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The feature subject in this issue is mammography and considerable space is devoted to the discussion because it is viewed as a very important aspect of modern medicine and because decisions about its merits are important to a large number of women and their families. This discussion was inspired by the new U.S. Preventive Services Task Force position that women between 40 and 49 years of age should not receive a recommendation for starting annual mammography. Based on ample historical precedent, a significant uproar could have been predicted with confidence and indeed occurred, as most readers already know. What most readers probably do not know is that this was an almost exact repeat of the reaction to National Institutes of Health consensus report in 1997, or that the subject has been debated endlessly in the medical literature with little change in the basic data for over a decade. They may also not appreciate how polarized opinions are. We will briefly review the pros and cons of breast cancer screening with mammography and cite an up-to-date leaflet available online for those concerned with this matter.

Obesity is constantly in the news. The views expressed at a recent symposium are examined and compared to the hypothesis carefully constructed and described by Gary Taubes in **Good Calories, Bad Calories**. Directly related to this is an interesting paper concerning the comparative roles of fat and muscle tissue in the context of insulin resistance and diabetes, as viewed from the perspective of our genetic makeup.

Other topics include the current status of controlling the incidence and progression of coronary artery plaque, which in fact is quite depressing, and recent studies on melatonin and breast cancer, green tea and depression, and how effective antidepressants really are in adults. Also, a new book **Knockout** by Suzanne Somers is reviewed and highly recommended for everyone.

Finally, a comprehensive review of the latest research on vitamin D is now available on-line at http://www.yourhealthbase.com/D_vitamin_update_2010.htm

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Wishing you and your family good health and well-being,

William R. Ware, PhD, Editor

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THE ONGOING MAMMOGRAPHY DEBATE

In November 2009 the U.S. Preventive Services Task Force issued a highly controversial report concerning screening for breast cancer (BC).¹ This task force was comprised of an independent panel of experts in prevention and primary care and was

so constituted as to avoid as much as possible all bias and influence. The principal bone of contention was the revised guideline concerning screening prior to age 50. It was the task force's position that the benefits were too small to justify universal screening, but that the balance between risks and benefits in the age group 40-49 was such that each woman should be helped to decide for herself when to start getting mammograms. This was interpreted as a blanket recommendation against screening for this age group, which is an oversimplification of the task force position. Most readers are aware of the immediate negative response which was at center stage for a week or so in the media, and several professional societies immediately stated that they would not be influenced by the task force position. Subsequently a steady stream of commentaries, editorials, perspectives, etc. appeared in mainstream journals. Five were just published in a recent issue of *JAMA* (January 13, 2010).

It is unlikely that most readers are aware that this is close to an exact replay of an attempt in 1997 to settle the question of BC screening for women between 40 and 49 years of age. The scene of the initial action was a National Institutes of Health (NIH) sponsored consensus conference in January 1997, which concluded that "data currently available do not warrant a universal recommendation for mammography for all women in their forties. Each woman should decide for herself whether to undergo mammography...a woman should have access to the best possible relevant information regarding both benefits and risks, presented in an understandable and useable form." Sounds familiar. What happened next was described by Suzanne Fletcher who chaired the writing group. In a commentary in the *New England Journal of Medicine*² she described the reaction as right out of *Alice in Wonderland*. The consensus committee's report was essentially disowned by the NIH, widely condemned by professional and lay "experts" and the matter was quickly taken up by the US Senate which held a brief hearing and then voted 98 to 0 in favour of mammography for women in their 40s!

Screening is not diagnosis. It is not comparable to culturing a sample from the throat or urine and identifying a pathogen or viewing a scan and identifying an aneurysm. Most screening protocols have their strengths, weaknesses and their grey areas of high uncertainty and it is what makes them imperfect. It is a common characteristic of screening procedures to be highly controversial and their merits endlessly debated, frequently with considerable emotion and bias. The most high-

profile are mammography and PSA screening for prostate cancer. The problem, simply stated, is that most screening protocols find a lot of disease which is not really there (false positive) while missing some disease which is indeed present (false negative). But it is more complex than this since some of the abnormalities labelled cancer are indolent or insignificant and present no risk to the patient during the foreseeable future and therefore do not need treatment, but their identification precipitates the diagnosis of cancer and sets in motion the therapeutic machinery and in many cases treatments far in excess of what is appropriate.³ In addition, some of the cancers are so aggressive that it makes almost no difference whether they are identified by screening or when they become symptomatic.

