INTERNATIONAL HEALTH NEWS

William R. Ware, PhD - Editor

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This issue features another flip-flop, this one having to do with saturated fat being a health risk. Now we are told this is not true and saturated fat may in fact have a number of protective functions, that is, it appears to be good for us. This just adds to a long list of flip-flops, some quite sensational. Recently we were told that medical science has decided dietary cholesterol is not a problem and there is no evidence of benefit from avoiding foods high in cholesterol such as eggs. This is after decades of eggs being vilified and after "low" or "no cholesterol" became a marketing tool. It is surprising that table salt was not labeled cholesterol free. We are well on the way to the view that cholesterol and fat are good for us, which incidentally is the title of a book by Uffe Ravnskov, MD, PhD, one of the principal critics of the fat-cholesterol-heart hypothesis. The Atkins diet was for several decades almost universally viewed by both mainstream medicine and nutritionists as a threat to the nation. Robert Atkins was even hauled before a congressional committee because he was viewed as a public enemy. Now the Atkins diet frequently appears in major diet studies as the low-carbohydrate initially ketogenic type diet, not to test its dangers which are rarely mentioned anymore and never demonstrated, but to test its comparative effects on various endpoints. For decades we have been told that LDL cholesterol in our blood, if elevated, must be reduced to specified targets governed by the patient presentation. Treat to target was the battle cry. Now we are told that there was never any convincing evidence and our physicians should forget about targets. Targets have been replaced by a new risk assessment threshold for using statins that would considerably increase the number of individuals worldwide on this class of drug. This has caused considerable controversy since even the risk assessment algorithms currently in use and the new one have recently received some very unflattering analysis.

IMPORTANT ANNOUNCEMENT. Attached to this issue is an index of subjects covered in IHN from 2011 to date. This index will also be available on the website. By using this index and the archives on the website, readers should find it convenient to research subjects covered by IHN.

Some call flip-flops reversals, a term defined in this context as when a current medical practice was found to be inferior to a less or prior standard. In a recent issue of the Mayo Clinic Proceedings (Vol.8, pp.790), a paper authored by a number of physicians found that for the decade ending in 2010 a total of 146 reversals were identified in the literature and these occurred across all classes of medical practice. But the treatments and protocols reversed had all been supported by what some term scientific studies. In some cases it was the common view that the matter was settled, science had spoken clearly. This is in fact an example of the misuse of the terms scientific and science.

The words "science" and "scientifically" have many meanings and uses. Our concern here is with the use of these words in an attempt to convince a reader or listener that the point being made or the position being advanced carries a very high level of credibility or corresponds to a "truth." Scientifically proven is frequently used in this context. Consider some examples of

the diverse use of these terms. We have academic courses and degrees in secretarial sciences, social sciences, scientific theology, physical sciences, biological sciences, medical sciences, mathematical sciences, natural sciences and this is an incomplete list. Then there is the pair of classifying terms, hard and soft. While usage varies, typically the hardest are physics (including astronomy), chemistry and the mathematical and computer sciences, with biology intermediate and the social sciences regarded as soft. Features of the hard sciences include a heavy use of higher mathematics, and a high degree of objectivity and accuracy with foundations of what might be termed facts which do not rely significantly on statistics for their validity. The hard sciences generally apply a purer form of the scientific method and rely on quantifiable data and mathematical models. The Merriam-Webster dictionary gives the general definition "knowledge about or study of the natural world based on facts learned through experiment and observation." It is easy to argue that most of the studies in medicine and nutrition that relate to guidelines and influence practice are close to soft science, simply because of the nature of the issues investigated, the methods used, the variability of the subjects participating and the heavy reliance on statistics. Recognizing this should nurture a high level of skepticism. Flip-flops reinforce this view.

Wishing you and your family good health,

William R. Ware, PhD, Editor

Highlights

THE SATURATED FAT SAGA CONTINUES

Two US organizations have recently taken positions concerning saturated fat. They are The American Heart Association in conjunction with the American college of Cardiology (AHA/ACC) and the Dietary Guidelines Advisory Committee (DGAC). The AHA/ACC recommends limiting intake to 5-6% of calories whereas the DGAC suggest less than 10%. Prior to this, 7% was a popular number. Added to these more or less exact thresholds was the advice to replace saturated fat with unsaturated fat, also a common recommendation for decades.

