INTERNATIONAL HEALTH NEWS

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NUMBER 251 **OCTOBER 2014** **23rd YEAR**

This issue features the Newcastle Diet and provides the details of the diet used in the clinical trial by the Newcastle University group led by Dr. Roy Taylor to reverse diabetes. This subject was discussed in the November 2013 and September 2014 issues of IHN. The diet involves using a 600-calorie meal replacement augmented only with non-starchy vegetables with a limit of a total of 800 calories. The clinical trial was a test of a hypothesis concerning how type 2 diabetes develops, which was discussed in detail in the September 2014 IHN. The results of the trial were sensational and fully confirmed the hypothesis. Diabetes can be reversed in at most 8 weeks and the results are permanent if one does not regain much weight. Also in this issue, two case histories are described, one in some detail, where either the Newcastle Diet or simply a usual diet with the same caloric restriction was found to actually produce normal fasting blood glucose in only 7 or 11 days, and the diabetes reversal also appears to be permanent, at least with the case history covering a year. One of the case histories describes a diet where the only aspect of the Newcastle diet used was calorie restriction. Also included is a summary of the case histories reported to Taylor's group, which are equally impressive given the variety of interpretations of the diet employed. The work of Dr. Taylor and his group appears to have ushered in a new era in diabetes treatment with results that cannot be achieved by any approach currently used in medicine. Type 2 diabetes is considered an incurable, progressive disease independent of pharmaceutical intervention. This new dietary approach appears to be the biggest event in the history of diabetes since Banting introduced insulin therapy, especially given that the type 2 of this disease is now clearly an epidemic and the rapid increase of type 2 diabetes in children and young persons a clear warning of a true disaster in the making for patients, parents, the health care systems, taxpayers and governments.

This issue also discusses in detail the matter of salt restriction, a topic currently being hotly debated, with new studies raising concerns about guidelines recommending dangerously low levels of this essential micronutrient. Also included are brief discussions of the relative merits of three standard surgical approaches to breast cancer treatment, results that will surprise many readers. In addition there is a discussion of a study involving comparison of the success for weight loss of popular "named" diets and finally, the impact of childhood immunity when exclusive breastfeeding for 6 months is compared to other options.

Wishing you and your family good health,

William R. Ware, PhD, Editor

Highlights

THE NEWCASTLE DIET AND REVERSAL OF TYPE 2 DIABETES

This is the diet used in the clinical trial described in the November 2013 IHN in the context of diabetes reversal and also the September 2014 issue in the context of the mechanism leading to type 2 diabetes.[1,2] The trial using this diet was designed to test the hypothesis concerning the metabolic and physiologic cycles involving liver and pancreatic fat and how they were connected by hyperglycemia and triglycerides. As has been discussed in IHN, the clinical study provided strong support for this hypothesis and accomplished the reversal of diabetes in the subjects. A subsequent informal study showed that the reversal was permanent.[3] Since the research group headed by Dr. Roy Taylor is at the University of Newcastle, the diet carries this name.

In the 2013 and 2014 reports in IHN this diet was called a 600 calorie diet. However, it actually involved 600 calories from a liquid meal replacement formula. Subjects were then told to add non-starchy vegetables to gain up to 200 calories, so in fact the diet, if implemented fully was an 800 calorie diet. Vegetables are low in calories and it is thus surprising that the subjects were able to consume the volume necessary to reach 800 calories. Together a cup each of asparagus, broccoli, cabbage and green beans give one only 140 calories. Two tomatoes are needed to make a total of 800. There were many restrictions imposed as would be necessary in a well-designed clinical trial, and this is now being called the Newcastle diet.[1]

The details of the Newcastle diet as given on the study group's website are as follows.

- A total of 600 calories per day are derived from a liquid meal replacement formula called O*ptifast,* which is 46.4% carbohydrate, 32.5% protein and 20.1% fat plus vitamins and minerals. Some would describe this as moderately high carbohydrate diet.
- At least three servings of non-starchy vegetables seasoned to taste if desired but salt is not allowed. This provided 200 calories.
- At least 2 liters of water.

Specifically prohibited foods were:

- Alcohol
- Salt
- Meat, poultry, fish, and eggs
- Bread, rice and pasta
- Dairy products
- Starchy vegetables
- Legumes
- Fruit

These prohibitions presumably deal with subjects who might decide to get some of the calories by cutting back on the *Optifast* and vegetables and gaining variety and more real food. One can understand the temptation given the prohibitions. Intentional exercise was not recommended due the unnecessary stress during the diet period. The issue with alcohol is purely caloric. It is important to recognize that this diet was designed for a clinical trial rather than as the optimum protocol for general use. The success of this diet was discussed in the November 2013 IHN.