The principal rationale of mammography is finding small abnormalities that cannot be palpated, i.e. the notion that early detection saves lives. The problem is that many of the abnormalities observed are benign or indolent, but frequently this cannot be verified. Thus unnecessary treatment results. The false positives also precipitate a cascade of additional tests, some invasive and not without risk, and in addition generate anxiety which can be severe and in itself highly unhealthy. Non-invasive tests that are used as follow-up after a positive mammography also suffer from false positives and false negatives.

Comparison of two mammograms a year or so apart can precipitate a malpractice proceeding against the radiologist on the basis of perceived injury by the patient due to a year delay in diagnosis. But many mammograms show features that are debatable and on which panels of radiologists would differ as regards interpretation. Some radiologists no longer read mammograms because of the potential legal issues. To call mammographic screening imperfect is clearly an understatement, but to communicate to a patient in a balanced and unbiased fashion the true magnitude of the imperfection is not simple, especially since the conventional wisdom is strongly pro-mammography. Given this, how does a woman make an informed decision? Many patients do not relate to statistical arguments, and yet in the final analysis this is all that can be used to amplify the simple statement that there are risks and benefits that should be weighed. Weighed how? Patients typically regard tests as black or white and do not like to think about big grey areas of uncertainty.

Thus it can be argued that there are huge barriers to the whole process of informed decision making,

and these reside with both the physician, the patient, and the constraints placed on the interaction, e.g. a short office visit to discuss a problem of considerable complexity that frequently has no definitive answer. This would seem to be a major problem with the task force's position which implicitly assumes that meaningful and relevant outcome will result from a discussion of the pros and cons for women between 40 and 49. The weight a patient gives, either consciously or unconsciously, to the various risks and benefits may bear no resemblance to a rational consideration, and in fact the patient may be incapable of appreciating the complexities of the problem. The widespread use of relative rather than absolute risks does not help to add clarity or neutrality to these discussions. The decision may be totally emotional

and have nothing to do with weighing the pros and cons. All in all, the situation is far from satisfactory, and underscores the need for a new solution to the problem, i.e. a screening protocol that really works. In the meantime, there remain such issues as overdiagnosis and unnecessary or excessive treatment. For breast cancer (BC) these are big issues.³ As well, there is the question regarding the real significance of screening in terms of its impact on BC-related mortality.

One way of looking at the risk-benefit analysis is to examine the impact of screening on the 10-year risk of dying from BC. Woloshin and Schwartz quote the following figures in terms of deaths per 1000 individuals:⁴

Age	<u>40-49 yrs</u>	<u>50-59 yrs</u>
No screening	3.5/1000	5.3/1000
Screening (regular)	3.0/1000	4.6/1000
Deaths avoided	0.5/1000	0.7/1000

Thus regular screening of 2000 individuals in the 40 to 49 age group avoids one BC-related death. It is interesting that the 50 to 59 age group actually is not that different with 1.4 per 2000 vs. 1 per 2000. But the fact that there is a mortality advantage, although barely measurable, is for some sufficient justification. If one death out of 2000 screened individuals is prevented, this is all that is needed to justify the widespread use of the procedure. But this is arbitrary.

The one per 2000 represents absolute risk reduction. The corresponding relative risk reduction considered most probable by both by the 2009 Cochrane group⁵ and the task force¹ was of the order of 15%, which sounds much more beneficial. How does one draw the line? In terms of absolute risk reduction should it be 1 in 5000 or 1 in 10,000? And the notion of cost-benefit analysis when lives are at stake offends many. Thus the belief that this problem has a clear, solid scientific solution ignores the arbitrary interpretation of very small benefits. The small *probable* benefit must be balanced by the potential harms of screening. These include overdiagnosis and overtreatment, more extensive surgery and post surgical treatment, psychological damage and problems from false alarms and false reassurance.

