



CANCER OPTIONS NEWSLETTER
APRIL 2010



Dear friends,

My newsletter contains the pick of the best information from both the orthodox and complementary worlds of cancer. There are frequently contentious issues particularly relating to Cam therapies, where possible I will bring you the balancing arguments so you can make your own mind up.

I am a strong believer in people with cancer being able to access on the benefits of safe integration of different approaches. We don't believe that people who wish to take charge of their dealing with cancer and tackle it from a holistic and multi-dimensional approach are either naive or unable to rationalise the arguments from viewpoints that are diametrically opposed for many reasons

Patricia Peat

Your thoughts and feedback on any subjects warmly welcomed!

Cancer Options and the Pathway Programme will soon be doing regular updates on Facebook and Twitter – tune in for the latest news once I find all the right buttons to press!

We aim for people to be:

PROACTIVE! WELL INFORMED! DETERMINED! DECISIVE!

We always say at Cancer Options; we don't mind what you do as long as you are well informed and have made your own decisions.

When we are working with people through the vast amounts of confusing and contradictory evidence our three golden rules for surviving cancer:

❖ **KEEP YOUR OWN PERSPECTIVE**

❖ **BECOME AN EXPERT ON YOURSELF**

❖ **LEARN WHAT HEALS YOU**

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The following is an open day for a residential living foods centre which is a welcome addition to the cam facilities in England

NEW RESIDENTIAL LIVING FOODS CENTRE OPEN DAY

Free Cancer Day!

22 May

Health Etcetera

10:00 Doors Open

10:30 The Role of Nutrition in the
Treatment of Cancer

12:00 Super Healthy Lunch available

13:00 Bill & Rian: Testimonial.
What we can do for you

14:30 Educational DVD. There is an
alternative way to deal with cancer

16:00 Finish

Refreshments and lunch available

To accommodate everyone, please let us know you are coming:

Call 01962 883 821 or e-mail info@healthetcetera.com

Address:

Hinton House, Hinton House Drive, Kings Worthy, Hants, SO23 7NH

www.healthetcetera.com

QUOTE OF THE MONTH

As always, doctors insist on practising good evidence based medicine listening only to the evidence from double blind randomised trials, I don't know where the following fits in the criteria

A client of mine asked her GP to be referred for mistletoe therapy, as you know from previous newsletters there is an evidence base to support this. Upon weighing up the evidence

And giving the request due consideration the reply was ***“Oh you can't have that, my mother had it and reacted to it”*** and duly refused to make the referral.

I did think of all sorts of clever quips to put at the end of this , throwing out all drugs that doctors mothers had reacted to etc, but I thought I would leave you to do your own.

AN ODD BIT TO TELL YOU

If you don't already, I would encourage you to pay a visit to the website for the Alliance for Natural Health www.anhcampaign.org there are a couple of important campaigns that we should support and also their latest newsletter. This makes intriguing reading for any of you that struggle with understanding why the so called pure science brigade can occupy the moral high ground when it comes to what is made available to you for your healthcare.

ARE YOU ENTITLED TO A SCAN?

Have you ever had to think about this? Would you imagine that when you have a serious illness that you would find yourself without any method of assessing your state of health? I would like to hear of peoples experience and views on this subject.

Many people for various reasons defer or decline chemotherapy and radiotherapy and pursue an holistic approach eg:

- ✚ They want to see how much they can achieve without the toxicity
- ✚ They have had previous treatment and is a smaller possibility that more will work
- ✚ They have a limited life span and do not wish to spend it having hospital treatments

IN ANY OF THESE SITUATIONS AN IMPORTANT ELEMENT FOR PEOPLE WHO ARE INVESTING THEIR TIME, EFFORTS AND FINANCES IN THERAPY THAT THEY ARE ABLE TO ASSESS HOW WELL THEY ARE DOING AND IF THEY HAVE ORTHODOX TREATMENT ON OFFER IF THAT NEEDS TO BE RECONSIDERED.

NOT UNREASONABLE YOU MIGHT THINK, AS YOU KNOW I AM ALL FOR FREEDOM OF CHOICE AND INDIVIDUALS RIGHTS. SO, YOU WOULD THINK ARE THE GOVERNMENT AND THE NHS IN THE HEADLINES ON PATIENT RIGHTS AND CHOICES, THE FOLLOWING IS A FRONT PAGE QUOTE FROM THE WEBSITE NHS CHOICES “ALL ABOUT CHOICE

“Your choices include more than just which GP or hospital to use. You also have choices about your treatment decisions and your everyday lifestyle”

Terrific, just what we want to hear, unfortunately that does not always apply if you want a scan to assess how you are doing. I am used to people getting a mixed reaction regarding this, some doctors happy to assist and help people make further decisions, others

reluctant and some outright refuse any cooperation if their treatment is refused.

I am sure we all have our own views on the morality and ethics of this, but I was recently asked what the legal stance on this is. I am currently trying to find out and it is slow getting answers, I don't think anyone has directly ruled on this and leaves it up to individual consultants, I will let you know when I find out. In the meantime I wanted to share with you a reply to a questions someone put regarding this to Cancer Research UK who left us in no doubt as to what our rights are, which are none at all apparently. The question concerned a gentleman who has lymphoma and is a year into his programme and thinks all is going well but would like to confirm that.

