Este Link descreve importantes resultados da relação dieta com a doença

Starving cancer cells with a Ketogenic Diet

(Chris Woollams) A number of expert scientists believe that the Ketogenic diet, involving a high ´good fat´, low carbohydrate, lowish protein combination, may have the potential to manage even advanced cancer cases - preliminary research shows it can stop cancer progression, inhibit metastases and kill off cancer cells.

Professor Thomas Seyfried of Boston is a biologist and after years of extensive research he believes cancer is a metabolic disease, not a genetic one. Dr Dominic D´Agostino Assistant Professor at South Florida University concurs and has been involved with treating patients with advanced cancer using a ketogenic diet.

However, before we get carried away by the euphoria, there is cautionary evidence that this effect may depend on the cancer type (see ´Caveats´ below), and nothing has been firmly established as yet.

The Ketogenic Diet has received great interest since we first wrote about it in 2006.

Simple Theories of the Ketogenic Diet

1.The fundamental tenet of the Ketogenic Diet is that cancer cells need to ferment to survive. And to do this they consume glucose and glutamine (from protein). While healthy cells can switch to burning fats if there is insufficient glucose available, cancer cells are inflexible and the theory is that if there´s no glucose available, they wither and die.

Moreover, cancer cells have defective mitochondria - energy metabolism leads to the production of harmful ´reactive oxygen species´. Glucose is essential to destroying these. Without glucose, they kill the cell. There are several caveats to this argument, and I will cover these below.

2.There is increasing evidence that high plasma glucose levels are linked to greater cancer risk and lowered survival in those already with cancer. One study fin the *Journal of Clinical Investigation (Jan 2, 2014* - CLICK HERE) concluded that increased glucose uptake CAUSED cancer.

In another study, researchers at Johns Hopkins showed that depriving colorectal cancer of glucose produced positive results (Click Here).

3. There is increasing evidence that calorie restriction (that is, eating about 15% less calories than you need in a day) can aid cancer survival. (Click here)

4. There is increasing evidence that fasting can increase survival because it reduces plasma glucose levels, and those of the hormones IGF-1 and insulin, both implicated in cancer development. Fasting also restricts glutamine levels, another energy source for cancer. And fasting boosts the immune system.

Note also, that both Calorie Restriction and fasting have been shown to improve chemotherapy outcomes, reduce side-effects, and allow lowered doses of chemotherapy to be used.

5. After 24 hours fasting starts to starve inflexible cancer cells of their fuel (glucose), while normal healthy cells, which are flexible, can burn fuel from other sources (for example, fats). *This is called KETOSIS.*

5. Unfortunately, in practice, 70 per cent of cancer patients cannot bear the thought of fasting even though it can halt cancer progression.

6. A ketogenic diet, which limits carbohydrate and protein consumption, but allows people to eat healthy fats, overcomes the need to fast while enhancing ketosis in the body. There is even a ´food´ made to a Ketogenic formula, and called Keto Cal, for the people who don´t want to fast.

What does the Ketogenic Diet involve?

While calorie restriction may have benefits against cancer, when you next have a meal glucose, insulin, IGF-1 and glutamine levels all spike. This causes mood swings, cellular inflammation and may refuel the cancer cells. Complete fasting (3-5 days) can prevent this. Fasting induces a state of ketosis in the body, where flexible healthy cells deprived of glucose switch to a fat burning system. But cancer cells do not have this flexibility, and so they starve to death.

So then we come to a **Ketogenic Diet** where the rules are simple:

1. Eat no carbohydrates other than non-starchy vegetables - definitely consume no glucose or high fructose corn syrup (think fizzy soft drinks).

2. Eat only a limited amount of protein - and make sure it is quality, fresh protein (fish, chicken)

3. Consume good fats - like virgin olive oil, fish oils, flaxseed, walnut, macadamia and other nuts and seeds, coconut oil, avocados. Eat no ´bad´ trans fats and no cows´ dairy, unless raw and from grass fed cows; even then in moderation.

The theory is that this maximizes the state of ketosis, reduces the drivers of cancer and can starve cancer cells out of existence. Clinical trials are taking place in America on the Ketogenic Diet and on the use of **calorie restriction** and **fasts** whilst having Chemotherapy and radiotherapy. It´s a hot topic.