Optifast as part of a soup or shake was suggested for breakfast, lunch and a snack. *Medifast* is a similar product. Other recommended foods were cabbage, celery, broccoli, bean sprouts, mushrooms, water chestnuts, cauliflower, onions, leeks, radish, tomatoes, cucumber, artichoke, Brussels sprouts, lettuce, peppers, carrots, low sodium vegetable stock, and fat-free salad dressing. Are the prohibitions important if only calories are really significant? Also, is 8 weeks necessary? Here are two case histories that provide hints of the answers.

CASE HISTORIES COLLECTED BY TAYLOR'S GROUP IN NEWCASTLE

In the following *case* histories, all blood sugar values are in mmol/L (to convert to the units used in the US, multiply by 18). Most modern meters are designed and calibrated to give results corresponding to those obtained from laboratory measurements which yield plasma rather than whole blood values. If this is not the case, then the meter will read about 11% high. The specifications should be in the users or online manual.

The publication by Taylor's group in 2011 describing the reversal of diabetes prompted a large number of inquiries from individuals with diabetes. Information regarding the details of what is now called the Newcastle Diet was supplied and a number of individuals tried the diet or some variation and reported back to the research group. Additional information was then obtained by personal contact. The results of 77 case histories have been published.[3] Diabetes reversal was considered to have occurred in 80%, 63% and 53% of those with > 20, 10-20, and < 10 kg weight loss respectively. Mean initial weight of the group was about 97 kg (213 lbs). Reversal rates according to the duration of diabetes ranged from 73% for < 4 years to 43% for > 8 years. About half the individuals used the meal replacements and energy was restricted without using this aspect of the diet in the remainder. The duration of the diet was also variable with a range of 1-104 weeks. Long-term data were available for 8 individuals who achieved reversal after undertaking the 8-week diet with half using meal replacements. The time since the end of dieting ranged from 3 to 8 months, HbA1c values ranged from 5.2% to 5.8% (normal or very near normal) and results from an oral glucose tolerance test indicated reversal of diabetes. Only 2 fasting blood glucose values were reported, 5.1 and 6.1. Weight loss ranged from 7 to 30 kg with all but one with ≥ 17 kg and small weight regain after the diet. Duration of diabetes prior to the diet ranged from 4 months to 4 years. For these eight, long-term reversal was based on laboratory results, not home measurements.

CASE HISTORY FROM THE UK

In August 2103 a fit 59-year-old reported in the British newspaper *Mail Online* that he had reversed his diabetes in 11 days with Dr. Taylor's diet. He had consulted with both Dr. Taylor and his GP prior to starting. At diagnosis his fasting blood glucose (FBG) was 9 but on the day when he started the diet it was 6 and about the same after one day. His starting weight of 147 dropped to 143 by day 3 and on day 4 his FBG was 4.6, day 7, 4.3 and day 11, 4.1 with a weight of 125. At this point he stopped the diet, but maintained this weight. At 2 months his FBG was 5.1 and a year later it was 4.9. He was pronounced cured by his GP.

A PERSONAL CASE HISTORY

Your editor has recently tried a shortened version of the Newcastle Diet, i.e. one week, but with significant variations. I was either diabetic or prediabetic depending on how much weight is given to HbA1c, since this was 6.2%, i.e. prediabetes, whereas I had FBG that was typically 8 to 9, and had become elevated over 15 years with values that just slowly increased along with the A1c. I had become concerned because recently my blood glucose 2-hours after eating was suggestive of deterioration in glucose control. In addition, signs of peripheral neuropathy (abnormal foot sensations) were becoming bothersome. Based on the notion that all that mattered was calories prompted a diet designed by ignoring the prohibited foods listed above as well as the alcohol and salt restrictions and simply eating only 800 calories per day, planning for just one week based on the second case history given above. My weight prior to this experiment fluctuated at between 160 and 170 lbs. BMI was about 22.

