The Anatomy of the Immune System

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This Article is the third in a series by Dr Barnes which explore the structure and function of the immune system, and how it fits into the changing medical paradigm.

Introduction

Immune therapies have long been the holy grail of cancer research with a huge prize. So far in mainstream research isolation of factors such as interferon and interleukins along with other factors such as colony stimulating factors have been where the research, particularly in America, has been focused. However there are some methods, which are proving to be useful in harvesting the attributes of the immune system. They have been in clinical use for many years with promising results.

Hyperthermia

Simple research on the internet reveals information on research into hyperthermia as a modality for treating cancer. Most of these papers will come from American research institutes and will have one believe this is a new direction in cancer therapy. Dig a little deeper however and a little more laterally and you can go back to ancient writings and traditional practices around the world, to find that heating the body is a time honoured method of healing. Traditional doctors used to treat tumours back as far as 5000BC with heat. Hyperthermia in the modern form has been practiced in America, Australia and Germany since the mid 1970's. Heating techniques range from microwave, radio wave and infra-red light techniques, along with wax baths and water baths. The technique that I have used and researched is the use of infra-red light as a way to increase body temperature.

Types of Hyperthermia

There are many different methods of applying hyperthermia and I list a few here:

1. Local superficial hyperthermia.
2. Local deep hyperthermia with microwave or radio frequency machines.
3. Intrastitial hyperthermia ie; heat application directly into the tumour.
4. Special hyperthermia such as heating up limbs or the heating of the prpstate via the urethra.
5. Cavity hyperthermia such as heating water and using this to heat pleural and abdominal cavities.
6. Whole body hyperthermia is used mainly in patients with advanced and/or drug resistant forms of cancer.

Research shows that cancer cells are less tolerant to heat than normal cell tissue. Cancer cells tolerate no more than 42 degrees, where as a normal cell can tolerate up to 43.5 degrees. Local hyperthermia exploits differentiation of temperature and can be used to heat tumours locally using this method.

A constant stream of heat through the tumour must be obtained for best results. These techniques have been developed in German clinics using short frequency waves 13.4 and 26 megahertz. This technique has also been used using microwave therapy.

These techniques can be used with solid tumours where the aim is for local tumour reduction and where there is no metastatic spread.

Whole body Hyperthermia

Whole body Hyperthermia can be divided into three categories – mild hyperthermia, moderate hyperthermia and extreme hyperthermia.

Mild and moderate hyperthermia can be conducted in an outpatient environment. However extreme hyperthermia requires full hospital facilities with anaesthetic and intensive care facilities. Clinics in Germany have used extreme hyperthermia extensively.

Mild hyperthermia describes the elevation of core temperature to 38 degrees. This therapy is used in conditions such as poor healing, hypertension and detoxification treatments.

Moderate Hyperthermia

Moderate hyperthermia involves the heating of the core temperature from 38.5 to 40.5 degrees. This current therapy can be used in an outpatient clinic and is probably the most used form of hyperthermia. It can be used as a method of treatment of cancer. It is not designed to kill cancer directly but to modulate various functions that aid tumour death. The functions that moderate hyperthermia performance are:

1. Activation by bio-chemical processes in the body.
2. Increasing permeability of cell membranes to water oxygen nutrients, break down products and aiding detoxification and if needed chemotherapy.
3. Increasing circulation – aiding transport of nutrients to cells.
4. Activation of the immune system.

Activation of the immune system

Immunological and biological effects of heat are categorised by:

1. Increase of phagocyte activity.
2. Activation of T effector cells (see previous article).
3. Induction of cytokine synthesis and function (cytokines being interleukins and interferon).
4. Expression of heat shock proteins.
5. Induction of Natural Killer cells.
6. Increase in the antigenicity of cancer cells increasing the ability of phagocytes to detect their presence.
7. Induction of apoptosis (spontaneous cell death).

Hyperthermia has been shown to act as a modulator for other therapies.

Thermo-chemo Therapy

The idea of heating the body to enable other therapies to work better and to have greater effect has been explored for many years. Extensive laboratory research has shown the enhancing effect of hyperthermia in conjunction with chemotherapy. Studies have shown that some chemotherapy can be maximised at temperatures between 39.5 and 43.0 degrees. The thermo-chemo effect has been seen in drugs that have an alkalising effect. The drugs effect can be increased up to fourfold. This has greatly improved the overall effect of chemotherapy because:

1. There is a lowering of doses of chemotherapy that are required.
2. The lower doses allow preservation of immunological function, in other words the immune system is not so severely disrupted and other modalities in therapy can be used to stimulate the immune function in conjunction with chemotherapy.

