Mistletoe makes further gains.


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One of the most obvious differences in the practice of oncology in the US and in Europe is the attitude toward mistletoe (*Viscum album*). European oncologists have used extracts of mistletoe for the past 90 years, and such usage is no longer controversial there. By some estimates, 40% of French (Simon 2007) and up to 60% of German cancer patients receive this botanical extract (Schonekaes 2003). On the other hand, the use of Iscador, Helixor, and other mistletoe extracts is virtually unknown in the US. Both Europe and the US have well-trained and highly competent oncology communities, yet they differ profoundly on this, as well as a number of other issues concerning cancer treatment. This difference is a vivid illustration of the effects of cultural norms on medical practice (Payer 1998).

Iscador is an extract of the white berries of the mistletoe plant, an unusual evergreen that grows as a kind of parasite in trees across Europe. Globular mistletoe is a familiar sight in Germany, especially in the winter, when it stands out in the bare branches of various deciduous trees. The plant has a fascinating history. Mistletoe was used medicinally by Celtic priests, who gathered it using golden scythes (to avoid contaminating the specimens). Much later, Rudolf Steiner (1861-1925), the founder of anthroposophical medicine, introduced it as a cancer treatment.

This year there have been several studies that have added weight to the pro-mistletoe argument. Jessica Burkhart, Stephan Baumgartner, et al. of the University of Bern, Switzerland, investigated the impact of mistletoe on the adverse effects of the drug cyclophosphamide (Cytoxan) in cell line studies. The experiment involved normal peripheral blood mononuclear cells (PBMCs) as well as the T-cell leukemia Jurkat cell line. All cells were first preincubated with mistletoe extract. Then a form of cyclophosphamide was added. After that, mitochondrial activity and replication were both measured.

The results were that mistletoe extract "strongly stimulated" healthy PBMCs but not malignant Jurkat cells. The level of activity of these cells was doubled by the addition of mistletoe (i.e., 197% level of activity with the lower dose and 225% with the higher dose compared with controls). In addition, mistletoe partially protected healthy PBMCs, but not malignant cells, from the damage inflicted by cyclophosphamide.
This is further scientific confirmation of the suggested use of mistletoe to reduce the adverse (side) effects of a widely used form of conventional chemotherapy. Mistletoe also exerts immunomodulating as well as direct antiproliferative effects. Mistletoe may also increase levels of various anticancer cytokines, including tumor necrosis factor (TNF-alpha).

Phase I Trial

This year, at the American Society for Clinical Oncology (ASCO) meeting, Washington, DC, scientists presented the results of a phase I clinical trial on the use of European mistletoe extracts and the drug gemcitabine (Gemzar) in patients with advanced solid tumors (Mansky 2010). The product tested was Helixor (not the more commonly used Iscador). These researchers' conclusions were highly positive. They reported that the combination had limited toxicity, no alteration in gemcitabine uptake, good tolerability, and a clinical benefit in 48% of patients. (This contrasts well with previously reported levels of benefit from gemcitabine alone.)

They concluded that the addition of European mistletoe extracts "may allow for use of higher doses" of gemcitabine and that the combination of mistletoe and this drug "warrant further study."

Studies of this sort continue to chip away at American oncologists' contention that all useful treatments are routinely employed in US oncology hospitals and that any other ways of treating...
the disease are without scientific validity. This is simply not true. In fact, American oncologists
could learn a great deal from CAM practitioners, domestic and foreign, if they would recognize
that other cultures have different ways of approaching the same problems and have something
valuable to contribute to the optimal treatment of cancer patients.

The Chemotherapy Concession Continues

A recent study provides evidence that some oncologists prescribe chemotherapy based on their
financial reward rather than the medical needs of their patients (Jacobson et al. 2010). This is a
continuation of the "chemotherapy concession," which came to public light a decade ago. It is a
system, unique in the US medical world, whereby oncologists can buy drugs at deep discount and
then dispense them at the higher, Medicare rate in their offices. In effect, participating oncologists
run a kind of pharmacy as a side business (although it is rarely identified as such to the patients).
This represents a considerable part of some oncologists' income.