The diet was as follows. For breakfast, blueberries (frozen source, no added sugar) and zero-fat, zero-sugar yogurt, lunch ½ meat lasagne serving of 160 calories (Stouffers frozen product), dinner either a piece of salmon or small, lean flank steak (London broil) plus a large serving of broccoli, green beans or asparagus and a raw tomato. Dinner included two small glasses of dry red wine containing in total about

160 calories included in the maximum of 800. Vitamin supplements were added and 2 liters of water consumed, the latter also observed to essentially eliminate hunger. No snacks were consumed. The only variation was in the vegetables. Comparison with the Newcastle will reveal that about the only similarity was the calorie content, although the macronutrient distribution was similar.

The results for fasting blood glucose (FBG) and blood glucose values before and after lunch and dinner are given below along with the morning weight before breakfast. The after meal values were determined at 2 hours, the common time interval used in the oral glucose tolerance test. Glucose is reported in mmol/L. Day 1 results can be taken as the baseline for comparison since during 12 hours of calorie restriction it is unlikely that there were significant metabolic changes.

DAY	WEIGHT	FBG	B-LUNCH	A-LUNCH	B-DINNER	A-DINNER
1	165	8.8	6.6	6.7	6.9	7.1
2	163	6.9	6.8	6.6	6.6	6.2
3	160	6.6	5.7	6.8	5.8	5.3
4	160	5.0	5.1	5.9	5.8	5.5
5	159	5.4	NM*	NM	5.6	5.2
6	157	5.1	5.9	5.6	5.6	5.9
7	158	5.3	5.7	NM	5.2	5.6

* NM—not measured

Guidelines give normal fasting glucose as ≤ 5.7 and ≥ 7 mmol/L for diabetes. In the set of case histories reported by Taylor' group and summarized above, < 6.1 was used as indicating reversal. The 7-day diet achieved reversal, just as was found in the second case study. All one can say about the post-meal values is that they are much lower than baseline or what the guidelines suggest, probably because of the low calorie meals. Both pre-and post-meal values were very low at the end of the experiment, even for dinner, indicating rapid and probably quite normal glucose metabolism. Even by the end of day 4, the diet appears to have normalized glucose metabolism throughout the day. The comparison between day 1 and day 7 seems quite dramatic.

Fasting blood glucose comes from liver production unless one snacks during the night. As already discussed at length in IHN, it is postulated by Taylor [2,4] that elevated FBG is the result of a pair of viscous cycles which involve liver insulin resistance related to deposition of abnormal amounts of fat in the liver and pancreas plus pancreatic beta cell damage due to elevated circulating fat (triglycerides), with the deleterious effects developing slowly over years until there is an accelerated failure of glucose metabolism and thus actual diabetes. The clinical trial reported by Taylors's group found normalization of liver fat in overweight or obese diabetics in 7 days.[1] It may be that this occurs even more rapidly in a lean, low BMI person who has crossed the threshold to diabetes but which is not yet manifest in HbA1c. The day one value for FBG of 8.8 was consistent with values commonly observed prior to this experiment. Furthermore, after this experiment there was a dramatic decrease in peripheral neuropathy presenting as foot sensation problems, a very common early warning sign. This improvement has continued for 3 weeks after ending the diet and the problem is almost completely resolved.

This diet violated almost all the prohibitions of the Newcastle Diet (meat, dairy products, fruit, salt, pasta, and alcohol), suggesting that those restrictions may not be meaningful outside of clinical studies. However, the diet was similar in ingredients to what your editor normally ate most of the time, and thus was satisfying. It even included about 160 calories from table wine with dinner. However, prior to the experiment, the normal diet had included snacks such as nuts which were very calorie dense, and a high calorie snack before bed. Thus, energy intake was above metabolic requirements, although not enough to produce being overweight but rather fluctuations. This suggests a gradual accumulation of liver fat over a number of years, which would be consistent with the gradual increase in FBG and HbA1c observed from 1998 to date, an increase consistent with the path toward diabetes, as described by Taylor.[2]

Will these results be durable? There is no way of telling at this point. For the three weeks after the end of the diet, FBG was 5.7 ± 0.3 (std. dev.) with a diet of fluctuating energy intake, but in the range of 1200 to 1500 calories. Stay tuned. An HbA1c should be available by late November, perhaps with an oral glucose tolerance test.

