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ENT indications for Hyperbaric Oxygen Therapy

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Abstract. *ENT indications for Hyperbaric Oxygen Therapy*. Hyperbaric Oxygen (HBO) therapy is a treatment where patients breathe 100% oxygen while exposed to high environmental pressure in a hyperbaric chamber. This hyperoxygenation has several beneficial effects as an adjunctive treatment in a number of ENT-related conditions and diseases. These can be summarized as anti-ischaemic effects (delivery of oxygen to otherwise ischaemic tissues, reduction of ischaemia-reperfusion damage), anti-infectious effects (bacteriostasis, improved leucocyte phagocytosis bactericidal activity and optimization of antibiotic therapy) and wound-healing effects (stimulation of granulation tissue formation and stabilization).
Since HBO therapy has a clear physiologic rationale, a demonstrated effect (although difficult to "prove" with placebo-controlled randomized trials) in certain indications and certain side-effects, it is proposed that it should be considered an integral part of the (combined surgical and pharmacological) treatment of patients, and not simply as a supplementation of oxygen. Furthermore, the importance of a well-trained medical and technical staff to ensure proper selection and the correct follow-up of patients should not be underestimated.

Introduction

Hyperbaric oxygen therapy (HBO) involves the administration of oxygen in high concentrations (typically 100%) to patients while they are exposed to increased atmospheric pressure. To achieve this, patients need to be physically placed inside a pressure container, a hyperbaric chamber. This can be either a "monoplace" chamber – a cylinder in which the patient lies or sits alone – or a "multiplace" chamber, where multiple patients and also healthcare staff, and possibly medical treatment and monitor devices, are placed under pressure (Figure 1).

The need for this chamber and the relative isolation of the patient during treatment limits the wide applicability of this treatment. Furthermore, as education regarding hyperbaric oxygen therapy is not commonly provided in the medical education curriculum, a shroud of "mystery" and "alternativism" often surrounds this particular treatment. The goal of this chapter is to highlight the principles that govern HBO therapy and to clarify the indications and diseases for which HBO can be used.

Part I: Hyperbaric oxygen therapy

1. Physical principles of hyperbaric treatment

Being exposed to increased pressure subjects patients to a number of the laws of physics, of which Boyle's law (Boyle and Mariotte's law) is the easiest to explain. Briefly, pressure and the volume of gases are inversely correlated, meaning that when pressure doubles, the volume of a gas-filled space (provided the enclosure has at least one mobile wall) will roughly decrease to 50% of the initial volume. While this may have therapeutic effects in itself, it is generally a complicating factor (see below).

A second law involved is Dalton's law, which permits for calculating the "partial pressure" of any gas contained in a (respiratory) gas mixture by multiplying the total pressure with the percentage (fraction) of this gas in the mixture. Oxygen is generally present at 21% in breathing air; therefore, the partial pressure of oxygen is 1 atmosphere x 0.21 = 0.21 atmosphere. Doubling the pressure of air will increase the partial pressure of oxygen to 0.42 atmospheres, even though the concentration

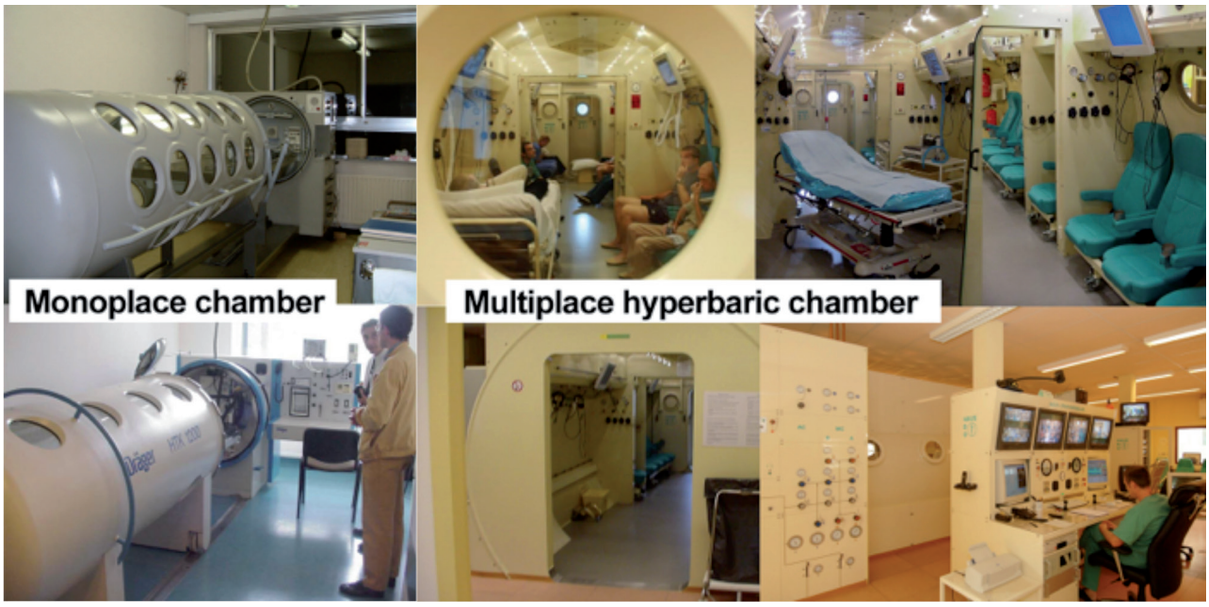

Figure 1
Monoplace and multiplace HBO chambers.

(percentage) of oxygen does not change. Increasing the percentage will of course also increase the partial pressure for a given total pressure.

Henry's law dictates the pressure of a gas inside a liquid (or, in physiology, in a tissue) based on the partial pressure of the gas that it is exposed to. This "saturation" of gas into a liquid or tissue is a dynamic process, attaining maximum tissue gas content after approximately 5-6 "half-time" periods. While the final gas content may be calculated by Henry's law ($Q = P \times \alpha$; with α being a solubility constant varying for each liquid and gas), the time scale (the "half-time" period) is dependent on the contact surface (and in tissues, the perfusion rate). For oxygen, this implies that an increased partial pressure in the alveoli will proportionally increase the arterial oxygen pressure, increasing the transport of oxygen molecules in blood plasma – independent of haemoglobin-bound oxygen. For nitrogen and other so-called "inert" gases, this means that there will be a progressive accumulation of the inert gas in the tissues, which upon "decompression" needs to follow the opposite route back to the lungs.

Finally, Pascal's law or Pascal's principle, states that pressure is directly and uniformly transmitted inside and through any non-compressible medium. Not only does this imply that patients subjected to higher atmospheric pressure do not change their body volume (only the non-communicating air or gas containing spaces in the body will), but also that any physiological pressure measurements will need to be related to the pressure sensor environment. Whereas the measured blood pressure of a patient will essentially be unchanged when measured inside a hyperbaric chamber, it will be increased (with the added chamber pressure) when the measuring device remains outside of the hyperbaric chamber.

In summary, physical principles, when applied to hyperbaric oxygen treatment:

- Reduce the volume of any gas-containing enclosed space (including vascular or tissue bubbles)
- Increase the partial pressures of respiratory gases and finally
- Increase the dissolved quantities of these gases in blood and subsequently in all tissues (the speed of which depends on the perfusion rate)

2. Physiological effects of hyperbaric oxygen

The most important effect of hyperbaric oxygenation is an increase in the transportation of molecular oxygen in the plasma of the arterial blood. Whereas the quantity of haemoglobin-bound

oxygen being transported is already near-maximal under "normal" arterial oxygen pressures (of approx. 100 mmHg), breathing 100% oxygen at 2.5 atmospheres (resulting in a PaO_2 of approx. 1800 mmHg) will add 5 ml O_2 per 100ml blood. This is roughly equal to the resting oxygen consumption of an adult human body. It has been shown on pigs that under such hyperbaric conditions, it is possible to remove all the blood (haemoglobin), while still sustaining normal resting metabolism.[1]

In practice, during hyperbaric oxygen therapy, venous blood will still be fully saturated with oxygen, indicating that tissue oxygenation is fully achieved with only the plasma-bound molecular oxygen. Therapeutically, this can be used in situations where haemoglobin levels are either too low (e.g., extreme blood loss anaemia, when no blood transfusions are possible) or non-functional (severe carbon monoxide poisoning). Furthermore, in patients with very low perfusion (arterial insufficiency, venous stasis) HBO may increase tissue oxygenation even in the absence of sufficient blood flow.

