A Review of Whole Body Hyperthermia and the Experience of Klinik St. Georg

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Whole body hyperthermia (WBH) is the deliberate heating of the whole body to achieve an elevated core temperature of 41–42°C for a shorter time frame (average of 2 hours) or 39–40°C (average of 4 to 8 hours). There are clinical trials all over the world, including in the US, demonstrating that WBH generally along with chemotherapy can have remarkable effects in late-stage cancers with advanced solid tumors, advanced refractory or recurrent cancers, mesothelioma, advanced metastatic sarcoma, advanced metastatic cancers (GI, breast, head and neck, sarcoma, neuroendocrine), ovarian cancer, metastatic colorectal cancer, pediatric renal cell carcinoma, metastatic cervical cancer, metastatic sarcoma, metastatic melanoma, nodular lymphoma, chronic lymphocytic leukemia, and a host of other late-stage, chemo-resistant metastatic cancers.

Most studies use a lower therapeutic dose of chemotherapy, since WBH has a synergistic effect and can lower the effective dose and overcome multidrug resistance. Several trials have also shown that WBH has a synergistic effect with radiation and can lower the effective dose, making the radiation therapy less damaging. Unfortunately, WBH is only being studied in advanced, refractory, and multidrug-resistant patients. Yet the results have been remarkable. WBH is being used all over the world, including in Austria, Eastern Europe, Japan, China, and most notably Germany as part of an integrative cancer treatment.

The use of heat to treat disease dates back to ancient times. Application of fire to cure breast cancer is recorded in an ancient Egyptian papyrus. The therapeutic value of elevated body temperature by fever was recognized by Hippocrates, who wrote: "What medicines do not heal, the lance will; what the lance does not heal, fire will." Parmenides stated: "Give me a chance to create a fever and I will cure any disease." Hot baths are considered therapeutic in Egypt, Greece, Rome, China, and India and also among many aboriginal tribes. German physicians in the 19th century observed regression of sarcoma in patients who suffered prolonged, high fevers due to infectious disease. William Coley, a famous physician from New York City, used bacterial endotoxins, now known as Coley's toxins, to induce fever and cure many types of cancer. Elevated body temperature has been recognized as a cure for cancer and other diseases for centuries.

The majority of WBH systems being used employ infrared (IR) radiation to achieve systemic heating. A period of steady temperature increase is followed by a plateau phase wherein the target temperature is maintained for 30 minutes to several hours, followed by a cool-down phase. The patient is normally sedated to induce sleep during the procedure. The device mainly used in German clinics is the WBH-2000 unit and Heckeal HT 3000, which are chambers that enclose all but the patient's head. Special light-emitting diode radiators deliver computer-generated, water-filtered IR-A wavelengths that penetrate the skin to deliver heat to the capillary bed. These units are generally used because they have been shown to preferentially stimulate the immune system (Figure 1). In the US, oftentimes microwave radiation units are used instead. These have minimal impact on stimulating immune function and are dangerous: they need to be extremely focused and controlled because they can cause hot spots and burn damage, whereas infrared units will not. IRA is a wavelength that specifically stimulates mitochondrial function; microwave radiation does not.

Therapeutic Effects of WBH

The effects of hyperthermia on natural killer (NK) cell activity have been examined in animal models. In a recent review article, WBH was shown to enhance NK cell cytotoxicity against tumor cells that is in part responsible for the improved clinical responses seen when hyperthermia is combined with other therapies. Animal studies have shown that WBH increases chemotherapeutic agent uptake (for example, liposomally encapsulated doxorubicin) into tumors. It also may increase the number of perfused blood vessels over a prolonged period, making it useful for improved tumor targeting of cancer therapies. WBH induces heat shock proteins (HSP) that can induce anticancer immune
responses by targeting associated tumor antigens to the immune system. HSP not only carry antigens but can also induce maturation of dendritic cells, resulting in a more efficient antigen presentation. Hyperthermia has been shown to have important stimulatory effects on several cellular and organismal endpoints related to the immune system. Dendritic cells are antigen presenting cells that play a central role in the generation of effective antitumor immunity. Not only do they have the potential to recruit, select, and expand T cells that are specific for tumor cell antigens within lymphoid organs, but tumor-associated or vaccine-delivered dendritic cells may also help recruit T cells to the tumor site and help maintain their survival once they arrive. Since dendritic cells have been shown to be thermally sensitive, using WBH in combination with immunotherapy strategies that are known to depend upon these cells such as vaccination may offer a superior benefit than using immunotherapy alone.

