

# INTERNATIONAL HEALTH NEWS

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*Clinical scientists doing studies are frequently investigating whether or not an intervention has merit. There may be much at stake. The study may involve a pharmaceutical with millions if not billions of potential profits. Alternatively, an academic clinical researcher may have dreams of a paper in a high impact journal, which will help gain a promotion, a research chair, or opening the research funding tap. However, in clinical research large absolute and thus in the view of some, clinically significant results are the exception. With the advent of antibiotics in the period after the Second World War, infectious diseases were a principal focus and it was normal to get results such that most treated were cured. Pneumonia, syphilis, gangrene, tuberculosis all yielded to antibiotics and no one probably even considered the possibility of a placebo effect or confounding. Statistics were not necessary. Anyone could see that the treatment worked.*

*However, the very nature of medicine evolved, and the important problems changed from mostly infectious diseases to mostly chronic diseases, which have in the hands of even the most distinguished researchers, almost completely eluded cures. This changes the game dramatically, since now two challenging issues come to center stage, preventing the major chronic diseases in the first place or halting, slowing or reversing their progression once present. Now, instead of having one species of infectious bacterium to deal with and one magic bullet that works, antibiotic resistance is common and chronic diseases present mind boggling complexity, an avalanche of theories, and hundreds of studies that nibble at the fringe but generally fail to yield significant guidance concerning the solution to the real problems, total prevention, a complete cure or at least halting progression.*

*Along with this evolution there was a change in how clinical study success was defined. Biostatisticians became an essential part of research teams. Since it was very rare to obtain study results benefiting more than a small percentage of those treated or undergoing some intervention, success was described in terms of deceptive relative benefits to downplay dimly small absolute benefits. This became universally acceptable. Otherwise, almost no one, even the very best clinical researchers would have any success at all. Small absolute benefits were viewed from a large population perspective to given them relevance, but this had little meaning for the individual. If an officially approved treatment had been required to provide absolute benefit to even just 15% of those treated, i.e. 85% out of luck, most drugs and other interventions used to treat or prevent chronic diseases would never have made it to the pharmacy shelves.*

*Medicine has evolved from the penicillin era to the modern era such that today it is a highly complex and technologically advanced undertaking involving many years of education and apprenticeship. Specialization became the norm but the burden of the job necessitated delegating very important activities to small, select groups. These are called the thought or opinion leaders and the guideline writers. Chronic diseases gave rise to national and international societies which took on this task and helped the practitioner who had neither the time nor training nor journal access for making independent assessments through literature research, analysis, and synthesis of an opinion. It is doubtful that it was anticipated that bureaucrats and administrators would take these guidelines and use them to attempt to actively control how doctors practice medicine, judge their performance and determine*

*personal financial benefits from their professional work. Nor were the harsh penalties probably anticipated that were handed out to those who dared think or practice outside the box. How could anyone have anticipated in 1960 that today the organizations that issue licenses to practice, journal editors, pharmaceutical companies and even academic deans have and use the power to destroy the careers of those perceived to be dangerously hostile to the conventional wisdom, saying they are protecting us from charlatans while in fact they are protecting their own turf and dogma, and in the case of the industry, profits that two or three decades ago would have been considered pure fantasy.*

*By and large the medical professionals have been innocent bystanders in a complex evolutionary process over which they had little control, and for many, inadequate knowledge of what was really taking place. After board certification it was too late for most to do anything more than accurately play the music to the beat of the conductor. Because few went on to train in research, most played no part in the development of the treatments they daily employed and were not responsible for the absence of effective treatments. Most of the training was in acute medicine encountered in the hospital setting and frequently not useful unless they remained in this environment. On the front lines they use what is available and approved. A few are brave and adventurous enough to engage in integrative medicine, but most are understandably afraid to think very far outside the box, try unorthodox therapies, or try protocols they have read about, even in the peer-reviewed literature, but are based only on case studies, even if the investigators had impeccable credentials and there was a high level of biological plausibility and the risk nil. Furthermore, the very nature of specialization and its gatekeepers deprives many patients from having their problem initially viewed from a broad, multidisciplinary perspective. This provides a major explanation for missed diagnoses which can plague patients for years as they go from specialist to specialist. A common complaint of patients is that they do not even get the opportunity to adequately describe their problems.*