Furthermore, there are issues of bias and design with almost all the studies on which these figures are based, and thus it is possible that there is no statistically significant BC mortality benefit at all rather than this very small one. *When the Cochrane researchers selected only trials they considered to have adequate randomization and a minimum bias favouring screening, they found no statistically significant effect at all on BC mortality associated with 10 years of repeated mammography.*⁵ Nevertheless, the possibility of small benefit is not rejected in the Cochrane review and analysis,⁵ although this 2009 report attempts to put it into perspective by saying that it corresponds to a life extension of two days, on average, per women who is invited for screening, and undergoes 10 years of regular mammography, even if the relative risk reduction were 29% rather than 15%. Swedish trials found this larger relative risk reduction for women between 50 and 69 years of age.

Central to the problem of overdiagnosis and overtreatment is the potentially cancerous ductal carcinoma in situ (DCIS). This abnormality is not palpable but is a very common finding from the positive mammogram. DCIS falls in the big grey zone between normal tissue and invasive cancer. No one knows the lifetime risk of DCIS developing into invasive breast cancer but it is thought to be considerably less than 50%. In fact, the best guess is that most abnormalities will not progress to invasive cancer.⁶ More than 50,000 American women will be diagnosed with DCIS each year, most by mammography, and virtually all receive some surgery. Recalling that overdiagnosis involves

the detection of abnormalities that meet the pathologic definition of cancer but will never progress to cause symptoms, the diagnosis of DCIS offers the potential for significant overdiagnosis. It is not invasive cancer but nevertheless patients believe they have cancer, especially when standard cancer treatments are recommended. But even the use of the term "carcinoma" in DCIS has been seriously questioned.⁶

There is actually very little known about what is called the natural history of BC and what happens to untreated patients.⁷ Autopsy studies show that a significant number of women die without knowing they have BC, including DCIS. Furthermore, there is some evidence that even invasive BC identified by mammography can spontaneously regress and disappear.⁸

In one study of DCIS patients, not only did the vast majority have surgery, but half received radiation and a third underwent a total mastectomy, a treatment pattern similar to that of early stage invasive cancer. Add to this the psychological aspect of "being diagnosed with cancer" and always fearing recurrence, and one has a picture of the real harm that can result from mammography and the identification of abnormalities that may never pose a problem. This in fact is the essence of the problem of screening. An almost parallel situation is seen in prostate cancer, where one of the major challenges is the identification, through biopsy material and other clinical information, of tumors that are indolent and probably pose no significant threat. Readers of *The Prostate Monitor* are well aware of this dilemma. For prostate cancer a solution of growing popularity is active surveillance where an attempt is made to determine by periodic assessment if the tumor is progressing to the point where intervention is indicated. Many men are avoiding treatment completely. It seems obvious that such an approach should be examined for DCIS. It is also noteworthy that curing "cancer" that is not really cancer artificially enhances statistics regarding the benefits of treatment.

The 2009 Cochrane review⁵ and the subsequent leaflet⁹ summarize the harms of mammography as follows. Screening of 2000 women regularly for 10 years will result in 10 healthy women being turned into cancer patients and treated unnecessarily. These women will have a lumpectomy or a mastectomy and will often receive radiotherapy and sometimes chemotherapy. Some of the cell changes associated with the diagnosis of DCIS are often found in several places in the breast which

prompts a mastectomy although only a minority of the cell changes would have developed into cancer. Of the 2000 screened women, 200 healthy women will experience a false alarm. This for many women causes anxiety, worry, despondency, sleeping problems, changes in relationships with family, friends and acquaintances, and a change in sex drive. This can persist for months and leave some women feeling more vulnerable about disease in general. Finally, not all cancers can be detected by mammography and a negative reading can result in false reassurance and might encourage ignoring future symptomatic evidence of BC (e.g. small abnormality found during self-examination).