As the capillary oxygen pressure is likewise augmented, reaching up to 300 mmHg, the diffusion radius of oxygen from the capillaries to the tissue will increase three- to six fold. Tissues with oedema, capillary stasis or microthrombosis, where the intercapillary distance is too high for adequate oxygenation (resulting in tissue ischaemia) may be salvaged by applying timely HBO.[2]

High oxygen pressures have a vasoconstrictive effect by antagonism of nitric oxide, reducing the arteriolar flow by 20-25%. Tissue oxygenation is not compromised, because of the high oxygen pressures; however, decreased fluid inflow will enhance oedema resorption.[3,4]

Normal or even supranormal tissue oxygen levels are important for a number of processes:

- Leucocyte function: polynuclear neutrophil white blood cells depend on a high oxygen level to achieve redox potentials capable of "killing" ingested (by phagocytosis) bacteria; it has been shown that even in healthy patients, neutrophil killing capacity is only half-maximal under normal tissue tensions[5]
- Antibiotic efficiency: aminoglycosides, penicillins and a number of other antibiotics have a markedly reduced inhibitory potential in hypoxic tissues[6,7]
- Bacteriostasis: the growth of anaerobic bacteria and facultative aerobic bacteria is suppressed in high oxygen tensions; this constitutes an important adjunctive mechanism of HBO in the treatment of infections in old or vascular compromised patients
- Reduction of ischaemia-reperfusion phenomena: whereas the re-introduction of oxygen after ischaemia may trigger deleterious effects such as leucocyte adherence, production of oxygen free radicals and apoptosis, the very rapid restoration of normal mitochondrial oxygen levels has been shown to (paradoxically decrease these phenomena; hyperbaric oxygenation is thus a more effective way of reintroducing oxygen than "normobaric" or even "hypoxic" re-oxygenation[8]
- Collagen synthesis and cross-linking: normal wound healing is characterized by fibroblast migration (mediated by oxygen gradients), pro-collagen production and collagen cross-linking (by oxidation of disulphide bridges); the intermittent elevation of tissue oxygen tensions stimulates the formation of healthy granulation tissue by providing a solid collagen matrix for neo-angiogenesis to occur in; whereas in hypoxic or ischaemic wounds, some granulation may be observed, this is generally very fragile and is constantly removed by friction or dressing changes[9,10]

3. State of current knowledge and evidence base for HBO

The above-mentioned effects have been well documented in laboratory and animal experiments. The application of HBO in the clinical setting should ideally be easily verified in human patients. However, because of the low number of hyperbaric oxygen treatment centres, lack of sufficient public healthcare funding and the rarity of many of the diseases that could optimally benefit from HBO, it has proven extremely difficult to set up and conduct prospective randomized controlled trials (RCTs), let alone conduct "placebo-controlled" trials.[11]

With modern-day healthcare evaluation relying heavily on RCTs to provide "proof of efficacy", HBO has not been widely accepted within the medical community, other than as an exotic treatment possibility. Funding of research in this area therefore remains a major problem, which does nothing to help progress the state of scientific evidence.

The application of HBO involves a degree of technicality, "isolates" the patient inside a hyperbaric chamber during treatment (even though hyperbaric chambers allow full monitoring and invasive treatment, permit in- and egress of nurses and physicians during the course of the treatment, and the treatment generally last less than two hours) and may have side-effects (which are mostly mild and generally preventable). Therefore, a cost-benefit analysis is essential for all indications and precise conditions for acceptable use must be defined to ensure that the added benefits of HBO outweigh these possible negative effects. It is not acceptable to apply HBO indiscriminately to any disease or condition, since it is in most cases an adjunctive treatment and often not mandatory, even if it may theoretically add some benefit to the evolution of the patient.

3.1. "Accepted" indications for HBO

In order to resolve the problem of an insufficient evidence base, scientific societies in Europe, USA, Australia and South-East Asia have used the consensus conference method to define and describe adequate use of HBO.[12,13,14] By examining published literature on the topic, either through a consensus jury (Europe) or by a specific scientific committee (USA, Australia), a list of "accepted indications" is compiled and regularly reviewed and adapted. This complies with the principles of evidence based medicine: when no "Level 1" evidence is available, one should resort to the next level in order to define guidelines and recommendations based on the "best available evidence".

Unfortunately, when it comes to public healthcare financing, the absence of Level 1 evidence is often interpreted as "proof that the treatment does not work".

In Europe, the European Committee for Hyperbaric Medicine (ECHM) organizes regular consensus conferences to re-evaluate the "list of accepted indications". A categorization into three distinct groups is made: Type I – highly recommended; Type II – recommended; Type III – optional. For each indication, the level of evidence is given (see Table 1).

Table 1

ECHM Recommendations for HBO use (from www.achobel.be)

CONDITION	ACCEPTED		
	Level of Evidence		
	A	B	C
Type I			
CO intoxication		X	
Crush Syndrome		X	
Prevention of Osteoradionecrosis (dental extraction)		X	
Osteoradionecrosis (mandible)		X	
Soft Tissue Radionecrosis (cystitis)		X	
Decompression Accident			X
Gas Embolism			X
Anaerobic or Mixed Bacterial Anaerobic Infections			X
Type II			
Diabetic Foot Lesion		X	
Compromised Skin Graft and Musculocutaneous Flap			X
Osteoradionecrosis (other bones)			X
Radio-induced Proctitis / Enteritis			X
Radio-induced Lesions of Soft Tissues			X
Surgery and Implant in Irradiated Tissue (preventive action)			X
Sudden Deafness			X
Ischemic Ulcer			X
Refractory Chronic Osteomyelitis			X
Neuroblastoma Stage IV			X
Type III			
Post-anoxic Encephalopathy			X
Larynx Radionecrosis			X
Radio-induced CNS Lesions			X
Post-vascular Procedure Reperfusion Syndrome			X
Limb Re-implantation			X
Burns >20 % of Surface Area and 2nd degree			X
Acute Ischemic Ophthalmologic Disorders			X
Selected Non-healing Wounds secondary to Inflammatory Processes			X
Pneumatosis Cystoides Intestinalis			X

The full list, as well as the reviews having led to the selection and evaluation of this list, can be consulted online (www.echm.org). Whereas some of the indications are related to the ear-nose-throat (ENT) specialty, it is clear that HBO does not constitute by any means a panacea or miracle remedy for these diseases. The evidence for the efficacy of HBO is often a combination of experimental and anecdotal data, coupled with the fact that for many of these diseases, the "classical" therapy is not very effective or successful.

To further define a list of possible applications of HBO, the ECHM has also published a "Code of Good Clinical Practice in HBO", in addition to establishing training and education requirements for HBO staff.[15] Only a few European countries have actually progressed to making HBO a (sub) specialty or university-level competence – Belgium not being among them.

3.2. HBO therapy in belgium

3.2.1. Availability

Since the 1970s, HBO has been available in a number of Belgian hospitals. In an unprecedented gesture, the (then) Ministry of Healthcare donated 10 hyperbaric chambers to university-level hospitals throughout the country, in order to "make HBO available to all Belgian citizens". The fact that the donation concerned "monoplace" hyperbaric chambers (extremely limited in their applicability) and that there was only a minimal social security payment for the treatment, has ironically been one of the main causes for the lack of scientific development of HBO in Belgium.[16]

In the following years, these single-person hyperbaric chambers were progressively taken out of service and were not replaced by more modern or capable chambers. In 1991, the Military Hospital in Brussels installed the first hospital-based multiplace hyperbaric chamber (the Belgian Navy having had a multiplace chamber in the Ostend Naval Base since 1968). In 1994, a major hospital in Antwerp acquired a multiplace chamber and since then, five more hospitals have installed a multiplace HBO chamber. In 1996, the Belgian Advisory Board for Hyperbaric Oxygen Therapy (ACHOBEL, www.achobel.be) was formed with the goal not only to harmonize treatment protocols and provide hyperbaric nurses with the necessary education, but also to propose an adapted social security reimbursement schedule.