The hypothesis that saturated fat causes heart disease goes back 50 years and was advanced before there was any significant evidence, but it took on a life of its own and became one of the most fervently believed dogmas of nutritional and medical science. Once belief in a dogma is close to universal, contrary evidence that falsifies the hypothesis is commonly ignored and even difficult to publish.

The key hazard to cardiovascular health was claimed to reside in the action of saturated fat to slightly elevate serum LDL cholesterol and this rationalization flourished during decades when LDL was described as the "bad" cholesterol by everyone from mainstream medicine and nutrition to health journalists and media commentators.

Thus it was surprising, even shocking to read a commentary in the April 2014 Mayo Clinic Proceedings which went into considerable detail concerning a contrary point of view.[1] The six

authors were from the US, Sweden, Scotland, Japan and Germany. The authors summarize the objections to this hypothesis as follows (see the free paper for references):

- Ten randomized controlled or cross-over trials found that a high intake of saturated fatty acids (SFAs), even up to 50% of total energy intake, had little effect or none at all on either LDL or total cholesterol.
- Two meta-analyses of follow-up studies found no association between CVD mortality and SFA intake
- In 10 cohort studies of patients who had experienced a stroke, 3 found no difference in SFA consumption between patients and controls and in addition for 7 of the studies, patients had eaten *significantly less* as compared to controls.
- In a meta-analysis of 16 long-term follow-up cohort studies, when the highest dairy consumption was compared to the lowest, the highest consumption was significantly *protective* for all-cause mortality, atherosclerotic heart disease, stroke and diabetes.
- Studies conducted in 1998 found that decreasing the intake of SFAs changed the LDL particle size in in a favorable direction as judged by the increased prevalence of large buoyant LDL particles.
- Three studies of patients with heart attacks were compared with healthy controls as regards to the concentration of short-chain fats (considered bad) in their fat cells because this reflects recent dietary intake. No difference in levels was found.

This large body of evidence nicely summarized by the authors of the commentary seems carefully ignored by groups that undertake to advise us on what to eat to avoid CVD events. Furthermore, the belief in the connection with LDL is clearly evident in the AHA/ACC recommendations since the advice to keep saturated fat intake at 5-6% is directed at adults who would benefit from LDL lowering. In other words, if your LDL needs lowering, don't do anything that might raise it if only slightly. Feeding trials find that for every 1% of energy from carbohydrates that is replaced with 1% of energy from SFAs, LDL is raised by 0.7 mg/dL.[2] Replacing 6% energy from carbohydrates with 6% from SFAs would increase LDL by about 4 mg/dL. Even at the old threshold of LDL level of concern of 160 rather than 189 mg/dL, is an increase to 164 really clinically significant? Recall, that the AHA/ACC guidelines abandon LDL targets as not evidence based (JUL 14 IHN). For those with ≥ 7.5% ten-year risk of adverse CVD events, the new guidelines simply recommend 30-50% LDL lowering. To focus on 4 mg/dL appears to be unwarranted fine tuning, probably even a change that falls within the daily fluctuations. One can also question the applicability of the feeding studies when, as discussed above, other studies that increased SFAs up to 50% of energy intake had no impact on LDL. As discussed in the March 2015 issue of IHN, the new calculator that is used to stratify individuals in order to apply the risk threshold of 7.5% is deeply flawed and severely overestimates the risk. This threshold is also being used in the guidelines to determine when one should worry about their SFAs intake since it identifies those who would benefit from LDL lowering and thus SFA lowering.

A study from Finland just published adds to the data concerning SFAs and coronary events.[3] This follow-up study of over 2400 patients, mean age 62 years, over about 5 years found no significant association between saturated fat (SF) intake and the risk of either coronary events or mortality in patients with established coronary artery disease. The authors speculate that because a high SFA intake was associated with several CVD risk factors at the start of the study but with no associations to clinical outcomes, a high intake of SFAs may have been protective in that it off-set the potential adverse effects predicted by these risk factors.

