Chapter 10
The Dilemma Between Hyperbaric Oxygen Therapy (Hot) and Ozone Therapy

HOT is better known than ozone therapy because it is considered an orthodox approach and is widely used in the USA. This explains why many physicians and the layman often ask me if ozone therapy is a sort of HOT.

The latter is a medical procedure by which 100% medical oxygen (Kindwall, 1993; Tibbles and Edelsberg, 1996; Leach et al., 1998; Cianci, 2004) is delivered at 2–3 times (usually 2.6) the atmospheric pressure (1 atmosphere = 760 mmHg) at sea level. In physiological conditions, at this level with normal air, the pO_2 in the alveolar space (O_2:14%) is equivalent to 100 mmHg and the pO_2 of arterial blood is about 98 mmHg; Hb is fully saturated to Hb_4O_8 and there is about 0.3 ml per decilitre of O_2 solubilized in the plasma. Tissues at rest extract from blood an average of about 25% O_2 (i.e., 5–6 ml of O_2/dl), so that venous blood has a pO_2 of about 40 mmHg and Hb_4O_8, having released at least one molecule of O_2, becomes Hb_4O_6. Thus the amount of O_2 physically dissolved in the plasma is grossly insufficient for the requirements of the tissues and the necessary 5.5 ml of oxygen derive from deoxygenation of Hb_4O_8. **In the hyperbaric chamber, administering 100% O_2 at 3 atmospheres, the O_2 solubilized in plasma is as much as 6 ml/dl and the Hb is fully saturated with oxygen**. In this situation, the dissolved O_2 content is sufficient to satisfy the cellular requirements and Hb_4O_8 hardly release any oxygen.

Rapid decompression (say from 4–5 to 1–2 atmospheres) causes decompression sickness due to nitrogen dissolved in plasmatic water, which suddenly forms inert gas bubbles that cause disseminated embolism. The diver can be saved if rapidly placed in the hyperbaric chamber, because during slow decompression the nitrogen is replaced by oxygen and slowly expired while the oxygen is metabolized by the tissues.

Carbon monoxide (CO) poisoning is a cause of death all over the world (Ernst and Zibrak, 1998) due to the fact that CO binds to Hb with an affinity 240 times that of oxygen. In the presence of CO, the oxyhaemoglobin dissociation curve shifts to the left and changes to a more hyperbolic shape, with the result of impaired release of oxygen at the tissue level, where CO also binds to myoglobin.

The hyperbaric chamber can save the intoxicated subject by delivering oxygen dissolved in the plasma to anoxic tissues and by accelerating the dissociation of COHb: its half-life decreases from about 300 min while air is breathed, to

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about 20 min with hyperbaric 100% oxygen. Moreover, HOT allows the dissociation of CO from cytochrome C oxidase, thus improving the cellular energy state. **The immediate administration of normobaric oxygen to a CO-intoxicated patient** is certainly useful, because the half life of CO-Hb is only about 60 min and tissue oxygenation is improved, **but it is not as effective as HOT**.

On rare occasions, **haemorrhagic shock may cause intensive anaemia**, unable to satisfy the metabolic demands of tissues: if suitable blood is not available or blood transfusion is not allowed for religious reasons, **HOT may temporarily compensate for the lack of erythrocytes**. These three examples suffice to illustrate **the unique importance of HOT**.

Adverse effects are rare and partly due to typical oxygen toxicity (optic symptoms in about 20% of patients), which can be prevented by administration of antioxidants and by shortening the period of hyperoxia (DuBois, 1962). In addition to **the high cost of installing a HOT facility, the oxygen presents a fire hazard**. Indeed, in the last decade, owing to incompetence and negligence, there have been two tragic explosions in Italy: one in Naples in a single-place chamber and another in Milan in a multi-place chamber with several deaths. These accidents should never occur, as the chamber should be regularly filled with inert air. In comparison, **oxygen-ozone therapy does not present risks, unless a mad ozonetherapist directly injects the gas IV, a procedure that is prohibited**. Moreover**, the cost of the material for ozonetherapy is almost negligible**.

There are fundamental differences between HOT and ozonetherapy. Although the bulk of the gas mixture is represented by 95–99% oxygen, ozonetherapy does not aim to oxygenate blood directly. Indeed, with all the procedures (AHT, EBOO, BOEX and RI), the arterial pO_2 hardly increases in vivo. Yet **if ozone is used properly, it has many virtues**: disinfectant and immunomodulatory (cytokine release) activities, increased delivery of oxygen to hypoxic tissue through vasodilatation ($NO^{\bullet}$, CO) and possibly a shift of the HbO_2 dissociation curve to the right (the venous pO_2 may fall to 20 mmHg), release of growth factors (PDGF, TGF-β1, etc.) thus enhancing tissue healing, possibly hormonal release due to a sudden homeostatic change and/or a placebo effect and, most importantly, a generalized metabolic improvement with enhancement of the antioxidant defence.