The new study showed that when the US Congress tried to reduce Medicare spending in 2003,
some oncologists responded by treating a greater number of patients with more expensive drugs
to make up for this lost income.

"Many doctors ended up prescribing chemotherapy for more of their patients, to make up for
lower prices," commented Reed Abelson, who has long followed this issue for the New York
Times. In some cases, doctors bought drugs for 20% below the Medicare reimbursement rate.
This generated "large sums" (ibid.) that oncologists realized between the wholesale and the retail
prices. The authors of the Health Affairs study analyzed the records of over 200,000 lung cancer
patients treated between 2003 and 2005. Contrary to expectations, when the Medicare cuts went
into effect, doctors wound up giving more extensive (and expensive) treatments. Before the law
went into effect, 16.5% of such patients received chemotherapy. After the law went into effect,
this rose to 18.9% of patients. Although the authors only analyzed lung cancer, this 2.4%
difference could be considerable, especially if applied to a substantial portion of the 1,529,460
Americans who are expected to develop cancer in 2010, according to the American Cancer
Society (ACS).

"In sum, far from limiting access," the changes under the law "actually increased the likelihood
that lung cancer patients received chemotherapy," said Dr. Mireille Jacobson of the RAND
Corporation, who was first author on the study. (Disclosure: I serve as a reviewer of scientific
studies for RAND.)

The authors chose to focus on lung cancer because of the various treatment options, some of
which are considerably more expensive than others. They found that doctors frequently switched
drugs to choose the more expensive options. There was, for instance, an increased use of
docetaxel (Taxotere), a drug for which oncologists get reimbursed about $2500 per patient per
month.

"The financial incentive seemed to have an effect where there's not strong evidence or more than
one equally good treatment option," said Craig C. Earle, MD, of Toronto, one of the study
authors.

Oncologists responded by treating a greater number of patients because they had been making so
much money under the old system, Prof. Joseph P. Newhouse of Harvard University, another
coauthor, told the New York Times. "These markups were a substantial portion of their
income" (Abelson 2010).

The bottom line is that some oncologists in private practice make crucial treatment decisions not
based on medical necessity but on what is most profitable.

Oncologists are highly skilled professionals, who deserve our support and respect. However, the
"chemotherapy concession" introduces a temptation for oncologists in private practice to
prescribe according to their economic interests rather than the medical needs of their patients.
This has no scientific or moral justification. Congress still needs to thoroughly investigate and fix
this problem.

Omega-3 Fatty Acids

Swedish scientists have published an important paper on the positive impact of omega-3 fatty
acids (found mainly in fish oil) on a certain type of childhood cancer called neuroblastoma
(Gleissman 2010). These Karolinska Institute scientists had previously shown that DHA (the most
unsaturated form of fatty acid in fish oil) could cause apoptosis (i.e., programmed cell death) in
cancer cells. They have now extended their work to experimental animals, showing that fish oil
supplementation caused either stabilization or actual regression of tumors in these animals. As
they state, DHA "is a promising new agent for cancer treatment and prevention of minimal
residual disease" (ibid.). Their conclusions, as I shall show, also have relevance to a broader range
of adult cancers.

The paper actually encompasses two parts, one on treatment, the other on prevention. In the
prevention half, they gave DHA as a food supplement to rats before the animals were implanted
with human neuroblastoma cells. (Because they lack a thymus, the rats in question are unable to
reject tissue from a foreign species.) In the treatment half of the study, athymic rats that already
had established neuroblastomas were force-fed DHA daily, and their tumor growth and DHA
levels were then monitored. The authors concluded that "untreated control animals developed
progressive disease, whereas treatment with DHA resulted in stable disease or partial response." The
response depending on the dose of DHA.

Neuroblastoma is a tumor of the sympathetic nervous system that occurs in children. In fact, it
accounts for 6% to 9% of all childhood cancers. It is the most deadly solid tumor of childhood
outside the brain. "Despite intensive treatment modalities, the cure rate for these patients is less
than 50 percent," the authors report, "and the majority experience relapse from minimal residual
disease." Needless to say, there is an urgent need for new treatment ideas.