*Patients are partly to blame by resisting implementing recommendations for lifestyle and diet changes and instead forcing the use of pharmaceutical interventions with insignificant absolute benefit. Patients are remarkably successful in demanding and getting drugs such as antibiotics, antidepressants, sleeping pills, painkillers, etc. even in some cases, against the better judgment of their physicians.*

*Change is needed but it is hard to imagine how it is going to come about. In IHN we frequently discuss approaches that, while seemingly of great merit, are doomed to remain virtually unknown and unapproved, partly because the bar has been raised very high by the advent of evidence-based medicine which now is revered with almost religious devotion with severe penalties for heretics. It seems that modern medicine has found a very good and easy to sell antidote for professional common sense and realistic attitudes.*

*Wishing you and your family good health,*

**William R. Ware, PhD, Editor**

**Highlights**

|   |      |
|---|------|
| Functional medicine                       | p. 3 |
| Radical remission of cancer               | p. 5 |
| Fasting to prevent chemo side effects     | p. 6 |
| Triglycerides and risk of type 2 diabetes | p. 8 |

## FUNCTIONAL MEDICINE

Consider the structure of modern medicine. The specialities, aside from those concerned with repair and trauma, can be subdivided into several sets. These involve specific organs or related sets of organs, systems or related sets of systems, specialities requiring a generalist approach, while perhaps restricted and finally, the service specialities. The following is not complete but provides the general picture of a large set of boxes. While there are of course exceptions, most specialists do not venture far from their boxes. One notable exception is the internist but here the box is very large.

- SPECIFIC ORGANS OR SETS OF ORGANS: *Cardiology, Dermatology, Ophthalmology, Nephrology, Otorhinolaryngology, (ENT), Rheumatology, Pulmonology, Hepatology (liver, gallbladder), Psychiatry.*
- RESTRICTED SYSTEMS: *Allergy and Immunology, Endocrinology and Metabolism, Hematology, Neurology, Obstetrics and Gynaecology (OB-GYN), Urology and Nephrology.* Surgery associated with specific body parts or organs.
- GENERAL: *Internal medicine, Pediatrics, General and family practice, Preventive medicine, Infectious diseases, Physical medicine and rehabilitation, Geriatric medicine, Emergency medicine, Sports medicine, Oncology.*
- SERVICE SPECIALITIES *Anaesthesiology, Pathology, Radiology, General surgery.*

Most models of the delivery of medical care use generalist gate keepers such as GPs, Family physicians and specialists in internal medicine (internists) to make initial evaluations and diagnoses. If the problem exceeds the expertise or experience of these gate keepers they then refer the patient to an organ specific or restricted system specialist. Reference to the list of organ specific and restricted system lists above makes it clear that once the patient leaves the care of the generalist they will be generally be viewed through a narrow focus lens of an individual whose knowledge resides mostly in a very restricted area. Furthermore, the referral is generally prompted by symptoms of a disease or disorder and not prevention. Preventive medicine really falls in the area of the generalist who relies on guidelines that dwell on exercise, lifestyle and diet, drugs that impact biomarkers of risk and vaccination, one of the principal interventions that comes to mind when one mentions prevention. Among generalists, one expects for example from internists, pediatricians and specialists in geriatric medicine the experience and knowledge not only in disease management but also in prevention of disease.

The reason for all this detail about what most readers understand is the contrast with what is called functional medicine. Functional medicine does not aspire to place the patient in the appropriate specialty box unless the presentation is compelling. Rather, they ask what is this patient's set of fundamental problems? What has gone wrong with the way their biological and physiological systems work as a whole that produces these symptoms and complaints and how can we fix this. Thus the functional medicine physician is concerned with whole body systems. In his book *The Disease Delusion*, Dr. Jeffrey S. Bland divides these essential systems as follows.

- *Assimilation and elimination.* The digestive system is the center of the immune system and the digestive, nervous and the immune and hormone producing endocrine systems that all function together in an interconnected manner. Included is the whole human microbiota represented by several hundred different species of friendly bacteria.
- *Detoxification.* Toxins produce nervous and immune system dysfunction, alter gene expression, and influence fetal and childhood development. Everyone in developed countries carries a burden of organic and inorganic toxins, the amount depending on exposure and the efficiency of elimination. When the former is excessive or the latter is impaired, multi-system dysfunction can occur.
- *Defense.* The immune system provides defense against both infectious and inflammatory disease. Proper function is essential to health and this depends on many complex factors including involvement of other systems. One common dysfunction is autoimmune disease.

