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This issue has no main theme but rather simply discusses a number of health issues. In addition, there is included at the end a commentary concerning the issue of diet and health viewed from a somewhat unconventional perspective. Nutritional research has been dominated for decades by what some term the reductionist approach. For example, typical issues might be is saturated fat associated with the risk of diabetes, does red meat increase your risk of heart disease, is vitamin D supplementation protective against influenza, which is better, a high-carb diet or a low-carb diet in the context of the risk of diabetes or heart disease. Does vitamin C decrease the severity or prevent colds? Diets for weight loss have always been popular but rarely informative and can almost universally be characterized with rapid drops in weight followed by steady regain until at the end of the study the comparative weight losses are small and frequently of no real significance. The worst macronutrient studies fail to differentiate the various types of carbohydrates or fats, may ignore the trans-fat component of the fat intake under study, and also fail to differentiate high from low glycemic carbohydrates or refined from truly whole grains. Generally, food additives including those that are toxic are ignored when simply looking at macronutrients. When studies attempt to ascertain the benefit of micronutrients, frequently the subjects involved have dose ranges that are too low, or doses that are only marginally greater in the treated as compared to the control groups. Low carbohydrate diets being tested are frequently moderately high in carbohydrates.

In the past decade, there has been growing interest in a more realistic approach to dietary questions which either attempted to identify beneficial dietary patterns or to compare them in head-to-head studies. Some attempt, at least in the discussion, to identify the components in the dietary pattern potentially responsible for good results, but this is generally by reference to reductionist studies. Modern Mediterranean diets are confused with the traditional Mediterranean diet of Crete.

*In the diet commentary included in this issue, the common suggestion that **you are what you eat** is embellished to include **you are what you do not eat**, and the hypothesis will be investigated that this latter statement is really the important one, and once one has solved the problem of what not to eat to maintain life-long health, the various guidelines associated with the former statement becomes much less compelling or meaningful. This approach recognizes that many foods and beverages by virtue of some of their contents are dangerous, toxic, fake food or simply unhealthy and should not just be limited, but rejected totally. Since it is necessary to eat something, the what-not-to-eat list places severe restrictions on what to eat since a major issue is not nutrition but toxicity and interference with normal metabolic and*

other processes. The solution is to find toxin-free foods and beverages whenever possible, and not to worry too much about the macronutrient content, something becoming easier as the organic food movement gains momentum and becomes better regulated.

This diet commentary has been strongly influenced by the landmark study of Dr. Weston A. Price who in the 1930s visited a large number of isolated, diverse groups of people around the world living according to the traditions developed over centuries and adjusted to changing environmental conditions, but without contact with the outside world that had any impact on diet and lifestyle. He was testing the hypothesis that the amazing degradation in health he was seeing in his practice in Cleveland Ohio over a period of 30-40 years was due to changes in nutrition brought about by the industrialization of food which had been taking place for 40-50 years. Highly significant comparisons were possible since he was able to study individuals who had migrated from these isolated societies and embraced the foods similar to those eaten by his patients in Ohio. His approach was similar to other famous studies such as Okinawa project and the Blue Zone research, but was characterized by the dietary and environmental diversity of the populations he studied and the comprehensive nature of his evaluation of both oral and physical health, reproductive success and micronutrient intake, the latter determined by samples brought back to his laboratory for analysis.

Wishing you and your family good health,

William R. Ware, PhD, Editor

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VITAMIN D--AN UPDATE

Some readers may have wondered why vitamin D gets so little coverage in IHN. The magnitude of vitamin D research is mind-boggling. In the past 10 years, over 28,000 papers have been listed with PubMed, the online search engine of the National Library of Medicine in the US. It is hard to understand how researchers keep current without severely restricting their field of interest. Likewise, it is quite impossible for IHN to keep readers informed about everything potentially significant to them or even a fraction thereof.

Consider the following list of health benefits listed by Dr. Michael Holick, one of the World's leading vitamin D experts, in the first chapter of a medical book he edited which was published in 2010. The percentages give are reductions in incidence that could be achieved by raising the population vitamin D levels to 50 ng/mL (125 nmol/L, note the conversion factor of 2.5).¹

- Rickets, 100%
- Osteomalacia, 100%
- Cancers, all combined, 75%
- Breast cancer , 50%
- Ovarian cancer, 50%
- Colon cancer, 67%
- Non-Hodgkin's lymphoma, 30%
- Kidney cancer, 67%
- Endometrial cancer, 35%
- Type 1 diabetes, 80%
- Type 2 diabetes, 50%
- Fractures, combined, 50%
- Falls (women), 72%
- Multiple sclerosis, 50%
- Heart attack (men)50%
- Peripheral vascular disease, 80%
- Preeclampsia, 50%
- Cesarean section, 75%

These estimates are of course based mostly on follow-up studies or other cohort studies rather than randomized controlled trials. Nevertheless, they illustrate the fact that vitamin D sufficiency is potentially protective for a remarkably diverse set of diseases. The message seems crystal clear. Is a more detailed discussion rather than just the above list necessary?

How about the impact on all-cause mortality? Studies concerning this question have been recently reviewed by Gröber *et al.*² One recent meta-analysis of 13 long-term (> 3 years) studies found that vitamin D supplementation reduced all-cause mortality by a significant 6%. Another meta-analysis found in comparing high vs, low vitamin D status blood marker 25-hydroxyvitamin D levels (25(OH)D) that for ≥ 30 vs. < 10 ng/mL, those deficient had a 35% greater risk of all-cause mortality and that each 10 ng/mL decline in this marker was associated with a 16% increase in this risk. Another meta-analysis found that those with deficiency in the range of 0-9 ng/mL had a 90% higher risk of premature death than those with levels > 30 ng/mL. This analysis also found that the point where the enhanced risk of mortality became non-significant was 36 ng/mL. The authors cite other studies that found similar results leading to the conclusion that sufficient vitamin D helps one live longer.

A whole book would be required to discuss in detail all the studies indicating health benefits, their weaknesses and strengths. In addition, the evidence-based medicine advocates appear unconvinced in the absence of randomized placebo controlled trials. There have been a few such trials, but they frequently had big problems such as too low a dose or studies that did not include sufficiently deficient individuals to allow an effect to become statistically observable. Some of these have been cited as evidence that the vitamin D advocates are wrong, misled by follow-up studies. Many vitamin D researchers regard this as nonsense. In addition, the doubters seem to ignore the fact that we evolved immersed in sunlight and probably had high vitamin D levels year around, at least in areas near the equator. Also, there appears to be a lack of knowledge among the general public that it is difficult to achieve vitamin D sufficiency entirely from food unless large amounts of fortified food is consumed, and that in northern latitudes where a significant portion of the population of the developed world resides, no vitamin D is generated by sun exposure to the skin between late fall and early spring, resulting an variations which can swing between deficiency and mild sufficiency. Therefore those who take supplements are not wasting their money, as the critics claim, but wisely playing it safe. The best case scenario is where an individual's physician actually monitors 25(OH)D on a routine basis and advises as to the dose regime indicated to maintain a high level of sufficiency year-round. It is your editor's observation based on family, friends and acquaintances that this is yet to become common. In fact in Ontario where your editor lives, most have to pay for the test whereas most tests are covered by the provincial health care system. Everybody (almost) knows their cholesterol levels but few know their vitamin D status. This is sad and illustrates one of the unintended consequences of the fixation on cholesterol, actually a very weak risk factor

for heart disease by some standards, while ignoring another blood marker which can expose a deficiency that has profound consequences. Consider the nursing home residents who get almost no sunlight-generated vitamin D no matter what the latitude. There might be quite remarkable results if all were brought up to sufficiency, although more nursing homes would then be urgently needed because of better health and lower mortality for the residents.

In spite of some critics reflexively suggesting potential dangers in large doses or even exceeding the official daily allowances (which are way too low), the consensus appear growing in mainstream medicine that 2000 IU/day is safe. A recent large study from the Mayo clinic confirms the safety of doses well above the limits suggested by conventional wisdom.³ In a large retrospective study they found that values of 25(OH)D above 50 ng/mL had increased in the cohort studied between 2002 and 2011 without a corresponding increase or even significant toxicity. Clinical toxicity was seen in only one case (out of 2000 observations). The recommendation of testing and achieving and maintaining a 25(OH)D level of > 50 ng/ml or greater appears to still be in the future which is unfortunate since both insufficiency and deficiency are widespread. There are considerable individual variations in the blood level of 25(OH)D achieved at a given level of supplementation, and getting vitamin D from sunlight depends on the latitude, season and sun exposure and use of sunscreen and skin color, reinforcing the need for measuring this marker to achieve a sufficient or better, optimal level.