This case history has revealed that reversal is possible after only about week of any sensible diet. The second case history found the same rapid change and in addition, found that the restoration of beta cell function proceeded after a return to a more normal diet and reversal was durable for at least a year. Both case histories demonstrate reversal in individuals at the low end of normal weight. Reversal might be possible even on a diet just containing ice cream, perhaps with celery and a tomato added, although the small amount of ice cream allowed would probably not be very satisfying. The carbohydrate in the meal replacement used in the Newcastle Diet was probably high-glycemic and ice cream contains protein and fat as well. Facetious or ridiculous, and too much sugar? Perhaps, but even this cannot be rejected at present. If only calories matter, a personalized one-week 800-calorie diet that appeals to children with diabetes should be easy to devise. Obviously a lot of research is needed.

It would appear that there is no downside to experiments such as described in these case histories. If the "cure" during the one week or 11 days is not permanent, it should be possible to resume the diet for a longer period or even adopt the Newcastle protocol in total. However, we now have two examples of durability, one over a year and one over three weeks, both involving very short-term diets. The case histories from the Taylor group also indicate significant durability. Your editor is not aware of any other approach to dealing with type 2 diabetes or prediabetes which can accomplish what is described above, over any period of time, with the exception of some forms of bariatric surgery. A careful examination of the literature reveals that very low carbohydrate or ketogenic diets will not in general bring one back to the non-diabetic state, and the prediabetic state, if achieved, may not be durable unless the diet continued. Such diets do not appear to address the fundamental problem. See the November 2013 issue of IHN. Furthermore, the prediabetic state may not be free of some risks, and it is my experience that a prediabetic HbA1c along with diabetic FBG does not protect one from diabetic neuropathy.

It is important to recognize the fundamental difference between drug-induced glucose control and what has been accomplished with this severe calorie restriction. The former merely takes advantage of a drug's action to interfere with one aspect of glucose production or utilization without addressing the cause of the disorder. Even aggressive glucose lowering with drugs fails to impact the major adverse effects of diabetes, as was shown by the famous trials ACCORD and ADVANCE, a topic discussed recently in IHN (December 2013/January 2014). One must never forget that type 2 diabetes as now treated is viewed as a progressive, incurable disease. After diagnosis, blood glucose levels rise steadily whether or not treatment is intensive. Ten years after diagnosis, 50% of diabetics are on insulin therapy.[4] Many have lost significant beta cell function at the time of diagnosis. Greatly enhanced mortality and morbidity follows with a serious deterioration in quality of life in the latter stages of this progression. The majority of foot or limb amputations are now directly related to diabetes. The Newcastle Diet and possibly its variations discussed above result in a permanent return, not to prediabetes, but to normal glucose (carbohydrate) metabolism. Drugs or insulin are no longer required. The significance of this is difficult to overstate, especially when it is projected that within a few decades, half the world's population will have type 2 diabetes. What is even more alarming is the new childhood epidemic. Anyone interested or concerned with this topic is urged to download and read the 2012 *Banting Memorial Lecture*. Simply Google the lecture title and a link to the PubMed abstract (www.ncbi....) will be found along with a button on the PubMed abstract page to obtain a free pdf of the full text. Consulting the Newcastle Diet website is also recommended – just Google the name.

Finally, the Newcastle or similar highly calorie restricted diets should only be undertaken after consultation with a medical professional familiar with the individual's history. Furthermore, the diet may not work for some forms of diabetes incorrectly called type 2. Examples include diabetes related to pancreatitis, and a rare genetic form called monogenic diabetes as well as type 1 diabetes which has come on slowly in adulthood and may be confused with type 2.

SODIUM, CARDIOVASCULAR EVENTS AND MORTALITY. THE DEBATE HEATS UP

Salt has joined fat and cholesterol as being demonized. Very low levels of intake are now being promoted by various high profile government and professional health organizations. The war on fat was highly successful, but had serious unintended consequences which will endure for decades after the death of the "fat is bad" hypothesis. The same can be said for the war on cholesterol, where the war is ongoing and controversial. Witness the current statin debate concerning benefit vs. risk, especially the risk of diabetes. Many aspects of these two hypotheses have been extensively discussed in IHN. Sugar is also being demonized, but in view of the huge annual consumption of sucrose and fructose by many individuals and the epidemic of obesity and diabetes, a war on sugar may have some real merit. Now salt is being rapidly elevated to the status of the latest threat to health even though primitive knowledge of its important place in human and even animal nutrition appears to predate recorded history.