On June 5th 2013 research results were published by researchers from the University of South Florida (*Angela M Poff, Csilla Art, and Dr Dominic D´Agostino*) and Thomas N Seyfried of the Boston College. In mice with metastatic cancer and using a Ketogenic Diet and Hyperbaric Oxygen in combination and alone, with control groups, the researchers reported that:

*A **"Ketogenic Diet alone significantly decreased blood glucose, slowed tumour progression and increased mean survival time by 56.7% in mice with systemic metastatic cancer.** While Hyperbaric Oxygen Therapy alone did not influence cancer progression, combining the Ketogenic Diet with Hyperbaric Oxygen elicited a significant decrease in blood glucose, tumour growth rate and a 77% increase in mean survival times compared to the controls (Ref: PLOS One).*

The latest thinking on the Ketogenic Diet

We have been telling you for 5 years about the increasing amount of important research on the Ketogenic Diet. The world experts are undoubtedly **Dr Dominic D´Agostino** of the Dept. of Molecular Pharmacology and Physiology, South Florida and **Thomas N Seyfried,** Professor of Biology at the Boston College.

The diet needs to be done under strict supervision by a competent professional (a nutritional therapist trained in the Ketogenic Diet).

Readers may also like to read the articles on Calorie Restriction, and on Fasting and Cancer. The links are provided at the end of the article.

The latest thinking on the Ketogenic Diet is as follows:

a. Carbohydrates, especially refined carbohydrates, glucose, fizzy soft drinks, high fructose corn syrup, high glycemic index foods should all be avoided. Remember, even honey is 50 per cent glucose and fructose! The Ketogenic diet involves the use of only non-starchy carbs from plants.

b. The diet focuses on ´good fats´ like extra virgin olive oil, flaxseed oil, coconut oil and those of raw nuts and seeds, avocado and eggs. Whilst ´bad´ fats like trans fats and cows´ dairy are to be avoided. More than 70 per cent of calorie consumption in the cancer diet comes from ´good´ fats.

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c. Protein consumption should be only light to moderate; and it should be from quality natural, fresh protein sources (pulses, fish, chicken), not dried meats and the like which can have added carbohydrate. High protein consumption can increase glutamine levels, the cancer cells reserve fuel when glucose levels have depleted. Protein also seems to stimulate the mTOR pathway which may drive cancer.

d. Healthy, normal cells have ´flexibility´ and can use carbohydrates (like glucose) or ketones (produced by the metabolism of the fats) as a fuel source. Cancer cells do not have this flexibility. They can only use glucose. In certain circumstances they may be able to use glutamine. By and large, without glucose they starve and die.

e. Dr Dominic D´Agostino and researchers from the University of South Florida Medical School showed in 2012 with animal studies, that animals with metastatic cancer can survive better using a carbohydrate-free diet than those on chemotherapy!

f. Dr D´Agostino refutes that such a high fat diet can be bad for your heart describing it as a myth. In his research, the consumption of good fats linked to a fall in levels of HDL and bad fats circulating in the body. In the last 30 months he claims he has spoken to many cancer survivors who had previously been ´written off´, with no further orthodox treatment available. He is convinced that the Ketogenic Diet is a viable anti-cancer diet.

g. D´Agostino believes that calorie restriction, fasting and particularly, the Ketogenic Diet offer patients the opportunity to control and restrict blood levels of important drivers of cancer - glucose, IGF-1, insulin, protein, glutamine. The inflexibility of cancer cells is their downfall.

For a 2014 Interview with Professor Thomas Seyfried go to

#TalkingKeto: Professor Tom Seyfried
www.youtube.com
Interview with Professor Tom Seyfried about treating Cancer with Ketogenic Dietary Therapies.

Foods that can Correct and Protect

First, a slight digression. In 2012 the **National Cancer Institute** in America conducted research (Cancer Watch) into what foods could restrict a cancer tumour´s regrowth. This followed the confirmation that at the heart of most tumours were cancer stem cells (Cancer Watch) and, currently, no drugs were available to kill them off.

At CANCERactive we firmly believe in using an anti-cancer diet as part of your Integrated Cancer Treatment Programme. Diets can fulfil several aims. **The Rainbow Diet**, where you incorporate a plethora of colourful foods into your diet, along with, for example, oily fish and sunshine to provide a nutritionally nourishing diet which includes highly ´bioactive´ compounds, these being both protective and corrective of cancer, fits totally with the NCI research that bioactive compounds like those in **sulforaphanes, curcumin, piperine, theanine and choline plus vitamins A and D, genistein, and EGCG from green tea**.

The idea that about 50 or 60 bioactive compounds can Correct, not just Protect, fits with the rapidly developing ***Science of Epigenetics***, which has proven that the term ´mutation´ is often used somewhat incorrectly to include changes in the methylation and acetylation around the core genetic code. These changes cause blockages and a loss of crucial messages but are reversible. In effect, cancer is a metabolic disease, not a genetic one. It can be reversed.