The Cochrane conclusions concerning risk and harm do not consider age, and thus apparently challenge the stratification of recommendations by age. The task force meta-analysis found that the relative risk reduction of about 15% was independent of age from 39 to 69 but the absolute risk increased somewhat with age with about 1400 rather than about 2000 required to be screened for 10 years to avoid one BC related death in the 50-69 age group. The difference between 1 in 1400 and 1 in 2000 was apparently the basis for their position on not recommending screening in the younger age group, but obviously this is debatable given the large number needed to screen, the barely immeasurable benefit, and as the Cochrane study points out, the dependence of risk estimates on which trials are selected for inclusion in the analysis.

There have been several publications recently asking the question: Are women really giving informed consent?¹⁰⁻¹³ At issue is the risk side of the equation and the use of relative vs. absolute benefits, perhaps outdated and inflated. A recent analysis in the *British Medical Journal* is very critical of the literature supplied to women in many countries in the context of considering mammography.¹¹ The view is that the benefits are overstated and the risks understated. Gotzsche *et al* give what they consider a reasonably balanced presentation for such promotional literature which is as follows (exact quote)¹¹

- It may be reasonable to attend for breast cancer screening with mammography, but it may also be reasonable not to attend because screening has both benefits and harms.
- If 2000 women are screened regularly for 10 years, one will benefit from the screening, as she will avoid dying from breast cancer.

- At the same time, 10 healthy women will, as a consequence, become cancer patients and will be treated unnecessarily. These women will have either a part of their breast or the whole breast removed, and they will often receive radiotherapy and sometimes chemotherapy.
- Furthermore, about 200 healthy women will experience a false alarm. The psychological strain until one knows whether it was cancer, and even afterwards, can be severe.

Note the absence of age. The 2009 leaflet based on the Cochrane review elaborates on these points. It is available free on the internet.⁹ The National Breast Cancer Coalition (NBCC) statement on mammography screening is also of interest. The position of the NBCC is that there is no statistically significant evidence that screening reduces mortality in the 40-49 age group and that for women

over 50, there is no strong evidence. Furthermore, they point out in reference to mortality risk estimate that biases in trials could “erase or create it.”¹⁴ This is the same point made by the Cochrane investigators.

Thus after decades of research regarding BC, there does not appear to be a satisfactory screening protocol and since it appears impossible to tell which DCIS abnormalities need to be treated, they are almost all treated as if they were cancer and in many cases unnecessary harm results which can be lifelong. This is not a particularly impressive report card. Judging by the criticism of the leaflets discussed above, many women are being given a distorted view, whereas a more realistic view would lead them to realize that there is no straightforward answer.

OBESITY—WHERE IS THE REAL SOLUTION?

In 2007-2008, 68% of American adults were overweight and 33.9% obese. While the rate of increase appears to have decreased somewhat, this in no way diminishes the seriousness of this problem nor its potential impact on public health and the cost of health care.¹⁵ Four papers appeared in the January 2010 issue of the *American Journal of Clinical Nutrition* summarize a recent symposium called “An Integrative view of Obesity.” When one reads these papers looking for the latest in solutions to this epidemic, there seems to be little that is new. The classic notion that decreasing calories and increasing exercise is a major part of the answer appears alive and well, and the goal post are now set such that for the obese, a weight decrease of 10% is considered clinically important as measured by small decreases in the risk of chronic diseases. If one is 69 inches tall and has a BMI of 40, the corresponding weight is 286 lbs, and the individual is on the threshold of morbid obesity. A loss of 10% is about 29 lbs, which still leaves the person obese. To be classed as not obese and in fact not overweight, the target would be about 180 lbs. The loss of an additional 77 lbs appears to be exceedingly difficult, and even the 10% reduction is not easy for many to either achieve or maintain.

In a talk that was described as anchoring the symposium, George Blackburn emphasized the energy gap, i.e. the energy consumed compared to the energy expended. He called for public health measures which include decrease in caloric intake,

improving the macronutrient content of diets, and increasing physical activity. In the published paper,¹⁶ Blackburn states that decreasing fat intake should be of particular concern in any lifestyle intervention, and his discussion of maintaining fat-free mass, while indicating the merits of higher protein diets, does not mention the matter of carbohydrates and carbohydrate metabolism. Other speakers also emphasized the role of the use of portion control and daily physical activity.¹⁷ These notions go back to the 18th century, but the obesity epidemic is very recent.

