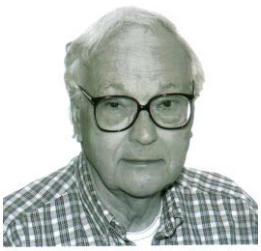
INTERNATIONAL HEALTH NEWS

William R. Ware, PhD - Editor

NUMBER 262 **NOVEMBER 2015** **24th YEAR**



In the past 100 years we have seen a major change from the importance of infectious diseases to a number of chronic diseases as a cause of mortality and morbidity, and we are also seeing an increase in these chronic diseases over time, in some instances dramatic, even in children. Many attempts have been made to explain this phenomenon. Since the changes involved must be major, this limits the field. We have had a major transformation in diet with the emergence of dominance of processed foods, high intake of refined, high glycemic index starches, the introduction of synthetic trans-fats as a significant dietary component and an incredible increase in the per capita intake of refined sugar. These are all modifiable factors. This hypothesis was discussed in the September International Health News.

The second major change has been the huge increase in environmental toxins from multiple sources with multiple avenues for entering humans. While daily intake is small, innumerable studies have revealed high toxic loads in human fat, tissue samples, blood, and breast milk. Some toxins are only partially eliminated and build up over a number of years. This got underway after 1945, the end of WWII, which had been responsible for the development of some very toxic chemicals, an activity which accelerated during the Vietnam War after which this field really took off and included chemicals for consumer products. First the populations of the developed world and then the whole world suffered exposure, either inadvertently or through ignorance. The body burdens we see today are the result of this constant and ever increasing exposure over decades. The detoxification mechanisms that had served us well over eons became overwhelmed in the flood of hundreds of strange new chemicals and the buildup, especially in fatty tissue, was underway. Today it is attractive to entertain the hypothesis that this is a major cause of the incidence and increasing prevalence of chronic diseases. How many readers know that when scientists want to induce cancer or, for example, Parkinson's disease in laboratory rodents, they frequently employ a single dose of one of the commonly used pesticides?

We are told that our toxin exposure is too small to cause concern. This does not take into account accumulation, nor does it acknowledge the impossibility of human toxicity studies that have any relevance whatsoever in the context of long-term exposure or take into account the fact that many toxin-related disorders take years to become symptomatic. In fact, meaningful studies are impossible. So what to do about toxic exposure? One can attempt to reduce exposure and thus decrease intake which is a worthwhile undertaking since this can reduce body load, but for many, it is too late now for there to be a significant impact. Even for prenatal exposure there are problems since many mothers already bear a significant toxic

burden. Eliminating all dietary toxins even with a totally organic diet is still impossible because of the many other sources of toxins.

The only alternative is detoxification. If one reads accounts of the experience of physicians who use detoxification as an important or even major aspect of their practice, you will read innumerable case histories of patients who had been to doctor after doctor with mysterious and frequently disabling symptoms with no success, only to be cured by detoxification. Detoxification is a very important way to deal with the body burden of toxins, and since these constitute not only heavy metals such as mercury, lead and cadmium, but also hundreds of organic chemicals for which there are no targeted agents available to accomplish the task. This means that a general rather than a specific approach is appropriate.

This subject has been discussed several times in IHN (see index). However, generalized detoxification is complex and the reader is referred to a recent book by Dr. Sherry Rogers, MD, which is a comprehensive and well-documented discussion titled "Detoxify or Die" and is based on over 30 years of clinical experience as a family physician confronted with an ever-increasing number of patients with toxicity problems.

Wishing you and your family good health,

William R. Ware, PhD, Editor

Highlights

ENDOCRINE-DISRUPTING CHEMICALS

One of the many things that human and animal life depends on is the proper functioning of numerous hormone-controlled processes lumped together by the term the endocrine system. Familiar examples of hormones are estrogen, testosterone, the thyroid hormones, and insulin. Dysfunction of almost any aspect of the endocrine system can produce serious deleterious developmental, reproductive, neurological and immune effects and thus illness. For example, exposure to endocrine disrupting chemicals can result in lowered fertility, increased risk of cardiovascular problems, cancer, and brain damage, obesity, stimulation of prostate cancer cells, and prostate enlargement. BPA (bisphenol A) from can liners and plastic bottles can elevate blood pressure in just a few hours. The chemicals in question are foreign to humans, are synthetic and are produced in huge quantities by the chemical industry. They are used in a large number of consumer products resulting in the potential for widespread exposure. They are also present in waste from the chemical industry and in garbage which goes into disposal sites and incinerators which can result in pollution of air and water. The large number of uses for these chemicals from plastics, building materials and food packaging to home and agricultural herbicides and pesticides result in their widespread presence in our environment.