3.2.2. Social security reimbursement

The RIZIV-INAMI nomenclature for HBO, created in 1970, includes two codes for "installation in and surveillance of a patient in a hyperbaric treatment chamber", one for the first day (regardless of the number of HBO sessions provided) and one for the second day. The financed amounts are, respectively, 75 and 62 Euros. There is no limitation as to which indication can be treated.

Actual cost calculations have been made, indicating that a HBO treatment in a multiplace chamber will cost between 100 and 120 Euros per session, per patient. The social security fee is thus virtually non-existent and Belgian hospitals offering HBO do so at their own expense. In the same 2008 Federal Knowledge Centre for Healthcare (KCE) report, it was concluded that the Level I evidence base for HBO was low and that geographically, hyperbaric oxygen therapy was adequately distributed in Belgium; no modification to the reimbursement rates was deemed necessary. Since then, two hyperbaric chambers in the south of Belgium have ceased operating due to a lack of funding.[17] Figure 2 shows the current status of HBO centres in Belgium (2016).

3.2.3. Discussion

It can safely be stated that HBO in Belgium is very much underutilized. There is no formal medical education regarding HBO in the university medical curriculum, resulting in a low level of knowledge and awareness among the possible referring specialist physicians. When it is used, HBO is often performed by nurses of the Emergency Department or Intensive Care ward, without specific medical supervision. The follow-up of patients is relegated

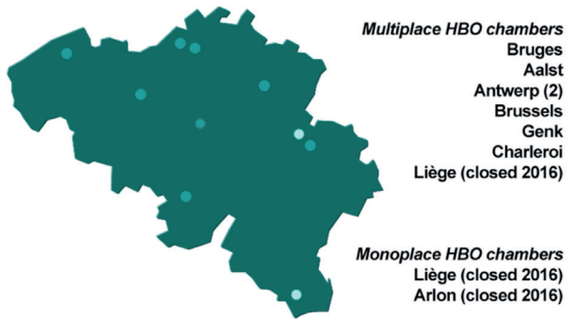

Figure 2
Geographical location of HBO centres in Belgium (January 2016).

to the referring physician, without much evaluation of the quality or consistency of the administered HBO. Allocating the correct number of properly trained personnel to HBO according to the European Code of Good Clinical Practice in HBO is expensive and as there is no formal obligation to comply with these minimum quality standards, they are in most instances not effected. To date, the Military Hospital in Brussels is the only hospital in Belgium capable of providing inside attendants during the entire treatment session and to have a specialized hyperbaric medicine physician directly supervising each treatment.

Part II: ENT-related indications for HBO

1. Sudden sensorineural hearing loss

1.1. Definitions

Sudden: the hearing loss has a rapid onset, within less than 72 hours.
Sensorineural: hearing loss is sensorineural by nature: abnormality of the cochlea, auditory nerve or higher aspects of central auditory perception.

Hearing loss: the most frequently used audiometric criterion is a hearing loss of 30dB or greater, affecting at least three consecutive frequencies between 125 to 8kHz, in one or both ears. When premorbid audiometry is unavailable, hearing loss in one ear is defined as related to the opposite ear's thresholds.

1.2. Incidence

The incidence of sudden sensorineural hearing loss (SSNHL) is reported as between five to 20 per 100.000, with about 4000 new cases per year in the United States.[18] In otologic and audiologic practice, 1.5% to 1.7% of new patients present with this complaint. Peak incidence occurs between the fifth and sixth decade of life. More than 98% of cases of SSNHL are unilateral. Tinnitus is present in 41% to 90% and dizziness in 29% to 56%.[19]

1.3. Natural course

Although the cause for SSNHL remains unknown, several hypotheses based on presumptive evidence have been identified. In a meta-analysis of 23 studies of SSNHL by J.K. Chau et al., the most frequent causes identified were infectious in 13% (herpes simplex, varicella-zoster, cytomegalovirus, mumps, meningococcal meningitis, lyme disease, syphilis, toxoplasmosis, measles, rubella), followed by otologic causes in 5% (Meniere's disease, hydrops), traumatic causes in 4% (perilymphatic fistula, temporal bone fracture, barotraumas, blast injury), vascular or haematological causes in 3% (stroke, transient ischaemic attacks, sickle cell anaemia, subdural haematoma, decompression sickness from SCUBA diving), tumour causes in 2% (vestibular schwannoma, leukaemia, myeloma, metastasis) and systemic auto-immune causes in 2% (Cogan's syndrome, systemic lupus erythematosus, temporal arteritis, Wegener's granulomatosis, polyarteritis nodosa, thyroid disorders).[20] In most of these diagnoses, hearing loss results from damage to hair cells or other cochlear structures. However, in more than 70% of cases, the underlying cause remains unknown or uncertain and is therefore classified as idiopathic.

Natural history and placebo-controlled studies have shown that for 32% to 65% of patients with SSNHL, a complete recovery occurs without any treatment, typically within two weeks of onset.[21] The prognosis for recovery is affected by the degree of hearing loss, age at presentation, duration, the presence of vertigo at onset, audiometric configuration, time between onset of hearing loss and treatment, and the presence of microvascular disease (e.g., diabetes). Idiopathic SSNHL has a better outcome than cases where an aetiological factor is identified, except in case of endolymphatic hydrops.[22]

1.4. Medical treatment and prognosis

SSNHL is a relative medical emergency. Diagnostic workup and treatment should be initiated without delay. Treatment options include systemic and/or intratympanic steroids, antiviral agents, antibiotics, vasodilators, anticoagulants, diuretics, osmotic agents, hyperbaric oxygen treatment, other medications, middle ear surgery for fistula repair and observation only.

A large body of articles on SSNHL is available (over 1200 on PubMed) with diverse and sometimes conflicting recommendations, which can complicate treatment choice for the practitioner. In 2012, the American Academy of Otolaryngology – Head & Neck Surgery, published a comprehensive review with recommendations which, although

(obviously) debated, appears currently to be the most up-to-date consensus paper.[18] The author panel views patient education and the exclusion of conductive hearing loss as strongly recommended, and further recommends evaluation for causal factors to be based on a combination of symptoms and prior episodes of hearing loss. In the diagnostic workup, complete and repeated audiometric (pure tone and speech audiogram, tympanometry) testing, evaluation for retrocochlear pathology by magnetic resonance imaging (MRI), or brainstem evoked response audiometry (BERA) is recommended, the former having better sensitivity for diagnosing tumours.[23]

With regard to the treatment of idiopathic SSNHL, the review recognizes that very little solid scientific evidence is available for recommending any one treatment above another. Although most studies do not currently meet criteria in terms of highest quality evidence, systemic corticosteroid treatment has been shown in a recent meta-analysis to provide a slight but not statistically significant improvement, compared to placebo.[24] Corticosteroids appear to offer the greatest improvement in the first two weeks and little change after six weeks. Considering the profound impact that hearing loss may represent, the possibility of improvement by corticosteroids make this a reasonable option if the onset of hearing loss is less than one month and if potential adverse effects are taken into account. To optimize treatment, the authors of a 2007 Belgian review propose combining methylprednisolone with other components that have individually shown to be effective. The following "Belgian cocktail" is proposed for all hearing loss, except for those affecting low frequencies only and only occured less a month previously: if the onset of symptoms: prednisolone 1mg/kg + piracetam 3x 3600mg/day + vitamin E 2x600 IU/day + magnesium 167mg/day. For hearing loss affecting low frequencies, the "Belgian cocktail" can be proposed if full recovery is not achieved at the end of one week of treatment with diuretics and oral steroids.[25]

The evidence-base for hyperbaric oxygen therapy is considered equal to that of initial corticosteroids. The major drawback to the application of this treatment is availability and cost. HBO is considered an optional treatment if delivered within three months from the onset of SSNHL.

Intratympanic corticosteroids are increasingly being used in the treatment of SSNHL. In animal models, a higher concentration can be delivered to the inner ear, compared to oral steroids.[26,27] Publications have shown inconsistent results for IT steroids. A systematic review concluded that IT steroids can be used for patients with SSNHL who cannot tolerate systemic steroid therapy.[28] IT steroids are recommended as a salvage therapy in the 2012 review.

