Hyperbaric oxygen. The role of oxygen, particularly hyperbaric oxygen, is underappreciated in cancer treatment. Historically, the work of Judah Folkman, MD, on angiogenesis implied that cancer could be destroyed by drugs which inhibit blood supply to cancer cells. We are now learning that decreasing blood supply actually makes cancers more aggressive.

As cancer cells become more hypoxic, a transcription factor described as hypoxia-inducible factor 1a is released, causing the cancer to become more glycolytic. The data show that the more hypoxic the tumor, the more aggressive.

Conversely, when we feed cancer cells oxygen, that reduces the aggressive nature of the cancer. In my experience, patients with cancer do better with therapies that increase the supply of oxygen to the tissues. Currently, a study is being conducted at Long Island Jewish Medical Center on the use of hyperbaric oxygen in cancer treatment.

Conditions Benefitted

- Post Radiation effects
- Osteoradionecrosis

HBOT effects Radiation injury in the following ways:

- Saturates the effected area as well as ALL tissues in the body with oxygen
- Fibroblastic proliferation begins
- Initiates efficient collagen synthesis
- Reduces inflammation and swelling
- Reduces pain and discomfort
- Heals damaged tissue with less scarring and no major side effects for most patients

Many patients, when following closely the prescribed protocol for Hyperbaric Oxygen Therapy notice the following cumulative benefits from the oxygen:

Following Medical protocol for HBOT and radiation injury is VITAL

Hypoxia has been noted in malignant tumors (Gray et al 1953). Anemia is common in the cancer population and is suspected to contribute to intratumoral hypoxia. The theoretical basis for the use of HBO as an adjunct to radiotherapy is as follows:

- A number of proliferating cells in many tumors are under severely hypoxic or anoxic conditions.
- The reproductive integrity of such cells is substantially more resistant to damage by radiation than that of cells oxygenated to normal physiological levels.
- The larger the number of cells that lose their reproductive capability, the greater the chance of cure or palliation.

Sergeev et al(1977) concluded: “Hyperbaric Oxygen employed in radiotherapy increases the rate of neoplasm damage and reduces the rate of recurrences… No rise in percentage of distant metastases was noted in cases irradiated under hyperbaric oxygenation.”

Experimental studies of the effect of HBO on tumor radiosensitivity

Fukimura (1974) Rabbits with implanted VX2 maxillary carcinoma. Two groups:

- -- Experimental radiotherapy under HBO
- --Control radiotherapy without HBO

1 tumor disappeared in 53% of the experimental group as compared to 13% in control group. 2 DNA synthesis inhibited more markedly in the experimental than in the control group.
McDonald et al (1996)

- Twenty golden Syrian hamster cheek-pouch carcinomas were induced with an established chemical carcinogen. Half of these underwent 30 HBO sessions (2.8 ATA/1h) while the other half served as controls.

At necropsy, animals receiving HBO therapy had significantly smaller tumors and fewer metastases.

Clinical studies of HBO as an adjunct to the radiotherapy of head and neck cancer

Glanzmann et al (1974) Malignant tumors of oropharynx and laryngopharyn. Combined radiation and HBO. Results compared with literature reports of treatment by radiation alone. Improvement observed in the healing quotient in advanced tumors particularly those of the oropharynx.
Nelson and Holt (1978) Advanced head and neck cancer. Three groups;

1. Colbalt radiotherapy
2. Cobalt radiotherapy
3. Radiotherapy & HBO & microwave hyperthermia

Group, Resolution, 3-yr survival

- Group 1: 36.5% /w 19%
- Group 2: 62.5% /w 29%
- Group 3: 94.0% /w 54%

Darialova et al (1985) Laryngeal cancer. Randomized. Method of mean fractionation to overcome tumor hypoxia and to raise selective radiosensitivity.
In the group with HBO plus radiation:

1. Less frequent radiation reactions
2. Less metastases.

Denham et al (1987) Squamous cell carcinoma arising from: anterior two-thirds of the tongue, oropharynx, hypopharynx, supraglottic larynx. Radiotherapy under HBO versus air. 5-year survival was higher in the HBO group than in the group treated in air.
Whittle et al (1990) Glottic cancer. Retrospective analysis of 397 patients. 240 treated in air

Clinical studies of HBO as an adjunct to the radiotherapy of head and neck cancer

and 157 under HBO. Local tumor control rate showed significant improvement in favor of HBO: Stage I, 10%; Stage II, 37%; Stage III, 73%

Haffty et al (1999) Randomized trial on 48 patients evaluating HBO at 4 ATA in combination with hypofractionated radiation therapy in patients with locally advanced squamous cell carcinoma of the head and neck (SCCHN). Long-term outcome from this study demonstrates substantial improvements in response rate with the use of HBO.

Advantages of HBOT as an adjunct to radiotherapy

Combination of HBO with radiotherapy is considered to be useful for the following reasons:

- It allows a more uniform kill by improving the oxygenation, and therefore the radiosensitivity, at the cellular level.
- It is useful as an adjunct to surgical repair after radiation.

HBO is considered to be the most effective method for counteracting tumor hypoxia for enhancing the effect of radiotherapy on cancer). The advantages of HBO combined with radiotherapy are:

1. HBO is also a useful therapy for radiation-induced necrosis of normal tissues.
2. In a controlled study of patients with or without HBO, the survival has shown to be higher in the HBO control group. The greatest advantage was seen in the less advanced tumors).
3. In experimental bladder tumor, tissue oxygen tension has been shown to be higher in the bladder trigone region (Nakada 1988). HBO was shown to enhance the effect of combined chemotherapy and radiotherapy in this model (Akiya et al 1988).

Machin et al (1997) have reviewed the survival outcome from the randomized Phase III trials in solid tumors published on behalf of, or in collaboration with, the *Cancer Therapy Committee (CTC)* of the British Medical Research Council over a 30-year period to 31 December 1995. In all, 32 trials, involving over 5000 deaths in more than 8000 patients, have been published. Tumor types have included bladder, bone, brain, cervix, colon and rectum, head and neck, kidney, lung, ovary, prostate and skin. The MRC trials have made an impact on both clinical practice and research activities. Trials of HBO have defined the biological activity of this approach, and the appropriate dose of radiotherapy in patients with brain tumors has been found.

There is considerable evidence for the presence of hypoxia in human tumors. Vascular insufficiency has been demonstrated on histopathology of the tumors, direct oxygen measurements, and mapping of hypoxic areas by imaging techniques. It appears that hypoxia is probably responsible for failure to cure some tumors such as squamous cell carcinoma, but even within tumors of the same stage and type, hypoxia does not occur to the same extent. Response to modifying agents also depends upon whether hypoxia is acute or chronic. New methods to detect hypoxic tumor cells (hypoxic cell stains) are being developed. The future prospects for the control of these tumors where hypoxia is a problem appear to be good. Of the various adjuvants to radiotherapy, HBO appears to be the best (Henk 1981). It can be combined with other radiation enhancers. The effect of HBO in enhancing radiosensitivity is most pronounced in head and neck tumors