Even automatic coffee makers bring hot water and acidic hot coffee in contact with plastics. When blood samples of large populations are examined, it is normal to find a number of endocrine disrupting chemicals in practically everybody. They even turn up in cord blood and newborn children. The winds and the ocean currents spread them around the world and even animals in remote places such as the high artic have a toxic burden of these substances as do the creatures that live in the oceans.

Toxicity depends on levels and thresholds and individual variation or otherwise we would all be dead. Instead, most of us are sick or getting sick, although not just from endocrine disrupting chemicals. However, some accumulate if the intake exceeds the natural ability to eliminate them, and thus presents an additional and long-term health threat. When the burden of evidence leads to a ban on one of these chemicals it is generally replaced with a similar one that is as bad or worse. Since definitive human toxicology studies are impossible, thresholds and ranges for risk are unknown and critics argue that only minute amounts are needed to produce adverse effects while the industry argues that this cannot be true since the amounts are so tiny, a view point which ignores the possibility of day after day accumulation. There are over 80,000 chemicals out there and almost all have never even been tested on animals, which is also a rather uninformative undertaking from the human point of view. Thus there are several major issues. What chemicals have been identified as endocrine disrupters, where do we encounter them, what is the mechanism of human exposure, and finally, how do we get them out of our systems. This last issue is very important since these chemical are ubiquitous, exposure inevitable, and detoxification probably the only solution to our problem of developing a toxic burden.

It is impossible to include a list of chemicals simply because it is too long. Consult the website *our stolenfuture.org* for a list that includes the hormone mimicked or the endocrine system impacted, as well as citations.[1] Listed are over a hundred chemicals. A short list is called the Dirty Dozen which will give the most common examples. Included are BPA, a chemical used in plastics which can come in contact with food and beverages, dioxin, a by-product of chemical manufacture, Atrazine which is used on most corn crops in the US, phthalates used in plastics, toys, food can liners, food packages and personal care products, perchlorate, a component of rocked fuel but a widespread environmental toxin, fire retardants present in carpets, fabrics, mattresses and electronic circuit boards, lead, arsenic, mercury, perfluorinated chemicals used in non-stick cookware, organophosphate pesticides, widely used in agriculture, and glycol ethers used as solvents in paints, cleaning products and cosmetics. Very sensitive individuals sometimes find a new house with new furnishings, drapes, carpets and an array of electronics as actually uninhabitable. Many workplaces are sprayed periodically with endocrine-disrupting pesticides. It is clear from the above why exposure is universal and yet this is just one class of environmental toxin. Since we encounter these chemicals at work, in the home, in food, beverages and drinking water, in bottled water sold or stored in plastic and as an air pollutant, they are almost impossible to avoid.

Since there are over a hundred of these endocrine-disrupting chemicals contaminating the environment all over the world, researching specific toxin-dependent methods of detoxification in humans is hopeless. The same intervention such as sweating can remove certain pesticides but not other similar ones. The accumulation and the binding or reacting with human biochemicals is variable and it is impossible to conduct meaningful studies even in vitro given the huge number of chemicals. There is no guarantee that organic produce is not contaminated unintentionally, especially if the ground had previously been used for modern chemical-based agriculture. About all one can do is boost their natural detoxification mechanisms, periodically sweat heavily (and wipe it off before it is reabsorbed) and minimize exposure as much as

possible. The latter is a tall order given that many have no choice but to live in cities with high levels of air pollution, employees have no control over what the company does about pest control, toxins are not on the food labels, washing produce may not be effective although it is reported that soaking and washing in alkaline water (e.g. water to which a bit of baking soda has been added) does a fairly good job of removing some toxins, people do need new drapes, carpets, mattresses TVs and computers and old items have to be quite old not to outgas fire retardants. In fact, water free of endocrine-disrupting chemicals is about the only thing that is easy to obtain. Just install an under-the-sink reverse osmosis system or use a counter top model, the latter being a relatively new product which uses an electric pump rather than water pressure. If working properly, reverse osmosis will get rid of almost everything. Some air filter systems will adsorb some toxins, generally on charcoal, but toxic molecules go right through HEPA filters, but these filters can stop some molds. Also, toxins can accumulate on dust particles, and the HEPA filter will get rid of these.