There is currently no evidence to support the use of other medical therapy for. Nevertheless, if started early, less than three days after the onset of hearing loss, the combination of acyclovir with prednisolone is certainly reasonable if clinical signs of the varicella-zoster virus (herpes zoster oticus, Ramsay-Hunt) are present.[29]

The most accurate and cost-efficient method for assessing the benefits of medical interventions is audiometric follow-up. When successive audiometries are compared, only a variation of more than 10 dB must be considered as significant. In a long-term follow-up report in 156 patients, final hearing levels were reached by 97% after three months. An audiometric evaluation follow-up at six months is generally considered reasonable.[18]

1.5. HBO treatment

1.5.1. Experimental studies and rationale

Even with an extensive work-up, the aetiology of SSNHL remains unclear in over 70% of cases. Vascular occlusion, impairment of labyrinthine blood supply and cochlear hypoxia, viral infections, abnormal cochlear stress response, cochlear membrane damage, labyrinthine membrane breaks, immune system disease, toxins and ototoxic drugs are among several potential pathophysiological mechanisms.[18,25]

As the cochlea is an end organ with no collateral vascularization, its direct vascular supply is limited. The cochlea and particularly the organ of Corti, requires a constant and high oxygen supply. Oxygenation of these structures is maintained by the diffusion of oxygen from cochlear capillary networks into the perilymph and endolymph.[30,31] In case of SSNHL, perilymph oxygen tension decreases significantly.[30] Experimental and human studies have shown that hyperbaric oxygenation (HBO) raises the perilymph oxygen pressure up to 9.4 fold, thereby creating very high oxygen concentrations.[31]

1.5.2. Clinical studies

Several retrospective and comparative trials indicate that in case of failure of classical medical therapy (usually consisting of high-dose corticosteroids), HBO therapy can still achieve a significant improvement in pure tone audiometry. In contrast, most comparative studies show no additional benefit for using HBO as a primary treatment, either in combination or without systemic steroids.

There are no prospective placebo-controlled or blinded randomized controlled trials on the use of HBO in idiopathic SSNHL. In recent years, two trials were initiated (one in Europe as part of the COST-B14 Project of the EU, the other in Sydney, Australia, in Alfred Hospital), but neither have been completed. Difficulties related to the enrolment of patients have been summarized as being the result of two primary factors:

- The refusal (direct or indirect) of referring ENT specialists to subject their patients to a blinded randomized controlled trial, the principal reason being the concept that earlier HBO will be more beneficial
- The time consuming nature of a cross-over trial, which implies adding a "treatment period" for patients of at least another 14 days (following on immediately after a 10-14-day-medication period)

1.5.3. Internationally accepted protocol for HBO treatment

From retrospective studies, case series and the (limited) knowledge of clinical outcomes with classical medication therapy, the currently accepted HBO protocol can be summarized as follows.[12,13]

- After (failure or an insufficient result of) a first treatment with high-dose corticosteroids (either IV or orally) and within a four-week time period:
- One HBO session at 2.5 ATA, 70-90 minutes, is given daily for 10 consecutive days (possibly a 5/7 or 6/7 schedule)
- Followed by a repeat tonal audiometry; in case an objective improvement is observed (of more than 10dB in three affected frequencies), a second series of five to 10 HBO sessions can be given; where no objective improvement is observed, HBO is stopped

There is generally no effect (or even a temporary increase) on tinnitus symptoms.

2. Radionecrosis of mandibular and/or soft tissues

2.1. Definitions

Osteoradionecrosis is a serious complication of radiotherapy for head and neck tumours and involves partial necrosis of the maxillary or the mandible, which persists without healing for three months. Radiotherapy induces inflammation that generates small thrombi and obliterates osseous blood vessels. An increase in free radicals, which alters collagen synthesis, is also involved. Both the mandible and maxilla are bones that are exposed directly to the external environment through the gingival attachment of the teeth. Any periodontal disease, pulpal infection or dental extraction can result in delayed healing and in some cases, develop into osteoradionecrosis.[32]

2.2. Incidence and risk factors

Osteoradionecrosis generally develops when tooth extraction and oral surgery are performed prior to radiotherapy. In this case, prevalence rates vary widely, with a range of 10% to 15% reported in most literature. Without this procedure, this affection occurs in only 2.7% after five years. Other risk factors are trauma such as that caused by poorly fitting dentures, post-irradiation tooth extraction, high-stage and high volume of tumour, high radiation dose (>65 Gy), periodontal disease, poor oral hygiene, alcohol and tobacco. The mandible is more often affected than the maxilla. Osteoradionecrosis is rare after radiation of less than 60 Gy and may have a higher incidence in case of concurrent chemotherapy and radiotherapy.

2.3. Natural evolution

Osteoradionecrosis can occur months or years after irradiation (22 to 47 months is the mean time reported in the literature) and may remain unnoticed for a long time; it is often discovered during a routine medical examination or because of discomfort in the mouth. The lesions manifest as an ulceration showing exposed and often necrotic bone. The most commonly affected locations in the mandible (80%) are the premolar and molar regions, likely due to the denser bone in this area, which tends to absorb a higher amount of radiation, as well as the poorer vascular supply of the mandible, compared

to other bones. The disease causes pain and may lead to pathological fracture, orocutaneous fistulas and infection with necrotic bone sequesters.[33]

In the current management of osteoradionecrosis, orthopantomography (panorex) and CT imaging findings are used in conjunction with clinical findings to determine if a patient has early, intermediate or advanced stage disease.

Stage I disease is characterized by small, superficial, localized areas of bone resorption with cutaneous or mucosal dehiscence.

Stage II disease represents larger and deeper areas of bone resorption. Cortical and medullary bone is involved and mucosal or cutaneous areas of breakdown are moderate in size.

Stage III disease is defined by full thickness devitalization of bone, resorption of the inferior border of the mandible and the presence of fistula or a pathological fracture.

2.4. Medical or surgical treatment

Preventive measures for osteoradionecrosis are the most important, as the treatment of established osteoradionecrosis remains difficult and often unsatisfactory. Prior to radiotherapy, a thorough dental exploration is indicated. Any extractions should be performed at least two to three weeks before radiotherapy starts. In stage I and II, conservative treatment can be considered, including oral care, local debridement, or hyperbaric oxygen and these may resolve over half of cases. In such situations, local irritants such as alcohol, smoking and ill-fitting dentures are strictly avoided, and regular debridement is advised to maintain oral hygiene.

Surgery must be considered when conservative methods fail and is indicated in any case of stage III osteoradionecrosis. This surgery includes resection of the necrotic bone, followed by microvascular free flap reconstruction, which is routinely performed immediately after resection.[34]

A new adjunctive treatment, PENTOCLO (pentoxifylline–tocopherol–clodronate) is currently under trial. Pentoxifylline acts as an anti-TNF-α and vasodilates and inhibits inflammatory reactions. Tocopherol has vitamin E activity and Clodronate is a bisphosphonate. PENTOCLO decreases the superficial fibrosis induced by radiotherapy and stimulates osteogenesis via antioxidant pathways. Long-term (six to nine months) PENTOCLO treatment appears to be effective and has been demonstrated to achieve clinical and radiological regression of osteo-radionecrosis, alongside a reduction of the indications for major surgery.[35]

2.5. HBO treatment

Patients with osteoradionecrosis generally suffer from all aspects of collateral radiotherapy damage (such as xerostomia, trismus, dysgeusia, dysphagia and decreased tongue mobility). They experience impaired quality of life and poor social contact (inability to communicate, eat and socially join with other people).

Due to the anatomical similarities between osteo-radionecrosis and avascular necrosis of bone (the 3H's concept: hypovascular, hypocellular and hypoxic bone), in 1983, Marx[36] proposed a treatment algorithm that includes hyperbaric oxygen therapy, either as a stand-alone treatment (for stages I and II) or as supportive treatment for surgery (stage III).[37] More recently, a "stromal" concept has been developed involving a pathological fibrogenetic process that includes chemotaxis and fibroblast proliferation.[38] This may explain the inefficiency of certain therapies based on oxygenation or anti-fibrotic drugs. However, these two concepts are not necessarily mutually exclusive; vascular compromised tissues undergo deterioration with accompanying fibrosis. This damage may eventually reach a critical point where tissue breaks down and an area of radionecrosis appears as a result. Infection and surgery may exacerbate this process.