The American Cancer Society in 2012 issued a report endorsed by the NCI stating that there had been an ´explosion´ in research into complementary therapies since 2006, and that there was **overwhelming evidence that diet, weight control and exercise could increase survival and prevent a cancer returning.**

And this is where we need to focus on the caveats:

Important - Counters and Caveats

In 1924, Warburg (who went on to win a Nobel Prize) wrote ´On Metabolism of Glucose´ where he suggested that the prime cause of cancer was the replacement of the normal respiration of oxygen in healthy cells by the fermentation of glucose.

Healthy cells make energy by converting pyruvate and oxygen in the mitochondria. Unfortunately, mitochondria are switched off in cancer by a loss of crucial messages due to blockages in gene transcription.

But it´s not that simple. When glucose is absent, cancer cells seem able to use glutamine, an amino acid in protein, as a reserve energy source. Indeed, some researchers think that some cancer cells are also ´addicted to glutamine´ (**Click here for a review**), which seems to support proliferation and survival. Indeed in certain cases of hypoxia (oxygen starvation) glutamine seems to drive the cancer, although this may not be the case for all cancers.

Johns Hopkins have researched colon cancer and a glucose restricted diet ´Colon cancer may yield to cellular sugar starvation (**Click Here**).

However, other researchers at the same medical school studied Lymph cancer. Johns Hopkins researchers showed that lymph gland cancer B cells could feed on a sugar-free diet due to their fondness of glutamine (**Click Here)**

Meanwhile brain tumours seem to thrive on glucose, but can also use glutamine (**Click Here).**

Seyfried himself has addressed this point **(Click Here)**. But I worry.

The Rainbow Diet - better than the Ketogenic Diet?

The Rainbow diet is about being SENSIBLE about sugar. Natural plant sugars are bound to be consumed. But added, empty calorie, sugar is not. 6 meals a day are eaten as a minimum. Such ´grazing´ and a lack of glucose and High Fructose Corn Syrup from fizzy soft drinks, no cakes, biscuits, chocolate, ice cream and so on, is sensible eating. But the strength of the Rainbow Diet is What You Eat - not what you leave out - the diet uses a host of epigenetic bioactive compounds - primarily the pigments in fruit and vegetables, to protect and correct.

There is more research of relevance:

1. In Cancer Watch we have covered about six research studies over the last three years all pointing to the fact that people with the highest levels of blood glucose develop more cancer, and those with cancer and high blood glucose levels have the poorest survival rates. But this is hardly surprising - uniquely, cancer cells feed on glucose. Research on high fructose corn syrup suggests it may be even worse (Click Here)

2. When it comes to fat, research from the VITAL study (Cancer Watch; November 2012) from the Fred Hutchinson Cancer Centre in Seattle showed that bad fats could drive the recurrence of breast cancer while fish oils could prevent it.

3. Research in the Oncologist. (2013;18(1):97-103; Champ et al - click here) showed that Calorie Restriction may well improve survival times for those undergoing radiotherapy and even chemotherapy, and clinical trials are planned.

You can read more about CANCERactive´s views on ´A Diet for Chemotherapy´ by Clicking HERE. You can read more about the Rainbow Diet by Clicking HERE.

This article is about the use of ´The Ketogenic Diet´. Although past work has focused on the Ketogenic Diet with brain tumours, this anti-cancer diet seems to have potential with almost any solid cancer.

Brain and other solid tumours

Let us start with a short review of research.

Brain and other solid tumours thrive on glucose - there are several research studies confirming this:

a. Researchers Seefried and Mukherjee from the Biology Department of Boston College first proposed in 2005 that brain tumour cells were inflexible in that they could use glucose but not ketones as an energy source, unlike flexible healthy cells which could use either. They argued that metabolic therapy was the way forward as little progress had been made with drugs for five decades.

b. Researchers from Ohio State University Cancer Center showed that a molecule miR-451 switches off in the absence of glucose and shuts down ´the engine of the tumour´ but causes the brain tumour to grown and spread where there is an abundance of glucose.

c In January 2009 researchers from Johns Hopkins noted that there was a strong link between hyperglycemia and cancer risk; and after following brain cancer patients they concluded that those with the highest blood glucose levels survived least. They also concluded this was likely to hold true for most cancers (Cancer Watch 2009; Click Here).

d. In 2009 researchers discovered that insulin resistance was linked to breast cancer. Where women had higher levels of blood glucose as a result, their breast cancer risk increased 1.7 times (Cancer Watch; Click Here).

e In 2010 researchers from the NCI showed that metformin, the diabetes drug which reduces blood sugar levels, was linked to lowered levels of lung cancer in studies (Cancer Watch; Click Here).

f. MD Anderson (November 2012) have shown that a protein, Pyruvate Kinase M2 (PMK2), which is active during infancy, is turned back on by cancer tumours and activates what they called The Warburg effect (after the Nobel Prize winner). They state, ´any solid cancer tumour, but in particular brain cancers, will use PMK2 to activate glycolysis´ (the burning of glucose to provide energy for cancer cells). (Nature Cell Biology - Weiwei Yang, Ph.D., Yanhua Zheng, Ph.D., Yan Xia, Ph.D., and Haitao Ji, Ph.D.)

g. In research by Elizabeth Maher et al March 2012, NMR in Biomedicine, the conclusion reached was that glucose was essential to a brain tumour but other sources from inside the cell, like glutamine, may also provide ´reserve´ energy.