In terms of public health, the critical question is the safe exposure in humans, not rodents. The most relevant evidence of unsafe exposure is clinical evidence of adverse effects. Exposure can occur prenatal, during childhood development, in adolescence and in adult life. Adverse effects of exposure in one time window may lead to clinical appearance of adverse effects years later when the connection cannot possibly be made. But the central problem is that experiments cannot be designed and executed on human subjects. Humans have different detoxification mechanism and different inherent sensitivities to endocrine disruption chemicals than animals and within a human population, there will be variations in sensitivity. The inescapable conclusion is that determining safe exposure in humans is not possible, and even if it was, the magnitude of the task involving male and female subjects from prenatal to adults and very long term follow-up with wide dose ranges is obviously a fantasy. The standard industrial and regulatory protocols for establishing safety are simply self-serving science fiction. Both publications from various national and international organizations and as well the academic literature reveal considerable interest, but it is far from clear how meaningful progress can be made. In fact, a common characteristic of guidelines on safe levels is that the levels almost always decrease over time and in some cases approach zero tolerance as the limiting case. If over 40 years of human studies were needed to get a clear picture of the dangers of ingesting saturated fat, then how can one expect significant progress in an undertaking as inherently complex as determining toxic exposure levels of even ten or twenty of the most prevalent endocrine disrupters known to be dangerous when definitive human studies are not even ethical and industrial, accidental and unavoidable high exposures not really relevant. Finally the political aspects of such undertakings are obvious.

We could discuss a variety of chemicals, the details of what is currently known about their involvement in various hormonal pathways and processes, but only provide cause for concern, not useful safe exposure limits, and already enough is known to justify great concern. The sad fact is that even avoidance has become nearly impossible.

THE BOTTOM LINE

In dealing with the present toxic environment, avoidance and detoxification are about all one can do. Awareness of the sources of endocrine-disrupting chemicals is essential in implementing avoidance, but this is challenging given the widespread contamination. Thus one should concentrate on the major classes of sources such as food and water, pesticides, herbicides, plastics, building materials, home furnishings and electronics, cleaning and personal care products. The more one can reduce intake the greater the chance that the body's natural detoxification mechanisms will be able to at least handle some of what must be dealt with. See

the March 2014 IHN for information on evidence-based detoxification and the book mentioned in the editorial.

ALCOHOL AND THE FETUS. ALCOHOL ACTING AS A TOXIN

The issue here is the *fetal alcohol spectrum disorder* (FASD), a nomenclature that emphasizes the diversity of the problems and expands on the older term *fetal alcohol syndrome* (FAS), which is the severest form. The American Academy of Pediatrics has just issued its latest clinical report on this disorder in the journal *Pediatrics,* and it is the source of most of the information provided below.[2] A free copy is available. Google PubMed and put 26482673 in the query box at the top of the home page.

Prenatal exposure to alcohol can cause damage to the developing fetus and is the leading preventable cause of birth defects and intellectual and neurodevelopmental disabilities in children. When a pregnant women drinks, it is well known that alcohol goes across the placenta and enters the fetal blood stream, and in the early stages of development the liver isn't fully formed or functioning and alcohol metabolism relies on the mother's liver.

FASD was first identified in 1973 and by 1984 a study concluded that the risk existed even when the alcohol consumption was limited to 1 standard drink per day (e.g. one shot of distilled spirits, 5 oz. of wine or 12 oz. of beer), the current maximum recommendation today for women in general and much more restrictive than for men. In other words, the view is that there is no significant threshold for risk to the fetus. While this has not been established with certainty, zero alcohol during pregnancy remains the recommendation since it guarantees the absence of FASD. For over 30 years governments have been active in attempting to inform women of this threat. Nevertheless in the US it is estimated that the prevalence of FASD is 2.4 to 4.8 cases per 100 live births. About half of all US women of childbearing age report past-month alcohol consumption with use ranging from sporadic intake to 15 % reporting binge drinking, a level of consumption that generally results in a blood alcohol level that is at or exceeds the impaired driving limit.