As mentioned above, the common recommendation over the years has been to replace SFAs with polyunsaturated fatty acids (PUFAs). When, starting in the 1960s, it became the rage to cut SFAs, the calorie replacement was typically carbohydrates, the heavy consumption of

which altered glucose metabolism, increased fat accumulation, elevated triglycerides, lowered HDL and increased the risk of diabetes and obesity. However, fat, including saturated fat, the great dietary evil, was being reduced which was the name of the game. Too much protein was considered bad and thus unsaturated fats had great appeal as a source of replacement calories. However, mostly omega-6 polyunsaturated fats were increased by consumption of safflower oil and margarine, which as pointed out below, is not a good idea. Many individuals either did not like fish or were not willing to eat significant amounts to get omega-3 PUFAs.

There have been a number of studies that addressed the issue of replacing saturated fat with other types of fat. A meta-analysis of replacement studies that used polyunsaturated fat found that when 5% of energy intake from SFAs was replaced by energy equivalent amounts of PUFAs, there was a significant decrease in the risk of coronary events including coronary-related mortality.[4] Since two variables were changed, such studies fail to establish the validity of the SFA hypothesis but rather indicate the merits of consuming PUFAs. However, the two major classes of PUFAs are omega-6 and omega-3, and a pooled analysis of 11 follow-up studies revealed that replacing saturated fat with the most abundant of PUFAs, the omega-6 linoleic acid, increased the rates of death from all causes, coronary heart disease, and cardiovascular disease.[5]

Another common recommendation in the context of this discussion is to eat only low-fat dairy products. As mentioned above, a meta-analysis of 16 studies did not support this recommendation. Furthermore, as pointed out in the commentary, in the famous Nurses' Health Study the difference in risk found on comparison of low-fat vs high-fat dairy products was trivial.

THE BOTTOM LINE

The commentary ends with the conclusion that there is no evidence that a lower intake of SFAs can prevent cardiovascular disease and a high intake of PUFAs without regard to the type may result in excessive intake of omega-6 PUFAs with adverse health effects. In addition, there is much evidence that saturated fat may even be beneficial. This is not the first time this position has been advanced, but it is unusual to see its view presented in a journal such as the *Mayo Clinic Proceedings*.

STATINS INCREASE RISK OF DIABETES. NEW STUDY

We have been told for decades that the benefits of statin drugs outweigh the harms. For the past few years there has been growing evidence that this is not true and that diabetes is one risk factor that may falsify this position.

A follow-up study has just been published on line which addresses this issue in a cohort of 8,749 men age 45-75 from Finland.[6] This cohort was part of a larger group of individuals randomly selected from the population of a town in Finland for the purpose of studying factors associated with the risk of type 2 diabetes, cardiovascular disease and insulin-resistance. Given that one of the endpoints was cardiovascular disease (CVD) it can be assumed that this cohort was free from CVD and primary prevention was the motivation for taking statins which determines the magnitude of the benefit side of the question of adverse effects vs. benefit.

Most of the subjects taking statins were on atorvastatin (Lipitor) or simvastatin (Zocor). Diabetics were of course excluded and the criteria for diagnosing the disorder were a fasting plasma glucose of ≥ 7.0 mmol/L (126 mg/dL) or a 2 hour glucose of ≥ 11.1 mmol/L (200 mg/dL) or a HbA1c of ≥ 6.5%. Insulin sensitivity and secretion were also measured.

The results were adjusted for confounders and presented as hazard ratios. Also the publication also presented survival type diagrams derived from the adjusted statistical analysis (Cox proportional regression analysis) which enables one to easily determine the absolute risk increase of diabetes associated with the use of these two statins including dose dependence. The results are presented in the table below. Absolute (note not relative) increases in risk of diabetes were dose dependent. The relative increases in risk of developing diabetes (relative harm increase—RHI) are also given to illustrate the poor correlation with what really counts, the absolute risk increase, which may also be viewed as the probability of occurrence of the adverse effect. For statins other than Lipitor and Zocor, the number of individuals in the study taking them was insufficient to generate statistically significant results.

