Autoschizis: a new word in cancer treatment

Subject: A combination of vitamin C and vitamin K-3 in a 100:1 ratio causes a unique form of cancer cell destruction that has been named autoschizis.

Researchers started playing around with a combination of vitamin C and a synthetic form of Vitamin K, called K-3 or menadione in the late 1990's watching what it did to cancer cells. Cancer cells really don't like this combination. Initial reports described the resulting cell death as due to apoptosis [1] but soon it became apparent that the process of destruction was different and of course needed its own name. The word autoschizis was coined I think by a group headed by J. Gilloteaux.[2

"VitC:VitK3-treated cells showed exaggerated membrane damage and an enucleation process in which the perikarya separate from the main cytoplasmic cell body by self-excision. Self-excisions continued for perikarya which contained an intact nucleus surrounded by damaged organelles. After further excisions of cytoplasm, the nuclei exhibited nucleolar segregation and chromatin decondensation followed by nuclear karryorhexis and karyolysis. This process of cell death induced by oxidative stress was named autoschizis because it showed both apoptotic and necrotic morphologic characteristics."

Or in another description:

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Let me translate this into simple language you can visualize. Apparently the cell membrane forms cuts or schisms which allow the cytoplasm to leak out. The cell shrinks in size until about only 1/3 its original size and only the nucleus and organelles remain surrounded by a tiny ribbon of cytoplasm. If apoptosis is a quiet cell suicide in which the cell curls up and dies, autoschizis is a bit more violent; the cell slashes itself open violently spilling out its insides.

Studies have looked at autoschizis in experiments with ovarian cancer [4,5] cells, liver tumors,[6] bladder tumors,[7] oral squamous cell and salivary gland tumors,[8] and leukemia [9] to name the abstracts I've come across so far. Pretreatment with this vitamin C/K combination also potentiates the effect of chemotherapy [10] and

radiation.[10] It also seems nontoxic, leaving normal cells unaffected.
"CK(3)-treatment selectively potentiated tumor chemotherapy, produced sensitization of tumors resistant to some drugs, potentiated cancer radiotherapy and caused inhibition of the development of cancer metastases without inducing toxicity in the host. We propose the association of vitamins C and K(3) as an adjuvant cancer therapy which may be introduced into human cancer therapy without any change in the classical anticancer protocols, and without any supplementary risk for patients."

At this point, I am unaware of any human clinical trials which have utilized this vitamin combination. So what sort of dose should we contemplate if we want to try this new treatment? Well if you took 10,000 mg of vitamin C a day, you need to add 100 mg of Vitamin K-3.

Menadion

the mediator of **cyclic electron flow**, added in catalytic amounts, elicited a characteristic transient in slow kinetics of chlorophyll a fluorescence in intact isolated chloroplasts. This transient (the M peak) was associated with the exponential increase in CO_2-dependent O_2 evolution and CO_2 fixation. It was largely affected by temperature and by the addition of intermediates of the **reductive pentose phosphate pathway**. Experiments with antimycin A suggested that endogenous cyclic electron flow is responsible for the creation of the M peak. Since the M peak was suppressed in a very narrow range of concentrations of exogenous dihydroxyacetone phosphate, 3-phosphoglycerate and ribose 5-phosphate, it was concluded that fluorescence transients in intact isolated chloroplasts could be observed only when a finite ratio and turnover of ATP and NADPH is reached.

Cyclic electron flow

Cyclic electron flow around photosystem I is essential for photosynthesis (Munekage Y, Hashimoto M, Miyake C, Tomizawa K, Endo T, Tasaka M, Shikanai T).
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Photosynthesis provides at least two routes through which light energy can be used to generate a proton gradient across the thylakoid membrane of chloroplasts, which is subsequently used to synthesize ATP. In the first route, electrons released from water in photosystem II (PSII) are eventually transferred to NADP+ by way of photosystem I (PSI). This linear electron flow is driven by two photochemical reactions that function in series. The cytochrome b6f complex mediates electron transport between the two photosystems and generates the proton gradient (DeltapH). In the second route, driven solely by PSI, electrons can be recycled from either reduced ferredoxin or NADPH to plastoquinone, and subsequently to the cytochrome b6f complex. Such cyclic flow generates DeltapH and thus ATP without the accumulation of reduced species. Whereas linear flow from water to NADP+ is commonly used to explain the function of the light-dependent reactions of photosynthesis, the role of cyclic flow is less clear. In higher plants cyclic flow consists of two partially redundant pathways. Here we have constructed mutants in Arabidopsis thaliana in which both PSI cyclic pathways are impaired, and present evidence that cyclic flow is essential for efficient photosynthesis.