- *Cellular communication.* This involves a wide range of messenger chemicals such as hormones, neurotransmitters, inflammatory mediators, etc. The proper function of this complex system is essential for not only for or health but our survival.
- *Cellular transport.* For cells to properly function, they need a variety of organic chemicals and minerals which must get into the circulation and then are transported via the circulation and in most cases must cross the cell walls. Waste products must also be transported. For example specialized chemicals transport fats in the bloodstream since they are water insoluble. If this complex system fails in any significant aspect, cellular deficiencies or toxicity develop.
- *Energy.* Energy production occurs in the mitochondria within cells and is where carbohydrates and fats are metabolized producing cellular energy. The complex biochemical processes depend on the proper intake of a huge number of nutrients such as vitamins, minerals, fatty acid and phytonutrients. Failure of this energy production system results in chronic diseases and accelerates biological aging.
- *Structure.* Human gross structure includes the skeleton, muscles, connective tissue and organs. These are not static but undergo regular renewal. Structural and functional problems include obesity, bone loss, brittle bones, muscle failure including heart failure, etc.

Two excellent examples of disorder where functional medicine has been successful are autism and multiple sclerosis, both of which are conventionally treated with symptom modification which in most cases fails to address the fundamental problems or produce reversal, prevent progression or affect a cure. Books describing these successes were listed in the December 2014/January 2015 issue of IHN.

Another example is Dr. Ron Taylor's diet-based cure for diabetes recently discussed in IHN. It was inspired by a "system view" of how diabetes originates and progresses which suggested how reversal could be accomplished.

The challenge is to identify the dysfunctional body systems and take corrective action. In his book Dr. Bland provides a set of questionnaires associated with each system which helps readers identify those that may be dysfunctional. He then offers dietary, supplemental and other interventions that target these problems. However, this is a rather specialized undertaking and if possible should be left to experts in the field who practice functional medicine on a daily basis. Unfortunately this is frequently impossible due to the fundamental structure of the modern practice of medicine described above and the professional disdain for those abandoning the rigid system of boxes by practicing functional medicine. Dr. Bland's book is highly recommended for anyone forced to try to solve their own problems. The reader is also referred to a recent review of personalized lifestyle medicine, which is free.<sup>1</sup> (Google D.M. Minich and J.S. Bland)

Finally, it seems the need for a paradigm shift towards functional and personalized medicine is becoming acute. Particularly in the US we are seeing financial forces taking over the most fundamental aspects of the practice of medicine. This was nicely outlined in an opinion piece in the *New York Times* (November 18, 2014) by two faculty members from Harvard Medical School, Pamela Hartzband and Jerome Groopman. They discuss the adverse impact of "pay for performance" initiatives put in place by insurers, hospital networks and regulatory groups. These initiatives attempt to force physicians to meet strict metrics for testing and treatment. These metrics arise from population-based studies, are generic and fail to take into account the individual characteristics of the patient or differing expert opinions on optimal practice. In addition, insurers are attempting to control the choice of medications. Financial incentives, penalties and peer pressure coerce physicians to comply. This is obviously the opposite of functional and personalized medicine and should be a cause for great concern. What is happening is no doubt also of great concern to some physicians who are losing one of the traditional aspects of their profession, the freedom to exercise their own clinical judgement independently without interference or artificial constraints.

The strongest indication for the need of attention from an expert in functional medicine is when an individual with a serious problem has been going from doctor to doctor with no success, suggesting that conventional therapies are probably not going to work and a different approach is the only hope. It

appears that there are a large number of individuals of all ages out there who fit this description. Dr. Brand's book gives a number of success histories in this context.

## RADICAL REMISSION OF CANCER

Radical remission in the context of this discussion is complete remission from cancer in patients for whom conventional treatment had failed or where most or all of the proposed treatment components had been rejected. This is the title of a recent book by Dr. Kelly A. Turner, PhD, and is based partly on her thesis research which involved a search for common factors in cases of radical remission, a search that involved traveling around the world and interviewing patients (survivors) and individuals who had provided advice and assistance. The book is reminiscent of *The Blue Zone* and *The Okinawa Program*, books which described the same research technique applied to extreme longevity. We will touch on some of the highlights of this fascinating book.