Dear Sirs

I wonder if you could answer a question for me? An acquaintance has been diagnosed with lymphoma and has made the decision to go down the complementary route rather than the orthodox route. However, the consultant treating her has refused to carry out a scan on the basis that he would prefer her to go down the orthodox route, commencing with chemotherapy followed by radiotherapy.

Is there a legal point of view regarding the withholding of treatment in such cases? For example, is the withholding of treatment perfectly legal and permitted when an individual chooses to follow a complementary path?

Dear Marie,

Thank you for your email to the Supporter Services department at Cancer Research UK, which has been passed to the nurse team for a reply. I was sorry to learn that someone you know has lymphoma. I can understand why you have questions to ask about this.

You explained that they have decided against orthodox treatment for their lymphoma and are determined to go down the complementary route. The consultant has refused to carry out a scan. You asked where they stand legally with this.

Firstly, I hope you do not think that I am 'nit picking' but I think that the person you know is probably having alternative treatment and not complementary treatment. If I might explain, complementary treatment is used alongside conventional medicine, to help people cope with their treatment. This tends to be the use of therapies such as massage and relaxation. Alternative medicine is any healing practice that does not fall within the realm of conventional scientific medicine. It is generally used instead of evidence based medicine and often uses therapies with a historical or cultural, basis rather than medicines and treatments which have been studied scientifically. Most doctors are supportive of complementary therapies as they can help patients feel better.

I must admit that I am not a legal expert and this makes it difficult for me to comment on the individual case. But as a general rule patients do not have the right to have treatment and tests that the doctor does not think it will benefit them. So if the specialist can argue that the scan is not of benefit, I would imagine that the law would support them.

Alternative therapies have not been extensively studied in the same way as conventional medicine. But to put it bluntly, those that have been studied at best do not appear to work and at worse, they are harmful. Having said this, conventional cancer treatments also have side effects and so occasionally patients do turn their back on what their doctor offers. I cannot know this for sure, but perhaps the specialist is thinking that a scan will not be of benefit, because the treatment is unlikely to change as a result of it. If nothing is going to change, there may be no point in having a scan.

If the person that you know is concerned that they not getting appropriate care, they could take this up with someone in the hospital. In England they could talk to the Patient Advice and Liaison Service (PALS), as they should be able to help the patient get answers to questions that they have about their care. But this service does not exist in the other UK countries.

Kind regards,

Jean

Cancer Information Nurse Cancer Research UK

WAS IT AN EPIC STUDY

Do you find you get confused, frustrated and annoyed with the continuing contradictory evidence regarding the benefits of a good diet with cancer, well if it is any consolation so do I! The recent EPIC study just added to that so I thought it would be helpful to provide some balancing discussion to this.

EPIC STUDY FINDS 'WEAK' LINK FOR FRUIT AND VEG AGAINST CANCER

THE CANCER PROTECTIVE EFFECT OF FRUITS AND VEGETABLES MAY BE MODEST AT BEST

An analysis of dietary data from more than 400,000 men and women found only a weak association between high fruit and vegetable intake and reduced overall cancer risk, according to a study published online April 6, 2010 in the *Journal of the National Cancer Institute*.

It is widely believed that a diet rich in fruits and vegetables can reduce the risk of cancer. In 1990, the World Health Association recommended eating five servings of fruit and vegetables a day to prevent cancer and other diseases. But many studies since then have not been able to confirm a definitive association between fruit and vegetable intake and cancer risk.

To address the issue, Paolo Boffetta, M.D., M.P.H., of the Mount Sinai School of Medicine in New York, and colleagues analyzed data from the EPIC study (European Prospective Investigation into Cancer and Nutrition), which included 142,605 men and 335,873 women recruited for the study between 1992 and 2000. The participants were from 23 centers in ten Western European countries--Denmark, France, Germany, Greece, Italy, the Netherlands, Norway, Spain, Sweden and the United Kingdom. Detailed information on their dietary habit and lifestyle variables was obtained. After a median follow-up of 8.7 years, over 30,000 participants were diagnosed with cancer.

The authors found a small inverse association between high intake of fruits and vegetables and reduced overall cancer risk. Vegetable consumption also afforded a modest benefit but was restricted to women. Heavy drinkers who

ate many fruits and vegetables had a somewhat reduced risk, but only for cancers caused by smoking and alcohol.

The authors caution against attributing any risk reduction to diet and they conclude that any cancer protective effect of these foods is likely to be modest, at best.

"In this population, a higher intake of fruits and vegetables was also associated with other lifestyle variables, such as lower intake of alcohol, never-smoking, short duration of tobacco smoking, and higher level of physical activity, which may have contributed to a lower cancer risk," they write.

ANOTHER OPINION

REVEALED: MAGIC FOODS TO HELP SAVE YOU FROM CANCER

TUMOUR BUSTER: Broccoli was one of the foods top of the list

Monday February 15,2010

A LIST of the best cancer-busting foods proven to slash the risk of tumours has been drawn up by two -leading international scientists.