Hyperthermia may also play a role in gene therapy. Inadequate systemic delivery of functional DNA seriously limits current cancer gene therapy. In an animal model, WBH was shown to enhance the efficacy of suicide gene therapy through selectively increased tumor gene delivery and expression. An increase in other immune cells such as CD56+, IL-2 (causing tumor lysis), cytotoxic T lymphocytes, IL-6, TNF-alpha, CD4+ T cells expressing the T cell activation marker CD69, monocytes, and macrophages have been observed. Human and animal studies have shown that WBH can have a profound and therapeutic effect on the immune function of an organism infected with cancer. The tumor goes into apoptosis with the IR-A heat due to metabolic exhaustion, loss of ATP production, hypoxemia and an increase in lactic acid, production of heat shock proteins; all cause destruction of the cancer. However, the surrounding healthy tissue is not affected but improved due to the better oxygenation, higher production of ATP, higher blood flow, and the increase and activation of immune cells. The tumor dies within the body, so now the immune system can recognize the cancer cells since the tumor antigens are presented by the invading macrophages to T cells and NK cells. NK cells are also activated by the production of heat shock proteins. Compared with what conventional oncology has to offer, it is clear that WBH when done correctly with the right machine can have a profound impact on cancer and patient survival.

Human Studies

Despite numerous human studies and case reports, WBH is considered experimental, particularly in the US. However, it is used frequently as part of an integrative approach to cancer in Germany and other countries. The vast majority of published data have been on patients with advanced disease as a last resort. In these studies, WBH was used either as a sole or adjunct therapy. Any response whatsoever is often remarkable and has been achieved with WBH.

Cancer multistep therapy was conceived by Dr. Manfred von Ardenne in 1965. It is a combined modality treatment with three process steps.

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Figure 1
SM’s PET-Scan taken in January 2007
The PET-Scan shows a massive infiltration in the peritoneum, the lymph nodes, liver, and spleen. The patient was at this time untreatable because of multidrug resistance.

Figure 2
SM after treatment at St. George Hospital with two whole body hyperthermias, local hyperthermia, and a complementary nontoxic cancer treatment program. No hot spots are visible; patient is in a complete remission. See also Figure 3.
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steps: WBH, induced hyperglycemia, and hyperoxemia. It was further developed into a systemic therapy of high efficiency and selectivity, since the knowledge of the synergistic-additive effects of chemotherapy became known. This is the manner in which WBH is generally administered chemotherapy, one remained stable and one progressed. These results indicate that WBH plus chemotherapy is a beneficial treatment choice for metastatic adenocarcinoma.

Fourteen patients with drug-resistant, advanced-bulky or metastatic cancers received 1 to 9 treatment cycles in Germany and will be discussed later.

