CHAPTER 14

GLUCOGENIC/KETOGENIC BALANCE EXPLAINED

Introduction

There are three pathways by which energy is produced with oxygen; the Krebs Tricarboxylic Acid Cycle, the beta oxidation pathway, and (primarily in the liver) the pentose phosphate pathway. Glucogenic and Ketogenic Imbalances each represent a deficiency of one of these principal energetics pathways, and an over-dependence on another.

(Due credit must be given to Watson (1) on whose (inappropriately named!) “fast/slow oxidizer” paradigm our Glucogenic/Ketogenic Balance was originally modelled.)

(An Anaerobic/Dysaerobic Imbalance also relates to oxidative energy metabolism. The best way to make a distinction between Anaerobic/Dysaerobic verses Glucogenic/Ketogenic is to think of Anaerobic/Dysaerobic as an excess of Anaerobic Glycolysis vs. excess Oxidative Stress, each decreasing ATP energetics, while Glucogenic/Ketogenic involves a deficiency of either Glucose energetics or fatty acid utilization. (A/D & G/K Imbalances often co-exist)).

Your patients with Glucogenic/Ketogenic Imbalances are just plain "pooped out." These individuals have lost the liver capacity to select, moment to moment, the ideal energetics substrate, Glucose & glucogenic amino acids, or fatty acids & ketogenic amino acids. This efficiency loss is analogous to an engine not firing on all cylinders. Only NUTRI-SPEC can get these people fired up again.

Hepatic function is the primary consideration in Glucogenic/Ketogenic Imbalances. To appreciate the clinical significance of this Imbalance you must understand the implications of what was until recently called Non-Alcoholic Fatty Liver Disease, which the research literature has more recently and more appropriately renamed Metabolic-Associated Fatty Liver Disease. The research literature reports the incidence of MAFLD among American adults to be somewhere between 35% and 60%, and the incidence increases with age. MAFLD is the disastrous consequence of a lifetime of eating sugar (fructose), and polyunsaturated oils (--- what Nutri-Spec terms HOHUM PUFAs --- Heated, Oxidized, Hydrogenated, and otherwise Un-Metabolizable Polyunsaturated Fatty Acids). Nutri-Spec clinical experience shows that the 60% incidence certainly applies to Americans over age 53 --- those in the oldest demographic of your Stage Of Life INFLAM-AGING Defense (SOLID) Diphasic Nutrition Plan.

Sixty Percent! How pathetic, and how tragic. MAFLD presents essentially the same phenomenon as Metabolic Syndrome. There is a direct association with high blood pressure, rising blood sugar and Type 2 diabetes, elevated cholesterol, elevated Triglycerides relative to low HDL cholesterol, cardiovascular disease, and cancer. Of the Nutri-Spec Metabolic Imbalances, G/K is the one most obviously and most directly self-inflicted. The dietary etiology begins in childhood consumption of sugar and seed oils. Abdominal weight gain? MAFLD is certain.

Glucogenic/Ketogenic Imbalance directly involves a breakdown in the communication line between the liver and adipose tissue. Both the Glucogenic & Ketogenic sides of this Imbalance show difficulty in regulating mobilization of fats for energy production, and storage of calories as fats.

The overall clinical picture involves a breakdown of critical communication lines including:

- the liver-adipose axis
- the liver-microbiota-gut axis
- the adipose-microbiota-gut axis
- the liver-pancreas axis
- the liver- muscle axis
- the liver-hypothalamus axis
- the liver-autonomic (Sympathetic/Parasympathetic) axis

The nutrition regimen Nutri-Spec recommends for G/K Imbalances shows a departure from what has been a decades-long Nutri-Spec position against megadose supplementation. The research shows unequivocally that deficient liver function associated with MAFLD can be well-supported with supplementation, but the supplementation required is definitely at a megadose level. Particularly vitamin B3 as Niacinamide, and vitamin B1 as Benfotiamine, are required in large doses to nutritionally support healthy liver function.