Analysis of donors of electrons to photosystem I and cyclic electron flow by redox kinetics of P700 in chloroplasts of isolated bundle sheath strands of maize.

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Bundle sheath chloroplasts of NADP-malic enzyme (NADP-ME) type C4 species have a high demand for ATP, while being deficient in linear electron flow and oxidation of water by photosystem II (PSII). To evaluate electron donors to photosystem I (PSI) and possible pathways of cyclic electron flow (CEF1) in isolated bundle sheath strands of maize (Zea mays L.), an NADP-ME species, light-induced redox kinetics of the reaction center chlorophyll of PSI (P700) were followed under aerobic conditions. Donors of electrons to CEF1 are needed to compensate for electrons lost from the cycle. When stromal electron donors to CEF1 are generated during pre-illumination with actinic light (AL), they retard the subsequent rate of oxidation of P700 by far-red light. Ascorbate was more effective than malate in generating stromal electron donors by AL. The generation of stromal donors by ascorbate was inhibited by DCMU, showing ascorbate donates electrons to the oxidizing side of PSII. The inhibitors of NADPH dehydrogenase (NDH), amytal and rotenone, accelerated the oxidation rate of P700 by far-red light after AL, indicating donation of electrons to the intersystem from stromal donors via NDH. These inhibitors, however, did not affect the steady-state level of P700+ under AL, which represents a balance of input and output of electrons in P700. In contrast, antimycin A, the inhibitor of the ferredoxin-plastoquinone reductase-dependent CEF1, substantially lowered the level of P700+ under AL. Thus, the primary pathway of ATP generation by CEF1 may be through ferredoxin-plastoquinone, while function of CEF1 via NDH may be restricted by low levels of ferredoxin-NADP reductase. NDH may contribute to redox poising of CEF1, or function to generate ATP in linear electron flow to O2 via PSI, utilizing NADPH generated from malate by chloroplastic NADP-ME.

Pentose phosphate pathway

(also called Phosphogluconate Pathway, or Hexose Monophosphate Shunt [HMP shunt]) is a cytosolic process that serves to generate NADPH and the synthesis of pentose (5-carbon) sugars. There are two distinct phases in the pathway. The first is the oxidative phase, in which NADPH is generated, and the second is the non-oxidative synthesis of 5 carbon sugars. This pathway is an alternative to glycolysis. While it does involve oxidation of glucose, its primary role is anabolic rather than catabolic

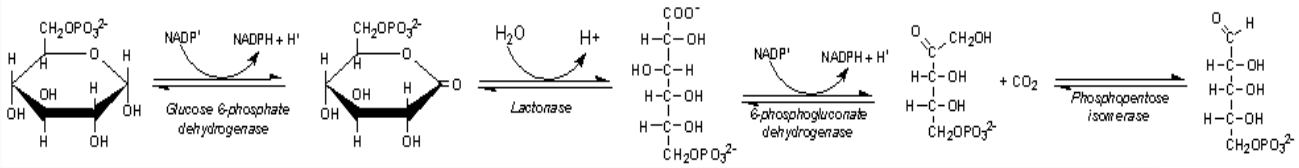
The pathway is one of the three main ways the body creates molecules with reducing power, accounting for approximately 60% of NADPH production in humans.

One of the uses of NADPH in the cell is to prevent oxidative stress. It reduces the coenzyme glutathione which converts reactive H_2O_2 into H_2O. If absent, the H_2O_2 would be converted to hydroxyl free radicals which can attack the cell.

It is also used to generate hydrogen peroxide for phagocytes.[1]

Oxidative phase

In this phase, two molecules of NADP$^+$ are reduced to NADPH, utilizing the energy from the conversion of glucose-6-phosphate into ribulose 5-phosphate.



Oxidative phase of pentose phosphate pathway

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