Metastatic adenocarcinomas of the GI tract are one of the more difficult tumors in which to slow disease progression. Standard chemotherapy has not significantly improved the long-term survival of these patients. However, WBH with chemotherapy was reported to improve survival. A phase II study was undertaken to compare the effectiveness of WBH-plus-chemotherapy with chemotherapy alone in patients with treatment-resistant, progressive disease. Nine patients were randomly assigned to a group. All received a continuous infusion of 5FU (425 mg/m2) and leucovorin (20 mg/m2) for 5 days followed by a 24-hour window without therapy, with either WBH (41.8°C for one hour) and chemotherapy or chemotherapy alone. After 2 monthly cycles, 1 progressive disease and 6 of 7 patients had a partial response who received the combined treatment. In those who received (every 28 days) with gemcitabine and cisplatin and interferon-alpha combined with long-duration WBH (40°C for 6 hours). In 13 patients, 6 objective responses included: 5 partial responses (2 pancreas, 1 gastric, 1 lung, 1 renal), (2/5 PRs were >90%) and 1 major response with a duration of 5 months (larynx). Additionally, 4 patients had stable disease for longer than 12 weeks. Four patients experienced progressive disease. The authors concluded that that the treatment is safe and well tolerated, and induces meaningful clinical benefit in patients with chemotherapy-resistant tumors.

Five patients with inoperable or metastatic pancreatic cancer were treated using a phase II protocol of a sequenced combination of whole body hyperthermia (6 hours at 40°C) with cisplatin (60 mg/m2) and gemcitabine (60 mg/m2) with daily metronomic, low-dose interferon-alpha (1 X106 IU). Patients received 1 to 5 treatments. The researchers documented 2 objective responses (40%), 2 partial responses (40%), and 1 progressive disease (20%) for an 80% overall response. Of interest are that 3 patients who had been heavily pretreated experienced meaningful tumor responses. This regimen appears to demonstrate clinical activity. The authors repeated the protocol with other patients (17 total) and demonstrated a similar clinical response, noting that responding patients experienced an increased quality of life, meaningful responses, and for one patient, clinical remission. More than 22 clinical trials have been completed for many types of advanced cancers, using various chemotherapeutic agents as an adjunct. Some studies used higher temperatures (for example, 1 hour at 41.8°C), while other studies used milder temperatures (39.5°C for 3 to 6 hours). The protocols also varied in terms of how many WBH treatments the patients received. More than 9 of these trials are phase II. Despite the fact that phase III trials have not been completed, clinics abroad, most notably in Germany, regularly use WBH as an integrative approach to cancer care. The reason is that most of these clinics see patients who have advanced disease and/or who have failed treatment, and they have seen firsthand the excellent results achieved using this modality. Furthermore, German clinics generally raise the patients' temperature to 41.6–41.8°C for 60 to 90 minutes – a substantially higher temperature and longer plateau than used in the US. Between the heating and cooling phase, the entire procedure generally lasts 4 to 5 hours.

The Klinik St. Georg Experience

Klinik St. Georg is located in Bad Aibling, Germany, approximately one hour from Munich. Since 1991, the clinic had existed under the medical direction of Dr. Friedrich Douwes. He is now president of the German Society for Oncology, having been recognized for his outstanding research and clinical contribution to the field of cancer treatment. He has received numerous medical awards for
research and clinical work in the field of hyperthermia. In addition to WBH, Douwes employs local-hyperthermia (the tumor is directly heated), transurethral hyperthermia (to induce tumor kill directly to prostate cancer), electrochemical therapy (electrical current is used to induce tumor lysis), immunotherapy (using both natural and prescription immune-stimulating compounds), detoxification (through chelation therapy and colonicis), and extensive nutritional support to complement the therapies. This discussion will focus on the results of WBH.

Douwes and his staff use high-temperature WBH, wherein the body is heated on average 41.6–41.8°C for 90 minutes. The procedure takes 4 to 5 hours to complete, as previously discussed. During the procedure, a temporary state of hyperglycemia using glucose is induced to improve tumor response. Low-dose chemotherapy and/or more natural therapy such as intravenous vitamin C (25–50 grams) are administered during the procedure. The high acidity and hypoxia that occur damage the vessels that nourish the cancer cells. WBH also damages the membranes, proteins, and enzymes of cancer cells, making them more vulnerable to anticancer agents – including herbal, nutritional, chemotherapy, and radiation. While Douwes has countless case reports of patients tracked for years, the following is a brief review of some of the success documented in scientific journals, at medical conferences, and from his own files.