Only you, with your NUTRI-SPEC testing and supplements, hold the key to reversing the G/K physical, mental, and emotional depletion. You can take patients who crave only sugar – and awaken their hunger for real life. You can take people who only make it through the day on coffee, tea, cola and chocolate – and empower them with real energy. You can take people who can only cope if they lean on anti-depressants, alcohol or nicotine – and move them out from under their dark cloud.

How many low vitality patients do you have? How many people do you know who are the victims of their life rather than the power in their life? Grab these people and give them a push with NUTRI-SPEC. Correcting Glucogenic/Ketogenic (along with the rest of the Five Fundamental Imbalances) is the only way to put the wind back in their sails.

Glucogenic and Ketogenic Energy Production

Glucogenic/Ketogenic balance represents a dualistic, diphasic model of oxidative energy metabolism. When this system is functioning normally, healthy individuals can cycle freely between the Krebs Cycle, the beta oxidation pathway and pentose phosphate energetics as dictated by their circumstances. Under normal variations in physiological demand there are times when glucogenic energy production is more desirable, and times when ketogenic energy production is more efficient. Your Glucogenic/Ketogenic patients have lost their ability to selectively utilize the most appropriate energy production pathway.

Just what is meant by the terms "glucogenic" and "ketogenic?" What exactly is happening?

We have used the analogy of an engine not firing on all cylinders. In a Glucogenic patient the misfiring cylinders relate mainly to fat metabolism; in a Ketogenic patient the cylinders not firing mostly relate to carbohydrate metabolism. So, Glucogenic and Ketogenic patients both have **deficient oxidative energy metabolism**. The Glucogenic patient has difficulty getting into the beta oxidation metabolic pathway, while the Ketogenic patient has difficulty getting into the Krebs Cycle. The Glucogenic patient is over-dependent on glucogenic means of energy production, while the Ketogenic patient is over-dependent on ketogenic metabolic pathways.

Your clinical objective in treating your Glucogenic patients with specific NUTRI-SPEC supplements and dietary recommendations is to improve their quantity and quality of energy production by pushing them into beta oxidation of fats and ketogenic amino acids. Similarly, your goal with your Ketogenic patients is to push them into the Krebs Cycle for greater quantity and quality of energy production.

THE RANDLE CYCLE (The Glucose-Fatty Acid Cycle)

The Randle Cycle (The Glucose-Fatty Acid Cycle) explains the relentless competition between Glucose and free fatty acids (FA) for uptake and oxidation in your muscles, adipose tissue, brain, liver, and pancreas. You can visualize the Randle Cycle as "Dr. Randle" having the last word in regulating the selection of either Glucose or FA as the preferred energy substrate, thus ultimately exercising control of Mitochondrial energy production in the Electron Transport Chain (ETC). As the supreme regulator, Dr. Randle is on duty hour after hour, choosing one or the other fuel to feed your metabolic fire burning in the Mitochondrial energy factory of every cell. Will he give your brain enough Glucose? Will he allocate enough FA to feed your muscle energetics?

The supply and demand of Glucose and FA involves a fine-tuning of metabolic energy pathways, leading ideally to maximally efficient oxidative phosphorylation (OXPHOS) along the Electron Transport Chain. That fine and final control is beyond, and can supersede, the coarse control exerted by your hormones (epinephrine, Insulin, cortisol, and glucagon). The cycle involves particularly the interaction between your muscles and adipose tissue as Glucose and FA fight each other for entry into the various pathways of energetics.

The Randle Cycle demonstrates that the exclusive utilization of one substrate thoroughly inhibits the use of the other, and does so independently of Insulin & glucagon hormonal regulation. It represents a survival adaptation to unpredictable nutrient availability, and establishes a close inverse relationship between adipose tissue and muscle tissue energetics, with the liver as the intermediary. The hormones and enzymes that control tissue Lipolysis also control circulating concentrations of FA, and FA in turn, control fuel selection in muscle.