A common thread found among many radical remission cases was diet change, and for many, extreme diet change. Turner lists:

- Drastic reduction or elimination of sugar, meat, dairy products and refined foods.
- Greatly increased intake of vegetables and fruits.
- Focusing on organic foods.
- Drinking purified water.

This list of course implies the elimination of junk foods, faux foods, soft drinks, fruit juices with added sugar, in fact a substantial fraction of the items on the Western grocery store shelves. As the author discusses in detail, these actions are justified by substantial evidence (key citations included), are familiar to many readers as healthy eating patterns and do not need a detailed review. Eating raw vegetables and juicing were a common practice and some survivors eliminated sugar with religious fervor. As has been discussed in IHN, eating organic foods actually aids in the natural detoxification by not feeding in new chemicals daily that need to be eliminated. Body loads go down dramatically for many toxins. In connection with water purification, recent research conducted by *Natural News* found that many simple water purification devices are totally inadequate, at least for heavy metals. Reverse osmosis appears to provide comprehensive purification. The diet chapter provides a number of compelling case histories.

Most survivors also made use of supplements. These could be categorized into digestive aids such as digestive enzymes and pre- and probiotics, aids for detoxification such as antifungals like stinging nettle, anti-parasitics, natural antibiotics and antivirals such as garlic and oil of oregano, and liver detoxifiers such as milk thistle. Other common supplements involved the whole spectrum of vitamins and minerals and omega-3 oil, grape seed extract, curcumin, quercetin, inositol, inositol hexaphosphate (IP-6) and bromelain.

The remainder of the interventions and practices common to the survivors involved exercise, attitude modifications and stimulating mind-body connections. For example, survivors found getting rid of suppressed emotions, increasing positive emotions, making use of social support, finding and emphasizing strong reasons for living, and deepening spiritual connections were all important aspects of successful programs. The details of these approaches are complex and to gain a comprehension of what the survivors did requires reading the relevant chapters. Nevertheless, this aspect of the programs many adopted appears highly important and there is a considerable literature concerning these mind-body interactions. When going it alone, one must become their own psychiatrist/psychologist. Dr. Turner helps by citing both books and publications from the medical literature. An excellent discussion of the mind-body connection with cancer can also be found in chapters 9 and 10 of the book by David Servan-Schreber, MD, PhD, titled *Anti Cancer. A new way of life*, but the entire book is highly recommended.

Another common thread was the success of multiple interventions rather than, for example just trying diet modification. This of course makes sense since it is difficult to weigh the potential impact of various interventions because of individual differences and this ignorance should inspire "throwing everything but

the kitchen sink” at the problem. When one looks at clinics that specialize in alternative and integrative cancer therapy, multiple interventions are generally the norm. See for example the website of the Schachter Center for Complementary Medicine and click on cancer.

Some survivors worked with individuals who some call healers, others engaged in extensive research using books and the internet. Nevertheless, in many cases, they were on their own and their success was entirely due to their own research and planned approach to cancer. Recall that most had rejected conventional medicine and had been given dismal prognoses. In a number of cases described in the book, the cancer professionals became angry, hostile and abusive when confronted with patients who rejected their proposals for treatment. A common characteristic of the survivors was an attitude of indifferent dismissal of this behavior and the belief that they were better off taking control of their own health. This is not a surprising result when one researches the dismal treatment success for metastatic cancer which can easily inspire the attitude of “what have I got to lose in going it alone?” However, some cancers respond very well to treatment, especially to chemotherapy, and rejection before failure would be a big mistake. Most are blood-related cancers.

It is interesting to speculate regarding the potential synergistic effects of combining Salvestrols with some or all of the approaches described in *Radical Remission*.

### **THE BOTTOM LINE**

The research Dr. Turner described in *Radical Remission* provides anecdotal evidence of the power the individual has to alter the course of cancer by optimizing the encouragement they can provide to enable their own bodies to solve the problem. The approach the survivors used has many similarities with functional medicine described above. Studies of any one of the interventions described above would probably produce small beneficial effects and be considered useless, but when a multifactorial assault on the problem is used, partly because of lack of knowledge of what has the best chance of working, and partly because the synergism is no doubt present, the probability of success appears greatly enhanced. There are numerous examples of this phenomenon. Oncologists probably dismiss these cases as simply spontaneous remissions of mysterious origin. The need for some serious studies is clear.