BOTTOM LINE

The 18 disorders where the prevalence is strongly modified by maintaining a high vitamin D status seem to send a simple message. Does one really need more detail, tables of outcomes with their statistics? The benefit/risk ratio appears near infinite given that there appears to be no evidence that maintaining blood levels > 50 ng/L or higher involves any risk. Why wait 5-15 years, as the evidence-based medicine advocates probably would advise, until the results of a few placebo controlled trials might report. Yet very frequently we are seeing studies which show vitamin D does not provide a benefit for some problem and the paper concludes that supplementation is not in general justified until randomized trials are conducted. Are randomized trials on dozens of disorders needed when there is a vast amount of epidemiological evidence of huge benefit? What planet do these evidence-based fanatics who demand this live on? It is actually most likely that meaningful trials may never be done. Vitamin D supplementation is cheap, simple, and vitamin D status should be easy to ascertain with the simple addition of 25(OH)D to routine blood tests. If mainstream medicine paid more attention to vitamin D and less to cholesterol, everyone would be much better off.

DIET AND COGNITIVE DECLINE. THE IMPORTANCE OF LIGNANS

A study recently published in the *British Journal of Nutrition* performed baseline cognitive examination on over 2500 Dutch middle-age subjects and then repeated the test 5 years later.⁴ Micronutrient intake focused on antioxidants and was assessed at baseline with a food frequency questionnaire. Included were vitamin C, E, beta-carotene, lutein, flavonoids and lignans. The four lignans judged most important in the diet were calculated from studies of the food contents.⁵ Cognitive functions included global cognitive function, memory, processing speed and cognitive flexibility.

In the lowest quintile (fifth) of vitamin E intake, the decline in memory was twice that in the higher quintiles. Higher lignan intake was strikingly and linearly associated with lower decline of

global cognitive functioning, memory function and speed of cognitive processes. For the other micronutrients, no statistically significant associations were found.

Lignans are polyphenols found in plants, and occur in a wide variety of plant-based foods, including seeds, whole grains, legumes, fruit, and vegetables. Flaxseeds are the richest dietary source of lignan precursors. When consumed, lignan precursors are converted in the intestine to compounds that have a weak estrogenic effect, so-called phytoestrogens, but may also exert biological effects through non-estrogenic mechanisms.

For the lignans, the global, memory speed and flexibility scores declined much more slowly over the follow-up than was found for the other micronutrients studies. The declines were measured by a cognitive function evaluations battery of tests. When the first vs. fifth quintile were compared, the declines for global cognitive function, memory, speed of processing, and cognitive flexibility were 0.14 vs. 0.04, 0.24 vs. 0.04, 0.15 vs. 0.07 and 0.14 vs 0.03, respectively. These are large retardations of cognitive decline and thus dietary interventions if easy to implement appear worth considering. The mean intake of lignans was 733 micrograms/day in the first quintile and 1350 in the fifth.

The authors suggest that the phytoestrogen capacity of lignans may be responsible for the observed effects. They cite studies which found beneficial effects of cabbage, nuts and red wine in slowing cognitive decline. Red wine contains resveratrol which is a phytoestrogen precursor. Supplementation with vitamin E is easy, and some recommend the mixture of the various forms of this vitamin which is also readily available.

However, the best sources are food. In the study, the researchers focused on four lignans they considered to have the greatest potential for influencing cognitive processes. They then used the results of a study where the food content of these four and the total were as well obtained for Dutch plant foods.⁵ The highest lignan-containing foods include the oil seeds flax and sesame and cashew nuts, brassica vegetables in general, kale, broccoli, white cabbage, garlic, apricots, strawberries and olive oil. The range is huge, with flaxseed at over 300,000 micrograms/100 g to olive oil at 250 micrograms/100 g. Flaxseed flour is readily available even from Amazon and offers the opportunity of making baked goods high in lignans. The most protective lignan intake could be gotten with only 100 g of broccoli, 200 g of white cabbage, 200 g of cashew nuts or 25 g of multigrain bread. Garlic and apricots and strawberries are also rich in lignans with 100 g providing 50%, 30% and 20% of the indicated desirable daily amount respectively. Flaxseed whole grain bread provides about 12,000 micrograms per 100 grams, 10 times that of the mean of the most protective intake in the study. For more choices, consult the paper which is in public domain with a free PDF available at the journal website or via PubMed using the ID number (PMID) of 15877880.⁵

Life Extension (www.lef.org) has three products that include lignan extract from sesame seeds. They are Super Omega-3 EPA/DHA formulation (10 mg lignan), Gamma E Tocopherol (20 mg lignan), and Tocotrienols (20 mg lignan), the latter containing the entire vitamin E family. Sesame seeds contain 40,000 micrograms of the 4 lignans per 100 g of seed and are one of the richest sources. The amounts in these supplements would correspond to 10,000 to 20,000 micrograms of the four lignans. This is clearly an excellent way to supplement without having to worry about specific foods.

In a previous study from the same research group with the same study cohort, it was found that total intakes of fruits, legumes and juices were not associated with baseline or changes in cognitive function.⁶ But the observation that consumption of some subgroups such as nuts,

cabbage and root vegetables were associated with better cognitive function and less decline prompted the above study.

BOTTOM LINE

This study illustrates a simple intervention that appears to delay cognitive decline, a serious concern as one ages. Furthermore, the health benefits of lignan containing foods appear to go well beyond this one benefit, and the foods high in lignans will be recognized as components of a healthy diet. Studies suggest reduced risk of breast cancer, prostate cancer and cardiovascular diseases as well as reduced osteoporosis and menopausal symptoms. Lignans are currently the subject of studies examining their impact on a number of disorders. See the website of the Linus Pauling Institute for more information (lip.oregonstate.org). Cognitive decline is obviously a big problem as one ages. Readers are encouraged to examine other discussions in IHN (see archive index under cognitive problems).

DUCTAL CARCINOMA IN SITU. IS IT REALLY CANCER?

Ductal cancer in situ (DCIS) which is also referred to as stage 0 breast cancer is a non-invasive condition where the abnormal (cancer) cells are found in the ducts of the breast. It accounts for about 20% of breast cancers detected through mammography. Five percent are diagnosed in women before the age of 40. Early detection has increased the prevalence dramatically from about 6 per 100,000 in 1973 to about 35 per 100,000 in 2011. It is estimated that between 25% and 50% of DCIS cases will progress to invasive ductal carcinoma with the probability strongly dependent on the degree of so-called cellular differentiation, an indicator, or the extent to which the cells have become abnormal. Another indicator is the size of the tumor. Thus there is a continuum of risk of progression from quite small to quite significant. Optimal management should depend on the individual risk present but historically DCIS has been simply regarded as a problem which must be as aggressively treated as all forms of breast cancer which can involve a lumpectomy or mastectomy followed by radiation and chemotherapy. In recent years this has changed with a much more conservative approach used on low-grade presentations which involve a lumpectomy but not necessarily radiation. Recently, two studies have been published which address the question of overtreatment and the survival (mortality) benefit provided by surgical treatment with or without post-surgical radiation.^{7, 8} A third study examined the issue of recurrence after lumpectomy with and without radiation therapy or tamoxifen.

In a Canadian study by Narod *et al* over 100,000 women with DCIS were followed for a mean duration of about 8 years (maximum 24 years) with the main outcome being breast cancer-specific mortality.⁷ The principal observations were:

- The 20-year breast cancer-specific mortality following diagnosis was 3.3%.
- Young age at diagnosis and black ethnicity were significant predictors of breast cancer mortality.
- Prevention of invasive in-breast recurrence with either radiotherapy or mastectomy did not eliminate death from breast cancer.
- The clinical course after treatment observed for women with DCIS was similar to that of women with small invasive breast cancers.
- Among patients who received a lumpectomy, radiation therapy was associated with a reduction in the risk of same-side invasive recurrence at 10 years (2.5% vs. 4.9% but not breast-cancer specific mortality (0.8 vs. 0.9%).

- The risk of breast cancer specific mortality increased after experiencing a same-side invasive breast cancer.
- Patients with small tumors (< 1.0 cm) vs. those with large DCIS tumors had cancer specific survival rates of 98.5% vs 97% at 15 years after diagnosis. A similar comparison for well differentiated vs. poorly differentiated tumors was 98.8% vs. 98%.
- Radiation therapy made no difference in breast-cancer specific survival following lumpectomy with a 10-year survival rate of about 99.3%.
- Comparison of lumpectomy vs. unilateral mastectomy yielded an absolute survival difference of only about 0.5% in favor of lumpectomy.