Of all those who have researched these topics, the independent researcher Gary Taubes, seems to stand out as one who has looked with great care at the totality of the literature to date, is not burdened by nutritional mythology or dogma, and appears to truly engaged in an unbiased search for the truth. His research is summarized in the 600-page book “*Good Calories, Bad Calories, Challenging the conventional wisdom on diet, weight control, and disease.*” (Knopf, New York, 2007). This book extensively and comprehensively documents the following conclusions regarding obesity (pp. 454):

- Obesity is a disorder of excess fat accumulation, not overeating nor sedentary behavior.
- Excess calories do not *cause* one to grow fatter and expending more energy than we consume

does not lead to long-term weight loss—it leads to hunger.

- Fattening and obesity are caused by an imbalance in hormonal regulation of adipose tissue and fat metabolism.
- Insulin is the primary regulator of fat storage, with high levels favoring accumulation and low levels favoring release of fat from fat tissue for use as fuel.
- By stimulating insulin secretion, carbohydrates cause obesity and make us fat. By decreasing carbohydrate consumption, individuals will become leaner.
- By driving fat accumulation, carbohydrates increase hunger and decrease the amount of energy expended on metabolism and physical activity.

These are generalizations of a vast amount of research. He of course is not advising against exercise. And obviously specific exceptions can be found, but these general conclusions are directly opposed to the conventional wisdom fashionable in nutritional circles and mainstream medicine and

evident in the above symposium. Critics may well wave banners stating that the First Law of Thermodynamics, like Horace Rumpole's wife, must be obeyed, but they should realize that within the confines of this law, human biochemistry and in particular metabolism is exceedingly complex, and oversimplification can lead down a blind alley. Until the hypothesis advanced by Taubes is considered seriously, there is probably no hope that the problem of obesity will be solved. It can even be argued that it will never be solved for political, social and psychological reasons. In addition, the problem needs a more sophisticated solution than simply condemning couch potatoes, drinks with high sugar content and calorie-dense junk food, although these actions are certainly defensible. Taubes' book seems like a breath of fresh air in this field and is highly recommended. He does not appear to "cherry pick" sources, discusses conflicting evidence, and the weight of the evidence he presents, some of which goes back several decades or more, appears devastating to the conventional wisdom.

FAT, MUSCLE, INSULIN RESISTANCE AND DIABETES

A paper by Eaton *et al* related to Taubes' hypothesis recently appeared in *Preventive Medicine*¹⁸. Two of the authors (Eaton and Cordain) have over a number of years played an important role in the what some call evolutionary medicine and in particular have engaged in research leading to an understanding of our Stone Age genetics in the context of diet and health and the implications of this genome in the modern era. The authors begin by pointing out that the genes and biochemistry that control carbohydrate digestion, blood glucose control, pancreatic insulin secretion and glucose clearance were selected eons ago and were appropriate to lean individuals with body mass index (BMI) estimated to be about 20 based on Stone Age surrogates from five continents. Another resemblance is to modern-day superior athletes. They also point out that until recently, the proportions of muscle and fat for most humans remained similar to the ancestral pattern. This is in marked contrast to present-day obesity epidemic encompassing even children and the dire predictions as to the proportion of obese adults in future years.

Our ancestors presumably had a very high ratio of muscle to fat. This is important because both fat

and muscle have insulin receptors, and when an insulin molecule attaches to a fat receptor, substantially fewer glucose molecules are cleared from the circulation than when an insulin molecule attaches to a muscle receptor. Being overweight or obese leads to increasing insulin receptor imbalance and appears to parallel the rise in insulin resistance characteristic of those with high BMI. Thus lean individuals in general exhibit greater insulin sensitivity as compared to those who have a high percent of body fat mass, and the latter are prone to so-called insulin resistance, the precursor of type 2 diabetes. Going back to Taubes' hypothesis, insulin resistance is associated with excess insulin secretion which is associated with fat storage, and a diet high in refined carbohydrates increases blood glucose, frequently dramatically, and thus insulin secretion. This looks like a vicious circle. The paper by Eaton *et al* focuses attention on muscle vs. fat and supports the notion, consistent with our genetic makeup, that exercise designed to increase muscle mass, i.e. so-called resistance training, is a very important aspect of any program designed to lower the risk or adverse effects of diabetes and the associated elevated blood glucose levels.