After years of research, the two experts said there is now clear evidence on what to eat to fight the disease.

Top of their list are fresh vegetables and fruit – broccoli, cabbage, brussel sprouts, cauliflower and oranges. They found these superfoods contain cancer-killing chemicals called phytochemicals and polyphenols which could kill or prevent the growth of cancer cells.

Professor Attilio Giacosa, a top gastroenterologist from Italy and Professor Jaak -Janssens, president of the European Cancer Prevention Organisation, said that the benefits of these fresh fruit and -vegetables can still not be gained through “magic pill” supplements.

But they warned the way you cook the superfoods is vital. Steaming or microwaving veg is the best way to preserve the essential nutrients.

Prof Giacosa said: “Many substances identified in these groups were found to be -beneficial. We speak mostly of phytochemicals, products we call

'biologically active' and polyphenols as well as other compounds. All have proven protective effects but we weren't able to use them to create a magic pill, a supplement able to replace the properties of vegetables. Why? Because it is the -vegetable product on its own that is the optimal source to prevent tumours."

More than 300,000 men and women a year suffer from -cancer in the UK and half will die of the disease. In recent years, survival rates – -especially for breast cancer – have soared because of earlier detection and -better -treatments. Now experts believe the greatest impact on -cancer deaths will come from prevention. This includes cutting out smoking, improving diet, increasing physical activity and reducing excess drinking. And an increasing amount of data shows which foods are best at preventing cancer.

Professor Giacosa, head of the Department of Gastroenterology at the Policlinico di Monza, said garlic may also help to prevent gastric tumours. It contains allyl -sulfur, a compound which stops or slows down the growth of cancer cells.

And there is major evidence drinking red and white wine can help to slash cancer risk.

Red wine offers 10 times the protection compared with white wine because of an antioxidant compound found in grapes called resveratrol.

It is recommended men should try to drink two glasses of red wine a day and women one. *(okay I will try if you insist!!)*

Professor Giacosa said that oily fish such as salmon, -herring and mackerel should also be eaten regularly because it is high in omega 3 fatty acids which improves blood flow. Pulses are also very healthy because they are low in fat but high in protein.

Professor Janssens said that diet plays an -important role in protecting against breast cancer. He said there is no -evidence that breast -cancer risk -develops at puberty and is higher in girls who hit puberty young.

And finally

AND NOW FOR THE OPINION OF ONE OF THE FINEST ANALYSTS OF THE ISSUES IN THE CAM WORLD RALPH MOSS

The Journal of the National Cancer Institute (JNCI) has published a paper that denies a major role to fruit and vegetable consumption in the prevention of cancer. Since this study contradicts many other studies, as well as a long-term US government recommendation ("5 per day"), it has gotten a lot of press. At this writing, there have been 520 news articles, almost all of them negative. "Simply eating your five a day will not protect you against cancer," is how the Independent (U.K.) phrased it.

However, there are several questions that need to be addressed about this study. Here are some initial thoughts. I hope to present some further thoughts after my visit with Prof. Colin Campbell this summer.

First, according to this European Prospective Investigation Into Cancer and Nutrition (EPIC) study, if the subjects had increased their fruit and vegetable intake by just 150 grams per day, they would have reduced their risk of getting cancer by 2.6 percent (men) and 2.3 percent (women). Now, 150 grams is the weight of one apple. In the United States in 2009 there were 766,130 cases of cancer in men and 713,220 cases in women, for a total of 1,479,350. Thus, by the study's own figures, one small apple or a handful of grapes could prevent 19,919 US cases of cancer in men plus 16,404 cases in women, for a total of 36,323 people. That's about the capacity of Fenway Park in Boston, where the Red Sox hold forth. So instead of minimizing the results (as virtually every media outlet chose to do) the authors of these articles could have put a positive spin on the EPIC findings. After all, is it a small thing to keep more than 36,000 Americans from getting cancer at such a minimal cost?

Looked at in another way, the patients in the study were divided up into five groups or "quintiles."

Quintile 1 consumed 0 to 226 grams per day (i.e. less than eight ounces maximum)

Quintile 2 consumed between 227-338 grams per day.

Quintile 3 consumed between 339-462 grams per day.

Quintile 4 consumed between 463-646 grams per day.

Quintile 5 consumed more than 647 grams per day (i.e., a minimum of 23 ounces)

The difference in the Hazard Ratio (i.e., the risk) of cancer between Quintile 1 and Quintile 5 was 11 percent. Thus, if everyone in the US adopted a diet in which they ate over a pound (23 ounces) of fruits and vegetables per day, the cancer incidence would drop from its present-day 1,479,350 to 1,316,621, for a savings of 162,729 cases of cancer. This could fill Beaver Stadium in State College, PA, with 55,000 left over!

The European Prospective Investigation Into Cancer and Nutrition (EPIC) encourages us to think internationally. The World Health Organization (WHO) has estimated that there are at least 12 million new cancers diagnosed worldwide (Science Digest 2008). According to the EPIC study, conversion to a moderately high fruit-and-vegetable diet could ideally save 1.3 million people from getting cancer each year. This astonishing fact was hardly conveyed by the negative press reports on the EPIC study.