Despite all this, all too often patients are given foods like ice cream, sugary tea, sugared buns and Ribena whilst lying in their post-operation beds. This is crazy. In fact, ten years ago I talked to Catherine´s oncologists about starving the brain of glucose. They actually laughed.

Katie Sheen´s Story

Katie Sheen, a nutritional therapist and lecturer at the University of Worcester, became interested in eating to combat cancer 10 years ago when her brother-in-law was diagnosed with a low grade astrocytoma. He and his family launched Astro Fund, the only charity in the UK to focus on low grade glioma research. Says Katie, "My brother-in-law saw that the astrocytoma is such a perversely beautiful cell: it looks like a starburst. So that´s how the charity was named; he wanted it to be a light in the darkness".

Katie´s focus on the ketogenic diet could be, at the very least, a torch or a beacon for those looking for an adjuvant therapy for brain cancer: working on her dissertation, she discovered that the **Mayo Clinic** was using this diet as a mainstream treatment for children with medication-resistant epilepsy:

"Basically its the antithesis of what you´d imagine." says Katie. "It´s a very high fat, calorie-restricted diet (whipped cream and animal fats permitted), with adequate protein and very low carbs. There are variations (MCT, Modified Atkins, which you can read about on the website Matthews Friends). But the whole point of the diet is that it put the body into ketosis. That´s the state the human body goes into under starvation, when it burns fat for energy. **Healthy brain cells can use ketones for energy but a brain tumour can only use glucose**". Says Katie, "It´s such an incredibly simply metabolic approach: you starve the tumour of sugar".

Investigating further, Katie came upon the work of Dr Thomas Seyfried at the Biology Department of Boston College, Massachusetts, who was researching the ketogenic effect on brain cancer. He cited the example of two children with high grade brain tumours, **both of whom were beyond further medical help**. Their nutrition department was allowed to try the diet: One child responded well and **survived at least another 10 years. (Nebeling et al, J Am Coll Nutr. 1995 Apr; 14(2): 202-8**). In Italy, a 65 year old woman with glioblastoma multiforme started a calorie-restricted ketogenic diet in combination with chemotherapy. Tumour regression was seen on scanning, but 10 weeks after lapsing from the diet the tumour progressed further (Zuccoli et al, Nutrition & Metabolism 2010;7:33).

A number of groups have researched this diet in animal models for brain and prostate tumours.

Nobody is suggesting that this approach is a substitute for medical treatment but it could a very useful adjunct:

"Now", says Katie, "a research group led by Adrienne Scheck in Arizona is doing experimental work on a glioma mouse model and getting very good results so we hope to be able to get a phase I clinical trial under way in the UK soon, to build on promising results from a German trial which has just published. (www.astrofund.org.uk)".

Summary

There can be little doubt that researchers in America are on to something. The inflexibility of cancer cells to use anything other than glucose (and high fructose corn syrup), apart from possibly glutamine, seems clear.

Calorie restriction is being researched in America in Clinical Trials as it seems to help the cause of Chemotherapy and Radiotherapy.

Glucose plasma levels seem inversely linked to survival - the more you have the worse your survival. While outright fasting seems to control the spike of glucose, IGF-1 and insulin better than calorie restriction, 70 per cent of patients aren´t interested. So maybe using a diet which has non-starchy plant carbohydrates, good oils and fats and a little quality protein makes it more tolerable, while having even more benefits. It is interesting to note that D´Agostino believes in the addition of three sessions a week of Hyperbaric Oxygen.

This is all becoming very interesting. Of course, there are some that would argue that you should still incorporate bioactive food compounds that are known to attack the various cancer stages (the Rainbow Diet; The NCI bioactive compounds ´that can be taken as supplements´ according to researchers.

There are even those who might argue that this is all getting closer and closer to the principles behind the controversial Gerson therapy.

We will be interested to see the results of the clinical trials.

To read about Fasting, Calorie Restriction and Cancer CLICK HERE.

To read about Hyperbaric Oxygen CLICK H