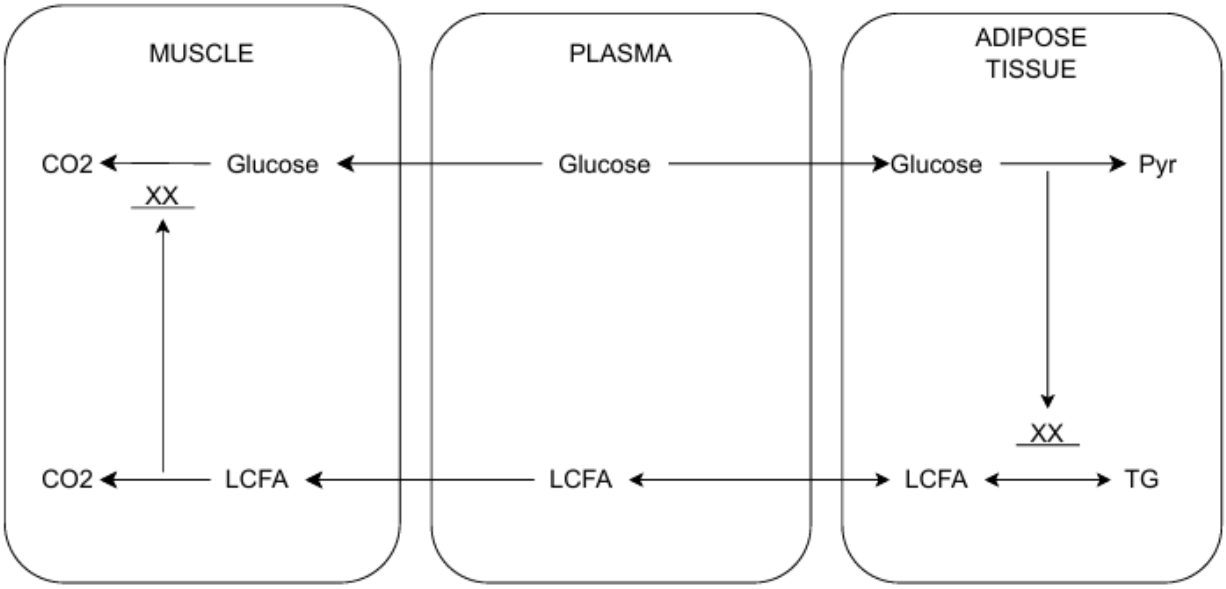
Such is the description of the Randle Cycle as an anthropologically-derived means by which humans adapt to inconsistent availability and quality of food. But modern dietary imbalances provoked by grotesque quantities of food, along with poor quality (particularly the consumption of the two major anti-metabolites, (polyunsaturated oils and fructose sugars), exceed adaptative capacity. In many individuals, Dr. Randle is overwhelmed, struggling to maintain energetics.

All the "diseases of aging" begin early in life, and are associated to some degree with "I just don't have enough energy" (both metabolically and subjectively) to meet the stresses of life.

The Randle Cycle is all about efficient use of scarce resources. Human metabolism never forgets that there are times when carbohydrate foods simply cannot be found; there may be environmental conditions when good saturated fats are impossible to find; in an unpredictable environment, sometimes Glucogenic or Ketogenic amino acids are unavailable.

As adaptation to scarcity, human energetics has become keenly focused on using the most efficiently burned fuel from moment to moment. Which fuel is ideal depends largely on whether a given cell is being called upon for high metabolic activity, whether it is metabolically quiescent at the moment, or whether it is in a stage of rest, repair, and rejuvenation. The cell will not waste precious fatty acids when carbohydrates are the ideal fuel of the moment; it will not squander Glucose, when supply of Glucose may be already running low. When metabolism is functioning optimally, it is because Dr. Randle has the situation completely under control.

Figure 1



Look at **Figure 1**. This represents the Randle Cycle as it operates healthfully from moment to moment, hour by hour, day by day in all cells.

You see in the center section that the plasma contains both Glucose and Long-Chain Fatty Acids. (LCFA). How did they get into the plasma, and where are they going?

The Glucose in the plasma may have come from a recent meal, or it may have been released into the blood from the liver via Gluconeogenesis.

And the fatty acids? They may have come from a meal, or they may have been mobilized from the liver, or more likely mobilized from adipose tissue.

Where are they going? Look at the arrows …

If the fatty acids came from the liver, they may be either heading toward adipose tissue for either energy production or storage there, or, may be going the other way, fulfilling their mission to supply an energy substrate for muscles.