I leave you to your own intelligent analysis

Half of breast cancer patients discontinue tamoxifen and any endocrine treatment before the end of the recommended treatment period of 5 years: A population-based analysis

BREAST CANCER RESEARCH AND TREATMENT, 01/19/10

I hear a lot of complaints about the side effects of tamoxifen but I was surprised to see the drop off rate was so high

van Herk-Sukel MPP et al. – Observational studies on long-term endocrine treatment among breast cancer patients have presented discontinuation rates on tamoxifen, but lack information on the continuance of any endocrine treatment [both tamoxifen and aromatase inhibitors (AIs)] within the same cohort. In this study we determined switching rates from tamoxifen to AIs, discontinuation rates of tamoxifen only, discontinuation rates of any endocrine treatment and determinants of first treatment switch and treatment discontinuation. up to half of the breast cancer patients starting tamoxifen continued 5 years of endocrine treatment. Identification of patients at risk of discontinuation will assist in the development of interventions to improve treatment continuation comparable to that of patients included in clinical trials.

Methods

- Patients with early stage breast cancer (stage I–IIIa) starting on tamoxifen were selected from the linked Eindhoven Cancer Registry-PHARMO RLS cohort in the period 1998–2006
- Continuous use (allowing a 60 days gap between refills) of tamoxifen only and any endocrine treatment were determined after various follow-up periods: 1, 2, 3, 4, and 5 years
- Time to first switch from tamoxifen to an AI was assessed

Results

- Total of 1,451 new early stage breast cancer patients started on tamoxifen
- 380 had a treatment switch to an AI during follow-up
- Of the patients followed for 5 years, 40% continuously used tamoxifen, which was 49% for any endocrine treatment
- Older age (older than 70 versus 50–69 years) was independently associated with increased discontinuation of tamoxifen and any endocrine therapy
- Patients with two or more concomitant diseases (versus no comorbidity) showed an increased likelihood to stop any endocrine treatment or switch treatment from tamoxifen to an AI

We do know there are many things that can be done to improve the side effects of tamoxifen or natural compounds which can lower circulating oestrogen levels themselves. Would encourage anyone considering discontinuing endocrine therapy to consult an integrative practitioner about other measures rather than just stopping treatment.

SWEET! SUGAR PLAYS KEY ROLE IN CELL DIVISION

Do tell your oncologist if he is telling you that you can eat anything and it won't effect the cancer

Using an elaborate sleuthing system they developed to probe how cells manage their own division, Johns Hopkins scientists have discovered that common but hard-to-see sugar switches are partly in control.

Because these previously unrecognized sugar switches are so abundant and potential targets of manipulation by drugs, the discovery of their role has implications for new treatments for a number of diseases, including cancer, the scientists say.

In the January 12 edition of SCIENCE SIGNALING, the team reported that it focused efforts on the apparatus that enables a human cell to split into two, a complicated biochemical machine involving hundreds of proteins. Conventional wisdom was that the job of turning these proteins on and off -- thus determining if, how and when a cell divides -- fell to phosphates, chemical compounds containing the element phosphorus, which fasten to and unfasten from proteins in a process called phosphorylation.

Instead, the Johns Hopkins scientists say, there is another layer of regulation by a process of sugar-based protein modification called O-GlcNAcylation (pronounced O-glick-NAC-alation). "This sugar-based system seems as influential and ubiquitous a cell-division signaling pathway as its phosphate counterpart and, indeed, even plays a role in regulating phosphorylation itself," says Chad Slawson, Ph.D., an author of the paper and research associate in the Department of Biological Chemistry, Johns Hopkins University School of Medicine.

Because the sugar molecule has some novel qualities -- it is small, easily altered, and without an electrical charge -- it is virtually imperceptible to researchers using standard physical techniques of detection such as mass spectrometry.

Suspecting that the sugar known as O-GlcNAc might play a role in cell division, the Hopkins team devised a protein-mapping scheme using new mass spectrometric methods. Essentially, they applied a combination of chemical modification and enrichment methods, and new fragmentation technology to proteins that comprise the cell division machinery in order to out and analyze their molecular makeup, identifying more than 150 sites

where the sugar molecule known as O-GlcNAc was attached. Phosphates were found to be attached at more than 300 sites.

They noticed that when an O-GlcNAc molecule was located near a phosphate site, or at the same site, it prevented the phosphate from attaching. The proteins involved in cell division weren't phosphorylated and activated until O-GlcNAc detached.

"I think of phosphorylation as a micro-switch that regulates the circuitry of cell division, and O-GlcNAcylation as the safety switch that regulates the microswitches," says Gerald Hart, Ph.D., the DeLamar Professor and director of biological chemistry at the Johns Hopkins School of Medicine.

Using a standard human cell line (HeLa cells), the scientists discovered abnormalities when they disrupted the cell division process by adding extra O-GlcNAc. Although the cell's chromosome-containing nuclei divided normally, the cells themselves didn't divide, resulting in too many nuclei per cell -- a condition known as polyploidy that's exhibited by many cancer cells.