In addition, statin treatment was shown to significantly increase the glucose level at 2-hours in the oral glucose tolerance test. Insulin sensitivity decreased by 24% and insulin secretion from the pancreatic beta cells by 12% and both effects were dose dependent for both statins.

Readers may recall that statin treatment in the context of primary prevention reduces the absolute risk of cardiovascular events by between 1 and 2% (See the tables in the February, 2015 issue of IHN). Thus if the absolute benefit is of this magnitude, then absolute risk increases in the table clearly indicate the risk of an adverse event such as diabetes far outweighs the small benefits associated with the prevention of cardiovascular events.

It is interesting that the spin provided in an online keep-up-to-date service for medical professionals quoted a prominent physician commenting on the study who pointed out that the benefits of statins had been clearly proven “in certain situations” and that “the benefit would outweigh the increased risk of diabetes for many people.” Nevertheless, as discussed in the February 2015 issue of IHN, even for diabetics who are at increased risk of cardiovascular events, the absolute benefits are small and pale compared the numbers given in the above table. Note that the NNH is approximate due to the variable length of treatment, but this is not a serious issue.

TABLE. Absolute risk increases (ARI), number needed to treat to harm one individual (NNH) and relative harm increases (RHI) for the risk of diabetes associated with statin treatment.

	ARI (%)	NNH	RHI
Total cohort (n=8749)	10	10	46
Atorvastatin (Lipitor)	10	10	21
Simvastatin (Zocor)	9.5	10	49
Other	3	33	NS
High dose Zocor (40-80 mg)	18	6	44
Low dose Zocor (10-20 mg)	7	14	28
High dose Lipitor (20-40 mg)	18	6	37
Low dose Lipitor (1 mg)	3	33	NS

THE BOTTOM LINE

It is becoming clear that two popular statins substantially and significantly increase the risk of becoming diabetic, that this risk is dose dependent and that those at high risk are those on aggressive treatment. Unfortunately the study does not provide significant guidance regarding high doses of other statins due to the low number of subjects available to provide data. Finally, diabetes is only one of the side effects, and it is highly unlikely that diabetes is the reason for the high rates of discontinuation since diabetes is a silent disease, aside from peripheral neuropathy. Then there are the side effects other than diabetes, some of which take a long time to become symptomatic and can be very dangerous. Finally, side effects in

clinical studies are notoriously underreported and it is not uncommon to ignore study drop-outs even when a side effect was the motivation.

When confronted with the common statement that some action or intervention reduces the risk of some health problem, one must always ask the critical question, b*y how much in absolute terms?* The problem is that in many cases the answer is not available in the published accounts of the relevant studies.

RISK VS. BENEFIT OF E-CIGARETTES

In the last few years E-cigarettes have become quite popular. The major international tobacco companies entered the market in 2013. E-cigarettes are promoted as a healthier alternative to tobacco smoking, as a way of quitting smoking or reducing cigarette consumption, and as a way to circumvent the smoke-free laws. In simple terms, they are a nicotine delivery system which provides some of the pleasure of cigarettes smoking although some brands are advertised as nicotine free.

This rapid development of a large market has left many health-related issues unanswered or not studied at the level of toxicological science they deserve. The study of risks is complicated by the variety of designs on the market, the rapid change in design, the variety of smoking habits such as inhalation and exhalation, and the temperature of the heating element, especially when devices with adjustable temperature are used. Furthermore, the "smoke", which is actually an aerosol vapor, contains a range of particle sizes and the locations and related amount of deposition of the aerosol contents in the body has not be carefully investigated. There is also a variation in the composition of the aerosol generating liquid from brand to brand and over time. Long-term health risks have obviously not been investigated. Commercial promotion and the approval by regulatory agencies lead to the false belief that they are tested and approved, and therefore must be safe. The salvation of smokers may have arrived, but the health costs are unclear.