The author's conclusions point out the DCIS have an inherent potential for distant metastatic spread and these should be considered as "de facto" breast cancers and not as preinvasive markers predictive of subsequent invasive cancer. Nevertheless, it is apparent from the above figures that treatment of this very prevalent type of cancer is associated with a high percentage of long-term survival.

The second study examined the breast cancer-specific survival in a group of about 60,000 DCIS cases where some elected not to have surgery and thus allowed a comparison of outcomes vs. a control.⁸ When stratified by grade, compared to no surgery those with low-grade tumors showed little difference in 10-year survival, but for high-grade tumors surgery yield a 10-year survival of 98.4% vs 90.5%. For all-cause mortality, those who did not receive surgery had a slightly longer 10-year survival rate but for high-grade tumors, there was significant higher survival in the surgery group (90.0%) vs. the non-surgery group (79.1%). The authors conclude that these results raise concern regarding the necessity of surgery for patients with low grade DCIS.

The third study examined recurrence after treatment of DCIS with a lumpectomy with and without radiation therapy.⁹ Endpoints included local (same side) recurrence and both-breast cancer-specific survival and overall survival. Study inclusion criteria included mammography detected low- or intermediate-grade DCIS with tumors measuring less than 2.5 cm. Tamoxifen use was optional (62% of those eligible). Exclusion criteria included age less than 26 (median age actually 58 with a range of about 34-85), presence of prior cancers except non-melanoma skin or cervical, and pregnancy or lactation. Eligible subjects (585) were randomized to either radiation or observation after lumpectomy (breast conserving surgery).

At 7 years follow-up the recurrence rate with or without tamoxifen was 0.9% for the radiation group and 6.7% for the observation group (no radiation) which yielded a statistically significant hazard ratio. Local recurrence rates by tamoxifen use and tumor grade were 1.2%, 5.3% 2.0% and 8.4% for yes/low, no/low, yes/intermediate and no/intermediate. Presumably, because the number of recurrences, with or without radiation therapy, was small (2 vs. 21 failures) further stratification was not meaningful. Overall survival also was not significantly different (91.7% vs. 95.1%) for observation vs. radiation, respectively), with again a non-significant hazard ratio. The authors comment that the addition of radiation therapy significantly decreased the local recurrence rate, the full clinical implications require further follow-up given the historic patterns of local recurrence over 10-15 years from diagnosis of what they term low risk DCIS.

An interesting question concerns what happens if DCIS is left untreated. This is termed the natural history of the disease. However, studies of the natural history of DCIS are very rare. Historically, clinical manifestations were the first sign of breast cancer and in most cases the disease had advanced beyond DCIS to invasive breast cancer (IBC) and aggressive treatment, if possible, was the only option. On rare occasions, a suspicious lump may have been declared benign while really DCIS and left untreated. With the advent of mammography, many more suspicious growths or tissue formations were found in ever increasing numbers as the technique became more sensitive and its use widespread. Sanders *et al* have recently reported on 45 women retrospectively diagnosed with DCIS who were “treated” only by biopsy at the time of the original evaluation.¹⁰ These cases turned up in a large review of surgical pathology diagnoses and original tissue slides for over 26,000 women where follow-up information was available. This is the latest of three studies that provide insight into the natural history. The study of Sanders *et al* reports on 16 patients who developed IBC, 3 who had a second DCIS diagnosis 3 to 28 years later, and 26 with DCIS who did not develop subsequent invasive cancer. Thirty-six percent developed IBC in the same breast and quadrant as their incident DCIS. Eleven IBC s were diagnosed within 10 years of the DCIS biopsy. Subsequent cases were observed at 12 to 42 years after the initial biopsy. Of those developing IBC, seven women developed distant metastasis resulting in death 1-7 years post diagnosis of IBC. One case developed IBC 29 years after the initial DCIS identification of DCIS and this occurred in the same location as the DCIS. In this study all the cases were reevaluated as low-grade ductal carcinoma at time of biopsy. This protracted natural history is quite different from that of patients with high-grade DCIS or any completely location-defined DCIS surgically removed with apparently negative margins. Sander *et al* also review two other studies which reach roughly the same conclusions. These may be summarized as follows. High-grade DCIS left untreated will develop into IBC in less than 5 years in 50% of patients. Untreated low-grade DCIS will evolve into IBC in 35-50% of patients but this can happen over a long time span up to approximately 40 years. Thus we are seeing a continuum where it is possible to have stable DCIS for decades even if left untreated. Even with treatment, recurrence is sometimes seen, but the recurrence interval may be well beyond the life expectancy of the patient.

Sander *et al* describe DCIS as the pivotal lesion in understanding the border line between malignancy and non-malignancy in the female breast. Untreated low-grade lesions give rise to a risk of developing IBC in 30% of patients within 15 years. Thus overtreatment seems hard to argue and the natural history of DCIS appears to justify the view that all cases should receive surgical therapy with additional therapy dependent on the grade and other related factors. This of course assumes that the verdict handed down by the pathologists(s) was correct. A recent study of diagnostic concordance (agreement) among pathologists in the context of DCIS found 84% concordance when 3 pathologists independently reviewed slides from test sets of breast biopsies with 3% declaring cancer more serious than DCIS and 13% declaring it absent.¹¹ In the absence of consensus, the pathologists then met to resolve the difference of opinion and obtain a consensus diagnosis. Some patients may ask for a second opinion from an independent pathologist, but most probably do not, and it is clearly not a completely black or white issue with no gray areas, nor is this a problem easily addressed.

There do not appear to be studies that address the issue of what is termed watchful waiting, where no therapy is initiated but evidence of progression is examined periodically. This has become popular with low-grade prostate cancer with significant avoidance of any

intervention over a number of years, but the presence of progression is followed with additional biopsies, generally annually. However, in breast cancer, an exception is what is called atypical hyperplasia which is also discovered during the examination of core needle biopsies of suspicious abnormalities seen in mammography. It is common that the atypical cells are seen in the ductal system and this is called atypical ductal hyperplasia. Atypical hyperplasia is not cancer but is considered to be a significant precursor. Thus the continuum of potential results from an initial biopsy are benign, atypical hyperplasia, grade one through 3 DCIS and finally invasive breast cancer. It is not uncommon for the initial biopsy to prompt a more extensive and invasive biopsy in order to adequately define where the patient actually is in this continuum, but there seems little doubt that aside from a benign result, there is progressive risk of invasive cancer as one moves through this continuum of manifestations of cellular abnormalities. Atypical hyperplasia is generally simply followed with watchful waiting and periodic reappraisal. The hope is that sooner rather than later watchful waiting will also come into wider use in early stage DCIS in order to avoid unnecessary surgery. The traditional practice of operating on any DCIS has naturally become a target for critics who fear overtreatment is out of control.

There is interest in finding biomarkers which would allow better identification of DCIS cases where monitoring could be potentially beneficial.¹² It is surprising that MRI is not used more extensively to monitor in watchful waiting in low grade DCIS. In addition, low grade DCIS does not generally progress rapidly and thus there would appear to be no urgency. Finally, the answer to the question posed in the title to this section appears to be yes, but women diagnosed with stage 1 or 2 DCIS should not panic and in fact should be advised that the potential for a cure is very high and can be accomplished with breast conserving surgery. There also needs to be a discussion between the physicians involved and the patient over the apparent contradiction when the patient is assured that their condition is low or even very low risk and yet they see themselves as getting more or less the same treatment as those they know with a well-established tumor. Stage 1 or 2 DCIS has even prompted individuals to elect bilateral mastectomies simply out of fear, especially when the genetic markers wave red flags, when there is only weak evidence of additional long-term benefit over a lumpectomy.

BOTTOM LINE

Being diagnosed with DCIS is significantly probable for any women and increases with age. It needs to be understood that there are a range of grades, and while all can be treated with breast conserving surgery, all grades carry a low risk of death from the disease and treatment which just includes post- surgical radiation is remarkable successful in producing close to 100% cure rate. Many individuals with only micro calcifications could avoid extensive imaging and even biopsy if properly diagnosed. For women diagnosed with DCIS, those with more favorable histology may be able to avoid radiation therapy as it is unlikely to affect outcome. While little natural history of DCIS exists, it appears to be sufficient to justify surgical treatment of all DCIS, with the qualification that better watchful waiting protocol could change this standard practice considerably.