The Glucose, just as the FA, is just as happy to follow the arrows in either direction --- to provide energy for adipose tissue, or be converted to fat there via Lipogenesis, or, it may be destined to energize muscles.

Observe in **Figure 1** as Glucose enters the muscle. It is fully intent on being energetically converted to carbon dioxide, after producing energy as ATP. But, if Dr. Randle decides that right now this muscle cell will more efficiently burn fatty acids for energy, he will push forward the FA pathway, as FA are equally intent as Glucose is on being burned into carbon dioxide in producing ATP.

Simultaneously, he slams the door on Glucose energetics (as the arrow hits **XX**). In this cell, at this moment, fatty acids rule. Dr. Randle stops Glucose in its tracks, and in some cases (as you will learn below) even kicks it out of the cell, back into the plasma.

Now look at the Glucose molecules that enter adipose tissue. Suppose Dr. Randle gives his full endorsement to Glucose energetics. At the same time he sees FA trying to assert themselves as an energetics substrate. "Oh no you don't!" Randle exclaims. He smashes the OFF switch to fatty acid metabolism. He blocks the Lipolysis of Triglycerides into fatty acids, no matter how strongly they beg to be released into the plasma to support the fatty acid energetics of other cells.

So, what **Figure 1** illustrates is the Randle Cycle as it operates in a perfectly healthy individual consuming a perfectly healthful diet. It is important to understand that the Randle Cycle is not a "problem" or a Metabolic Imbalance in any way. It is how human beings are designed to function most productively in a natural environment, on a diet marked by scarcity, as (was!) commonly found in that natural environment.

Picture the Randle Cycle not so much as a cycle but as two sides of the same coin. That coin should achieve perfectly efficient cellular energetics using the superior fuel, Glucose or FA, ideal at that moment, for each tissue type — brain, muscle, liver, etc. But Dr. Randle, even though he has his PhD in Biochemistry, too often "flips out" when confronted with the stresses of gluttonous or anti-vital eating. In many of your patients, the coin flips out of control, landing with either the Glucose or the FA side up, and the other side deficiently responsive thereafter. The resulting cellular energy deficit invariably results in patho-physiology, and eventually, chronic disease.

One side of the coin that we can call a Ketogenic Imbalance, is an excess dependence on FA energy production through Beta-Oxidation, which severely inhibits the uptake and utilization of Glucose.

The flip side of the coin, which we can term a Glucogenic Imbalance, represents an increased uptake of Glucose (in parallel with the action of excess Insulin). But in this energetics imbalance the flow of Glucose is more than the cell can handle, such that the excess use of the Glucose energetics pathways inhibits FA oxidation. That excess Glucose can be diverted into the production and storage of fats, in the form of both Triglycerides and Cholesterol.

Both sides of the coin are indications of Insulin Resistance, though by somewhat different mechanisms, which may ultimately lead to Type 2 Diabetes. Typically, your patients with Ketogenic Imbalance will show gradually rising blood sugar beginning as early as the teen years and progressing throughout adult life.

In contrast, the Glucogenic Imbalance will tend to show frequent bouts of reactive hypoglycemia (rapidly falling blood sugar, even though it may never reach absolutely low levels), until at some point there is pancreatic beta-cell exhaustion, and the blood sugar tends to rise, and hyperglycemia progresses from that point on.

Consider the FA-dominant side of the Randle Cycle. Ketogenic inhibition of Glucose utilization is a form of Glucose intolerance and Insulin Resistance that, when chronic, causes an impaired capacity of Insulin to increase Glucose uptake by both muscle and adipose tissue. That impairment is accompanied by increased adipose tissue Lipolysis and increased hepatic Glucose production via Gluconeogenesis.

The biochemical mechanism by which FA oxidation inhibits Glucose utilization in muscle (= Ketogenic Imbalance) was fairly well elucidated by research done decades ago (Randle introduced the term "Randle Cycle" in the 1960s). But the flip side, the inhibition of FA oxidation by Glucose (= Glucogenic Imbalance), was much more difficult to explain. There is an inhibition of adipose tissue Lipolysis by the presence of excess Glucose and Insulin. The mechanism of that inhibition

involves over-stimulation of Glucose uptake along with its re-esterification in the liver into Triglycerides and Cholesterol globules.