The emphasis on muscle vs. fat mass is consistent with the well known benefits of resistance exercise as well as exercise in general for type 2 diabetics. Even short periods of resistance exercise produce improvements in sugar control comparable to taking diabetic medication. For example, a study just published used a combination of aerobic and resistance exercises for 16 weeks.¹⁹ Subjects were post-menopausal women with type 2 diabetes. Significant decreases were found in HbA1c, a long term average measure of blood glucose, and an improvement in a measure of insulin resistance (HOMA2), and as well fasting insulin and glucose levels. In addition, there was a large increase in muscle strength but no change in weight. Similar results were found by Cauza *et al*²⁰ where strength

training in obese type 2 diabetics resulted in significant decreases in body fat and HbA1c and increases in lean body mass, a surrogate for muscle mass, but no change in weight. In another study, moderate aerobic exercise, when added to rather severe calorie restriction, attenuated the loss of muscle mass associated with dieting and the muscle mass that was maintained was leaner.²¹ This is an important finding since in general aerobic exercise is less effective than resistance exercise in the context of muscle mass building. It is interesting to note that excessive loss of skeletal muscle mass is common as one ages and in older diabetics and that this is manifest even in the early stages of the disease.²² While not discussed in the paper, this seems to suggest a positive feedback loop.

PROGRESSION OF CORONARY CALCIFICATION—NO THERAPY IN SIGHT

The evidence is compelling that coronary plaque burden is a risk factor for adverse coronary heart disease (CHD) events. The extent of coronary artery calcification as measured by the coronary calcium score using non-invasive electron-beam tomography (EBT) or coronary angiographic tomography is a surrogate for the extent of atherosclerosis, and the greater the burden of atherosclerosis the greater the risk of adverse events. Conversely, a zero calcium score implies a very low probability of any significant coronary plaque. Thus if one is interested in primary prevention of CVD, a primary target is coronary plaque and the goals are to halt its progression and/or reverse the formation process. A recent survey of randomized trials with these endpoints has just reported.²³ All used EBT. Five trials involved subjects with cardiovascular disease and five involved subjects with chronic kidney disease. There was no reproducible or consistent treatment that was found effective in connection with the progression of coronary calcification over a period of one year. An editorial accompanying this report took the position that screening is not justified since there is no treatment and that the same applied to rescanning at a later date to determine the rate of progression.²⁴ Since individuals can get a heart scan on demand in many countries, there is an increasing incidence of patients presenting to discuss their CAC score and some come with a recommendation of a follow-up scan after 1 to 5 years. Unfortunately, it appears from this survey of treatment effectiveness that there is nothing evidence-based to tell these individuals.

An examination of the literature will reveal a number of papers recommending statin treatment for asymptomatic individuals of intermediate Framingham risk and an elevated calcium score. As has been pointed out in this newsletter and in a paper by your editor in *Medical Hypotheses*,²⁵ coronary plaque burden and progression are independent of LDL cholesterol levels and, consistent with the above analysis of studies, statin treatment has no significant therapeutic benefit on these two endpoints. Nevertheless, it is almost certain that this approach is being practiced and prime-time TV commercials tell us it works.

A recent open-label study designed to look beyond LDL-lowering is of interest. The study was motivated by the failure of LDL-lowering to arrest plaque progression or reduce coronary plaque. Combined therapy involved statins for most subjects plus niacin, omega-3 fatty acids from fish oil, and vitamin D3 supplementation. The non-LDL goals consisted of triglycerides \leq 60 mg/dL, HDL \geq 60 mg/dL, and 25 hydroxyvitamin D serum levels of \geq 50 ng/mL. Subjects had a wide range of coronary calcium scores with a quite high median value. The mean follow-up with a repeat calcium scan was 18 months. Compared to expected calcium score progression, 49% achieved slower plaque growth and in addition, 44% had a substantial reduction in calcium score.²⁶ No information was acquired regarding the relative importance of the individual components of the intervention.