Then there is the increasing level of popularity of E-cigarettes among never-smoker adolescents which raises a multitude of issues including what is viewed as a relatively harmless introduction to a strongly addictive drug.[7]

The E-cigarette functions by feeding a volatile liquid into contact with an electrically heated filament. This creates a stream of vapor containing the components of the liquid and any products formed by thermal chemical reactions on the filament. A recent study of the liquids from seven manufacturers found 141 volatile flavor substances.[8] Obviously the long-term (say 5 years) effects of inhalation of these substances has for the most part never been investigated. However, the authors identify three that are potentially allergenic. They also comment on the switch of aerosol generating liquids to include ethylene glycol, a known toxic substance used in antifreeze. Most pet owners know that if their cat or dog laps up some spilled ethylene glycol it may be fatal. The amounts of the aerosol generating liquid that end up in the respiratory system and how it is distributed in the body appears unknown.

A serious toxicological issue concerns formaldehyde. Some brands of E-cigarette allow the user to adjust the filament voltage and thus the temperature to generate more vapor. It has been found in several studies that there is a threshold in filament temperature for significant formaldehyde production. In models tested, an increase from 3.2 V to 4.8 V resulted in a 4 to 200-fold increase in formaldehyde in the vapor.[9] Formaldehyde is severely toxic, reacts rapidly when in contact with tissue, and is associated with a number of health problems. Readers will perhaps recall the articles (June and December 2012) on aspartame which decomposes into an amino acid and methanol. The methanol circulates and when it encounters a particular enzyme, formaldehyde results which then reacts and damages tissue

and DNA close to the point of encounter with the enzyme. The E-cigarette introduces the formaldehyde directly suggesting that it will then react throughout the respiratory system from the mouth and throat to the lungs. Many E-cigarette users are no doubt unaware of this risk associated with turning up the voltage on their devices.

Another concern is sub-acute bronchial toxicity induced by the E-cigarette. A case report was recently published. The patient had moderate COPD and was recovering from right upper lung resection.[10, 11]

Some decide the way to smoking cessation is to take a pill, and a widely advertised one is Chantix (varenicline). The FDA has announced a label change (package insert with information both the physician and patient needs to know but few read) warning of an interaction of this drug with alcohol resulting in decreased psychological tolerance, aggressive behavior and amnesia. There is a risk of seizures, mostly in patients with no seizure history. The drug already has a black box (High Alert) warning regarding neuropsychiatric adverse events including suicidal ideation (thoughts and plans).

THE BOTTOM LINE

Because of the short period of use and what are probably unsatisfactory and unrealistic testing protocols, the risks associated with inhaling the vapor from these devices must be considered an open question. Furthermore, there is little incentive to critically study this issue in the industry and the potential that the well tested and very successful approach to downplaying health risks that was developed decades ago by the tobacco industry may prevail for this device. Absence of proof that a problem exists is not proof of its absence.

METABOLIC SYNDROME AND CANCER RISK

A recent paper in the journal *Metabolism* examines the enhanced risk of certain cancers associated with having the metabolic syndrome.[12] The metabolic syndrome (MetS) is defined in terms of five markers. If any three of these exceed guideline thresholds, the syndrome is diagnosed. These thresholds for North America are

1. Waist circumference ≥ 103 cm
2. Triglycerides ≥ `1.7 mmol/L (150 mg/dL)
3. HDL cholesterol < 1.0 mmol/L (38 mg/dL)Fasting blood glucose
4. Fasting blood glucose ≥ 5.6 mmol/L (100 mg/dL)
5. Blood pressure ≥ 130 and/or 85 mm Hg

The authors list six cancer sites where significant enhanced risk has been observed in epidemiologic studies: Breast (post-menopausal), liver, colorectal, endometrial, prostate and pancreatic. Colorectal cancer is the centerpiece of this list with a strong and well-established connection. The mechanism is complex, but in simple terms involves insulin and the overstimulation of the insulin receptor and the insulin like-growth factor, the role of other hormones and as well the very important pro-inflammatory state found in individuals with MetS.