The researchers not only mapped O-GlcNAc and phosphorylation sites but also measured changes in the cell division machinery, because, Hart says, the chemical changes act more like "dimmer" switches, than simple on/off ones.

As important as the discovery is to a deeper understanding of cell division, Hart says, this extensive cross talk between O-GlcNAc and phosphorylation is paradigm-shifting in terms of signaling. Signaling is how a cell perceives its environment, and how it regulates its machinery in response to stimuli. The new sugar switches reveal that the cellular circuitry is much more complex than previously thought, he adds.

The research was funded by the National Institutes of Health.

HOW GENES INTERACT WITH THEIR ENVIRONMENT TO CAUSE DISEASE

A UCLA study reveals how human genes interact with their environment to boost disease risk. Published in the Feb. 18 online edition of the AMERICAN JOURNAL OF HUMAN GENETICS, the findings shed light on why the search for specific gene variants linked to human diseases can only partly explain common disorders.

"We know that genes and environmental factors influence common human diseases like heart disease, diabetes and cancer," explained principal investigator Jake Lusic, professor of medicine, human genetics and microbiology, immunology and molecular genetics at the David Geffen School of Medicine at UCLA. "Most research, however, has focused on unraveling the genetic component of disease risk while ignoring the effect of environmental stimuli. Our study examined how the molecular interaction between the two helps lead to disease."

"Smoking and high cholesterol, for example, each increase a person's risk for heart disease," he said. "But when you add them together, the total risk exceeds its parts. Their interaction creates a dangerous synergy that causes damage beyond what the two can cause independently."

Unlike earlier studies that focused on a single gene, the UCLA team scrutinized the activity of thousands of human genes both at rest and under stress. In particular, the scientists zeroed in on gene expression -- the process by which a gene's DNA sequence is converted into cellular proteins.

Using arteries that surgeons had trimmed from 96 donated hearts prior to organ transplantation, Lusic and his team cultured cells from the inner lining of the blood vessels. To mimic environmental stress, the scientists exposed the cells to fats that incite inflammation and lead to atherosclerosis, or hardening of the arteries. Then they looked at the cells' genes and compared their normal expression patterns to their activity under stress.

"The genes responded differently to inflammation depending on their genetic makeup," said first author Casey Romanoski, a UCLA graduate student in human genetics. "About 35 percent of the most affected genes were influenced by the interaction between their genetic variants and the fats."

"You can't effectively study genes divorced from their environment," she added. "The missing link lies in the intersection of genes with their environment."

"Our findings demonstrate that these interactions are important in humans and should be considered in genetic research," said Lusi. "Improving our understanding of the molecular architecture of disease may one day provide us with a new tool for how we address common disorders like cancer, diabetes and heart disease."

The National Heart, Lung and Blood Institute and the American Heart Association funded the research.

FIGHT-OR-FLIGHT HORMONES HELP TUMOR CELLS ESCAPE TO SPREAD

Previous studies have so far shown no relationship between stress and cancer development, yet our instincts and common sense tells us these elements have a direct effect on our health. We know we all develop cancer cells, and may have tumours that will never be potential be harmful, the following indicates the importance stress may play in cancer becoming a real problem

Chronic stress triggers a chain of molecular events that protects breakaway ovarian cancer cells from destruction, a team of researchers led by scientists at The University of Texas M. D. Anderson Cancer Center reports April 12 in the early online publication of the JOURNAL OF CLINICAL INVESTIGATION.

In preclinical research, the team found that heightened levels of the fight-or-flight stress hormones epinephrine and norepinephrine permit more malignant cells to safely leave the primary tumor, a necessary step in metastasis and cancer progression. They also found that ovarian cancer patients face earlier mortality when a crucial protein activated by the hormones is present at high levels in their tumors and that depressed patients have higher levels of the protein.

"When normal cells become detached from neighboring cells or from the supportive scaffolding known as the extracellular matrix, they die from anoikis, a form of programmed cell death," said first author Anil Sood, M.D., professor in M. D. Anderson's Departments of Gynecologic Oncology and Cancer Biology.

"Cancer cells find a way to bypass anoikis, so they survive as individual cells circulating in the blood or in ascites, fluid that accumulates in the abdomen of ovarian cancer patients," Sood said. Resistance to cell death helps malignant cells migrate from the primary tumor and re-attach to colonize new sites.

"Restoring cancer cells' vulnerability to anoikis would open a new avenue for suppressing tumor growth and metastasis," Sood said. Two promising approaches -- directly silencing a crucial protein or using beta blockers to preempt its activation -- worked in cell culture and mouse models, making them candidates for human use.

FAK activation protects cancer cells

The team showed that increases in epinephrine, also known as adrenaline, and norepinephrine reduced the number of ovarian cancer cells killed by anoikis by activating focal adhesion kinase (FAK), a protein known to promote tumor survival and to protect against anoikis. The researchers previously showed that FAK is abundantly present in ovarian cancer cells.

Lab experiments showed that resistance to cell death by anoikis begins when one of the hormones connects with the β 2-adrenergic receptor (ADRB2), which activates FAK via other intermediate proteins. Treating cells with beta blockers to inhibit the ADRB2 connection or using small interfering RNA (siRNA) to shut down FAK increased cell death.