Although Marx's concepts have been used for more than 30 years in clinical practice, scientific evidence of its efficacy has been extremely difficult to provide. Most trials are retrospective and not randomized; prospective trials suffer from important methodological limitations.[39] The angiogenic effects of HBO therapy have been experimentally quantified by Marx, indicating that more than 20-25 sessions are needed to obtain a maximal vascular density in irradiated tissues.[40] There exists a frequently expressed concern that HBO treatment may exacerbate or stimulate cancer growth; while this remains unproven in the literature data (the contrary in fact being the case),[41] recurrent or persistent cancer may appear like (osteo-) radionecrosis and must be ruled out in case of the absence of a clinical effect.

In general, HBO treatments still reflect the initial propositions made by Marx:

- In cases of mild or beginning osteo-radionecrosis, 30 sessions of HBO are given five to seven times a week, at 2.5 ATA for 70-90 minutes
- In case no healing has occurred or in more severe cases, this is either followed by 10 more sessions or surgical intervention to debride necrotic tissue and a possible cover with a flap
- In stage III osteoradionecrosis, surgical intervention is planned from the onset, to be performed after preparation of the irradiated surrounding tissue with 30 HBO sessions. Post-operatively, 10-15 sessions are given to optimize wound healing. It is of vital importance that these post-operative sessions are started as soon as possible after surgery, as they have both an effect on infection risk (bacteriostatic) and on the wound healing.

The exact role of HBO in relation to newer emerging treatments (such as, the recently proposed PENTOCLO schedule) needs to be defined.

3. Compromised grafts and flaps in the ENT region

3.1. Overview of commonly used flaps and grafts in ENT

Head and neck reconstructive surgery is a challenging discipline for surgeons aiming to restore function and form with minimal surgical morbidity. Small defects can be successfully managed with primary closure, or can be resurfaced using skin grafts or small local flaps. Bigger defects require a flap transposition (free flap or pedicled flap) in order to attempt a restoration of form and function and to ensure rapid and adequate wound healing.

All head and neck defects should be evaluated in terms of lack of support. Indeed, anticipation of the resulting defect prior to surgery is crucial for proposing the most pertinent reconstructive solution. The chosen flap should ideally approximate the resected tissues in terms of type, thickness, texture, mobility, sensation and function. Over the past number of years, head and neck reconstruction has evolved from the use of a limited choice of pedicled flaps to a broad variety of free-tissue transfers. However, the essential question of whether free tissue reconstruction has a cost or a functional benefit over pedicled flaps remains controversial.[42]

3.1.1. Skin grafts

A skin graft is a section of epidermis and dermis that has been completely separated and transplanted to another area of the body to cover a wound. A skin graft does not need its own blood supply; the microvasculature from the recipient tissue bed will grow through into the graft and allow its survival. Both split thickness and full thickness skin grafts can be used, based on the localization and surface of the wound to be covered.

The most common cause of autologous skin graft failure is haematoma or seroma, which isolates (elevates) the graft from the recipient site and prevents revascularization. The second most common cause of graft loss is infection. Immunosuppressed patients and those in whom intraoperative time is prolonged are particularly at risk. Bacteria secrete proteolytic enzymes that lyse the protein bonds needed for revascularization. Infection can be avoided by carefully preparing the wound and meshing the graft surface to allow free egress of subjacent fluids, in this way allowing fibrin to deposit and form natural glue for graft adherence.[43]

3.1.2. Free flaps

A free flap is an island flap detached from the body and reattached at the distant recipient site by microvascular anastomosis. The introduction of microvascular reconstructions provides surgeons the possibility of choosing among a wide variety of more than 20 free flap donor sites including the fibula, radial forearm, rectus abdomini, lateral arm, scapula, jejunum, latissimus dorsi, scapula, lateral thigh, omental, iliac crest, ulnar and gracilis.[44]

There is no universal agreement on the optimal choice of free tissue donor, or the best technique for performing microvascular anastomosis. Randomized controlled trials comparing one free flap reconstruction to another are not available. Surgeons must always carefully evaluate the regional anatomy of each patient, as well as the patient's general health status in order to propose the most pertinent solution among the various possibilities. Factors that work against free flap surgery can be increased risk with prolonged anaesthesia time and patients with a compromised venous condition. In such cases, for patients considered to be suboptimal for microvascular reconstruction, pedicled regional flaps still represent a valid alternative.

Microvascular techniques continue to evolve and the success rates for free tissue transfer are high, exceeding 95%. Vessel thrombosis, primarily venous, represents the most common postoperative complication that may affect tissue viability. Therefore, close postoperative monitoring must be realized with frequent assessment of flap colour, bleeding rate, capillary refill, skin surface temperature and Doppler investigation.

3.1.3. Pedicled flaps

A pedicled flap is a muscular flap with or without skin cover, which is left attached to the original site to provide a blood supply and which is transferred by rotation to a recipient site. Pedicled flaps remain the most frequently used approach in many head and neck tumour centres compared to free flaps, because of the latter's high cost and a requirement for highly specialized microsurgical expertise. Furthermore, the shorter period of anaesthesia required for pedicled flaps is often the best choice for critically ill patients. Due to the aggressiveness of chemotherapy and radiation therapy protocols, the ability to introduce oxygenated tissue with a nourishing blood supply into the defect may be critically important. Moreover, many of these flaps can be transferred without the need for repositioning the patient during surgery. For these reasons, pedicled flaps continue to play an important role in many institutions worldwide.[45]

The most frequently used pedicled flaps include the pectoralis major myocutaneous flap, nourished by the pectoral branches of the thoraco-acromial artery, as well as the latissimus dorsi myocutaneous flap, a broad flat muscle of considerable length, allowing it to be subcutaneously tunnelled over the pectoralis major muscle, under the pectoralis major insertion, or under the clavicle itself; it is vascularized by the thoracodorsal artery.

3.2. Rationale for the use of HBO therapy in compromised flaps and grafts

With proper planning and preparation, the success rate for flaps and grafts in the ENT region is high; however, partial necrosis of the elevated and repositioned flap is not uncommon. This may occur due to pedicle oedema, venous thrombosis or sludging, arterial thrombosis and/or underlying haematoma or seroma. Careful monitoring is therefore a necessity, especially during the first days following surgery. In case no remediable cause can be determined and the flap or graft looks ischaemic or cyanotic, hyperbaric oxygenation would be a logical step. However, the limited availability of emergency HBO therapy and concerns about possible ischaemia-reperfusion damage by oxygen free radical formation have hampered its widespread acceptance.[46] Nevertheless, a large volume of experimental literature precisely indicates a reduction of ischaemia-reperfusion effects with HBO, as opposed to slower re-oxygenation by "normobaric" oxygen therapy, or even simple revascularization.[47] However, limited flap necrosis appears to be generally accepted as a risk, even if this means a second surgical intervention at a later stage.

3.3. HBO treatment protocol

As in this indication, HBO serves primarily to salvage ischaemic tissue from necrosis and/or reperfusion injury, the proposed HBO protocol is quite intensive: three sessions during the first 24 hours, thereafter two sessions per day for four to six-days or until a clear demarcation of necrotic and "healthy" tissue is obtained.

The exact optimal treatment pressure is not defined and some authors propose guiding treatment pressure by transcutaneous oxygen pressure measurements; others propose using lower-dose hyperbaric oxygen (2 ATA) to avoid the generation of oxygen free radicals.

It is important to ensure that any arteriolar thrombosis (in free or pedicled flaps) is relieved and that no haematoma is present under the flap, as this will invariably lead to flap failure.

4. Severe anaerobic infections in the head and neck regions

Anaerobes are predominant components of the oropharyngeal bacterial flora and are therefore a common cause of infections in the upper respiratory tract and neck region. Treatment of anaerobic infections is complicated by the polymicrobial nature of such infections, by the slow growth of these organisms and by the growing resistance of anaerobic bacteria to antibiotics. Anaerobic bacteria can be involved in sinusitis, tonsillitis, chronic otitis and in the complications caused by these infections.

