Antioxidants - An Unusual View

Antioxidants, principally Vitamins A, C and E also including a whole range of other supplements, claiming to have high levels of antioxidant activity, are commonly consumed on a worldwide basis as part of a health lifestyle. Indeed, the rise of interest in nutritional medications, has recently provoked serious interest from Big Pharma especially as many of their current drugs are running out of patent, and the flow of new drugs onto the market has been significantly slow of late.

Claims that antioxidants enable us to live longer and healthier lives do not in fact stand up to scrutiny. No significant clinical trial shows any particular improvement in cancer incidence or indeed cardiovascular disease, which are the most likely candidates to kill us. Indeed, a recent large scale trial to see whether the antioxidant Vitamin E prevents cancer was halted as there was an increase in the number of prostate cancer cases in the treatment group.

It is easy to see how antioxidants have become so attractive. When oxidants are produced at too high a level, they cause DNA damage and also damage many proteins in the cell. What we do know in cancer is that cancer is caused by damage to DNA, so therefore the assumption is or rather has been, that taking antioxidants will reduce the damaging effects of oxidants and therefore reduce DNA damage and therefore in turn reduce the incidence of cancer.

This is much oversimplified. For example, vegetables such as those in the Brassica family, Broccoli in particular, have been connected with anticancer benefits, but they manage to achieve this through pro-oxidative cellular processes rather than antioxidant mechanisms.

Life at its absolute simplest consists of a cell membrane across which there exists a voltage, that is essentially a spark, so you could call this 'the spark of life'. That spark in the cell is in fact due to a collection of oxidation processes which are called Reactive Oxygen Species (ROS) such as Superoxide, the Hydrogen radical, Singlet Oxygen and Hydrogen Peroxide. Indeed, with the use of high dose Intravenous Vitamin C in Cancer, which has to be given intravenously, we cannot achieve anything like the serum levels required by giving it orally, acts entirely as a pro-oxidant by releasing Hydrogen Peroxide, which kills tumour cells. All chemotherapy works on the pro-oxidant basis. Essentially these Reactive Oxygen Species are the 'spark of life'. As an analogy think of your lawnmower lying in the garage, unused over the winter, and then you try to start it up again in the Spring. You pull the starter cord and it simply won't fire because there is no spark, without the spark there is no life, so much the same for the body. Cells need to be 'fired' by ROS in order to activate the process of programmed cell death (apoptosis), this is a normal process and is downregulated in cancer, chemotherapy works by causing apoptosis.

Recent research has been particularly intriguing in Pancreatic Cancer, because aggressive pancreatic cells have high antioxidant levels, and therefore they switch off the Reactive Oxygen Species, and so that leads on to looking at therapies which drop the antioxidant levels in Pancreatic Cancer cells, which should make them less aggressive and more amenable to standard treatments such as chemotherapy or other pro-oxidant cancer treatment approaches.

One other interesting thought is that it is generally assumed that when a cell divides it's genetic material is at its most vulnerable, i.e. when single stranded DNA occurs as the DNA unravels in the cell replication process. However, what we now know is the antioxidant levels in these cells is very high indeed, and it may just be that the opposite may be the truth.

So, my approach clinically with anybody who has cancer is to stop all antioxidant preparations, principally Vitamins A, C and E but also any other supplement with antioxidant properties. Also, I advise cutting out Blackberries, Blueberries, Strawberries and Cranberries. Also supporting this is the observation that cancer stem cells which drive cancer, and are not killed by chemotherapy, they have high antioxidant levels, therefore switching off the Reactive Oxygen Species, therefore there is no 'spark' in the cell and consequently no means of killing these cells.

Is there any counter-argument to the use of antioxidants? There is in fact another mechanism to consider and this relates to our discussion later in the piece on the drug metformin for drug resistant cancers. This is a known inhibitor of a particular bio-chemical pathway called the mTOR signaling pathway. Inhibition of this can cause resistant cancer cells to die by unleashing another form of cell death. Some of the antioxidants in fruit and vegetables are also inhibitors of mTOR and they have the same beneficial effect. So any anti-cancer benefits of these are probably happening in this way, rather than by a direct antioxidant effect.   ***So what does that mean in terms of patient advice ?*** I would say the best approach is that if you have cancer, don't take antioxidants. If you don't have cancer then use antioxidants such as vitamin C. ***Can we be absolutely certain about this advice ?*** The answer is probably 'no' and there will be no definitive clinical trial that can be carried out that can make an absolute conclusion for this one way or the other.

Are there any simple treatment available that kill cancer stem cells? The answer is potentially "Yes", particularly Metformin, which is the most commonly used drug in Type 2 Diabetes. The incidence of Diabetes is rising in the developed world, in some instances to almost epidemic levels. Metformin is used all over the world and is shown to be safe, what it does is to make the insulin receptors on our cells more receptive and therefore less insulin resistant, therefore we need less insulin to open the cell up for glucose

to get into the cell to give it energy. Also, recent work over the past few years has shown that Metformin has a cancer lowering effect of something like 30% lower incidence of many major cancers, such as the lung, pancreas and colon. Also moving on from these observations, the discovery that Metformin kills cancer stem cells by unleashing the Reactive Oxygen Species in the cell, which then drives the programmed cell-death process, which is downregulated in cancer. So it occurs to me that it would be sensible to look at antioxidant levels in cancer cells before and after the administration of Metformin.

Taking this argument further, in Type 2 Diabetes antioxidants block essential Reactive Oxygen Species signaling in the liver, which normally heightens insulin sensitivity and lowers the rate of glucose synthesis. Recent work has shown that physical exercise reduces the incidence of Type 2 diabetes by an increased Reactive Oxygen Species production, yet exercise has no such positive effect in those who simultaneously consume antioxidants and so quench the ROS. What we also know is that Men who exercise frequently have a 20% lower incidence of colon cancer, again almost certainly due to the production of increased Reactive Oxygen Species due to exercise, so why quench these important 'sparks' by using antioxidants?

So where do we go from here? Can we prove this once and for all? The answer is probably not, because any clinical trials would have to be impossibly large. However, there is intriguing epidemiological evidence from certain neurodegenerative diseases which are associated with high oxidant damage, particularly so in Parkinson's Disease, which results in damage to the basal ganglia, which are collections of nerve cells in the centre of the brain. This may explain why Parkinson's patients have 30% fewer solid cancers across the whole range of solid tumours as compared to age-matched individuals without Parkinson's Disease, and this may well be due to lower levels of antioxidants in their cells.

This is therefore why I give this unusual advice to cancer patients, that they should avoid all antioxidants at all times.

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