In a mouse model of human ovarian cancer, mice subject to restraint stress had smaller tumors with fewer nodules and greater cell death when treated with siRNA to suppress FAK. Treatment with the beta blocker propranolol had a similar effect.

The researchers examined 80 cases of invasive epithelial ovarian cancer to assess the role of stress-induced FAK activity. They found increased FAK expression in 67 percent of patients and heightened levels of phosphorylated FAK in 50 percent.

FAK abundance tied to earlier death

Patients with high levels of either measure had greatly reduced overall survival over three years. About 65 percent of those with low FAK expression survived at least three years compared with 30 percent of those with high expression. For activated FAK, the difference was 65 percent vs. about 15 percent.

Using depression as an indicator of stress, the researchers found major depression was associated with higher levels of activated FAK and increased levels of norepinephrine in the tumors. Major depression was defined as a score greater than 16 on the Center for Epidemiological Studies Depression [CESD] scale for the purposes of this study.

Sood said future research will include investigating whether similar effects occur in other types of cancer, prospectively assessing the significance of FAK activation in chronic stress settings, and ultimately bringing strategies to clinical settings that can block the deleterious effects of chronic stress on tumor growth and progression.

This research was funded by grants from the National Cancer Institute, M. D. Anderson Cancer Center Ovarian Cancer Specialized Program in Research Excellence, Zarrow Foundation, EIF Foundation, Betty Ann Asche Murray Distinguished Professorship, Blanton-Davis Ovarian Cancer Research Program and the Marcus Foundation.

Sood also is affiliated with M. D. Anderson's Center for RNA Interference and Non-Coding RNA. Co-authors are Koen DeGeest, M.D., and Susan Lutgendorf, Ph.D., of the Department of Obstetrics and Gynecology, Division of Gynecologic Oncology at the University of Iowa; Lutgendorf also is with the Departments of Psychology and Urology in the Holden Comprehensive Cancer Center at the University of Iowa. Other M. D. Anderson co-authors are Guillermo N. Armaiz-Pena, Ph.D., Jyotsnabaran Halder, Ph.D., Alpa M. Nick, M.D., Rebecca L. Stone, M.D., Wei Hu, M.D., Ph.D., Amy R. Carroll, M.D., Whitney A. Spannuth, M.D., Julie Allen, B.S., Liz Han, M.D., Aparna Kamat, M.D., Mian Shahza

Okay so where is all this research going, let's see – diet, sugar, stress, environment all contributing to cancer, stop me if you have heard it all before!!!

EARLY TERMINATION OF CLINICAL TRIALS MAY OVERESTIMATE TREATMENT EFFECTS

Laurie Barclay, MD

Early termination of clinical trials may overestimate treatment effects, according to the results of a systematic review and meta-regression analysis reported in the March 24/31 issue of the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

"Although randomized controlled trials (RCTs) generally provide credible evidence of treatment effects, multiple problems may emerge when investigators terminate a trial earlier than planned, especially when the decision to terminate the trial is based on the finding of an apparently beneficial treatment effect," write Dirk Bassler, MD, MSc, from McMaster University in Hamilton, Ontario, Canada, and colleagues from the Study of Policy of Interim Truncation 2 Study Group. "Bias may arise because large random fluctuations of the estimated treatment effect can occur, particularly early in the progress of a trial. When investigators stop a trial based on an apparently beneficial treatment effect, their results may therefore provide misleading estimates of the benefit."

The goal of this study was to compare the treatment effect from truncated RCTs with that from meta-analyses of nontruncated RCTs studying the same question, and to evaluate factors associated with overestimates of effect. To identify truncated RCTs, the reviewers searched MEDLINE, EMBASE, Current Contents, and full-text journal content databases up to January 2007. In addition, they searched MEDLINE, the Cochrane Database of Systematic Reviews, and the Database of Abstracts of Reviews of Effects up to January 2008 to find systematic reviews from which individual RCTs were extracted.

Independent reviewers blinded to trial results and with medical content expertise matched RCTs reported as having stopped early for benefit with nontruncated RCTs from systematic reviews, based on their similarity to the truncated RCTs. Data were extracted independently by reviewers with methodological expertise.

The investigators compared 91 truncated RCTs asking 63 different questions with 424 matching nontruncated RCTs. For truncated RCTs vs matching nontruncated RCTs, the pooled ratio of relative risks was 0.71 (95% confidence interval, 0.65 - 0.77). This difference was not affected by the presence of a statistical stopping rule or by methodological quality of the trials in terms of blinding and concealment of randomization.

"Our research shows that in most cases early stopping of clinical trials resulted in misleading estimates of treatment effects," corresponding author Victor Montori, MD, from the Mayo Clinic in Rochester, Minnesota, said in a news release. "These misleading estimates are likely to result in misguided decisions about the trade-off between risks and benefits of a therapy."

For truncated RCTs having fewer than 500 events, there were large differences in treatment effect size between truncated and nontruncated RCTs (ratio of relative risks < 0.75). The pooled effects of the nontruncated RCTs showed no significant benefit in 39 (62%) of the 63 questions.