4.1. Overview of major anaerobic infection syndromes in the area of ENT

4.1.1. Anaerobic sinusitis

Chronic sinusitis is an inflammatory process that involves the paranasal sinuses and which generally persists for 12 weeks or longer. Symptoms include nasal congestion, postnasal drip and facial fullness. Polymicrobial infection is frequent, but anaerobes predominate, involved in more than 50% of such cases (compared to 8% in acute sinusitis). Anaerobes are common in chronic maxillary sinusitis associated with odontogenic infection, primarily of the premolar or molar teeth. Chronic sinusitis caused by anaerobes is associated with complications such as mucocele formation, osteomyelitis and orbital and intracranial abscesses.[48] CT scanning is the gold standard for assessing damage to the sinus and for visualizing bone and soft tissue.

Many of the pathogens isolated from chronically infected sinuses are resistant to penicillin through the production of beta-lactamase; this should be taken into account in the choice of treatment drug. The antibiotic of choice is clindamycin, a combination of penicillin and a beta-lactamase inhibitor, or alternatively, a quinolone with anti-anaerobic coverage (moxifloxacin). The duration of the treatment is not clearly established, but may be given for three weeks to three months. Daily saline irrigation and topical corticosteroid therapy is also recommended. For patients with nasal polyps, a short course of systemic corticosteroids (one to three weeks), a short course of doxycycline (three weeks), or the addition of a leukotriene antagonist may be considered.[49]

Sinus puncture and aspiration can be performed and allows for the removal of purulent secretions, and also provide culture material for guiding antibiotic treatment. A trocar is inserted into the opening of the maxillary sinus via the inferior meatus to allow drainage and antibiotic irrigation of the sinus. A local urfamycine injection (500mg) with methylprednisolone (40mg) is recommended, followed by a new injection of urfamycine (500mg) four days later.

Surgical treatment may be indicated in case of failure of medical treatment.

4.1.2. Malignant otitis externa

Necrotizing external otitis, also called necrotizing malignant otitis, is an external otitis resistant to local treatment and involves the temporal and adjacent bones. The infection results from an invasion of the external ear canal by a pathogen. The typical patient at risk is an elderly diabetic (or immunocompromised) male. Traumatic factors are often found in such cases (forceful or frequent use of cotton swabs, prosthesis and exposure to swimming pool water). The most frequently involved pathogen is *Pseudomonas aeruginosa*, found in 75% to 90% of cases.

Clinical symptoms are otalgia, which worsens at night and purulent otorrhoea. Hearing impairment is inconsistently present. An important otoscopic finding is granulation tissue in the bone-cartilage junction of the external auditory canal. If the infection, while spreading into the temporal bone, reaches the cranium, it may cause cranial palsies and will consequently have poorer prognosis. The facial nerve is usually the first involved (in 20% to 50% of cases), resulting in facial paralysis.

A culture of ear secretions is required to investigate resistance to antibiotics. Pathologic examination of granulation tissue is essential to exclude malignant processes.[50] CT scanning appears to be the more easily available and effective test. It is useful for assessing the location and extent of diseased tissue. Only early stages of bone erosion may remain invisible on a CT scan. Technetium scanning (Tc99) has a sensitivity of 100% and when negative, may exclude necrotizing external otitis. However, its poor specificity makes it inadequate for follow-up application. Gallium citrate (Ga67) scintigraphy is suggested by a small number of authors for diagnosis; however, scientific evidence to support this claim is unavailable. It is instead more frequently used as a baseline for follow-up after treatment. Magnetic resonance imaging can be used to assess the extension of disease toward the petrous apex, deep soft tissue spaces and intracranial organs.[51]

The mainstay of treatment is systemic antibiotics, which are effective against *Pseudomonas aeruginosa*. A common parenteral combination treatment associates a third-generation cephalosporin (ceftazidime) with a fluoro-quinolone (ciprofloxacin) for a period of four-to-six-weeks. Local treatment is also important and includes daily meticulous cleaning and debridement of the auditory canal, with topical application of antimicrobial agents. Surgery currently has a limited indication, as it may expose healthy bone to the infection. Nevertheless, surgery remains

recommended in the absence of improvement with adequate medical treatment after two weeks.[52]

4.1.3. Anaerobic soft tissue infections of the neck: peritonsillar, retropharyngeal, parapharyngeal and deep neck abscesses

Deep neck infections are a life-threatening disease and need early medical management. Most deep neck infections arise from pharyngeal or from dental infections. Less frequent causes include salivary gland infections, sinusitis, mastoiditis, upper respiratory tract infections, trauma and foreign bodies. Immunocompromised patients are particularly at risk.

Symptoms depend on the specific neck space involved and include cervical pain, neck swelling, dysphagia, dyspnoea, dysphonia, lockjaw, odynophagia and torticollis. Characteristic symptoms of infectious processes such as fever, malaise, anorexia and tachycardia are also present.

The predominant anaerobic organisms isolated in peritonsillar, lateral pharyngeal and retropharyngeal abscesses are prevotella, porphyromonas and fusobacterium. Aerobic organisms are Group A Streptococcus, *Staphylococcus aureus* and *Haemophilus influenza*.[53]

Peritonsillar abscess is reported as the most common deep neck infection in adolescents and young adults. Retropharyngeal abscess is more commonly seen in young children and is more likely to have aerobic pathogenic isolates.

Lemierre's syndrome is a rare and severe complication of a parapharyngeal infection, where *Fusobacterium necrophorum* is the predominate genus. This syndrome is characterized by thrombophlebitis of the internal jugular vein, causing pulmonary emboli.

Computed tomography is essential for more accurately providing the dimensions and localization of infected areas. Laboratory testing including haemogram, renal function, culture and antibiogram test are useful for assessing the general state of the patient, and to determine the microorganisms involved for establishing the antimicrobial therapy needed.

Initial antibiotic therapy should be empiric and should later be adapted to the antibiogram. Generally, the drug of choice is penicillin G (or a third generation cephalosporin in case of a penicillin allergy) at high doses, intravenously, associated with metronidazole.[54] Some authors recommend corticosteroids for reducing the swelling of the upper airways. When a diseased tooth is detected, extraction should be performed as early as possible. If there is no improvement of infectious signs within 48h with intravenous antibiotics, surgical treatment should be performed.

4.1.4. Phlegmon of the buccal floor (Ludwig's angina)

Ludwig's angina is a type of cellulitis affecting the soft tissues of the submandibular, sublingual and submental area. This infection can have an aggressive evolution and may be life-threatening, either because of airway obstruction or subsequent mediastinitis, necrotizing fasciitis or sepsis. In more than 70% of cases, dental infections are at its origin, with second and third molars most often being involved. Other possible causes include submandibular sialadenitis and parapharyngeal or peritonsillar abscess. A variety of micro-organisms have been recovered from cases of Ludwig's angina. However, anaerobic bacteria predominate.[55]

At physical examination, the patient will indicate a painful swollen area in the oral floor and the submandibular region. The tongue will be pushed in a posterior direction, causing significant dyspnoea, dysphagia, odynophagia and dysphonia.

Antimicrobial therapy is similar to that applied for other neck abscesses. Monitoring and protection of the airways is particularly crucial. Endotracheal intubation is not recommended, because of the risk of unexpected extubation with difficult re-intubation and the possibility of infecting other sites during intubation. Tracheostomy is indicated for the most severe cases but is difficult to execute, due to a loss of anatomic references. Surgery may be needed to drain the abscess via intra-oral incision for the sublingual space, or by external incision for the perimandibular location.[56]

4.2. Rationale for the use of HBO therapy

HBO may be able to increase the oxygen pressure in the infected and ischaemic/oedematous tissue to higher than normal values. This depends on the degree of necrosis and pus, and early debridement will often be necessary to relieve tissue tension and allow for good penetration of oxygen and antibiotics.

The addition of HBO will help control the infection primarily by (see the beginning of this chapter):

- Preventing indirect tissue cell necrosis induced by oedema
- Exerting a bacteriostatic effect on anaerobic bacteria, which will limit or slow down further expansion of the infection
- Optimizing the efficacy of antibiotic treatment
- Optimizing the leucocyte "bacterial killing" capacity

4.3. HBO treatment protocol

In severe cases, HBO will be administered three times in the first 24 hours, twice daily for four to six days thereafter and then once daily, primarily to prevent recurrent anaerobic infection and to stimulate granulation tissue formation. The proposed treatment pressure is 2.5 or 3 ATA and may be guided by clinical response and/or transcutaneous or intratissular oxygen pressure measurements.