One serious issue is the time window between conception and recognition of the existence of a pregnancy which can easily exceed one month. The latest information updated this year from the US Centers for Disease Control cites a 2011 study indicating that in 2006, 49% of pregnancies were unintended, an slight increase from 2001. Among women aged 19 years and younger, more than 4 out of 5 pregnancies were unintended and for those younger than 15 it was 98%. It is doubtful that these numbers are much different in 2015. Thus there must be significant post-conception alcohol consumption and as well, a failure to address in a timely fashion such issues as folic acid supplementation. Thus many women and especially younger women can be well into the first trimester before even listening to a doctor's probably strongly worded advice to avoid alcohol.

This time window problem is important. A baby's facial features are formed during the first six to nine weeks of pregnancy and mothers who drink during this window are more likely to have babies with facial deformities associated with FAS. Damage to the baby's organs through drinking appears most likely to happen during the first trimester. However, it is thought that damage to the baby's brain can occur any time during the pregnancy. Incidentally, children born of mothers who have FASD do not appear to be at risk since there is no evidence of inheritance.

Facial abnormalities include a shortened eyelid opening and absence or decreased size of the upper lip. The report in *Pediatrics* has a good set of pictures of the lip defect from early age and how it persists into adulthood. Cleft palate is also recognized to co-occur with maternal alcohol exposure. In the fetus, alcohol affects the structural and/or functional aspects of the brain and other organs and systems, particular the cardiovascular, kidney, musculoskeletal, ocular and auditory systems. Cognitive and behavioral difficulties range from subtle learning and/or behavioral problems to significant intellectual disability. Maternal alcohol exposure is associated with greater incidence of attention deficit hyperactivity disorder (ADHD) and learning disabilities. Neurocognitive problems associated with FASD include deficits in visual-spatial and executive functions of the brain, impaired impulse control, and memory skills and difficulties with problem solving. In addition, problems are seen in abstract reasoning, auditory comprehension and language use. Impaired social function is observed in adults diagnosed with FAS as children.

Unfortunately treatment is symptomatic and involves helping with coping. The problems can be life-long in duration. In some cases standard coping therapies fail, as is the case with ADHD where stimulants may not provide relief. Children with FASD generally qualify for special education.

From an economic, educational, societal, and family or health perspective, FASD obviously represents a significant public health problem and as well a personal burden for all involved. A just published review in B*iomolecules* addressing the issue of how alcohol induces developmental or neurological damage, advances a number of hypotheses, and makes it clear that the mechanisms involved are in fact unclear, especially in embryonic development.[3]

THE BOTTOM LINE

The reports cited above are not very encouraging. While it is claimed that early recognition and diagnosis of neurocognitive and behavioral problems can result in improved outcomes, the report in *Pediatrics* admits there is no cure. In fact, the section on treatment is short and depressing. Thus there are two challenges. One is universal awareness of the potential for very serious consequences associated with alcohol consumption during pregnancy. Full appreciation of this should provide a very strong incentive for total alcohol abstinence. The second challenge is much more complex since it involves alcohol abstinence by anyone at risk of becoming pregnant. The numbers given above for the prevalence of unintended pregnancy indicate a significant problem in this context. Finally FASD is but one example of the extreme fetal sensitivity to toxins, and we live in a world where were we are immersed in toxins, a recurring theme in IHN. At least alcohol is one of the few that can be easily and totally avoided when special circumstances warrant this. The toxicology is obviously complex given the differences in the threshold for adverse effects between men and women, the benefits of moderate wine consumption among men in many different contexts, and the presence of this practice as part of the Mediterranean diet, one of the most healthy diet patterns.