HOW EFFECTIVE ARE NEWER CHEMOTHERAPY DRUGS?

An editorial in the April 23, 2015 *British Medical Journal* examined the recent accelerated drug approval process for cancer drugs in both the US and Europe.¹³ The subtitle was “Rushed approvals result in a poor deal for both patients and cancer research.” This editorial contains some extremely disturbing statistics and information the authors obtained from reviewing the chemotherapy clinical study literature and other papers over the last 8 to 10 years.

- Between 2007 and 2010, when almost 9000 oncology clinical drug trials were compared with trials for other diseases, the former were 2.6 times more likely not to use a comparator and 1.8 time more likely not be blinded (open to bias from the investigators). They point out that not only does this undermine the validity of the outcomes but reflect what regulators will allow.
- A review of drugs approved by the European Medicine Agency in its first 10 years found that new oncology drugs improved survival by a mean of 1.5 months and a median of 1.2 months.
- The 71 drugs approved by the US FDA from 2002 to 2014 for solid tumors have resulted in median gains in progression-free survival of 2.5 months and overall survival of 2.1 months. These survival time in fact represent distributions, which given the small times involved, must seriously overlap to include no difference in benefit.
- Only 42% of these FDA approved drugs met the criteria of the American Society of Clinical Oncology Cancer Research Committee as representing meaningful results for patients.
- Post-marketing changes in the package insert (so-called label) were substantially greater for oncology drugs given priority approval as compared to those going through the much longer standard process, which the authors suggest reflects deficiencies in the accelerated review process.
- Once oncology drugs are being marketed, withdrawing them due to observed lack of efficacy can be a lengthy process. They cite bevacizumab for metastatic cancer as an example.
- Both the European and US regulators allow companies to test cancer drugs using a surrogate endpoint rather than survival or other more patient-centered outcomes. Tumor size is given as an example of an unreliable endpoint since it is highly variable in predicting overall survival. In the US, surrogate endpoints were used for all 14 applications granted approval between 1990 and 2002. In Europe, from January 1995 to December 2004, most cancer drugs also were approved on the basis of surrogate outcomes.
- In 2013, two peer-reviewed papers appeared where a total of over 100 oncologists protested against the high prices being charged for cancer drugs when 11 out of 12 approved in 2012 provided only small benefits for patients.

The authors term the approval process an “Easy Ride” and suggest that this serves both patients and research badly. The latter refers to the lack of incentive to find something of real clinically significant benefit rather than some small but statistically significant benefit. It can also be argued that the majority of cancer drug development research currently leading to new drug approval is bogged down in merely getting more ineffective drugs approved in the hope that marginal improvements in survival will lead to enhanced profits. The few exceptions where

efficacy is high are generally priced so high that the choice is between bankruptcy or declining treatment except for the wealthy. It might be added that the points raised in the BMJ editorial should be included in discussions between patients and oncologists concerning informed consent and that this discussion should not emphasize relative risk reduction on the basis that deception in this context is hardly appropriate.

The results discussed above are consistent with those presented in 2004 by Morgan *et al*¹⁴. Based on reports from Australia between 1992 and 1997, the contribution of curative and adjuvant cytotoxic chemotherapy to 5-year survival in adults was 2.3% whereas in the US it was 2.1%. These results suggest that over this period in these two countries chemotherapy made little contribution to cancer survival. Furthermore, not much appears to have changed between 1992 and 2014 from the patient's perspective. It is important to note that we are talking about cancers that involve solid tumors.

BOTTOM LINE

When offered one of the new “wonder” chemotherapeutic drugs, it is important to ascertain the actual expected life extension in order to weigh this against the side effects. Trivial life extensions are sufficient to gain regulatory approval and allow patients to be told the treatment will extend their life. Unless carefully qualified, such an approach appears unethical.

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REVIEW AND COMMENTARY

THE ROLE OF DIET IN CHRONIC DISEASE

"It is easier to change a man's religion than to change his diet."
Margaret Mead

"Over the past 100 years, we have completed the single most comprehensive dietary shift in the history of our race." Catherine Shanahan, MD in *Deep Nutrition*

Almost everything we need to sustain life comes from what we eat. The goal should obviously be a diet that maintains health and quality of life. So what should one eat now that we are in the 21st century and probably living in developed countries with many options? As most readers know, both options and opinions vary quite considerably, and the answer also depends to some extent on where one lives and how much one can afford to spend on food. There is a saying **"You are what you eat."** This needs to have a footnote **"You are also what you do not eat."** Actually, this may be the more important statement. The modern world is a minefield of unhealthy foods and environmental toxins.

Judging by the huge number of diet books available, there is strong interest in this subject. Unfortunately, a significant part of this interest involves weight loss, not overall health and the avoidance of chronic disease. For many, a diet is something one goes on, tries to lose weight, and then stops. The end result is frequently little weight change. However, conventional wisdom holds that just as important is the composition of the diet in the context of health independent of the benefits of weight loss.

Views on healthy diets among dietary "experts" are so varied as to suggest there may in fact be no experts, only individuals who have bought into certain ideas. This is exemplified by pure plant-based diets, *Paleolithic* diets, diets that mimic living hunter-gatherer diets, diets that are similar to those eaten by micro societies that have remarkable longevity and health such as the *Okinawa Diet*, the traditional *Mediterranean Diet of Crete*, low-fat diets, low-carbohydrate diets, high-protein diets, diets designed to control hypertension (*DASH* diet), etc. Visit Amazon and take time to look at what is available. Alternatively, look at the official dietary recommendations of governments and academic nutritional experts. View their food pyramids. These represent the ultimate one-size-fits-all advice.

The end result is probably confusion, especially if there is the notion that there is only one diet that is really optimal for humans and yet one group of experts will favor a diet that is dramatically different to that favored by another group. Proponents of the plant-based diets will tell you that you do not need meat or fish, those favoring the low-fat diet will probably maintain that fat is bad, causes atherosclerosis, elevates LDL cholesterol, promotes cancer and makes you fat whereas those who favor the low carbohydrate diet will tell you that your need for carbohydrates is low, and those consumed should not significantly raise post-meal blood sugar. Some favoring ancient diets will favor high meat intake whereas others will attempt to convince you that ancient diets were entirely plant-based.

The confusion and associated loss of faith in experts is reinforced when there is a flip-flop such as recently occurred with regard to dietary fat, especially saturated fat. Once considered public enemy number one, we are now told that this was nonsense, that there was no evidence, and that fat and even saturated fats by and large are good for us and even necessary. A defense of saturated fat was very recently published in the journal *Mayo Clinic Proceedings*.¹ Dietary cholesterol was also recently declared innocuous after decades of advice to severely limit intake and never eat eggs or at least the yolks. Suspicion grows that expert opinion with regard to some important issues is controlled by other considerations than honest, unbiased science and sincere debate and that in fact, politics, academic egos, and corporate greed may be characteristic features of what is really going on.

Nutritional research for decades has been dominated by a reductionist philosophy. Food was viewed as a set of components such as red and processed meat, high and low glycemic carbohydrates, fiber, three basic types of fat which were then further subdivided, and particular, individual micronutrients such as vitamins, minerals, individual fatty acids, hormones, flavonoids, etc. Studies focused on the role of each in connection with various health questions such as the risk of chronic diseases, all-cause mortality, birth defects, mental disorders, diabetes and a variety of other health problems. Frequently the so-called endpoints of the studies, the data collected and tabulated, were simply biomarkers such as blood lipids (e.g. cholesterol) or blood glucose rather than events such as a heart attack or the development of diabetes or acute liver disease or cognitive impairment. Many studies were not or could not be randomized and controlled and thus regarded as second-class.

The fundamental weakness of the reductionist approach was that it ignored the possibility that what mattered was the nature of the total diet, and that the study of the importance of one component was likely to be of no real significance. Furthermore, measurement of macro- and micronutrient intake was difficult and prone to error, and intervention studies involving a specific dose of one or more supplemental micronutrients or dietary intake of one of the macronutrients were easily rendered meaningless by too low doses or too low or high intake. In addition, control subjects who already took the supplement or started to do so after the study began or adherence to the study protocol were especially serious problems. Dietary studies where macronutrients were compared, e.g. low-fat vs. low-carbohydrate diets added to the confusion. In fact, most low carbohydrate diets used in studies were not low-carbohydrate at all, but merely reduced carbohydrate diets. The role of fat in heart disease and cancer has been extensively studied for decades and the above flip-flop indicates the latest and perhaps final result. Many studies yielded small effects or statistically insignificant results and conflicting conclusions were common. The very best were merely hypothesis generating. Early in this period of epidemiological activity, dogma replaced true science and many academic careers and reputations were deeply enmeshed in dogma. Guidelines telling people what to eat were held up as scientifically based and should not be questioned by reasonable individuals, but were really nothing more than dogma. However, this provided immensely successful marketing tools for the food industry and, for example, the label "low-fat" or "no cholesterol" became equated to a healthy product.