There is independent evidence that vitamin D prevents the incidence of coronary plaques. A study

of about 1400 patients measured calcium scores at baseline and after 3 years follow-up. Of this group, 394 had chronic kidney disease which is a risk factor for atherosclerosis. While the prevalence of coronary artery calcium was independent of 25(OH)D levels, incidence over the study period was significantly associated when the measure was per 10-ng/mL lower concentration, with an adjusted risk increase of 23%. The mean group baseline concentration was 21.4 ng/mL which suggests a considerable number were deficient.²⁷

It is a sad commentary of medical progress that in 2010 there are no effective therapies for preventing

or halting the progression of coronary artery atherosclerosis. Medical scientists have been studying CHD for decades. Perhaps in retrospect, the focus on the diet-heart hypothesis and the cholesterol-heart hypothesis was an unfortunate distraction. Research reports in this newsletter over the past several years have tried to put these hypotheses in perspective and discuss their severe limitations. In addition, the ease of examining evidence of atherosclerosis in the carotid arteries also probably played an unfortunate role, given that such studies are only marginally relevant to the coronary arteries.

NEWS BRIEFS

NEWER ANTIPSYCHOTIC DRUGS FOR CHILDREN. A CAUSE FOR CONCERN?

This topic is discussed in the April 2009 issue of *Therapeutics Letters* (www.ti.ubc.ca). The authors report a tenfold increase in the use of newer antipsychotics (olanzapine, quetiapine and risperidone) for children under 14 in British Columbia. These drugs are used for indications such as schizophrenia and bipolar disorders. The authors of the perspective comment that there is widespread disagreement among psychiatrists about the diagnosis of bipolar disorder in children, some claiming that it is in fact impossible. They quote a Cochrane systematic review that found little conclusive evidence concerning benefits of antipsychotic medication for those with early onset schizophrenia, and in one study an atypical antipsychotic was associated with increased risk of serious adverse effects. Also cited was another systematic review regarding schizophrenia which was unable to draw any conclusions regarding relative effectiveness of current available treatments but concluded that adolescents might be particularly vulnerable to side effects and suggested caution in extrapolating from adult studies. This perspective also discussed a recent study which concluded that the nearly exclusive use of atypical (newer) antipsychotics was a problem given the safety findings related to weight gain and metabolic problems.

Finally, the authors comment that in the U.S. much of the increase in prescriptions for antipsychotics is for attention deficit disorder and hyperactivity and that there are no controlled trials supporting this use. While the authors do not use this precise language, the above appears to suggest somewhat reckless over treatment of children using these newer atypical drugs with marginal net effectiveness and the potential for severe side effects. This review is in the public domain.

GREEN TEA AND DEPRESSION

A recent study has established a strong association between green tea consumption and the presence of depressive symptoms in community-dwelling older population.²⁸ A group of 1058 Japanese individuals aged ≥ 70 years was examined for the presence of depression and their green tea consumption ascertained. When the comparison was made with those who drank ≤ 1 cup per day, mild and severe depressive symptoms were 46% less likely in those who drank ≥ 4 cups per day, but not 2-3 cups. The risk of very severe depression was 52% lower for those drinking ≥ 4 cups per day as compared to ≤ 1 cup. The authors suggest that one mechanism might be an amino acid component in green tea which in animal studies has been shown to cross the blood-brain barrier and influence brain serotonin and dopamine concentrations. They suggest that green tea leads to a decrease in the response to stress. One limitation of their study was its cross-sectional nature (like a picture at a fixed time) and there exists the possibility that depression itself decreased the consumption of green tea. They suggest that a prospective study would be informative. Green tea is a pleasant drink which has numerous other possible health benefits, and 4 cups or more a day is not that much. There are also green tea extracts where one capsule provides 2-4 times the polyphenols contained in 4 cups of tea.