YOUNGEST IN THE CLASS SYNDROME. A PROBLEM HARD TO IGNORE AND SOLVE

In school systems where there is an age threshold used, each class tends to contain a one-year distribution in ages with inherent within class pupil maturity differences accentuated in the earlier grades. A number of studies have examined the impact of pupil relative age and academic performance, behavioral problems and the diagnosis of so-called mental disorders. The concentration of the diagnosis and treatment of ADHD in the youngest members of a class

has been discussed in IHN (April 2012) and held up as an argument for overdiagnosis, in this case attributing normal behavior to mental disease, a result that has horrific implications associated with both unnecessary medication with highly dangerous drugs and the stigma attached to the diagnosis. It is now well known that students who are relatively younger at grade entry tend to perform worse on achievement tests, are more likely to be held back a grade in elementary school, and are less likely to attend college or university. There is also evidence going back to 2003 that what is also called the "within-grade maturity disadvantage" has long-lasting negative effects on personal achievements and health outcomes.

A study from japan just published in PLOS One examined the issue of teenage and young adult suicide rates in terms of the educational experience as measured by being the youngest vs. the oldest in each class through school.[4] Japan is very strict regarding setting April 2 as the cut-off date which does not vary by region and has not changed since 1947. Furthermore, children are expected to stay in school to finish junior high school, typically at age 15. Vital statistic records were used to identify cases and a statistical technique was use to seek out prevalence gaps.

A significant gap was found in the rate of mortality from suicide around the birthdate of April 1. The figure they show, complete with statistical fluctuations, is compelling. Furthermore, the results did not depend on what they called the bandwidth, the range of days around this threshold used in the analysis, which went from 7 to 28 days. Finally, they observed that those born before and after the cutoff seemed to pursue different career paths with being among the oldest associated with higher educational attainment than being among the youngest. There was no mention of ADHD or other mental or behavioral issues, but the database involved made this impossible. This is unfortunate since the medication of children with ADHD can include not only the old standby, stimulants, but also antipsychotic drugs traditionally reserved for serious mental disorders and there is a the problem of enhanced suicide risk from these medications which is described in the package inserts in a black box that no one reads.

An article in *The Japan Times* based on a peer-reviewed journal article helps address the study limitation concerning psychiatric drugs in Japan. The report states that the number of ADHD drug prescriptions for patients between 13 and 18 surged 2.5 times between the periods 2002-2004 and 2008-2010. In addition, prescriptions for 6 to 12 year olds increased 84% over this same time range, and that prescriptions for antidepressants jumped 31 % for the 13-18 age group. Also, the number of children seeking medical care for mental health issues grew from 95,000 in 2002 to 148,000 in 2008. Thus is highly likely that psychiatric drugs may have played a role in the observed suicide prevalence gap.[5]

Since the piece in the April 2012 IHN which discussed a study from Iceland which revealed the relative age of the school entry threshold problem,[6] a study conducted in three London, UK boroughs found that being among the youngest in a class cohort was associated with a higher risk of referral to mental health services, while being among the oldest was by comparison a protective factor.[7] However, a Danish nationwide study, failed to find similar effects and attributed his partly to a high proportion of young children held back by one year in the Danish school system and/or the generally low prevalence of ADHD diagnosis in the country.[8]

THE BOTTOM LINE

The above further strengthens the warning given this summer in IHN (July-August) that the start of the school year present serious risks to children in the context of being misdiagnosed with a mental disorder which may result in devastating medication side effects, which can even appear in later years, and as well there is the stigma of having a false diagnosis of mental problems

which may impact future educational and occupational opportunities. This is a serious problem that is not being addressed by public school systems.

DO BLOOD PRESSURE MEDICATIONS RESTORE CARDIOVASCULAR RISK TO IDEAL LEVELS?

Blood pressure (BP) guidelines have focused on starting antihypertensive therapy when BP exceeds a threshold, for example systolic BP ≥ 140 or diastolic BP ≥ 90 mm Hg. It is generally agreed that reducing the use of antihypertensive drugs to reduce BP in patients above the treatment threshold results in lower risk of cardiovascular adverse outcomes including heart attack, stroke and heart failure. However, it is also recognized that patients who achieve a target BP still have elevated cardiovascular risk compared to untreated individuals at the same BP level. This phenomenon or paradox is readily seen in the results obtained from online heart disease risk calculators.

Here is an illustration using two online calculators for a 65-year-old male non-smoke and non-diabetic with total cholesterol of 180 mg/dL and HDL cholesterol of 55 mg/dL. The 10-year heart attack risk is an absolute risk. Risks are over 10 years.