In the last decade we have seen growing interest in nutritional studies that concentrated on comparing dietary patterns rather than focusing on individual components. This seems a significant move in the right direction and has provided guidance, but the diets suspected as being really bad were rarely used for comparison, even though they are common. An example is the American junk food and highly processed packaged food diets which are probably worse than the commonly used comparison, the Standard American Diet (SAD). Definitions of

unfavorable patterns also frequently included intakes of saturated fat above the guideline levels, which as mentioned above, is now viewed as a non-issue.

Arguments in favor of adopting ancient diets such as the Paleolithic generally evoke the notion that our genetic makeup (code) has changed little since then. Mutation rates are viewed as very small and the essentially fixed nature of the genome does not allow for rapid adaptation. Thus it is argued that we have not adapted to the changes that came with the agricultural revolution about 10,000 to 20,000 years ago or the profound changes that took place in dietary choices and options starting in the late 18th century. However, it now appears that this genetic hypothesis has been falsified by the recent emergence of what is called epigenetics which opens an entirely new vista on the subject under discussion and provides an explanation for rapid adaptation which is sometimes then inheritable.

DIETS, NUTRITION AND DISEASE IN EARLY 20TH CENTURY PRIMITIVE GROUPS LIVING ISOLATED FROM CIVILIZATION

In the 1930s a Cleveland Ohio dentist named Weston Price noticed the deteriorating dental and general health of his patients. These changes were observed by Price starting about 1910 and extended until 1925. The changes he saw among his patients involved all ages and allowed comparison of several generations, but nevertheless, were occurring over a very short period of time. He hypothesized that the causes were environmental and mostly nutritional. Until the late 19th century, there had been an extended period of rather stable history of food in America with distinct regional traditions that stemmed largely from England. In the early and mid-19th century city dwellers consumed lots of saturated and unsaturated fat, almost all natural, and their diet included butter, eggs, meats, whole milk, whole grains, fruits in season and vegetables. Farmers lived mostly off their land. Prepared foods were almost nonexistent, canning common to supply winter food, agricultural soil mostly still rich in nutrients, and the animals raised for meat grazed or were fed hay in the winter. Then in the late 19th century the industrial revolution got around to food. The practice of making white flour and in the process removing almost all nutrients was introduced about 1870. Development of other industrial foods was off and running. Commercial crackers in 1861, the invention of the common can opener in 1870 along with margarine as a butter substitute, Wesson vegetable oil in 1900, hydrogenated or partially hydrogenated vegetable oils contaminated with trans fats around 1900, ginger ale in 1901, Royal Crown Cola in 1905, Kellogg's corn flakes and also A-1 sauce in 1906, Aunt Jemima pancake flour, Crisco shortening (hydrogenated), Mazola salad and cooking oil and the first corn oil in 1910, and the favorite of carp fishermen, Wonder Bread in 1921. During this period, sugar became much less expensive and more widely used and several brands of candy bars and packaged cookies were introduced which still exist. In 1850 per capita sugar consumption in America was 20 pounds per year, about the same as in 1800. It then increased to about 80 pounds by 1900 and 90 pounds by 1925. Thus there was a rapid development of high calorie, nutritionally poor foods during the period when Price not only observed a strong increase in dental problems including cavities, but also the increase in health problems his patients mentioned which alarmed him greatly.

Consumption of industrial food would have been presumably much greater in cities, and thus it is reasonable that Dr. Price's patients who lived in and around Cleveland, Ohio were taking advantage of these modern advances in time saving and enjoy the tasty foods emerging from factories rather than from the land and barn. It is interesting that already concerns were being expressed about dangerous and toxic food additives. Initially, there was little or no regulation. These changes may have been the driving force for nutritional deprivation significant enough to influence the dental arch development during gestation and early development and cavity

prevalence, both of which Price found so alarming. The time-line clearly corresponds to the advent of nutritional deprivation and its adverse health effects.

What he observed in oral health and jaw anatomy was a radical departure from the norm that had existed for hundreds of thousands of years according to extensive fossil evidence. It was an amazing and abrupt deterioration. He formed the hypothesis that nutrition was at the root of what he was observing and decided to test this hypothesis by making a number of expeditions, visiting different groups of people who were isolated from what we loosely call civilization and who followed a way of life that was in keeping with traditions developed generations before. He studied a number of different native cultures including Eskimos in Alaska, people living in isolated villages in the Swiss Alps, on the islands off the coast of Scotland, in the Andes Mountains in Peru, and in several locations in Africa, Polynesia, Australia and New Zealand and also visited and studied northern Canadian natives including those living near the arctic circle. He examined their dental and physical health, their diet and way of life and returned with food samples which allowed him to establish levels of micronutrient intake. The research was published in a book *Nutrition and Physical Degeneration* in **1943** which was required reading in anthropology courses at Harvard for a number of years. Reprints are available from online booksellers. His work has been largely ignored by modern nutritionists.

The groups Price studied were all extremely healthy and essentially free from the chronic disease common to modern humans. Their teeth were near perfect and their jaw structure (dental arches) corresponded to the invariant norm set over hundreds of decades by fossil evidence. As expected because of the wide variety of locations, Price found a very wide range of diets, some very high in fat and some very limited in variety. Animals were hunted or raised or both for meat and some also provided milk which was partly turned into cheese or fermented. When fruit was available, it was a normal part of their diets.

The following generalizations are of interest if one is searching for guidance as to what to eat. Deviations from practices going back hundreds of generations were only dictated by changes in climate, and availability of food. These observations apply to populations and cultures totally isolated from the modern world and its commercial food that could be observed, interviewed and even coaxed into providing food samples.

- Not surprisingly, all food was raised without commercial fertilizers, pesticides or herbicides.
- All foods were natural foods. There were no sources of commercial food available to these groups.
- All diets contained saturated fats from animal sources.
- Fish and fish eggs, when available, were held in high regard.
- Fermented foods were almost universal, including what we call yogurt and foods similar to sauerkraut.
- Meat eaters always consumed the entire animal and organ meats and bone marrow were highly prized. Organ meats such as liver are generally high in micronutrients. Today liver may be high in toxins.
- Grains were soaked or sprouted, soured or fermented, which it turns out removed unhealthy or toxic substances. Refined grains such as commercial white flour or refined sugar were not available if the group in question was truly isolated from civilization. Rye was ground and used for bread.

- Analysis of the foods indicated vitamin and mineral levels that were vastly higher than found in modern foods such that the intake of these individuals exceeded the modern recommended daily allowances by as much as hundreds of percentage points.
- Price found no vegetarian societies.
- Fruit and vegetable (plant) consumption varied considerably with some populations consuming limited amounts.
- Some population such as the Masai of Africa existed on a diet that was almost exclusively meat, blood and milk. Pictures on walls of caves indicate that the Masai milked cows thousands of years ago as the do today.
- Nearly every culture consumed some foods that the conventional wisdom of modern nutrition considers to be unhealthy. In some cases, for example fat including saturated fat in large amounts was commonly eaten.
- Some groups did not come close to eating what modern nutritionists consider a “balanced” diet, but with no adverse effects.

All these diets resulted in robust, amazing health, almost totally cavity-free teeth, and freedom from the chronic diseases that characterize modern civilized societies. One of Price’s interesting observations was the high premium put on perfect babies. He discusses how some cultures went to great lengths to maximize the probability of this happening, even supervising preconception nutrition of both parents and postnatal maternal nutrition to insure healthy milk. This also illustrates their recognition of the critical importance of nutrition in general and in childhood development and this was a strong driving force for finding healthy food and preparing optimum meals. Remember, these groups had had many thousands of years of trial and error, given what was available, to reach the level of optimization they achieved. Some groups were traditionally very secretive and reluctant to reveal their health and dietary secrets. Price frequently commented that all of the groups studied were not only healthy but had an inherent beauty which was hard to miss, and it involved much more than perfect, beautiful teeth.