HBO is always to be considered an adjunctive treatment and surgical debridement and targeted antibiotic therapy remain the primary therapeutic measures. However, in patients with vascular or metabolic risk factors, HBO is an important adjunctive therapy.

5. Inner ear decompression sickness after SCUBA diving

Middle ear and inner ear barotrauma from pressure changes (underwater diving, aircraft travel) are described in Chapter 15 of this report (and only briefly summarized below, as they may arise as complications of HBO therapy). Inner ear decompression sickness (IEDCS), however, is an urgent indication for therapeutic recompression with oxygen.

5.1. Mechanism of decompression sickness

When breathing, all components of the breathing gas come into contact with blood plasma in the alveoli. According to Dalton's law of physics, each component of the breathing gas has a partial pressure equal to its fraction of the total gas pressure. For air, nitrogen gas takes up 79% and will thus have a partial pressure of roughly 79% of the total alveolar pressure (disregarding, for simplicity, the CO_2 and H_2O components of alveolar air).

When SCUBA (self-contained underwater breathing apparatus) diving, the respiratory gas pressures increase with depth and the partial nitrogen pressure will increase accordingly. According to Henry's law of physics, this increases the dissolved nitrogen "tension" in the arterial blood and further downstream, nitrogen gas will start to accumulate in tissues. As nitrogen is not used in metabolism, after some time, a new state of equilibrium will be reached where tissues are said to be "saturated" with nitrogen.

Upon ascent from a SCUBA dive, the saturated tissues will release nitrogen into the bloodstream (as the nitrogen tension is lower again at this stage); this will transport nitrogen molecules to the alveoli, to be equilibrated with alveolar air and exhaled.

The preceding paragraphs are a simple explanation; complicating the process are factors such as:

- Not all tissues take up and release nitrogen at the same speed (this depends on their perfusion rate) and as nitrogen is more soluble in fat than in water, the total "capacity" of one tissue for nitrogen can dramatically differ from another
- It is not possible to physically define exactly the speed and capacity of each tissue; therefore, these "tissues" are virtual in nature, not anatomical or functional
- When ascending to a certain depth after a deep dive, some tissues may already be desaturating, whereas others may still take up nitrogen
- A too large pressure differential between tissue and blood may cause nitrogen to exit the tissue in the form of microbubbles, which dramatically decreases desaturation speed
- The maximum tolerable "supersaturation" of tissues (before bubbles form) varies according to tissue type and according to the depth of the pressure change transition
- After surfacing, some excess nitrogen remains present in the tissues and these continue to desaturate for up to 12 hours after the dive. When performing a second dive before this time, tissues still containing nitrogen will saturate more slowly (as they already contain a certain nitrogen gas tension; the speed of saturation is dependent on the nitrogen tension differential); however, their nitrogen content is already high at the start of the dive
- All of the above factors and mechanisms apply to all so-called "metabolically inert" gases that are present in the breathing mix. Advanced, deep diving often involves the use of special gas mixes

containing helium and the various gas percentages may change during the course of a single dive. This makes calculations of decompression schedules complicated.

When nitrogen (inert gas) bubbles form in the venous blood stream (despite careful calculation and execution of a decompression schedule), these may either block the blood flow locally (resulting in decompression sickness) or be swept away and end up in the right-sided cardiac cavities. In most cases, these bubbles continue to the pulmonary capillaries, become lodged in the alveolar network and progressively disappear by nitrogen diffusing out of the bubble towards the alveolar air; however, there may be instances where they transgress to the arterial circulation. In the right-sided atrium they may pass through a patent foramen ovale (PFO) or other intracardiac shunt.[57] They may also bypass the lung capillaries through pulmonary arteriovenous anastomoses (which may open up in case of heavy physical effort or high bubble load, which causes a rise in pulmonary artery pressure).[58] They may then embolize arterioles or capillaries further downstream and also cause decompression sickness.

5.2. Symptoms of inner ear decompression sickness

A complete review of the possible mechanisms for inner ear decompression sickness is beyond the scope of this review. Symptoms are generally quite dramatic and arise shortly (within one hour) after the dive. Most prominent is the sudden onset of rotational vertigo, accompanied by nausea and vomiting, often after physical effort or a respiratory "straining" manoeuvre. Hearing loss may also be present, but is often only described at a later stage, when severe nausea abides.[59]

Other symptoms of decompression sickness may also be present (visual disturbance, skin blotching or "cutis marmorata", paresthesia, paralysis), but in most cases, these are often absent.

5.3. Diagnosis of IEDCS

The diagnosis of IEDCS is essentially clinical: an acute vertiginous/cochlear syndrome shortly after a "suitable dive". A suitable dive is one that has a certain degree of saturation (i.e., a certain depth and certain duration) and a certain statistical risk for decompression sickness (i.e., close to the calculated limits of obligatory "decompression stops", according to the decompression schedule used). There is no single threshold depth or duration and many temporary environmental and personal factors play a role; therefore, experience in diving medicine is often needed to evaluate whether a dive is potentially capable of causing decompression sickness.

A further diagnostic workup should not delay prompt recompression treatment, as the prognosis of IEDCS relies on the speed of starting hyperbaric treatment. There are no other hyperacute vestibular syndromes that occur shortly after a dive in previously healthy people, except perhaps for benign paroxystic positional vertigo (BPPV). In case of clear Hallpike provocation testing and a significant reduction of symptoms by the Epley manoeuvre, such a differential diagnosis may be considered. Acute hearing loss after diving should prompt interrogation and clinical examination for exclusion of severe middle ear or inner ear barotrauma. Again, in case of doubt, treatment should be directed at IEDCS.

5.4. Treatment of IEDCS

Even with early recompression treatment, the prognosis of IEDCS is not good. Up to 90% of patients treated within six hours from the onset of symptoms retain residual cochleovestibular symptoms.[59] Recommendations for using treatment schedules at higher pressure and using oxygen-helium mixtures as breathing gas seem to have less impact on the final outcome than early recompression (ideally within one hour). In case of uncertain diagnosis (especially in the case of inner ear barotrauma), a bilateral paracentesis is recommended to obviate the necessity for Valsalva manoeuvres during compression. Several follow-up HBO treatments may be given; however, early vestibular re-education is also important. It is recommended that early caloric testing be performed to ascertain anatomical and functional damage and at a later stage, pendulum chair testing, to verify the degree of central compensation.

Part III: Precautions and possible complications of HBO

Hyperbaric oxygenation has a number of side-effects; contra-indications are those conditions or

diseases where the risk of side-effects is judged too important, or when the consequences of these side-effects are considered too dangerous. Therefore, each patient should be subjected to an individual evaluation, based on the expected benefit of HBO and the possible risks or side-effects. The conclusions of this evaluation will also be dependent on the type and capabilities of the hyperbaric chamber that will be used (mono- or multiplace, ICU capacities – or lack thereof–, available monitoring and in-chamber treatment devices, as well as the training and availability of HBO chamber staff, nurses and physicians).

1. Barotrauma

The most common complication or side-effect of HBO therapy is barotrauma. As all gas-containing spaces in the human body must "equalize" their pressure to outside pressure, failure to do so will invariably result in pain, exudation, and bleeding or rupture of membranes.

1.1. Middle- and inner-ear, sinus barotrauma

The most common complication of HBO is middle ear barotrauma. For a detailed description of causes and pathophysiology, see Chapter 15.

In patients with ENT region infection or surgery, or with a history of radiotherapy or previous surgeries, the ventilating orifices of sinuses and the Eustachian tube may become blocked. Extra care is therefore needed before starting HBO treatment to evaluate these patients' ability to equalize. Although tympanometry and visual observation of tympanic membrane movement during the Valsalva manoeuvre can be used, there are no 100% reliable methods for determining the risk of middle ear and sinus barotrauma. An extensive patient briefing and careful observation during the compression phase of the HBO session should permit for detecting possible equalization difficulties early, thus stopping the treatment before severe barotrauma can occur. Again, in this instance the training and dedication of HBO staff play a major role, as patients will often not spontaneously report "squeezes" unless the pain is excruciating or if bleeding occurs.