Systolic BP	Treated	Heart Attack Risk	AHA/ACC CVD Risk*
mm HG	Yes or No	%	%
150	Y	15	17
	N	12	15
140	Y	14	15
	N	11	13
130	Y	12	13
	N	10	11
120	Y	11	12
	N	9	10
115	Y	9	11
	N	9	9

**CVD risk, AHA/ACC: fatal or non-fatal heart attack or stroke due to atherosclerosis*

The heart attack risk comes from the Framingham Study data. The CVD risk comes from the data used for the guidelines introduced by the American Heart Association/American College of Cardiology in 2013. The identical heart attack risk at a BP of 115 represents rounding-off of the numbers. The expected difference persists in the AHA/ACC results at that BP Some readers of IHN may have discovered this difference between treated and untreated individuals at the same BP while using these calculators and wondering why they want to know if the BP is treated or untreated and what is the difference in the calculated risk. Also, comparing untreated BP at 150 with treated BP at 115 yields absolute risk reductions due to treatment of 3-4% with numbers needed to treat to prevent on event over 10 years of 25-33.

A recent study attempts to clarify the underlying pathophysiology of this phenomenon.[9] The researchers examined data from both the Multi-Ethnic Study of Atherosclerosis (MESA) and the Coronary Artery risk Development in Young Adults study (CARDIA). The results were as follows:

- In the MESA cohort aged ≥ 50 at baseline, those with well-controlled hypertension (<120/<80 mm HG, i.e. “ideal”) who were on antihypertension medication still had more than twice the *relative* risk of incident CVD events over 9.5 years than those with ideal BP without treatment.

- The CARDIA results indicated that middle-aged adults with well-controlled BP on medication had longer exposure to higher BP (cumulative elevated BP) than adults with ideal BP without medication. The treated group also had higher end-organ damage (major organs fed by the circulatory system such as heart, kidneys, brain and eyes). This was even observed in CARDIA subjects with mean BP levels below the typical threshold for diagnosing hypertension.

- In the current study it was found that when cumulative systolic blood pressure was high there was acceleration in a measure of heart damage obtained from Doppler echocardiography. This provides a clue to the pathophysiology of the paradox.

The authors point out a number of studies with results consistent with the view that elevated BP over a number of years prior to diagnosis and treatment of hypertension is associated with the paradox associated with CVD risk illustrated in the above table, presence of coronary calcium years later, and that not only enhanced CVD risk but also mortality risk was present for those on antihypertensive medication as compared to those who were not. However, they caution that the results do not suggest that antihypertensive medication is ineffective for CVD risk reduction, and that whether earlier treatment to lower cumulative exposure to elevated BP would eliminate the excess CVD risk in treated vs. untreated patients with the same BP is unknown. More studies are needed. However, they suggest the results clearly indicate that from a public health standpoint health care providers should place more emphasis on the prevention of BP elevation much earlier in its natural history to further reduce CVD morbidity and mortality. In other words, attempt to maintain ideal BP from youth into older age. While the focus of this study was on medication, it should be pointed out that early intervention with exercise and diet might provide an equally satisfactory outcome. Also, there is still not general agreement on what constitutes ideal BP in the older age group.

THE BOTTOM LINE

This study and related studies highlight the risk of the threshold system which is an integral part of the guideline based practice of medicine. In this case it appears that a very low threshold for concern about blood pressure in early adulthood is appropriate. The paradox that treated blood pressure presents a greater cardiovascular risk than untreated blood pressure has been known for a long time and we now have new evidence encouraging one to pay attention to early hypertension with a low threshold for concern. Nevertheless, there are gaps in knowledge that need to be filled.

DIETARY AND SUPPLEMENTAL CALCIUM: BENEFITS AND RISKS

The notion that calcium and vitamin D deficiency contribute to the development and progression of osteoporosis goes back at least to the 1940s. In 1956 the recommended intake in the US and Canada was 800 to 1000 mg/day. In 1974 a lower recommended intake of 400 to 500 mg/day was favored by the World Health Organization (WHO) and the UN Food and Agricultural