When members of these isolated societies moved to adjacent areas where they had access to early 20th century commercial foods, Price observed a large and significant deterioration in dental health. Many children now had narrowed dental arches, crowded teeth, and big changes in the jaw and facial bone structure. General health was also observed to deteriorate.

The dietary changes that presumably were responsible were not that great, judging by the timeline of new food introduction up to the time of Price’s observations in the 1930s. As discussed above, there was only the introduction of refined wheat flour devoid of most nutrients and its use in commercially prepared foods, new cooking oils and fats, some of which contained trans-fats, and increased sugar consumption from soda, candy, and sugar added in cooking and processed foods. In many cases the meat must still have been derived from grass fed cattle. These dietary changes were apparently all that was required to produce profound changes in health over just a generation. In addition, this deleterious effect was independent of the regular traditional diets that were abandoned. Price’s observations offered the first glimpse of what the early 20th century human should not eat. Also highly significant was the power these changes, and perhaps just some of them, had in influencing *in utero* and early childhood development as judged by dental arch distortions and adverse changes in facial bond structure. Price was describing the equivalent of the canary in the mine sending a warning loud and clear. No one paid much attention.

In sharp contrast to the primitive groups who did not migrate, in the late 19th and early 20th century, over the subsequent years city dwellers in many countries shifted more and more to prepared and commercial foods. Fundamental change was driven by the realization that fortunes were to be made in manufacturing and packaging foods and E.I. DuPont coined the slogan “Better Things for Better Living through Chemistry” which turned out to include chemicals we ate which the human body had never before encountered. Per capita sugar consumption increased steadily and has continued to do this throughout over 100 years. The prepared food industry blossomed until today grocery stores contain mostly processed foods and pesticide, herbicide and drug containing fish, meat and produce. Individuals living in the late 1800s would probably have difficulty even comprehending a prediction that in the 21st Century population could have changed to the point of needing so many pharmaceuticals, measured in multiple doses of multiple drugs per day with little apparent benefit, especially with regard to significant prevention. Eventually chronic diseases took over as dominating mortality.

After World War II, the fat-is-bad hypothesis ruled supreme and was joined by a fear of dietary cholesterol. Processed foods could be successfully marketed with the labels indicating low or no fat or cholesterol. By 1994, the American Diabetes Association was recommending Americans consume 60-70% of their calories from carbohydrates, but poor choices in carbohydrates became increasingly the norm. Every decade diets became more corrupted with highly processed, chemical-containing foods, drinks sweetened with synthetic chemicals, some of which are dangerous including one that breaks down to ultimately yield large quantities of formaldehyde, a known carcinogen, in selected locations of the body (determined by the location and prevalence of a critical enzyme). There has been an ever increasing level of added refined sugar until today the per capita sugar consumption is astounding. As Price observed when he had the occasion to compare two groups from the same culture, one that remained isolated and one that was exposed to some of the modern foods, it was clear that the latter rapidly became unhealthy with the second generation even more affected. This has repeatedly been observed in modern migrating populations who abandoned their original food practices, and as well occurred when vendors of modern processed foods established stores in previously totally isolated regions.

Price’s observations also suggest that the reductionist research that has characterized nutritional science, especially since the end of the World War II, has been rather ill-conceived. It appears that the relative amounts of fat, protein and carbohydrates are to some extent irrelevant, and that studies of micronutrients almost always look at levels that are way too low. Price found that what humans had evolved and adapted to by trial and error over thousands of years, while highly variable, always appeared to yield a high level of superb health and perfect babies.

WHAT NOT TO EAT OR DRINK

The following list of what not to ingest has been compiled from various sources including *Deep Nutrition* by Catherine Shanahan, MD and Luke Shanahan and Nora Gedgaudas’ book *Primal Body, Primal Mind*. Prior to 1900, most of the items on this list would not be a problem since they did not exist. Diet patterns that are restricted to organic foods would obviously satisfy many of the following restrictions. However, many individuals do not have the opportunity or money to make organic produce a significant part of their diets, and those with a pessimistic view of the whole subject of avoidance no doubt suspect that some organic produce or packaged products are faked. As well, in many jurisdictions, organic is not well defined and largely not subject to effective regulation. Fortunate individuals know vendors or farmers they trust and can get a large variety of organic foods or free-range or grass-fed meat, poultry and free-range eggs. Finally, it is important to understand that very small amounts of toxic materials can still be very important due to the very large number of atoms or molecules in even a microgram of the

chemicals in question. Those who remember their chemistry will recall Avogadro's number of 6×10^{23} atoms or molecules in a molar mass of a molecule or atom. This is, for example, the number of H₂O molecules in 18 mL (about 3 teaspoons) of water. Also compare Avogadro's number with the approximately 10^{13} cells in the adult body and you will see the problem we face even if only low levels of toxic materials are ingested.

The general principle is to avoid anything man made, synthetic or industrially or genetically manipulated and to aim for essentially zero tolerance. It is important to understand that the prepared food industry has gone to great lengths to conceal dangerous food additives by naming them in ways that most people cannot recognize or understand. Many of the items on this list are also discussed in Dr. David Perlmutter's book *Brain Maker* in the context that they promote damage to the gut and the bacteria that reside there which results in serious problems throughout the body, not just in the brain.

- Bad fat: Vegetable oils: Canola, soy, sunflower, cottonseed, corn, grapeseed, and safflower. Instead use good fats that can handle the heat involved in cooking: peanut, coconut and palm oil, butter, lard, tallow. These have a decreased tendency to oxidize or change into trans-fats on heating and do not contain trans-fats to start with. A common suggestion is to try to fry at as low a temperature as possible to avoid the formation of toxic modified proteins and fats.
- Partially hydrogenated vegetable oils, generally solid and containing trans-fats such as, margarine, shortening, and the fake, indigestible fats. Partial hydrogenation is also used to prepare the bad liquid fats listed above, also called industrial oils.
- Sugar and honey and foods with added sugar, although wild honey has been reported to have medicinal benefits when used short term.
- Fruit juices, especially commercial. Get fruit juice by eating fruit.
- Energy and "health bars," although there may be some exceptions for a few health bars.
- Fried restaurant or packaged foods, fried, fast and snack foods. These generally are rich sources of trans-fats.
- Most canned goods and especially acid foods like canned tomatoes which leach toxins out of the plastic can liner.
- Powdered milk and powdered "protein" preparations. Some would avoid milk altogether since whole, organically produced, unpasteurized milk is not easily found, and the milk sold in the stores has generally been homogenized and some or all the fat removed. Milk can contain a number of pharmacologically active contaminants including hormones, antibiotics, and as well toxins such as pesticide residues, dioxins, and even arsenic. Modern store milk should be viewed with serious reservations. Some stores sell organic milk in traditional glass bottles.
- Cereals that come in boxes or bags.
- Ready to use salad dressings unless free of vegetable oil (unlikely). Substitute extra virgin olive oil and vinegar, but be aware of the growing practice of faking the quality of olive oil.
- All soy products. The dangers are too numerous to include here. See Gedgaudas' book *Primal body, Primal Mind*, Chapter 4 for a good discussion.
- Soda type drinks, diet or otherwise, including energy drinks
- Genetically-modified foods (obviously hotly debated and a highly politicized issue) which are hidden in many prepared foods. To believe that the safety issue is settled is simply a fantasy.