Twenty-one patients with recurrent, multidrug-resistant advanced ovarian cancer were treated with WBH and platinum-based chemotherapy. During WBH, a core temperature of 41.5–42°C was achieved. The WBH was combined with artificial hyperglycemia (300–400 mg/dl). The plateau temperature was held over an average of 90± 30 minutes and the artificial hyperglycemia on average 240± 30 minutes. The treatment was repeated every 3 to 4 weeks for several months. One patient (4.8%) had complete remission, 7 patients (33.3%) had partial remission, stable disease was noted in 10 patients (47.6%), and 3 (14.3%) did not respond and had progressive disease. Median time to progression was 6.4 months and median survival time was 16.5 months. For the responder group, other studies have shown excellent response rates for ovarian cancer as well as for other types of cancer such as sarcoma. An example of an excellent clinical case is SM, a 47-year-old woman diagnosed with stage 3C metastasizing adenocarcinoma of the ovary in August 2005. She had previously had her ovaries removed, after which she received 6 cycles of chemotherapy with taxol and carboplatin, beginning December 8, 2005. She experienced a continuous increase in tumor markers, and a CT scan July 1, 2005, revealed metastatic spread. She received further chemotherapeutic treatment with Caelyx (liposomal, encapsulated doxorubicin) and did not achieve any results. The therapy was aborted; and she was told to get her affairs in order, since she had only a few months to live. She was seen for the first time at Klinik St. Georg on August 22, 2007. She received 50 mg of cisplatin intraperitoneally with simultaneous systemic mitomycin C 10 mg and 20 mg liposomal doxorubicin (Doxil).
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Her core temperature was elevated to 41.6°C for 120 minutes. She also received locoregional hyperthermia to her abdomen 3 times per week at a temperature of 42-44°C, as well as immunotherapy (e.g., thymus extract), nutritional support, intravenous vitamin C (25 grams), and detoxification (chelation therapy). On August 29, 2007, she received the same protocol. On October 24 and 31, 2007, she received the same WBH protocol without the intraperitoneal infusion. Peritoneal infuson was no longer necessary, since there was no longer any ascites. She was in remarkably improved condition, with no pain and normal bowel function. Her initial CA-125 was 112 U/L and it was now down to 4.5 U/L. The patient received her final treatments on March 12 and 19, 2008, with the same systemic protocol. Prior to the treatment, her PET scan was negative. Her CA-125 was now down to 3.7 U/L. She remains alive and well today.14

Another case is RF, a 69-year-old woman diagnosed with breast cancer in 1986 (moderate differentiated invasive ductal, pt2aN0MxG2L1). She had conventional treatment with removal of the right breast, followed by 3 cycles of chemotherapy (with FAC schedule; polychemo treatment). She then stopped because she could not tolerate the chemotherapy and was put on Tamoxifen. In 1989 (3 years later), she had a local recurrence that was removed by surgery. In 1992 she again had a local recurrence, although she was under antihormonal therapy with Tamoxifen. She was then treated by radiotherapy (50, 4 Gray). After this treatment she developed a lymphedema in her right arm. In 1994 she had again a local relapse in the right thoracic wall, this time also with involvement of her lymph nodes in the right supraclavicular area. She refused any further conventional treatment and went to Klinik St. Georg. RF received 4 whole body hyperthermias (initial treatment July 8, 1996) in combination with 10 local hyperthermias with low-dose chemotherapy (FEM schedule, 50 mg Epirubicin, 30 mg Mitomycin, 750 mg 5-FU) (5-FU, Epirubicin, Mitomycin). She received one whole body hyperthermia treatment each week for 4 weeks (7 days apart) and local hyperthermia 3 or 4 times per week. This brought her into a long-lasting remission. The after care follow-up was negative up to her last visit in December 2008. She is on a complementary medicine maintenance program.13