Organization (FAO). This was about to change when calcium balance studies in 1977-8 indicated that intakes of 1000 to 1500 were inadequate to replace calcium losses in women and this was supported by studies showing the beneficial effects of calcium supplementation on bone density published in the 1990s. By 2002 the WHO and the FAO recommended 1300 mg/day for post-menopausal women and men over 65. In late 2013 the US National Institutes of Health recommended daily intake for 19-50 years of age of 1000 mg for men and women, for 51-70 years an intake of 1000 to 1200mg for men and women, and for >70 years, 1200 mg for both. The upper end of these recommendations is difficult to reach unless supplements are used, especially if the intake of dairy products is low. Thus over the years, calcium supplementation has become popular, generally combined with vitamin D. However, in the past 2 years reconsideration of both benefits and risks has resulted in serious question about the wisdom of higher intakes and supplementation. Essentially, the benefits now appear to be small to insignificant and the risks, while not large, nevertheless now have moved to center stage.

In 2015 Tai *et al* published a systematic review and meta-analysis of calcium intake and bone mineral density.[10] Literally dozens of studies from1978 to 2012 looked at the change from baseline to one year. An overall effect for various locations in the body was typically an increase 1% over this entire time span when high vs. low intake is compared, a change regarded as not clinically significant, and the 95% confidence limits frequently included a negative lower limit, i.e. no significant effect at all. The large number of studies with the same results reminds one of Albert Einstein's definitions of insanity, doing the same thing over and over again and expecting different results. The study concluded that increasing calcium intake from dietary sources or by supplementation produces a small non-progressive increase in bone mineral density which is unlikely to lead to a clinically significant decrease in the risk of fractures.

The conclusion regarding no impact on the risk of fractures was reinforced by a systematic review also published in 2015.[11] Total fracture risk and risk of hip and vertebral fracture were examined in a number of studies. The three meta-analyses were stratified by risk of bias, but nine such analyses yielded non-significant results in seven and the overall results for the three unstratified analyses, each combining the three levels of bias, all failed to find statistically significant risk reduction. The authors concluded that dietary calcium intake is not associated with the risk of fracture, there is no clinical trial evidence that increasing calcium intake from dietary sources prevents fractures, and that evidence is weak and inconsistent concerning the value of supplements. This lack of clinically significant benefit based on an amazing number of studies that have accumulated over decades turns the focus to the risks.

This has been discussed on the basis of a number of reports including a recent one by Reid, Bristow and Bolland from Auckland, New Zealand.[12] Mark Bolland from the Faculty of Medicine and Health Sciences, University of Auckland, was also involved with the the studies discussed above and is a prominent expert in this area. The risks of high dietary and supplementary intake of calcium are as follows:

- *Gastrointestinal*. These include constipation, bloating, severe diarrhea and abdominal pain. One study they cite found that the absolute risk for admissions to hospital with acute abdominal symptoms was 6.8% compared to a 3.6% for a control group and this was statistically significant.
- *Adverse kidney events.* The woman's Health Initiative (WHI) study found a significant increase in the risk of kidney stones. This study also failed to find benefit in terms of fracture risk.

- *Cardiovascular effects*. This area has by far received the most attention. The National Institutes of Health sponsored AARP Diet and Health study examined this question.[13] They found that a high intake of supplemental calcium is associated with a significant enhanced risk of cardio vascular-related death in men but not women. For men there was also a significant association with heart disease death but the increased risk did not reach statistical significance for stroke risk. Meta-analysis by Reid *et al*[12] involving 5 trials plus the WHI study (restricted to women who were not taking calcium at baseline) confirmed the presence of significant risk. While the cumulative incidence over 5 or 10 years indicated the absolute risk increase of cardiovascular effects compared to a placebo was of the order of 1%, this must be considered in the context of an intervention with no evident benefit and other adverse effects as well.

The authors concluded that it seemed sensible for older individuals at risk of osteoporosis to maintain calcium intakes in the range of 500-1000 mg/day but that there appeared to be no need for supplements except in individuals with major malabsorption problems or substantial abnormalities in calcium metabolism. Calcium supplements were deemed to have very little role to play in the prevention of osteoporosis and this view includes the combination of vitamin D and calcium. This is after dozens of studies, tons of calcium supplements ingested, panels of experts and various health organizations producing recommendations and guidelines, and now we see strong evidence that tells us to get our calcium from food and the minimum suggested of 500 mg/day is easy to meet, especially if some dairy products are consumed and that rather than benefit, supplementation is a risky action since it is easy to exceed 1500 mg/day, especially when some prepared foods have added calcium (e.g. cereals). It is worth noting in passing that a recent study of calcium and vitamin D for the prevention of colorectal cancer also failed to find significant reduction of the risk of colorectal adenomas (precursors to cancerous tumors) over 3-5 years.[14]

Sad to say, we now have another major flip-flop which will probably detract from the confidence of the general public in official recommendation, guidelines and the conventional wisdom.