Thermo-chemotherapy is generally reserved for advanced cases when the effect of hyperthermia alone will not be seen as sufficient.

Combination Radiotherapy

In April 2000 a paper was published describing a comparison of radiotherapy with radiotherapy plus hyperthermia in locally advanced pelvic tumours. This was a prospective study meaning it was closely followed through the course of the treatment. 358 patients were enrolled between 1990 and 1996 in a number of cancer centres in the Netherlands. Most patients suffered from bladder cancer, cervical cancer or rectal cancer, patients were assigned radiotherapy or radiotherapy plus hyperthermia. In this study complete responses were noted in 39% of the patients with radiotherapy and 55% of the cases with radiotherapy plus hyperthermia. Together with this the duration of local control of the disease was significantly longer with those patients who received both radiotherapy plus hyperthermia. The group with the best response were patients with cervical cancer. The complete response rate with radiotherapy plus hyperthermia was 83% compared with 57% with radiotherapy alone. The three year survival of the combined group was 51%, whereas with radiotherapy alone it was 27%.

Hyperthermia plus vaccines and other immune stimulating substances

Researchers are now continuing to explore the combining of hyperthermia with vaccines together with the use of other forms of immune modulated therapies. In my clinic we have explored the use of hyperthermia with mistletoe therapy and another therapy called Jomol therapy, which works very similarly to colicoxins.

Jomol is a bacterial wall fragment from a bacteria called Norcordia Opacica. This bacterial lives in the intestines of most mammals and is seen to be non-pathogenic. However, researchers and developers in Germany have suggested that this bacteria may play a part in stimulating a immunological response to cancer.

We use the preparation of JOmol during the heating phase of hyperthermia. The bacterial wall treatment (Jomol) is injected causing an immunological reaction. Research has shown that it stimulates many of the required immunological reactions such as increase in Natural Killer cells. A combination of Jomol and hyperthermia potentially increases the total immunological effect against cancer.

Jomol has also been shown to have a unique property in that it seems to have infinity for the wall of cancer cells. The bacterial wall fragment (Jomol) sticks to the cancer cell wall and acts as a target for the immune systems affecting a phagocyte response. This leads to T-cell activation against the cancer.

Conclusion

Hyperthermia in its many forms remains a very powerful immunological tool. Not only does hyperthermia weaken cancer cells and make them more vulnerable to other therapies, but it also stimulates the immune response. Research in animals suggests that after treatment hyperthermia and reintroduction of inoculation of cancer cells, the body retains a memory which enables the immune system to mount a secondary, more appropriate immunological response against the cancer, second time around.

Hyperthermia on its own in advance cases may not be the solution, however, its combination with conventional therapy such as chemotherapy and radiotherapy have improved overall responses and at the same time decreasing some of the side effects encountered by these particular therapies.

References

1. Comparison of radiotherapy in line with radiotherapy plus hyperthermia.
   Lancett 2000, April 1.355 (2510), 1119-2.

2. Invited review for the clinical application of thermo-chemotherapy given at mild temperatures.
   M. Uramo, et al International Journal of hyperthermia 1999 volume 15-2, pages 79-207

3. Effect of Fever like whole body hyperthermia on leucocytes spectrum distribution protein carnase C activity and uropoa
   Wang X Y, J Immuno Volume 62, 3378-3387, 1999.

4. Hyperthermia , a new treatment modality in oncology
   Frederich R Douwes, St George Hospital, Bad Aibling, Germany.

5. Too hot for cancer, hyperthermia and electro therapy.
   Alternative Medicines, November 2000

6. Effects of vivo hyperthermia on Natural Killer cells.
   Tibor Hajto e tai laboratory of immunology at Lucus Clinic, Artesheinm, Switzerland, Clinical Trials Journal 1985 – 1992, volume 6

7. Deep hyperthermia with radio frequencies on patients with liver metastases from colorectal cancer.

D. Hager, Anti-cancer research, volume 19 also 90, 3403-3408, 1999.

8. Heckel infra-red whole body hyperthermia product manual 2000.
   Heckel-H2 2000

9. Categorisation of mild whole body hyperthermia protocols using human breasts, ovarian and colon tumours grown in severe combined immuno deficient mice.
   E A Repasky, Journal of Infectious diseases in obstetrics and gynaecology, vol 7. 91-97, 1999.