ANTIDEPRESSANT DRUGS EFFECTIVENESS IN ADULTS

The effectiveness of antidepressant drugs was assessed in a recent study by examining data from 6 randomized placebo controlled trials involving a total of over 700 patients and lasting at least 6 weeks.²⁹ It was found that on

average, patients with mild or even moderate symptoms experienced minimal or no benefit. The magnitude of the benefit of antidepressants increases with the severity of the depressive symptoms *and was found to be significant only in individuals with severe depression.*

MELATONIN, LIGHT EXPOSURE AND BREAST CANCER

In the May 2009 issue of this Newsletter, the connection between breast cancer, night-shift work and the circadian rhythm of melatonin secretion was discussed. An interesting study on women with total blindness, which relates directly to this problem, has just been published.³⁰ This study compared two groups of blind women, one with light perception and one without. Thus in one group there was presumably a circadian variation of melatonin with nocturnal secretion, whereas in the other group, living in total darkness eliminated this variation. A significantly lower rate of breast cancer was found in the totally blind group when compared to those who were blind but had light perception. When risk factors for breast cancer were introduced into a multivariable analysis, for all women the risk reduction due to total blindness was 57% and was statistically significant. For Postmenopausal women, a 51% risk reduction was observed which just missed statistical significance. This incidentally was a small study. Furthermore there were no measurements of melatonin so it is merely a hypothesis that the totally blind individuals had higher levels of melatonin. But the authors point out that the results are consistent with observations on night-shift workers and flight attendants, both of which may lack the normal circadian rhythm of melatonin secretion.

This study highlights the importance of sleeping in a totally dark room and avoiding light exposure during the night. The secretion suppression from light exposure during the night depends on wavelength distribution of the light, its intensity and the duration of the exposure. Some modern bathrooms are very highly illuminated with six to eight 75 watt bulbs and even an exposure of a few minutes can reduce melatonin secretion, although spending fifteen minutes to a half hour having a midnight snack in a brightly illuminated kitchen would be much more significant. Ideally, lights left on around the house at night should be very low wattage and bedroom curtains should exclude street light from mercury lamps, or in the case of the shift worker, daylight. Moonlight does not appear to be intense enough to be significant.

BOOK REVIEW

KNOCKOUT. Interviews with doctors who are curing cancer and how to prevent getting it in the first place. Suzanne Somers. Crown Publishers, New York, 2009

This is a book every adult should read, period. Put simply, cancer will directly or indirectly influence the lives of almost everyone. Those who personally escape this affliction will still encounter it in family and friends. That is a certainty given cancer's current prevalence and the frightening and relentless increase in prevalence.

Suzanne Somers is of course a very well known author whose books on diet, hormones and aging have been bestsellers. She is herself a cancer survivor now free of the disease for a number of years. Her book begins with an account of a recent close brush with death which was successfully prevented by emergency department doctors. But what took place after this when she was admitted for the purpose of finding out what was really wrong provides a splendid and highly pertinent introduction to this book. It would spoil the story to give the details, but if this introductory chapter does not scare the wits out of readers, it is hard to predict what will.

At the conclusion of her story, Ms. Somers presents four chapters which provide short reviews from her point of view of cancer treatment and prevention in the context of mainstream medicine plus an interview with Ralph Moss, a well known critic of modern oncology. The second and third parts of the book are made up of interviews with doctors who are at the frontier of alternative and integrative treatments for cancer as well as interviews with leaders in the field of cancer prevention who emphasize alternative approaches. This provides the reader with a unique opportunity to "listen in" on highly targeted and up-to-date interviews dealing with the most important issues we face, both now and in the future. An interview with William Faloon, director and cofounder of Life Extension Foundation, ends the main part of the book. This interview deals with the prevention of *treatment-induced* metastasis, something many readers will have rarely if ever heard about. These chapters provide an excellent opportunity for the reader to judge the credibility of both the individuals interviewed, their philosophy

and their approaches. And throughout the interviews, one obtains important insights as to how modern medicine does and does not work. The reader should go away with a more realistic view of the “standard of care” for cancer patients. Finally, there is a very good set of resources and related material included at the end of the book.

To say that the book should be ignored because the author is not a doctor is nonsense. Somers is a keen and experienced observer of mainstream medicine in general and cancer treatments and prevention in particular. Furthermore, the bulk of the material in the book involves doctors answering questions and discussing issues. It is worth repeating—everyone should read this book.

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