Severe middle ear barotrauma or excessive and forceful attempts at equalization (forceful Valsalva manoeuvres) may result in inner ear barotrauma, characterized by sudden hearing loss and instability. This is a complication that should, in normal practice, not ever occur. Patients who are unable to equalize their ears can be safely treated after placement of bilateral tympanic ventilation tubes or grommets. In some HBO centres, these are placed prophylactically. It is our experience that even patients with a history of equalization difficulties may be able to safely and comfortably equalize, and as such, we do not recommend routine placement.

Maxillary sinus barotrauma is often described as pain in the upper premolar teeth, or frontal sinus squeeze in the form of a sharp pain above the eyes. Here, an attempt may be made to open up the ventilation orifices by either applying local vasoconstrictive nasal sprays or using oral antihistaminic drugs. In case barotrauma occurs, it is generally necessary to interrupt the HBO treatment for a number of days.

1.2. Pulmonary barotrauma

Whereas pulmonary barotrauma has been described occur among divers, mostly as a result of ascending without exhaling properly, it is very rare in hyperbaric treatments.[60] The decompression phase is generally extremely slow (0.1 to 0.15 atmospheres per minute, which equals 1 to 1.5 meters per minute in diving), so that expiration blocking will have to continue for an exceptionally long time in order for pulmonary alveoli to rupture. However, vulnerability to pulmonary barotrauma may be increased in patients with chronic obstructive lung disease, pulmonary cysts or bullae, or local areas of air-trapping, such as in severe bronchial stenosis, or abundant bronchial secretions.

Pulmonary barotrauma will result either in the occurrence of pneumomediastinum, pneumothorax or arterial gas embolism. Pneumomediastinum is treated conservatively, with rest and normobaric oxygen treatment. Pneumothorax may present a life-threatening situation when it occurs "at depth". According to Boyle's law of physics, gas in the pleural space will expand as the pressure decreases, possibly causing a tension pneumothorax during hyperbaric chamber decompression.

Arterial gas embolism will be diagnosed by sudden central neurological symptoms, such as general weakness and progressive stupor to even coma, or hemi-paraesthesia, paresis or paralysis, all occurring during ascent or within minutes after the hyperbaric chamber pressure has returned

to atmospheric pressure. Here, the immediate treatment should be recompression on oxygen and new hyperbaric treatment according to diving medicine "treatment tables" (typically, a 285 minute US Navy Treatment Table 6). As the patient will generally still be in or in the immediate vicinity of the HBO chamber, no delay is acceptable; the diagnosis is quite easy on clinical grounds alone and prompt recompression will in 99% of cases reverse the symptoms and cure the patient. Performing other diagnostic tests (chest X-ray, CT scan, laboratory tests, etc.) will simply delay the start of the only effective treatment and compromise the final outcome. Even if classical resuscitation measures (haemodynamic stabilization, oxygen administration) succeed in clinical recovery and symptom reduction or disappearance, recompression treatment is necessary.[61]

1.3. Implanted medical devices

An increasing number of patients are carrying implanted medical devices, whether it be cardiac pacemakers, implantable cardioverters-defibrillators (ICD), neurostimulators or pain medication pumps. These devices may malfunction or break by exposure of the patient to hyperbaric pressure and manufacturers sometimes include SCUBA diving or hyperbaric treatment restrictions in the "instructions for use". However, if no such information is available and certainly, in emergency situations, sometimes a decision must be made either to not treat the patient with HBO or risk possible malfunction of the device. Here again, a risk-benefit analysis is made individually.

1.4. Other pressure-related barotrauma

1.4.1. Tracheal leaks

Uncommonly reported, but in our experience not rare, is the occurrence of subcutaneous emphysema in patients with recently closed tracheostomy. There is some testimony of a very slightly elevated tracheal pressure during HBO therapy (breathing in a mask or hood requires an expiratory pressure of approximately 3-4 mmHg above normal) and this possible complication requires careful consideration. Post-operative HBO sessions may for these patients best be scheduled a few days (4-5) post-surgery, with a lightly-compressive bulky dressing, preventively applied around the neck.

2. Oxygen toxicity

Breathing oxygen at high pressures generates a certain degree of oxygen free radicals (OFR) and these are responsible for a number of possible side-effects. Even though frequently cited, their incidence is low and they rarely have lasting consequences.

2.1. Acute neurological oxygen toxicity

Commonly referred to as the "Paul Bert effect", hyperoxic convulsions are related to the cerebral accumulation of OFR. Whereas each aerobic cell and tissue can recruit "anti-oxidant defences" (catalase, peroxidase, glutathione, vitamin E), an excess of OFR may affect the synthesis of gamma-amino-butyric acid (GABA) and thus permit, after some time, an uncontrolled neurological discharge, resulting in an epileptic fit. The mechanism is similar to that of hyperthermia convulsions in children, the result of an imbalance between GABA (the "regulating" or suppressing neurotransmitter) and glutamate and acetylcholine (the "stimulating" neurotransmitters). Incidence of hyperoxic convulsions increases alongside higher inspiratory oxygen pressures that are breathed for longer periods of time. In HBO at 2.5 atmospheres absolute, it ranges between 1/699 and 1/8945 treatments.[60,62] There appears to be a correlation between indication/patient condition and risk of hyperoxic convulsions, more stressed and more severely ill patients having a higher incidence. Convulsions generally occur without clear premonition signs after more than 45 minutes of treatment and last for one to two minutes, are self-terminating and are followed by a period of postictal confusion. There is full recovery after 10-15 minutes. Hyperoxic convulsions are an undesired but unavoidable side effect of HBO, but do not contra-indicate further treatments, although these may be given at a lower pressure or with medical pre-treatment using benzodiazepine or valproate.[63]

2.2. Ophtalmologic changes

After a series of 20 or more HBO treatments, most patients develop a change in refractive power of the ocular lens. The average change is -1.61D, which sometimes causes these patients to complain about progressive myopia. This change is for the most part fully reversible after 4four to six weeks

after cessation of HBO therapy; however, it can be a disturbing side effect. De novo occurrence or accelerated development of nuclear cataract has been described, but it is exceptional and occurs typically after an exceptionally high (more than 150) number of treatments.[64]

2.3. Other

Pulmonary oxygen toxicity (the "Lorrain Smith effect") is well known even in non-hyperbaric intensive care medicine. It is linked to an excessive duration of oxygen breathing at inspired oxygen fractions of 0.5 or more. Its risk of occurrence, in contrast to the previously mentioned neurological oxygen toxicity, can be quite accurately calculated using a table of Units of Pulmonary Toxicity Dose (UPTD). In normal hyperbaric practice, there is no risk of pulmonary toxicity, except when the patient receives continuously high oxygen in between HBO sessions (e.g., on the intensive care ward).[65]

3. Claustrophobia and mask intolerance

Being enclosed in a hyperbaric chamber may be a stressful experience for sick and older patients; however, depending on the physical environment, the quality of patient information and psychological attention, HBO is generally well tolerated. In exceptional cases, patients may have difficulties supporting an orofacial mask; in such a case, a clear transparent plastic "hood" of oxygen is proposed. Claustrophobia can, if present, further be reduced by minor anxiolytic therapy.

4. Physical accidents and their prevention

The hyperbaric chamber and associated systems contain an oxygen-enriched atmosphere, which necessitates appropriate fire-prevention measures. These should be enforced in a non-threatening manner so as not to cause stress for the patient, but should be enforced nevertheless, as accidents, however infrequently, do happen. It has to be kept in mind that fire requires the presence of a "fuel" to be combusted, a "spark" to generate ignition and "oxygen" to sustain and facilitate fire. Each of these corners of the "fire triangle" can and should be minimized; the responsibility for doing so is that of the medical-technical team of the HBO centre. While fire and explosive accidents are spectacular and usually result in serious bodily harm, they have a very low incidence and are generally the result of human error.[15,66]

5. Patient selection and follow-up

The usefulness of HBO as an adjunct in the treatment of many diseases is difficult to prove scientifically. Careful patient selection and precautionary measures are necessary to ensure that side-effects and complications remain within the current acceptable rate. Oxygen by itself is not generally a substitute for proper care; therefore, it is equally important to ensure that the "classical" treatment is administered and followed-up on in an optimal manner. It is unavoidable that such meticulous patient care influences outcomes and this may obscure (or enhance) the effect of HBO therapy. Whether this is necessarily a negative factor remains debatable.

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