"Truncated RCTs were associated with greater effect sizes than RCTs not stopped early," the study authors write. "This difference was independent of the presence of statistical stopping rules and was greatest in smaller studies."

"On average, treatments with no effect would show a reduction in relative risk of almost 30 percent in stopped early trials," Dr. Montori said. "Treatments with a true relative risk reduction of 20 percent would show a reduction of over 40 percent."

Limitations of this study include the fact that the literature search missed some truncated RCTs and failure to evaluate publication bias in the systematic reviews.

"To the extent that substantial overestimates of treatment effect are widely disseminated, patients and clinicians will be misled when trying to balance benefits, harms, inconvenience, and cost of a possible health care intervention," the study authors conclude. "For trial investigators, our results suggest the desirability of stopping rules demanding large numbers of events. For clinicians, they suggest the necessity of assuming the likelihood of appreciable overestimates of effect in trials stopped early."

GOOD NEWS FOR PROBIOTICS

Carcinogenesis

The anticancer effect of probiotic *Bacillus polyfermenticus* on human colon cancer cells is mediated through ErbB2 and ErbB3 inhibition

ABSTRACT

A wealth of data implicates that ErbB receptors have essential roles in tumor development. Probiotic bacteria are known to exert an anticancer activity in animal studies. *Bacillus polyfermenticus* (B.P.), a probiotic bacterium, has been clinically used for a variety of gastrointestinal disorders in East Asia. Here, we investigated the effect of B.P. on the growth of tumors and its putative mechanism of actions.

Conditioned medium of B.P. cultures (B.P. CM) inhibited the growth of human colon cancer cells including HT-29, DLD-1 and Caco-2 cells. Moreover, B.P. CM suppressed colony formation of HT-29 cells cultured on soft agar and reduced carcinogen-induced colony formation of normal colonocytes. Furthermore, data from the mouse xenograft model of human colon cancer cells showed reduced tumor size in B.P. CM-injected mice when compared to *E. coli* conditioned medium-injected mice. Exposure of B.P. CM to HT-29 cells for 24 hr, 48 hr and 2 weeks reduced ErbB2 and ErbB3 protein expression as well as mRNA levels.

Moreover, cyclin D1 expression that is required for ErbB-dependent cell transformation was decreased by B.P. CM. Furthermore, transcription factor E2F-1 that regulates cyclin D1 expression was also decreased by B.P. CM. These results show that B.P. inhibits tumor growth and its anticancer activity occurs, at least in part, through suppressing ErbB2 and ErbB3. Taken together, our study suggests that this probiotic may be clinically used as a prophylactic treatment to prevent colon cancer development.

TOWARD SAFER PLASTICS THAT LOCK IN POTENTIALLY HARMFUL PLASTICIZERS

Scientists have published the first report on a new way of preventing potentially harmful plasticizers -- the source of long-standing human health concerns -- from migrating from one of the most widely used groups of plastics. The advance could lead to a new generation of polyvinyl chloride (PVC) plastics that are safer than those now used in packaging, medical tubing, toys, and other products, they say.

Helmut Reinecke and colleagues note that manufacturers add large amounts of plasticizers to PVC to make it flexible and durable. Plasticizers may account for more than one-third of the weight of some PVC products. Phthalates are the mainstay plasticizers. Unfortunately, they migrate to the surface of the plastic over time and escape into the environment. As a result, PVC plastics become less flexible and durable. In addition, people who come into contact with the plastics face possible health risks. The U.S. Consumer Product Safety Commission in 2009 banned use of several phthalate plasticizers for use in manufacture of toys and child care articles.

The scientists describe development of a way to make phthalate permanently bond, or chemically attach to, the internal structure of PVC so that it will not migrate. Laboratory tests showed that the method completely suppressed the migration of plasticizer to the surface of the plastic. "This approach may open new ways to the preparation of flexible PVC with permanent plasticizer effect and zero migration," the article notes.

IS IT RIGHT FOR DRUG COMPANIES TO CARRY OUT THEIR OWN CLINICAL TRIALS?

On bmj.com, two experts debate whether the conflict of interest is unacceptable when drug companies carry out clinical trials on their own medicines.

Their views come as new guidance on the standards required for communicating company sponsored medical research is published.

Vincent Lawton, a healthcare consultant and non-executive director at the Medicines and Healthcare products Regulatory Agency in London, argues that having invested billions of pounds in medicine development, it is unrealistic to expect the drug industry to "surrender its intellectual property." He adds that taking away research from pharmaceutical companies will lead to delays, inefficiency and a lack of innovation.

Ben Goldacre, a doctor and writer from London disagrees and argues that "it is hard to see any justification" for allowing the current situation to continue.

Goldacre says that increasing evidence points to a conflict of interest for the drug industry which "results in bad evidence, which distorts medical decision-making, and harms patients."

One of the problems, argues Goldacre, is that the industry can choose which data to publish, and which to leave unavailable. He refers to the difficulties in getting clear information about the number of suicide attempts in industry trials of SSRI antidepressants or the number of heart attacks in individuals taking the anti-inflammatory drug rofecoxib (Vioxx).