THE BOTTOM LINE

This is a good example of how simplistic views of complex biochemical and metabolic processes as well as flawed studies can result in potentially dangerous practices which are promoted by expert advice and guidelines and followed over decades as the part of the path to health. The take home message appears to be that one should not take calcium supplements unless there is some significant problem with the utilization of dietary calcium, or if dietary preferences favor very low calcium intake. In addition, lead contamination has been found in some calcium supplements.[15]

REFERENCES

(1) Accessed 10/16/2015. http://www.ourstolenfuture.org/basics/chemlist.
(2) Williams JF, Smith VC. Fetal Alcohol Spectrum Disorders. *Pediatrics* 2015;136(5):In press.
(3) Yang F, Luo J. Endoplasmic Reticulum Stress and Ethanol Neurotoxicity. *Biomolecules* 2015;5(4):2538-53.
(4) Matsubayashi T, Ueda M. Relative Age in School and Suicide among Young Individuals in Japan: A Regression Discontinuity Approach. *PLoS One* 2015;10(8):e0135349.
(5) Breggin P. *Medication madness. The role of psychiatric drugs in cases of violence, suicide and crime.* New York; 2008.

(6) Morrow RL, Garland J, Wright JM, Maclure M, Taylor S, Dormuth CR. Influence of relative age on diagnosis and treatment of attention-deficit/hyperactivity disorder in children. *CMAJ* 2012 March 5.
(7) Berg S, Berg E. The youngest children in each school cohort are overrepresented in referrals to mental health services. *J Clin Psychiatry* 2014 May;75(5):530-4.
(8) Pottegard A, Hallas J, Hernandez D, Zoega H. Children's relative age in class and use of medication for ADHD: a Danish Nationwide Study. *J Child Psychol Psychiatry* 2014 November;55(11):1244-50.
(9) Liu K, Colangelo LA, Daviglus ML et al. Can Antihypertensive Treatment Restore the Risk of Cardiovascular Disease to Ideal Levels?: The Coronary Artery Risk Development in Young Adults (CARDIA) Study and the Multi-Ethnic Study of Atherosclerosis (MESA). *J Am Heart Assoc* 2015 September;4(9).
(10) Tai V, Leung W, Grey A, Reid IR, Bolland MJ. Calcium intake and bone mineral density: systematic review and meta-analysis. *BMJ* 2015;351:h4183.
(11) Bolland MJ, Leung W, Tai V et al. Calcium intake and risk of fracture: systematic review. *BMJ* 2015;351:h4580.
(12) Reid IR, Bristow SM, Bolland MJ. Calcium supplements: benefits and risks. *J Intern Med* 2015 October;278(4):354-68.
(13) Xiao Q, Murphy RA, Houston DK, Harris TB, Chow WH, Park Y. Dietary and supplemental calcium intake and cardiovascular disease mortality: the National Institutes of Health-AARP diet and health study. *JAMA Intern Med* 2013 April 22;173(8):639-46.
(14) Baron JA, Barry EL, Mott LA et al. A Trial of Calcium and Vitamin D for the Prevention of Colorectal Adenomas. *N Engl J Med* 2015 October 15;373(16):1519-30.
(15) Rehman S, Adnan M, Khalid N, Shaheen L. Calcium supplements: an additional source of lead contamination. *Biol Trace Elem Res* 2011 October;143(1):178-87.

Editor: William R. Ware, PhD

INTERNATIONAL HEALTH NEWS is published 10 times a year by
Hans R. Larsen MSc ChE, 1320 Point Street, Victoria, BC, Canada, V8S 1A5
E-mail: editor@yourhealthbase.com World Wide Web: http://www.yourhealthbase.com

ISSN 1203-1933

INTERNATIONAL HEALTH NEWS does not provide medical advice. Do not attempt self-diagnosis or self-medication based on our reports. Please consult your healthcare provider if you are interested in following up on the information presented.