Current guidelines for daily sodium intake in the context of minimizing cardiovascular events such as heart attack and stroke represent very low levels of consumption. The guidelines originate with the American Heart Association (AHA), the World Health Organization (WHO) and the US Institute of Medicine (IOM). These numbers are derived from studies on the effect of sodium on blood pressure and then extrapolation using models which generally assume a linear relationship between sodium intake and blood pressure and between blood pressure and cardiovascular events. Implicit in these models and thus the guidelines is the frequent assumption that there is no unsafe lower limit for sodium intake, i.e. no threshold. This model conflicts with the known role of sodium in human physiology where low sodium intake activates a compensatory response to conserve sodium, a response which produces an increase in the risk of, among other things, heart attacks.[5] The notion of no unsafe lower limit also flies in the face of human history where salt has always been regarded as important, even to the point of being used as a surrogate currency and an issue for hostilities.

Studies examining the association between sodium intake and cardiovascular disease outcomes, while extensive, have been highly inconsistent and the AHA very recently recommended that guidelines be based only on evidence linking sodium and blood pressure and a few (selected) population trials of the effects of sodium reduction on cardiovascular events.[6] This 12 page paper with over 50 pages of supplementary data presumably was intended to support the US guideline recommendation of a limit of 1.5 g/day or 2.4 g/day of sodium the former for high risk individuals. This is equivalent to about 4 to 6 g/day of sodium chloride, i.e. salt per day. Thus a study just published in the *New England Journal of Medicine* by O'Donnell et al, the PURE study[5], which found that these guidelines in fact appears to put one at a significantly elevated risk of cardiovascular events, created a big reaction in the media and among researchers.

A second study published simultaneously in the same journal found that the association between sodium intake and blood pressure was not linear and this was most pronounced in persons consuming a high sodium diet, persons with hypertension, and older persons, but the risk was flat and nil over a significant range of intake well above the guideline recommendations.[7]

A third paper also appeared in the same issue which represented a statistical *tour de force* using the above mentioned approach that salt elevates blood pressure, blood pressure is associated with the risk of cardiovascular mortality and therefore salt is associated with cardiovascular mortality.[8] This study was based on models, used international data and concluded that 1.65 million deaths from cardiovascular causes occurred in 2010 which could be attributed to sodium consumption exceeding 2 g/day (5 g of salt/day), a conclusion inconsistent with the results of the PURE study.

The PURE study used the sodium and potassium content of fasting morning urine samples as a surrogate for intake, an approach representing a practical solution to what is otherwise a difficult study design problem, especially when the alternative is using food frequency questionnaires or collecting 24-hour urine samples on a large international cohort of over 100,000 individuals. The 24-hour excretion was

then calculated from morning sample by a validated equation and considered equivalent to the daily intake since over 90% of the intake is normally excreted.

The PURE blood pressure study[7] involved 102,000 individuals from 18 countries and combined the morning urine sample with a blood pressure measurement using an automated device. Both potassium and sodium intake were estimated as described above and expressed as g/day of excretion. The study population mean blood pressure was 132/82 mm Hg and 35% had values ≥ 140/90. Sodium excretion was 4.9 g/day for sodium and 2 g/day for potassium. Very few participants had sodium intake less than 2.3 g/day and almost no one had an intake less than 1.5 g/day. Both systolic and diastolic pressure showed a nonlinear dependence on sodium excretion. When the data were separated between China and the rest of the world (China provided almost half of the subjects), for the rest of the world the diastolic pressure showed an increase of 0.7 mm Hg per g excretion for intake up to 3 g, 1.7mm Hg per g in the range of 3-5 g, and 2.6 mm Hg per g for > 5 g/d. Increases in systolic pressure were smaller, not exceeding 1 mmHg per g over the entire range. The subjects with 3-5 g/day values for excretion had systolic pressure of close to 130 mm Hg, whereas for 7 to 7.9 g, it was 135 mm Hg and for 2-3 g/day it was 128. For the Chinese group values were slightly higher in absolute pressures but similar in rates of change with amounts excreted. Slightly higher changes were found for those with hypertension and increasing age. Anyone who takes their blood pressure at home will no doubt recognize that these changes are similar if not smaller than the day to day fluctuations they observe and may be unwilling to attach much significance to the role of salt. However, older hypertensive individuals will experience a larger effect and most do not know their total sodium or salt intake, something that is worth investigating. An intake of 8 g/day of sodium is equivalent to 20 g of salt or 3.6 teaspoons.