There appears to be a very special relationship between DHA and nervous system tissue. For
instance, a deficiency of DHA will lead to delayed neural development. Compared with normal
nerve tissue, neuroblastoma is "profoundly deficient in DHA," whereas the level of the competing
omega-6 fatty acid arachidonic acid (AA) is increased. This suggested to the authors that "an
imbalance between omega-3 and omega-6 fatty acids may serve as an adaptation mechanism in
nervous system tumors." Logically, then, one might expect the addition of DHA to slow or even
stop the growth of neuroblastoma.

This is indeed what happened when they gave DHA supplements. The authors reported: "In the
DHA-supplemented group the mean time to tumor take was significantly delayed compared to the
control group" (ibid.). One rat receiving the DHA-enriched diet did not develop tumors at all. In the treatment part of the study, the median tumor volume index at the end of the experiment (day 12) was 3.72 for animals receiving 1 gram of DHA per kilogram of body weight, 5.47 for animals receiving half a gram per kilogram of DHA, and 9.48 in the control animals. The results were statistically significant. Put another way, a high dose of DHA decreased normal tumor growth by about two-thirds. As was predicted in the authors' "omega-3 deficiency" theory, the level of DHA in the tumor tissue tripled in the higher-dose treatment group versus the controls.

The finding that DHA supplements cut the amount of tumor formation by two-thirds in experimental rats was in line with previous findings that a fish oil-enriched diet could inhibit the formation of various other kinds of tumors, including papillomas (Akihisa 2004), breast cancer (Manna 2008, Yuri 2003, Noguchi 1997), cancers of the large and small intestines (Toriyama-Baba 2001), lungs (Toriyama-Baba 2001), colon cancer (Takahashi 1993, ligo 1997), sarcoma (Ramos 2004), and prostate cancer (Kelavkar 2006). Other studies have shown that omega-3 is strongly associated with a decreased risk of aggressiveness in prostate (Fradet 2006), kidney (Wolk 2006), and breast cancer (Kim 2009).

But DHA supplementation worked better at preventing the occurrence or recurrence of tumors than at treating established tumors. "Our study shows that DHA given as a daily oral supplement displays a moderate capacity to reduce neuroblastoma growth in the majority of treated animals," Judith Gleissman and her Karolinska coworkers wrote, "but not in all." Some animals simply did not incorporate DHA into their tumor tissue, and it was precisely those animals that did not respond to the treatment.

Do these recent Swedish findings have relevance to cancers in humans, including children with neuroblastoma? I believe that they do. The authors point to a study in an Inuit population of Alaska, with a DHA intake severalfold higher than that of typical Caucasians. In one study, this group's neuroblastoma rate was 1/10 that of a comparable lower-48 American population (Dewailly 2001). It is a matter of concern that, in most of America, the ratio of omega-3 to omega-6 fatty acids has "dropped precipitously" over the past few decades. This bodes ill for American children and their parents and loved ones.

Eating more fatty fish seems, even more than ever, a prudent thing to do. Children, too, should be encouraged to increase their DHA intake through fatty fish consumption. However, with the Gulf of Mexico oil spill, finding good sources of noncontaminated fish is likely to become even more difficult than it already has been. High-quality supplements of DHA and EPA may therefore be the best solution for most readers. For vegetarians, getting sufficient amounts of DHA and EPA can be a challenge. Various vegetable foods, such as flaxseed oil, contain alphalinolenic acid (LNA), which is a short-chain omega-3 fatty acid that our bodies convert into longer-chain EPA and then potentially into DHA. Although the conversion percentage is debated, it is low, perhaps just 10%. It is not large enough for infants to fully meet their needs for DHA from LNA, which is why DHA is added to infant formulas. DHA supplements derived from microalgae, not fish, are also available.

There are also three or four clinical trials under way to test the effect of DHA and other omega-3 fatty acids in various kinds of cancer, such as lung, breast, and lymphoma. Readers can find out about these by entering the terms DHA, EPA and cancer into the Clinicaltrials.gov database.

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