The author's stated goal in presenting the details of various proposed mechanisms is that this would encourage targeted drug development and testing. Examples they give include the anti-hyperglycemic drug metformin, monoclonal antibodies against insulin like growth factor and other drugs targeted at various pathways postulated to be involved in the initiation and progression of cancer.

However, it would seem sensible to instead eliminate MetS. For individuals free of cancer, this might solve the problem. For those with cancer, it also seems like a good idea. The authors do not discuss this, probably for the very good reason that most individuals with

MetS cannot get rid of it, simply because conventional dietary and lifestyle approaches do not seem to produce large enough changes so that the syndrome can be declared eliminated. Difficulties in adherence are of course factor.

In the November 2014 issue of IHN, there was a short piece on how the Newcastle Diet was incredibly successful in reversing diabetes. As the table indicated, all the subjects qualified for the diagnosis of MetS with three factors strongly and significantly present, but HDL was just above the threshold and not impacted by the diet. Blood pressure was not measured, but given the presence of other factors, this is not important. The 8-week severely calorie restricted diet put the three markers back to normal. Even if one added the standard deviations, the numbers were all comfortably below the thresholds. This included the waist circumference indicating that the diet also very significantly eliminated "belly fat."

It can be argued that eliminating the MetS does not alter permanent damage already present which might lead to cancer, but it is certainly a step in the right direction since it eliminates many of the factors viewed as creating a pro-cancer milieu. For the subjects in the trial, this was an added bonus on top of getting rid of diabetes.

THE BOTTOM LINE

Between 1999 and 2010 the prevalence of MetS in the U.S. population actually declined from 25.5% to 22.9%.[13] However, the prevalence of abdominal obesity increased from 45.4% to 50% during this period. Declines in the other parameters were attributed to successful interventions. Nevertheless, the roughly 23% prevalence continues to present danger and the definitions of three factors out of 5 is somewhat arbitrary since having two factors instead of three probably does not drop the risk to zero. Since the Newcastle diet has a strong impact on abdominal obesity, triglycerides and fasting blood glucose and as well eliminated diabetes which includes reducing significantly the daily average circulating glucose levels. The merits of this approach are obvious. The substantial loss of weight is a huge added bonus.

NEWS BRIEFS

ANTICHOLINERGIC MEDICATIONS AND RISK OF DEMENTIA OR CONFUSION

This class of drugs blocks the action of the neurotransmitter acetylcholine in the brain. These prescription drugs are used to treat asthma, incontinence, gastrointestinal cramps, and muscle spasms. They are also used for sleep disorders and as antidepressants. Use prevalence in the age group 60-75 ranges from 8% to 27% whereas for those over 75, it goes up to 90%. The reader is referred to the internet for a long list of drugs in this class.

A recent retrospective study from Australia examined the connection between the use of these drugs and hospital admission for acute confusion or dementia [14] Taking two drugs increased the risk by a factor of 2.6 whereas three or more resulted in an almost four-fold increase in risk. The increases were similar when patients on antipsychotic medications were excluded and the outcome restricted to acute confusion.

In Australia antipsychotic drugs are commonly used in the management of behavioral and psychological symptoms of dementia. Nine such drugs were included in this study. The authors comment that hospitalization for acute confusion is uncommon and the implications for patients may be significant if the association between these medications and confusion is not recognized and thus the medication continued. The authors concluded that strategies to reduce anticholinergic medication burden are likely to yield significant health benefits. Awareness of the above is also important for anyone with family members being treated with this class of drug.

THE BOTTOM LINE
Pay attention to what elderly parents are given especially in nursing homes. It may do them more harm than good and merely make life easier for the staff.

CHOLESTEROL AND STROKE RISK

It is a common belief that elevated cholesterol is a risk factor for stroke. On the webpage of the US NIH National Institute of Neurological Disorders and Stroke (updated October, 2014) one finds "Excess LDL can cause cholesterol to build up in blood vessels, leading to atherosclerosis. Atherosclerosis is the major cause of blood vessel narrowing, leading to both heart attack and stroke." This NIH webpage gives a way of calculating stroke risk. Eight risk factors are given: age, systolic blood pressure untreated, systolic blood pressure, diabetes, smoking cigarettes, having a history of cardiovascular disease, atrial fibrillation or left ventricular hypertrophy. Numerical points are given to each risk factor. Add up the points and look up the 10-year probability of a stroke. Incidentally, this approach presented in 2014 is taken directly from a 1994 report based on the Framingham study.