- Monosodium glutamate (MSG). Check the internet for long lists of alternative names for this common food additive and popular flavor enhancer used in commercially prepared foods. Some Chinese cookbooks have the cook adding MSG to every dish. MSG is an excitotoxin and overexcites brain cells to the point of damage or death and lead to worsening of learning disabilities, Alzheimer's and Parkinson's disease, and Lou Gehrig's disease (see *Excitotoxins: the Taste that Kills* by the neurosurgeon Russell Blaylock).
- Processed meats (ham, salami, hot dogs, bacon, sausage) contain nitrates and nitrites. When studies find red meat carries a risk of some disorder, it is generally the processed meat component.
- Any artificial sweeteners: acesulfame-potassium, cyclamate, aspartame (NutraSweet), saccharin. Aspartame is one of the worst due to the release of formaldehyde (a carcinogen and powerful toxin) during metabolism, first from the generation of methanol (highly poisonous methyl alcohol also called wood alcohol) and then the conversion of methanol to formaldehyde. Available by the pound at the grocery store and widely used as a sweetener.
- Preservatives: butylated hydroxyanisole (BHA), propyl gallate, tert-butylhydroquinone (TBHQ).
- Thickeners: carrageenan, acacia gum, gum Arabic, brominated vegetable oil
- Miscellaneous: Aloe Vera, caramel coloring, artificial food coloring, potassium bromate (white flour, bread, rolls—interferes with thyroid function), bisphenol A (BPA), dioxins (common source is from heating chlorinated synthetic sweeteners), and phthalates found in plastic food containers and cosmetics.
- Municipal water supplies (tap water) should be viewed with profound suspicion and in most cases is best reserved for toilets, washing machines, mopping the floors and watering the garden. The reason of course is variable and is, in some cases, high levels of toxins of every description, pharmaceuticals both from human excretion and from consumer disposal, added chemicals such as fluoride and chlorine compounds, and traces of other chemicals added in the water treatment process, etc. Read chapter 4 of McKay Jenkin's book listed in the bibliography for a good discussion of municipal tap water. The best solution is to drink and cook only with reverse osmosis water. Recently a stand-alone generator has come on the market that uses a pump rather than domestic water pressure to force the water through the osmosis membrane. The standard solution is an under the sink unit consisting of a set of filters and a storage tank the size of a propane barbeque tank, with a separate counter top spigot for "potable water." Those who say reverse osmosis water is bad because important minerals have been removed are not seeing the big picture. Trust other filter systems at your own risk. Most do a poor to fair job of removing contaminants. The challenge is to remove all undesirable chemicals and organisms. This blanket condemnation of tap water of course goes against the conventional wisdom that tap water is safe to drink because the authorities involved say it is. It depends on the standard one applies and it is not financially possible in general for municipalities to provide truly pure water. Well water should be tested by a reliable laboratory or subjected to reverse osmosis filtration prior to drinking or using for cooking. Showerheads should include a chlorine filter with replaceable cartridges. However, it is not clear how well they work. This is because in the shower one inhales contaminated mist or droplets. Bottled reverse osmosis water sold in glass bottles would probably be a solution, but clearly not very practical. Your editor stores an emergency supply of reverse osmosis water in screw-cap wine bottles.

This is a very long list and the risks to human health not well studied or quantified. Long-term risks, prenatal and childhood developmental risks, etc. are impossible to adequately study, animal studies potentially irrelevant, and all in all, potable water is a highly disturbing and frustrating subject. All one can do is avoid known sources and when this is impractical or impossible, attempt to detoxify (see the IHN Archive Index for discussions of detoxification).

Gluten is not mentioned because the issue here is gluten sensitivity unless one has the acute form called celiac disease. However, when this sensitivity is present the results can be disastrous to general health. The prevalence of gluten sensitivity (suspected to be much higher than mainstream medicine admits) suggests that a strict gluten-free diet should be tried much more often than is now common, especially when the root cause of a set of symptoms is unclear and various therapies have failed. Perlmutter's books *Grain Brain* and *Brain Maker* are highly recommended, not only to increase awareness of the problem of gluten sensitivity and the magnitude of the damage that can result, but also because both extensively discuss the critical issue of the gut and health.

Big Agriculture, Big Chemical and lax, indifferent, or conflicted government agencies have made it very difficult in some cases to avoid food additives because of the use of obscure names or turning a blind eye to deliberate attempts to conceal their presence. Naturally, the pesticide and herbicide content of foods is never seen on labels, but the internet has a number of sites devoted to listing foods by the *probable* content of these toxins. Many of the items in the don't eat list reflect the impact of modern lifestyles where fast food, ready to eat packaged food and convenience and snack foods have come to dominate the diets for many in the developed world. The traditional way of living where produce was acquired from farmers who avoided chemicals or through trusted local vendors and where meals were prepared from scratch is no longer convenient or even practical or possible for many individuals and families. Food and chemical companies have taken advantage of this growing market with little apparent regard for the health of consumers and very much concern for shelf-life of products, addictive foods, cheap substitutes for real food, edible synthetic food, marketing to false beliefs (low-fat, for example) and most of all, the bottom line as the all-encompassing principle guiding practices. Rejection of the modern culture of food and eating will be challenging for most. Many modern foods have highly appealing taste, undeniable convenience and the trade-off in terms of healthy eating is obscured by the observation that almost everybody eats this stuff so it must be OK. Pessimists simply say we are all doomed to have poor health because the modern world makes anything else virtually impossible. They are right in the sense that poor health is becoming the norm.

DIET REFORM

One can get started on a program of diet reform by altering the way the supermarket is viewed. Consider mentally placing a do-not-cross yellow tape such as the police use around most of the aisles leaving only the produce section, the meat and fresh fish sections and dairy, and cross the yellow tape only for things like carbonated water, eggs, coffee, garbage bags and similar necessities. Consider purchasing laundry and dishwasher detergents and personal care items at a store which sells natural types. Select free range eggs if available and organic items whenever possible, recognizing that "organic" may not always be organic. Both the US and Canada have official certification seals that can be found on some products.

The above allows avoiding the vast majority of modern manufactured foods implicated in chronic diseases. However, there is a problem in that the supermarket produce, beef and chicken may (probably) contain items contaminated with pesticides, herbicides, hormone mimics and actual hormones, antibiotics, toxins, etc. Apples for example are notorious as carrying high levels of pesticides. Genetically modified foods are also present in a significant

fraction of all processed and faux foods. Thus the next step in the diet reform is to find stores or vendors that carry produce and meat which are free of these objectionable offerings from modern food production, Big Chemical and Big Agriculture. Maximize the organic food content of the diet if at all possible. Some may have the opportunity to buy directly from organic farmers. Even organically produced wine of good or even high quality is now available. In general, it is important to put the intake and excretion of toxins and objectionable chemicals way out of balance in favor of natural detoxification, which has been demonstrated to occur with organic diets. If one is gluten sensitive, even that is not good enough. Zero tolerance is the rule and watch out for gluten in personal care products.

Finally, there is the decision as to what to eat. Weston Price's observations suggest that it may not matter much since in the cultures he studied, there was a huge variation in the type of diet with no significant differences in achieving essentially excellent health and freedom from the chronic diseases that now plague the Western world. The list given above which was based on Price's observations of diet patterns can serve as a rough guide. The currently promoted versions of the Paleolithic diet have some of the features of a diet based on Price's observations as does the traditional Mediterranean diet of Crete. However, Price found no vegetarian cultures, perhaps because over the eons, the problems caused by nutritional deficiencies inherent to the plant-based diet either became apparent or the culture died out. Rather, of central importance in all the cultures studies were animal-sourced foods and richly abundant fat-soluble micronutrients.

However, some of the diets Price found among the healthy primitive cultures would certainly be criticized by nutritional experts, and especially unlimited fat and saturated fat and red meat. The issue here is inflammation and the suspected merits of a non-inflammatory diet in the context of general health. However, a recent review of the literature by Santos *et al* found little evidence for the association between saturated fat and inflammation.² As regards red meat, the issue is the relevance of red meat studies which included mostly so-called grain fed beef which contains high levels of omega-6 fats which are viewed by some as inflammatory. The "grain" of grain-fed beef is a concentrate food made up of a slurry consisting of corn and corn byproducts including husks and cobs, soy and soy hulls, spent brewery and distillers' grain residues and other cereals. The people Price studied ate the meat of wild animals or domesticated animals which grazed and had high levels of omega-3 fats, and the meat did not contain any potentially dangerous substances such as antibiotics, hormones, pesticide and herbicide residues or who knows what else. In addition, some meat studies do not separate out the effects of processed meat which everyone appears to agree is something to be avoided, and which is on the above do-not-eat list. Thus the advice to limit red meat sold in the local supermarkets is probably good advice, and can be justified because red meat currently a staple is not the kind of red meat we should eat. Diets high in omega-3 fatty acids and low in omega-6 fatty acids are viewed as minimizing systemic inflammation.³ The exact reverse taken to an extreme is the norm today.

The conclusion seems obvious but not that easy to implement. In simple terms, eat as much organically produced food as possible and avoid all processed foods. Eat a variety of food without being concerned about macronutrients except for getting enough fat. The implication that one should eat lots of organ foods carries the concern regarding toxins which concentrate in the liver and thus the sources should be free range and not doctored up with hormones and antibiotics or fed commercial foods. Fish should be wild caught but it is difficult to get wild shellfish and farmed fish can easily be sold as wild and thus misrepresented. Fix most meals from scratch and do not ignore the merits of bone marrow and stock made from bones. Fossil evidence makes it clear that for eons humans split or crushed bones to get at marrow. This basic dietary philosophy outlined above is not easy to follow today, especially in urban areas.

