should be mentioned here that some facilities, where people work at high altitude, provide oxygen-enriched rooms (e.g. some mines or telescopes in the Andes). Every additional 1% of oxygen corresponds to a 'reduction' of 300 m of altitude without increasing the risk of fire (at least within a wide range). With this technology, some facilities provide an interior environment, which corresponds to 3000 m, which is well tolerated.

If the person will be exposed without having the chance to escape from hypoxia (e.g. business trips to destinations at high altitude), an ascent profile according to international recommendations (e.g. (Küpper *et al.*, 2008a) should be an integral part of the strategy when the respective work is planned. If the place of work is situated >3800 m, the person should sleep at least one night under controlled conditions (hypobaric room at a training centre with physicians experienced in altitude medicine) at the respective equivalent altitude before his/her first departure to such places. Depending on the final altitude, this may include several nights in hypobaric conditions to realize an altitude profile and acclimatization according to the 'Gold Standard' as recommended (Küpper *et al.*, 2008a).

Employees should be advised to contact an experienced high-altitude physician in the event that he/she does not feel well at high altitude and cannot descend. Painkillers, nifedipine, dexametasone, and acetazolamide and information on how to contact the physician to manage an emergency should be given to him/her before departure for any destination >3800 m. Below 3800 m, a standard painkiller (no aspirin at altitude!)

should be sufficient (Küpper *et al.*, 2008a). For some destinations, where portable hyperbaric chambers are available, the employees should be instructed in detail how to use them safely (Küpper *et al.*, 2008b).

Expatriates and immigrants

This group should be informed about AMS as described above. Before they leave, they should get a more detailed medical examination, especially with electrocardiography and echocardiography included. This aims at two topics: (i) to exclude pulmonary hypertension and (ii) to get initial values for a comparison with later controls. Subacute altitude disease, the main risk for this group, causes a hypertrophy and dilatation of the right ventricle, a pulmonary hypertension, and sometimes a pericardial effusion. In many places where these expatriates work there will be no possibility for echocardiography. In this situation, a follow-up investigation may be performed during a holiday trip home or similar convenient time. A control echocardiography should be performed at least once a year or if symptoms arise. Note that accompanying children need special attention (Meijer and Jean, 2008). If any pathologies, which indicate increased pulmonary pressure or right ventricle hypertrophy or dilatation, are found at echocardiography, the patients should be advised to leave their high-altitude residency as soon as possible.

Altitude populations

As mentioned above, altitude-related problems are rare in this group. Employees descending from altitude for holidays or for other reasons for more than a week should be advised to avoid re-entry HAPE. They should also be trained in First Aid if a HAPE should occur, especially in the use of oxygen an Nifedipin or—if available—in the use of a portable hyperbaric chamber (Küpper *et al.*, 2008a, b).

South American highlanders should be surveyed by occupational medicine for CMS. As a minimum, these checks should include an analysis of haematocrit, haemoglobin, and erythrocyte cell count and should be performed annually. If symptoms arise which suggest CMS additional echocardiography should be performed, if possible.

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