The cardiovascular part of the PURE study helps put the above results in perspective. Morning fasting urine was used to estimate 24-hour excretion and this was used as a surrogate for intake as in the above study. Subjects numbering almost 102,000 were followed for a mean of 3.7 years. The combined primary endpoint was death and major cardiovascular events with secondary endpoints of any cause death and major cardiovascular events. The most stunning result was that for all these endpoints a pronounced J-shaped curve for the odds ratios (in this study almost identical to the risk ratios) was associated with the 24-hour sodium excretion. Minimums of the J-shaped results at the range 4 to 6 g/day were taken as the reference with an odds ratio of 1.00, i.e. no effect. Below this range, there was a sharp increase in risk for all three endpoints. For the primary endpoint, at an excretion rate of 1.5 g/day, the recommended AHA target especially for hypertensives and older persons, the increased relative risk was 80% with a number needed to have this excretion rate (intake) to harm one person over 4 years of 40. For all cause death the numbers were 115% and 38 and for major cardiovascular events, and 60% and 88. Numbers needed to harm (the number with that excretion rate needed to observe one event) were based on odds ratios and the incidence in the group used as a reference. This strongly enhanced risk at low intake was not influenced by adjustments in the analysis for hypertension and blood pressure and thus was apparently not being influenced by these factors, a point to seriously consider when considering the validity of the linear model calculations.

Above the reference range of 4-6 g/day, there was a slow increase in risk until at 12 g/day (30 g of salt, over 5 teaspoons), the primary endpoint carried a 20% increase in relative risk, all-cause mortality a 40% increase, and cardiovascular events a 20% increase. The numbers needed to have this high intake to harm one individual over 4 years were 161, 141 and 175, respectively. Two of the three odds ratio curves extending from the reference range upward were not linear. Thus, the assumption of linearly increasing risk with no threshold in salt intake was not supported by these results, and the risks of adverse events at the 2.3 g/day recommendation of the WHO were large and just slightly lower than those for the 1.5 g/day target.

The authors of the PURE study point out that there are 4 other studies in the literature that have reported J-shaped risk curves for risk vs. salt intake. While some participants in these studies had high cardiovascular risk, in the PURE study the vast majority did not have a history of cardiovascular disease or diabetes and those with such a history were more common in the group of participants with low sodium excretion. However, exclusion of participants with prior cardiovascular disease, cancer, diabetes or

current smoking, and those who had an event in the first two years of follow-up did not materially alter the findings in the PURE study. The increased risk at low sodium intake remained.

The PURE studies also looked at the impact of potassium intake, again using 24 hour excretion as a surrogate measure, and found the expected protective effects. While the use of 24-hour excretion is less accurate in the case of potassium, nevertheless the protective effects were attenuated when the results were adjusted for fruit and vegetable intake which is the major source of potassium. Thus the suggestion that there should be more emphasis on increasing potassium intake. However the absolute protective effect of having high potassium levels is very small, according to a just published study based on the Woman's Health Initiative. While comparison of lowest to highest quartiles of dietary potassium intake yielded adjusted relative risk reductions as high a 27%, the prevalence of stroke even in the postmenopausal women involved was very low and this resulted in almost negligible absolute benefit for this endpoint.[9]

In a news release, the AHA more or less dismissed the PURE results citing methodological concerns. However, in an editorial accompanying the three papers, Suzanne Oparil took a positive view of what were termed provocative results from the PURE trials which she stated beg for a randomized controlled outcome trial to compare reduced sodium intake with the usual diet. In the absence of such a trial she took the position that the results argue against reduction of dietary sodium as an"isolated public health recommendation." The third study was more or less dismissed because of numerous assumptions and lack of high quality data.[10] She failed to mention that that study did not take into account the strong J-shaped risk vs. intake results not only found by PURE but several other studies as well.

The bottom line appears to be that one must be concerned about low as well as very high sodium intake, whereas the guidelines are pushing for low intake that may be quite dangerous.

NEWS BRIEFS

MORTALITY ASSOCIATED WITH THREE COMMON SURGICAL OPTIONS IN EARLY BREAST CANCER

A study just published in *JAMA* examined the important question of the comparative mortality associated with bilateral mastectomy compared with unilateral mastectomy or breast conserving surgery plus radiation, the latter commonly referred to as a lumpectomy with radiation.[11] The study population consisted of all female California residents newly diagnosed with a first primary breast cancer from 1998 to 2011 and numbered almost 190,000.