What happened to LDL cholesterol mentioned in the NIH introduction? Certainly cholesterol was on the minds of the Framingham investigators. In fact it was a very big deal and launched almost universal cholesterol testing, dietary avoidance and the demonizing of this chemical vital in human biochemistry and present in cell walls. Ultimately the result was a significant fraction of the older members of the populations in the developed world were on statins and other cholesterol lowering drugs. It appears that the Framingham study could not find a significant association that would motivate them to include the LDL level in their point system calculator. Furthermore, as your editor has pointed out many times in this newsletter, the notion that circulating cholesterol drives atherosclerosis is falsified by a large number of studies based on autopsy results and more importantly, imaging of coronary artery plaque. There is no correlation.[15] Consistent with this, cholesterol lowering has no impact on coronary artery calcium scores or coronary plaque progression.

However, it is part of the conventional wisdom that statins reduce the risk of stroke. Dr. David Newman, MD has examined the literature to obtain the absolute risk reduction. For individuals without known heart disease, the number needed to treat to prevent one event was 154 over 5 years whereas if there was a history of heart disease, it was 125. Converging these into percentages of those treated who do not benefit, we get 99.5% and 99.2%, respectively (see NNT.com). Individuals at risk need something a lot better than this.

THE BOTTOM LINE
Cholesterol appears to be a non-issue in stroke risk. This is consistent with the failure of statins to impact risk with what at least some consider clinical significance.

ELEVATED BLOOD GLUCOSE AND PANCREATIC CANCER

Pancreatic adenocarcinoma is the most deadly of cancers with a five-year survival of only 5%. Furthermore, both the incidence and mortality are increasing and it is now the fourth leading cause of cancer deaths in the US. The problem is clear when one considers that the development is silent and 85% of the tumors are unresectable at diagnosis. Given this picture, prevention becomes paramount. Type 2 diabetes along with chronic hyperinsulinemia and hyperglycemia are recognized risk factors.
A recent study has clarified the dose (circulating level) relationship between blood sugar and risk.[16] Nine studies were identified for analysis with a total of about 2400 patients with pancreatic cancer. It was found that there was a strong linear dose response association between fasting blood glucose (FBG) and the rate of pancreatic cancer across the range of prediabetes and diabetes. An increase in the rate ratio of 1.15 was found for per 0.56 mmol/L (10 mg/dL) increase in FBG. Perspective can be gained by considering that the threshold for prediabetes is 5.7 mmol/L and 7 mmol/L for diabetes. Progression from prediabetes to

diabetes and then steadily increasing FBG for many underscores the problem for many individuals.

THE BOTTOM LINE

The obvious solution is to get rid of the diabetes, for example using the Newcastle Diet described recently in the October 2014 issue of IHN. However, there are no studies and no guarantee that this will impact pancreatic cancer already present or slow its progression. It does seem likely that identifying prediabetes at the first sign of glucose metabolism dysfunction is a really good idea if one wants to reduce the risk of pancreatic cancer. It is thus alarming that there are vast numbers of individuals unaware that they are prediabetic, and it is estimated that 1/3 of all diabetics are undiagnosed and going about their daily activities totally unaware of the time bomb ticking away which involves not only this cancer, but as discussed repeatedly in IHN, a depressing variety of disorders which will adversely impact future quality of life and predict early mortality. Those who regard 8 weeks of a semi-starvation diet as too high a price to pay in suffering do not comprehend what is in store for them, and in addition, since food choices do not seem to matter, it is nonsense to regard an 800-calorie diet as more than a mild hardship, if that.

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BOOK REVIEWS AND READING LISTS

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- ***The Disease Delusion****. Conquering the causes of chronic illness for a healthier, longer and happier life.* Jeffrey Bland, PhD. HarperCollins, New York, 2014.
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