## **FASTING TO PREVENT CHEMOTHERAPY SIDE EFFECTS AND ENHANCE BENEFITS**

It is well known that for many cancer sites or for dealing with metastatic disease, chemotherapy is only modestly effective, sometimes producing such short life extensions that the specialty of oncology exposes itself to ridicule. Furthermore, all but a few chemotherapy agents cause serious side effects and systemic damage since they function by taking advantage of a differential in cell sensitivity that is not very large. Finally, cancer cells develop resistance to the toxic effects of the therapeutic agents.

The undesirable side effects are a significant issue. Over 20% of cancer related deaths are hastened or even caused by the toxic effects of chemotherapy. Systemic toxicity reduces the overall efficacy by limiting treatment dosage and frequency. Cancer patients have enough to worry about without having the fear of dying from the treatment, but unfortunately this represents the present state of affairs if one ignores the few new and targeted drugs that mostly cost a fortune and may not be covered by insurance. In addition, chemotherapy increases the risk of secondary cancers, severe damage to bone marrow, immunosuppression, anemia and possible bone marrow failure.<sup>2</sup> Furthermore, there may not be full disclosure concerning the magnitude of the benefits, which may in just months of life extension, due to professional conflicts of interest or a distorted view that this is the best we can do and we have to do something. However, to be fair, there are some chemotherapeutic protocols that are very successful in producing satisfactory long-term results, and this of course depends on the stage and type of cancer.

However, there is something cancer patients can do to minimize the collateral damage and devastating side effects of chemotherapy. Cancer cells and normal cells differ in their response to severe nutrient deprivation and it turns out that fasting can result in a protective effect for normal cells against toxins, and

for some cancer cell types, enhanced sensitivity to the cytotoxic effects of chemotherapy. This discovery is significant and is gaining interest as a way to overcome to some extent a classical and serious problem. Nutrient deprivation is frequently achieved by total fasting, water only, from 24 to 48 hours prior to chemotherapy and some protocols even continue fasting during the treatment and for a day or so after it. The pioneer in this area is Professor Valter Longo at the University of Southern California.

Prior to human studies, fasting was already indicated as a potential beneficial action based on cell culture studies where mixtures of cancer and normal cells were starved and then treated with a chemotherapy agent. When compared with controls, much less cytotoxicity to normal cells was found and, there was a significant enhancement in the cancer cell cytotoxicity of the agent used. Also, animal studies have consistently and dramatically shown the same fasting effect. In fact, both studies of the microbiological effects and as well animal studies suggest fasting also appears to have the potential to affect cancer progression with or without chemotherapy.<sup>3;4</sup>

While the mechanistic details are still the subject of research, a simplified version is that malignant cells have entirely different cellular requirements since macronutrients such as glucose are utilized not only to provide energy but also to facilitate the synthesis of biochemicals needed for frequent cancer cell proliferation. Thus malignant cells consume abnormally large amounts of nutrients and the excess over energy requirements goes into producing lipids, amino acids etc. required for cell division. During fasting, normal cells, unlike cancer cells rapidly adapt to fasting with the focus on cellular protection and maximizing survival. The so-called oncogenes in cancer cells prevent this normal response to starvation; but the decreased availability of glucose and other changes also create an extreme environment detrimental to many types of cancer cells. This is called differential stress resistance and the view is that the starvation condition protects normal cells from chemotherapy without interfering with the killing of malignant cells but rather also enhancing cytotoxicity.<sup>4</sup>

There are significant reservations among cancer specialists concerning the advisability of fasting since some patients are underweight and even in a fragile state of health. However, in an interview published in the *Natural Medicine Journal* (2013, Vol, 14, #1, free on line), Professor Longo commented that his patients after fasting regain weight easily after returning to normal diet and thus the protocol appears safe. However, he comments that individuals with diabetes and metabolic disorders should be carefully assessed before trying this protocol.