When breast-conserving surgery with radiation was used as the reference, mortality over the study period of 15 years associated with bilateral mastectomy did not significantly differ from the reference treatment in a statistical analysis that corrected for a large number of confounding factors. The same comparison with unilateral mastectomy yielded evidence of enhanced risk for this traditional procedure.

According to the authors, this observational study is the first to compare the three surgical procedures side by side. The authors cited other studies that also found enhanced mortality of unilateral mastectomy compared to breast conserving surgery. However, there are no randomized trial data to inform concerning the question of whether or not the bilateral mastectomy improves survival, and the authors suggest it is unlikely that such a trial will ever be performed. Thus one must rely on observational data corrected for multiple confounders.

This study also examined the increase over time in the use of the bilateral mastectomy. Over the period in question, the rate increased from 2% to over 12%. They mention proposed explanations including the increased use of highly sensitive MRI imaging, increased anxiety driving the desire for preventive surgery, and the increase in genetic testing which facilitates the identification of high-risk patients. High profile celebrity endorsements, which increased general awareness of the bilateral procedure, occurred after the

end of this study. The authors also remark that patient satisfaction after bilateral mastectomy is variable with noteworthy areas of concern over deleterious effects, reconstruction failures and infections.

COMPARISON OF NAMED DIETS FOR OVERWEIGHT AND OBESE ADULTS

A meta-analysis (study of studies) comparing the popular "named" diets such as the Atkins, Zone, Jenny Craig, South Beach and Weight Watchers has just been published in *JAMA.*[12] Thirteen studies based on a comparison between diet and no diet were included. Six and 12-month weight loss data was recorded and analyzed.

Significant but small differences were found between any low-fat and low-carb diet with the latter producing more weight loss. However, weight loss differences between individual named diets were small. The authors conclude that these results support the current view that recommending any calorie reducing diet that a patients will adhere to when the goal is weight loss.

In all these diets, the number of kg lost can look impressive, but when the subjects are overweight or obese, the actual percentage weight loss is frequently rather modest. This is not to say such changes lack benefit, but the path from obese to normal weight seems to continue to be elusive for many individuals unless heroic calorie restriction and adherence is present. Thus the growing popularity of bariatric surgery for the obese and morbidly obese.

CHILDHOOD INFECTIONS RELATED TO BREASTFEEDING FOR AT LEAST 6 MONTHS

The American Academy of Pediatrics recommends mothers initiate and maintain exclusive breastfeeding for at least 6 months. A study just published in the journal *Pediatrics* provides strong evidence for the two features of this recommendation, exclusive and 6 months, in the context of infection risk during the first 6 years.[13] The study collected breastfeeding data from a study conducted in 2005-2007 and then collected follow up data for the incidence of infections during the past year among the 6-year-old children. The sites were upper respiratory tract and cold, ear, throat, sinus, lung or pneumonia and urinary tract. Also examined was the frequency of doctor visits in the past year among these 6 year-olds. There was no effect seen for cold or upper respiratory tract or urinary tract infections. However, for ear, throat, sinus and lung or pneumonia, when the exclusive breast feeding of no more than 4 months was compared with 6 or more months, the incidences as percentages were 26.4 vs. 11.6, 24.2 vs. 7.0, 15.9 vs. 2.3 and 4.8 vs. 2.3, respectively. In addition, smaller, but still significant benefits for the ear, throat and sinus infections were found when the breastfeeding extended to 6 months but was not exclusive. Odds ratios corrected for a number of confounding factors presented the same picture of infection protection. In addition, the prevalence of ≥ 2 office visits was 43% vs. 19% when no more than 4 months breastfeeding was compared with 6 or more months.

According to the authors, the mechanism whereby human milk provides protective effects that last beyond infancy and after the termination of breastfeeding is unclear. While they offer a number of possible explanations, there is of course the simple explanation, how the early immune system evolved over the eons prior to the advent of baby formulas. It is unfortunate that in the developed world, modern lifestyles interfere with prolonged exclusive breastfeeding, and in some situations, the mother has no choice.

It is of interest in this context that a recent study using rhesus macaques compared breast-fed to formula-fed infants. The study demonstrated that a natural vs. a formula infant diet has profound and durable effects on the infant gut microbiota, the development of their immune systems, and the metabolic profiles of their plasma and stool.[14] The differences between the gut microbiota were pronounced, both in individual taxa and community-level measures or richness, diversity and evenness, and remained pronounced 6 months after all animals in the study began receiving an identical diet.

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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