Another significant difference is that **ozonetherapy induces fairly long-lasting and interconnected metabolic changes, while the effects of HOT, being due mainly to a transitory oxygen hyperconcentration, are of shorter duration**. Interestingly, increased DNA damage was detected immediately at the end of the first HOT, while no effect was found 1 day later (Dennog et al., 1996). They also suggested that HOT, under the same conditions, may increase antioxidant defences but this result is not surprising. This suggestion is now supported by interesting experimental data (Kim et al., 2001). Cianci (2004) has provided evidence that HOT i.e., a high oxygen tension favours cell replication in vitro and wound healing in vivo. The finding of significant oxidative base damage after the first HOT treatment reinforces my conviction that ozonetherapy should always start with a very low dose followed by a gradual increase to minimize any possible damage.

An objective comparison of the therapeutic efficacy of HOT versus ozonetherapy is not possible, mostly because valid RCTs of ozonetherapy are few and small, while there are many publications dealing with HOT. However, even though as many as 64 different disorders seemed to be improved with HOT, in most of them the evidence to warrant its clinical use was insufficient (Kindwall, 1993). There is only one paper comparing rheological parameters (but not clinical efficacy) between HOT and ozonetherapy: Verrazzo et al. (1995) claimed that only the latter approach caused a significant increase of erythrocyte filterability and a decrease of blood viscosity. On the basis of our data, these results need to be confirmed because a rational ozonation. Process does not involve the cell membrane. This claim appears to be a reliquiae of the previous procedure of treating blood with ultraviolet light, which was an extremely imprecise approach.

In Table 10.1, I attempt to summarize the diseases for which either HOT or ozonetherapy are used and to express an opinion, based on personal experience and not on hard data, about which of the two approaches seems more beneficial.

It may seem that I favour ozonetherapy and the reason is that, in some affections, ozonetherapy is very effective. In most cases, we can apply both parenteral administration, in the form of AHT, EBOO, BOEX and RI, and topical application, either as a gas mixture (bagging and dynamic insufflation) or ozonated water and oil. **The combination favours an incredible synergic effect, which acts on several targets**. Indeed this explains the efficacy of ozonetherapy where there are several components at work simultaneously (infection, inflammation, cell necrosis, ischaemia, dysmetabolism, impaired healing, etc.). Several of these affections have been discussed in the previous chapter (Sections I and VII).

Table 10.1 Diseases for which HOT and ozonetherapy are used

		Hot	Ozonetherapy
(1)	Arterial gas embolism	+++	——
(2)	Decompression sickness	+++	——
(3)	Severe CO poisoning and smoke inhalation	+++	——
(4)	Severe blood-loss anaemia	+++	——
(5)	Clostridial myonecrosis (gas gangrene)	+++	++
(6)	Compromised skin grafts and flaps	+	+++
(7)	Prevention of osteo-radionecrosis	+	+++
(8)	Radiation damage	+	+++
(9)	Refractory osteomyelitis	+	+++
(10)	Necrotizing fasciitis	+	+++
(11)	Traumatic ischaemic injury	+	+++
(12)	Thermal burns	+	+++
(13)	Chronic ulcers and failure of wound healing	+	+++
(14)	Multiple sclerosis	——	+?
(15)	Chronic fatigue syndrome	+	++
(16)	HIV-AIDS	+?	+
(17)	Senility	+	++

Legend: +, little; ++, modest; +++, good activity; ——, no activity; ?, uncertain

Bevers et al. (1995) proposed HOT (20 sessions at 100% O_2 at 3 bars for 90 min) for patients with severe radiation-induced haematuria. Dr. R. Dall'Aglio informed me to have solved this problem with only three intravesical applications of ozone gas (once weekly!).

HOT was proposed for patients with AIDS (Bocci, 1987a) and a subsequent study showed a transitory improvement of the quality of life (1993, Hyperbaric oxygen therapy for the treatment of debilitating fatigue associated with HIV/AIDS, *JANAC* 4(3), July–September). An interesting comparison between the therapeutic value of HOT and ozonetherapy administered by intraperitoneal ozone has been reported by Bulent et al. (2010) Rats undergoing an experimental acute necrotizing pancreatitis were better protected by ozonetherapy than HOT.

Thus there is no doubt that HOT has a precise and unique rationale in affections no. 1–5. In all other diseases, the use of HOT is not well supported and the risk of transferring the patient, who often lives far away from the site of the chamber, discourages its use.

The purpose of this chapter was to clarify that ozonetherapy is very versatile, practical, inexpensive, without side effects and quite beneficial in several affections. I would like to believe that orthodox physicians, rather than being biased against ozonetherapy, simply do neither know about it, nor how to perform the therapy.

10.1 Conclusions

The reader may find useful the objective comparison between OHT and ozone therapy. In my opinion, both approaches are important and basically use oxygen as the vital element for maintaining life and activating wound healing. However, while HOT uses only oxygen under pressure, ozone therapy uses a small and precise dose of ozone as the compound able to generate messengers crucial for activating several biological functions. This fact DEEPLY differentiates their practical applications and, in order to maximize their usefulness, either HOT or ozone therapy must be used within their specific fields.