An excellent review article was written by H. Kaltas in 2000, titled “Too Hot for Cancer: Hyperthermia and Electrotherapy.” Several of Douwes’s patients were interviewed, including a patient with late-stage terminal ovarian cancer that after 8 years had spread to her liver, colon, and bladder. After several WBH treatments with low-dose chemotherapy and locoregional hyperthermia, the patient was in excellent health. She returns to the clinic once or twice a year to keep up the remission. A 56-year-old man with extensive non-Hodgkin’s lymphoma visible throughout his body received several WBH treatment with excellent results. He was able to tolerate the chemotherapy, since with WBH the dose used was 60% less than what is normally used.11 Douwes has excellent case studies of advanced breast, colon, lung, sarcoma, and many other types of cancer that have responded remarkably to WBH along with an integrative approach. Perhaps that is why he is achieving even greater success than what is being reported elsewhere.

A Different Philosophy

There is a fundamentally different philosophy to the cancer treatment at Klinik St. Georg. Douwes is not going to wait for phase III trials to confirm what he already knows about WBH. Furthermore, most of the published clinical trials using WBH have already shown remarkable results.1,11,13 He has practiced oncology since 1975 and was unsatisfied with the results of the conventional approach to cancer. He is clear that the “war on cancer” has not been won with the vast majority of conventional therapies available. This is what led him on the path to finding the very best modalities that can add meaningful and quality time to the life of a cancer patient. He was also not pleased with patients being “scared to death into treatment”: being told they will die if the malignancy is not treated immediately and rushed into therapy (whether the research shows it works or not) without time to explore other options. Douwes prefers to have a more positive attitude with patients; so many come to him already hopeless, it is important that they now still have a chance.

Dr. Lieberman earned her PhD in Clinical Nutrition and Exercise Physiology from the Union Institute, Cincinnati, Ohio, and her MS degree in Nutrition, Food Science, and Dietetics from New York University. She is a Certified Nutrition Specialist (CNS); a Fellow of the American College of Nutrition (FACN); a member of the American Academy of Anti-Aging Medicine (AAM); a former officer, present board member, and chair of the exam committee for the Certification Board for Nutrition Specialists, and immediate past president of the American Association for Health Freedom. She is the recipient of the National Nutritional Foods Association 2003 Clinician of the Year Award and is in the Cambridge Who's Who Registry of Executives and Professionals. Her newest books, The Gluten Connection (Rodale 2007) and Transitions: Glycerin Index Food Guide (Square 1 Publishers 2008), were recently released. Dr. Lieberman’s best-selling book The Real Vitamin & Mineral Book is now in its 4th edition (Avery/Penguin Putnam, 2007). She is the author of The Mineral Miracle (Square 1 Publishers 2008). User’s Guide To Brain-Boosting Supplements (Basic Health Publications, Inc., 2004), Dana To Lose! - 4 Simple Steps to a Bodie Body (Avery/Penguin Putnam, 2003). Get Off the Menopause Roller Coaster (Avery/Penguin Putnam, 2002), Maitake Mushroom and D-Isation (Woodland Publishing, 2001), Maitake King of Mushrooms (Keats Publishing 1997); and All About Vitamin C (Avery Publishing Group, 1989). Dr. Lieberman is the founding dean of New York Chiropractic College’s MS Degree in Clinical Nutrition; an industry consultant; a contributing editor to the American Medical Association’s 5th Edition of Drug Evaluations; a peer reviewer for scientific publications; a published scientific researcher; and a presenter at numerous scientific conferences. Dr. Lieberman is a frequent guest on television and radio, and her name is often seen in magazines as an authority on nutrition. She has been in private practice as a clinical nutritionist for more than 20 years.

Dr. Lieberman's letter to Townsend Letter for Nutrition 2008. Dr. Lieberman is a frequent guest on television and radio, and her name is often seen in magazines as an authority on nutrition. She has been in private practice as a clinical nutritionist for more than 20 years.

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with their lifestyles and find successful treatment options, there is no reason why someone cannot live a full and productive life with cancer.

Notes

References