Professor Longo's group has recently developed an alternative to water-only fasting. This uses a nutrient package they developed which after the first day of a reduced calorie, high fat diet, this meal kit is used. The researchers hope this will make the fast more acceptable with greater compliance while maintaining the physiologic impact of fasting. The product is trademarked as *Chemolieve*. The contents are proprietary, but according to an article in the Denver *Naturopathic Clinic News* by Dr. Jacog Schor (June 6, 2013) a version he has seen contains daily rations of teas, nut bars, vegetable broth and selected nutrients. According to Schor, it provides < 300 calories per day. It is being manufactured but is not yet on the market due to ongoing trials. Details at [www.l-natura.com](http://www.l-natura.com)

Interest in this approach has grown to the point where, according to a *NCI Cancer Bulletin*, clinical trials are underway. These are at USC, the Mayo Clinic, and Leiden University. As well, a consortium of 12 universities in the US and Europe are planning two trials, each with 800 patients. However, results do not appear to have been published. Instead, all we seem to have are anecdotal reports, the most comprehensive of which included 10 case histories (7 female) presented in a report in the journal *Aging* by a group led by Professor Longo.<sup>5</sup> Four suffered from breast cancer, two from prostate cancer and one each from ovarian, uterine, non-small cell carcinoma of the lung, and esophageal adenocarcinoma. All patients fasted for a total of 48 to 140 hours prior to and 5 to 56 hours following chemotherapy. All the patients experienced fewer adverse effects and less severe chemotherapy-related toxicity. Nausea, vomiting, diarrhea, abdominal cramps and mucositis were virtually absent from the reports of all 10 patients. Four patients also fasted throughout their treatments and reported low severity of majority or side effects. These results were in sharp contrast to the typical experience of cancer patients receiving the same chemotherapy regimens and thus serving as controls. Interested readers can download the paper free from PubMed (use the PMID number 20157582 in the search box). While we must wait for

clinical trials that address the issue of enhanced benefit or the possibility of lower chemotherapy doses, animal studies suggest this is a very reasonable expectation.

### **THE BOTTOM LINE**

While the evidence is limited at present, it nevertheless involves a combination of biological plausibility and case histories describing considerable benefit which deserve consideration by cancer patients and their oncologists. It will be some time before what has been described above will qualify for consideration as a standard protocol.

## **TRIGLYCERIDES AND RISK OF TYPE 2 DIABETES**

In recent issues of IHN we discussed the work of Professor Roy Taylor concerning a dietary intervention capable of completely reversing type 2 diabetes. A key factor in the biological plausibility of this cure involved pancreatic dysfunction associated with circulating triglycerides. Evidence for this goes back some time in animal studies,<sup>6</sup> and in 2007 the first human study provided confirmation by showing a strong negative correlation between pancreatic fat as measured by imaging and pancreatic beta-cell function as measured by several parameters.<sup>7</sup> It is also well known that type 2 diabetics very frequently have elevated circulating triglycerides that accompany elevated pancreatic fat levels and impaired beta-cell function.

A recent observational study (follow-up) has provided additional evidence in favor of this model for the development of diabetes. Lee *et al* have proposed an index (TyG Index) based on routine blood measurements that provides strong evidence for the risk of developing diabetes.<sup>8</sup> The index involves the product of the fasting blood sugar and triglyceride concentrations (calculated by multiplying the fasting blood (plasma) glucose and the blood triglyceride level, both in mg/dL, dividing by 2 and then taking the natural logarithm to give values typically around 8 to 10). In the study, 5354 non-diabetic subjects had a set of parameters measured at baseline and were followed for a mean of 4.6 years to determine the number who had developed diabetes. When the cohort was arranged by increasing TyG index and divided into four groups of equal number (quartiles), in comparison with those in the lowest quartile, those in the highest had a statistically significant four-fold increase in risk (absolute risk ratio after adjusting for a large number of potential confounding factors). The results are summarized in the table given below. Note that the fasting glucose levels at baseline were well below the threshold for prediabetes, but that there was a considerable range of baseline triglyceride values. Some had triglyceride levels well above the level where guidelines indicate cause for concern. Lee *et al* also stratified their results by gender and obesity (BMI  $\geq$  25) and obtained similar results. Thus the TyG index appears to be a simple, powerful and independent predictor of the risk of diabetes and these results should help focus attention on dietary measures to reduce triglyceride to normal, not just by 10-20% from a high value as drug therapy frequently does.