Goldacre concludes that the current situation "is dangerous and absurd" and that "doctors who are making treatment decisions need access to good quality trial data, presented transparently, and all of it, not just the positive findings that drug companies choose to share."

Vincent Lawton, however, believes that it is acceptable for the drug industry to make a profit and still undertake rigorous clinical trials that stand up to regulatory scrutiny.

He points out that, in January 2005, the industry made a commitment to increase the transparency of clinical trials by registering its trials in central, publicly accessible databases. Most major companies also publish trial results, whether positive or negative, on their own websites.

Lawton sums up by saying that it is unlikely that publicly sponsored academics would have the infrastructure to conduct all clinical trials on all new medicines, leading to regulatory approval.

An accompanying paper, also published on bmj.com, sets out new guidance for communicating company sponsored medical research.

Written by the International Society for Medical Publication Professionals, the good publication practice (GPP2) guidelines have been updated in response to changes in the environment in which authors, presenters, and other contributors work together to communicate medical research.

They include guidance on defining the roles of authors, sponsors, and other contributors, recommendations about reimbursement, and confirmation of the role of professional medical writers, and apply to peer reviewed journal articles and presentations at scientific conferences.

Lead author, Chris Graf says the guidelines "make recommendations that will help individuals and organisations maintain ethical practices and comply with current requirements when they contribute to the communication of medical research sponsored by companies."

PHOTODYNAMIC THERAPY SHOWN TO BE EFFECTIVE IN THE TREATMENT OF MESOTHELIOMA

Hopefully a welcome development in this hard to treat disease. More support for the development of this in England would not go amiss as I have watched the team at UCL struggle for funds for years.

Among the experimental therapies that are currently being investigated for the treatment of the asbestos cancer mesothelioma, one of the most promising is a technique called photodynamic therapy (PDT).

Mesothelioma, which is an aggressive and fatal cancer that affects the linings of the chest and abdominal cavities, is generally less responsive to traditional treatments like chemotherapy and radiation. It is rarely caught in time to be operable. A number of other treatments, such as gene therapy, immunotherapy and alternative approaches have all given some hope to sufferers of this deadly cancer.

Photodynamic therapy is one of the front-runners in the field of promising treatments. This method combines three separate elements—a nontoxic, photosensitizing compound, oxygen and visible light—to target the cancerous cells. Usually administered during or after surgery in order to remove residual portions of the tumor, it can also be used when surgery is not feasible—as is often the case with mesothelioma patients.

Unlike chemotherapy and radiation, which tend to have a scorched-earth effect on the patient's body, photodynamic therapy has a clear advantage in that it does not kill non-cancerous cells. This means that the side effects are lessened, and the patient is not debilitated by the treatment.

Photodynamic therapy has been approved by the Food and Drug Administration for several kinds of cancer, although its use for mesothelioma remains in the experimental stage.

Roughly 3,000 new cases of mesothelioma are diagnosed each year in the United States, and around the world, 20,000 people die from the disease annually. Nearly all mesothelioma diagnoses can be traced back to contact with asbestos, a mineral material which was once incorporated into many different commercial and consumer products in order to make them fireproof. Although asbestos use peaked in the 1970s, mesothelioma has a

long latency period and therefore may not be diagnosed until years, or even decades, after the contact took place.

NANOTECHNOLOGY TACKLES THE TWO BIGGEST PROBLEMS ASSOCIATED WITH CHEMOTHERAPY

And finishing on more good news, let's hope it is not years before we see these things become a reality

Huixin He, associate professor of nanoscale chemistry at Rutgers University, Newark, and Tamara Minko, professor at the Rutgers Ernest Mario School of Pharmacy, have developed a nanotechnology approach that potentially could eliminate the problems of side effects and drug resistance in the treatment of cancer. Under traditional chemotherapy, cancer cells, like bacteria, can develop resistance to drug therapy, leading to a relapse of the disease.

As reported in the December 21, 2009, issue of the journal *Small*, He, Minko and their co-researchers, including investigators from Merck & Co. and Carl Zeiss SMT, a global nanotechnology firm, have designed nanomaterials that allow for the delivery of both a chemical (doxorubicin) to destroy cancer cells and a genetic drug to prevent drug resistance.

When administered to drug-resistant ovarian cancer cells, the treatment was more than 130 times lethal than when doxorubicin was administered alone. "The drug can only be released when it is inside the cancer cells," He said. "This controlled internal release mechanism can dramatically eliminate side effects associated with anticancer drugs to normal tissues."

Battling Aggressive Breast Cancer with Nanotubes

In related research, Professor He and another team of co-researchers have developed single-walled carbon nanotubes that hold the potential of providing a more effective means for detecting and selectively destroying aggressive breast cancer cells.

In a paper published in *BMC Cancer* late last year, the researchers showed that by chemically bonding a special antibody onto the nanotubes and taking advantage of two unique properties of carbon nanotubes, single cancer cells can be detected and selectively eradicated while leaving the nearby normal cells unharmed. The uniqueness of this approach is that it is more easily extended to other types of cancer cells. He's research in the areas of cancer detection and treatment is funded in part with grants from the National Science Foundation and National Cancer Institute.

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