Organic foods are still not that common. Individuals living on farms are in the best position to imitate these primitive cultures, in some cases almost entirely, but this means giving up the modern convenience of most supermarket food, spend much more time preparing meals, and probably enduring the complaints or even boycotts of younger family members.

The cultures Price studied had not always consumed the diets he observed. They descended from pre-agricultural societies which also did not practice animal husbandry. And some moved from place to place. However, they evolved to adapt, and over a fairly short period. One can argue that this is simply epigenetic adaptation, which does not involve DNA code changes, and they came to do well on such foods such as grains and the milk of domesticated animals. To quote Jeffrey S. Bland, PhD (from *Genetic Nutritioneering*):

Throughout your life the most profound influences on your health, vitality and function are not the doctors you have visited or the drugs, surgery or other therapies you have undertaken. The most profound influences are the cumulative effects of the decisions you make about your diet and lifestyle on the expression of your genes.

While the observations of Price used to help guide healthy dietary practices are rather similar to the principles behind the *Paleolithic*, *Evolution* and *Stone Age* diets, Price had the additional advantage over promoters of these diets in having associated with and studied living examples of the dietary cultures he describes and having observed firsthand the almost total lack of chronic disease and strong evidence of superb health by every measure he could use. This sort of information for early man is of course indirect and in some cases controversial.

If one believes the general principles outlined by Price based on the primitive but early 20th century groups he studied, then the conclusion is that it does not really matter how the calories are distributed between the three major macronutrients as long as one avoids most foods that are part of the modern diets. Most of the reductionist research about the relative merits of various diets can be ignored. However, the diets Price documents were not low-fat, high carbohydrate nor vegetarian. Aside from that, the type of diet did not seem very important. This is a dramatic departure from modern reductionist thinking about diet.

HIGHLIGHTS OF THIS REVIEW

Weston Price looked at over a dozen primitive cultures that had not interacted in any meaningful way with the “modern” societies which surrounded them. He noted their splendid dental health including the almost total absence of tooth decay, the success of proper facial bone development during gestation and early growth, and their superb general health and vigor. Perfect evenly spaced teeth were almost universal, produced by an appropriate so-called dental arch which controls the spacing of teeth and the appearance of facial features. These isolated populations enjoyed what he judged to be a high level of freedom from disease and unusual vigor. Proper development of the facial bone structure provided open nasal passages rather than the common deformities seen today which force mouth breathing. This was in the 1930s in regions all over the globe. When migration from isolation took place into adjacent living areas where there was access to modern processed foods, he found that huge and highly significant deterioration of dental health and dental arch deformities in the children these individuals produced. Vastly increased susceptibility to infectious diseases was apparent among those that migrated, whereas in isolation this disease was virtually unknown, although there are exposure and immunity issues here. There was a huge variation in diet types, climate, presence of vegetation and availability of fish. Nevertheless, these groups followed a lifestyle that they had developed over centuries which gave them health and satisfaction with life and a realistic hope

for future generations based on their significant attention to producing “perfect babies.” What have we learned from these people Weston Price studies so carefully?

The most striking observation involved the importance of what they did not or could not eat. Between 1870 and the 1930s when Price made his many expeditions, humans in the developed world were being offered and eating a number of new commercial foods and cheap refined sugar as discussed and documented above with dates of introduction. Price’s populations not only did not consume any of these foods or even adopt the methods of producing white flour, and when individuals genetically identical migrated to places where these foods were available, it was a disaster. In many of the populations studied, animal husbandry was widely practiced, but the animals grazed except when snow forced the owners to feed hay. The animals were what we call grass-fed, free-range and thus the eggs and chickens produced were also free-range. The land was uncontaminated by chemicals foreign to the human body.

It would therefore appear that even the initial changes brought about by the industrialization of food produced items one should not eat. What started in the 1870s has by today gone completely out of control, which might help explain why the abstainers who are now very hard to find remained healthy and so it seems, almost everyone is now sick with everything from mental disorders to the standard chronic diseases or their precursor disorders. Price had considerable experience with the presentations of human chronic diseases since he saw them frequently in his practice and would have certainly identified them in his studies of isolated populations, especially since he was looking for them.

One of the most common sources of nutrition was meat, it was not what we call meat today since it was produced by grazing in the absence of corn-based fodder contaminated with chemicals and GMO varieties and there were no vets to provide antibiotics, hormones and who know what else. Modern studies which suggest limiting red meat consumption (and of course processed meat) are not referring to the red meat from wild and domesticated animals that these healthy primitive groups ate, sometimes as the major source of calories throughout the year. There was no such thing as farmed fish fed unnatural food and being kept alive with drugs.

One of the most remarkable things Price observed was how rapidly health deteriorated when migration took place and “modern” foods introduced. This occurred even though the number of choices of commercial food was vastly more limited than today and modern toxins largely absent. The toxic effects on childhood development were immediate as these migrants reproduced and carried over to poor dental health very rapidly as the offspring matured into adults. There is certainly some element of truth in the notion that adopting a diet that included foods purchased from stores and other vendors of these produces was tantamount to eating poison.

The second most striking observation is what the healthy people living in isolation ate. First there were no vegetarians. If one gave a modern nutritional expert Price’s summary according to groups of what people ate, they would have to conclude that diet details did not matter since there were no consistent patterns except that most ate meat both wild and raised, fish when available and lots of fat. Food made from ground rye was common including rye bread, but the consumption of fruits, roots and vegetables and gathered greens was highly variable depending on location. These observations of Price would defy the best efforts of reductionists to come up with a healthy diet common to all the micro societies he studied. To favor heavy consumption of meat and saturated fat would be taboo and his observation of the importance of fat in connection with the assimilation of the major fat soluble vitamins would be ignored since today

we could not even get the vitamin and mineral intake common to all these groups except by supplementation and the doses would never be recommended by the conventional nutritional experts.

Thus the hypothesis is advanced that one should look for dietary guidance to totally isolated micro civilizations existing in modern times which have been virtually without contact with the outside world for generations and thus not only eat according to the general principles derived by trial and error over many generations, in fact over eons, but also avoid almost everything in modern diets. The evolution from real to fake and processed food has taken place over about five generations which indicates how far back we must look to see the major features of traditional diets.

Evidence suggests that what one does not eat is vastly more important than the macronutrient balance in what is eaten, with superb health and longevity achieved on highly variable diets independent of the distribution between the reductionist's favorite categories of fat, protein and carbohydrate. However, modern farming has created the potential for serious micronutrient problems which can be aggravated by many foods on the "don't eat" list. The industrial revolution produced industrialized food at an ever-increasing pace until today our great grandparents would not recognize most of the stuff in our shopping carts as food and would gaze with wonder if they toured a supermarket. They would be shocked to learn the extent to which the chemical and food processing industries has become involved in what we eat. Thus the sage advice, eat only what your distant ancestors would recognize as food. It is not good enough to go back only a generation or even two. But it is not that simple! These ancestors would of course recognize an apple, but today apples are notorious as being loaded with toxic chemicals that are sprayed on them with abandon.

Eating only organically grown or produced food is virtually a necessity as part of a program to avoid all the things we should not eat. Ideally, find sources that can be trusted and whenever possible, buy directly from the farmer or farmer's markets. Internet searches will frequently yield surprisingly close by sources. Your editor has just recently found a farmer raising grass-fed cattle of a magnificent Swiss breed less than 30 km from his home in Ontario. Also, Amish and Mennonite farmers will almost always reject all the modern agricultural practices that are poisoning us and robbing food of its nutrients. As more people come to appreciate the merits of not eating most of the food that their friends and neighbors eat, demand will almost certainly increase the availability of genuine organically produced food. The loss of convenience, the added time required preparing meals and the probable rejection by the younger generation is the price to be paid to gain health rather than disease promoted by diet. Also, there will be an increased incentive to improve culinary excellence, for example by imitating the principles of traditional French cuisine, in order to heighten the pleasure of eating real food. It will take time, but the guarantee of "organic" will become more reliable as this revolution gains momentum and we may eventually even see a return to heritage varieties of fruits and vegetables.

Finally, this review and commentary only mainly concerns what we eat and drink. Risks to our health go way beyond this and include environmental and other toxins to which we are exposed outside of food, beverages and water and occur through inhalation and absorption through the skin (e.g. cosmetics, personal care products, cleaning aids, bug repellants etc.) Read McKay Jenkins' book *What's Gotten Into Us?* for an excellent, comprehensive and modern discussion of this huge problem.

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