*Predicting development of type 2 diabetes from fasting plasma glucose and fasting triglycerides. Adjusted risk ratio given for four quartiles of population according to TyG Index. Adapted from Lee et al<sup>8</sup>*

| <b>PARAMETERS</b>               | <b>Q1</b> | <b>Q2</b> | <b>Q3</b> | <b>Q4</b> |
|---------------------------------|-----------|-----------|-----------|-----------|
| Quartile mean values, TyG Index | 8.0       | 8.4       | 8.8       | 9.4       |
| Fasting glucose (mmol/L)        | 4.86      | 4.96      | 5.02      | 5.10      |
| Triglycerides (mmol/L)          | 0.77      | 1.17      | 1.66      | 2.86      |
| Adjust Risk Ratio (REF Q1)      | 1         | 2.9       | 2.0       | 4.1       |

A second study<sup>9</sup> conducted in Scotland revealed the same diabetes-triglyceride connection found by Lee *et al*. This large population study examined the clinical determinants of the progression of type 2 diabetes. It used medical records from 1992 onward for 15 years and examined the rate of progression from diagnosis to the requirement of insulin treatment (defined as either insulin treatment or an HbA1c  $\geq$  8.5%



the latter being a three-month average of blood glucose. Aside from younger age at diagnosis only two independent factors were found to be significant, elevated triglycerides and low HDL. Mean triglyceride levels at the time of diagnosis were 2.77 mmol/L (245 mg/dL). Normal is considered below 1.7 mmol/L (150 mg/dL). An elevated liver enzyme ALT level was also a risk factor for rapid progression to insulin dependence but was not an independent risk factor in the final statistical analysis. The authors comment that it was not possible to determine if the triglycerides and liver enzyme were simply markers of insulin resistance or whether they had a primary effect associated with triglyceride toxicity on pancreatic beta-cell decline. The risk with BMI (body mass index) was found to be U-shaped with a minimum at a BMI of at 24-26, with both low and high BMI presenting roughly equal enhanced risk.

In Taylor's clinical study of severe calorie restriction and the reversal of diabetes, triglyceride levels were elevated in all the diabetics and dramatically decreased to normal at the end of the 8 week, 800 calorie diet. In addition, this was accompanied by a return to normal of the fat levels in both the liver and pancreas as measured by imaging as well as the normalization of liver enzymes. Very low carbohydrate diets with somewhat reduced calories intake also can have a strong impact on triglyceride levels.<sup>10</sup> In the lowest quartile of the Lee *et al* study, triglyceride level had a mean of about 125 mg/dL. The conventional level for concern is about 160 mg/dL. A low carbohydrate diet should be able to bring a level 150-160 down to 120 mg/dL although it may be necessary to also increase calorie restriction to achieve a desired reduction. In Taylor's clinical study, mean baseline triglycerides were 2.4 mmol/L and at the end of the 8-week diet, were 1.3 mmol/L (212 and 115 mg/dL)

The results of these two recent studies are entirely consistent with Taylor's view of how diabetes develops. Consuming excess calories results in the conversion of excess carbohydrates to fat which increases not only the liver fat content but also the pancreatic fat content due to elevated circulating triglycerides. The resultant beta-cell dysfunction enters into a vicious cycle which results ultimately in glucose metabolism becoming sufficiently impaired to justify the diagnosis of diabetes.

### **THE BOTTOM LINE**

Mainstream medicine thinks about triglycerides mainly in terms of cardiovascular risk, but the association is controversial. Triglycerides are always measured along with cholesterol because the value is needed to calculate LDL cholesterol which is not generally directly measured. Perhaps the focus should to change to diabetes. Individuals wishing to avoid diabetes need to watch not only their fasting sugar levels but also their triglycerides. This should not be a problem since both are routinely measured in physical exams. When either starts creeping up from normal, action should be taken. It is at the first sign of trouble where interventions work the best and frequently require only modest adjustment of diet and lifestyle. If one is at the upper end of prediabetes and has high triglycerides, then more drastic action is called for, normally with diet, more severe calorie restriction, and exercise. The intensity of the interventions is increased until normality is reached. The time required will depend on the intensity of the actions undertaken. One must be sure actions being undertaken are consistent with general health and fitness. In addition, it may help to mentally focus on the huge benefits of avoiding diabetes and the multiple comorbidities that accompany it. For individuals with diabetes, elevated triglycerides are clearly a significant risk factor with a simple solution provided by Taylor. Readers should be aware that the low-fat, high carbohydrate diet is associated with elevated triglycerides and low HDL. Even though diabetes carries the risk of cardiovascular disease, anything that increases the risk of progression should be avoided. A low-fat high carbohydrate diet was recommended for decades as part of a heart healthy diet and universally recommended in programs to reduce the risk of cardiovascular disease. This may have had the unintended consequence of the current diabetes epidemic.

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