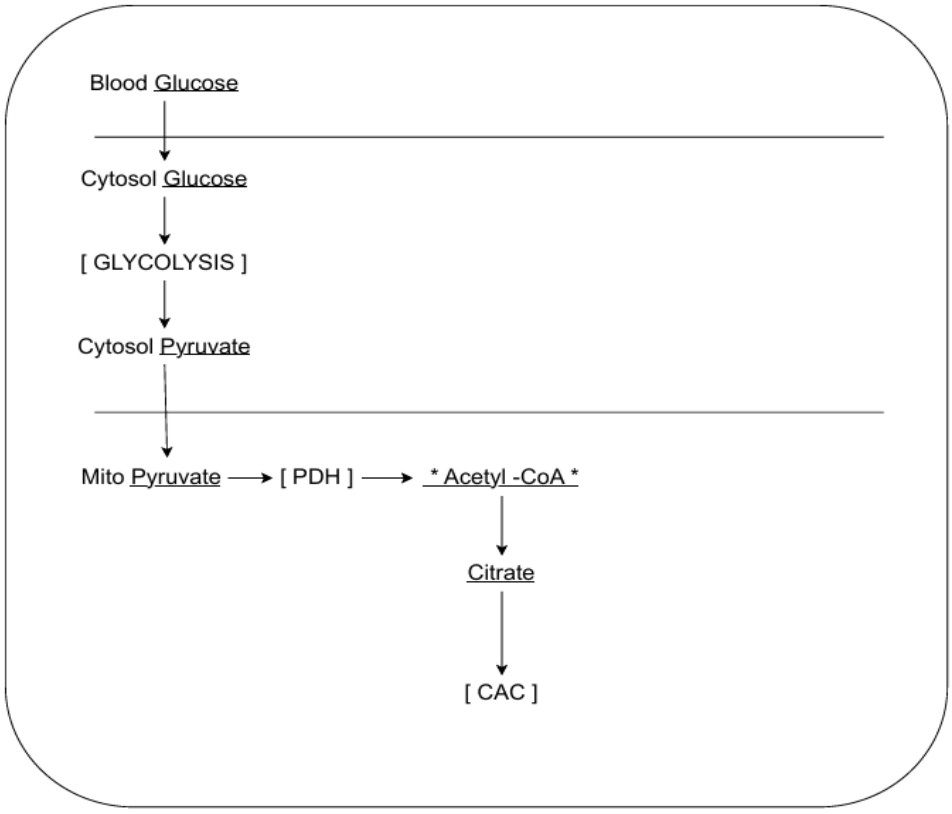
The Randle Cycle largely explains that the patho-physiology of dysregulated fuel metabolism associated with Insulin Resistance and ultimately Type 2 Diabetes can result from two opposite derangements – either Glucose dominance (= Glucogenic Imbalance) or FA dominance (= Ketogenic Imbalance). Similarly, patients with either Glucogenic or Ketogenic Imbalance will develop Metabolic-Associated Fatty Liver Disease (MAFLD) (which is a more accurate term than the outdated Non-Alcoholic Fatty Liver Disease (NAFLD)).

The controlling influence of hormones on Glucose vs. FA metabolism has been well-known for decades. In healthy energetics, the high Insulin/Glucagon ratio of the absorptive state (for several hours after a meal) promotes lipid and carbohydrate storage; in contrast, a high Glucagon/Insulin ratio, as characteristic of the fasting state, stimulates adipose tissue Lipolysis as well as hepatic Glucose production to preserve Glucose supply to tissues entirely reliant upon it for energy (e.g., the brain). But when the Randle Cycle is imbalanced, it will either exaggerate or inhibit those hormone influences.

KETOGENIC IMBALANCE: How does the metabolism of FA suppress the utilization of Glucose? The mechanism is easy to understand if you just picture the normal healthy use of Glucose for fuel.

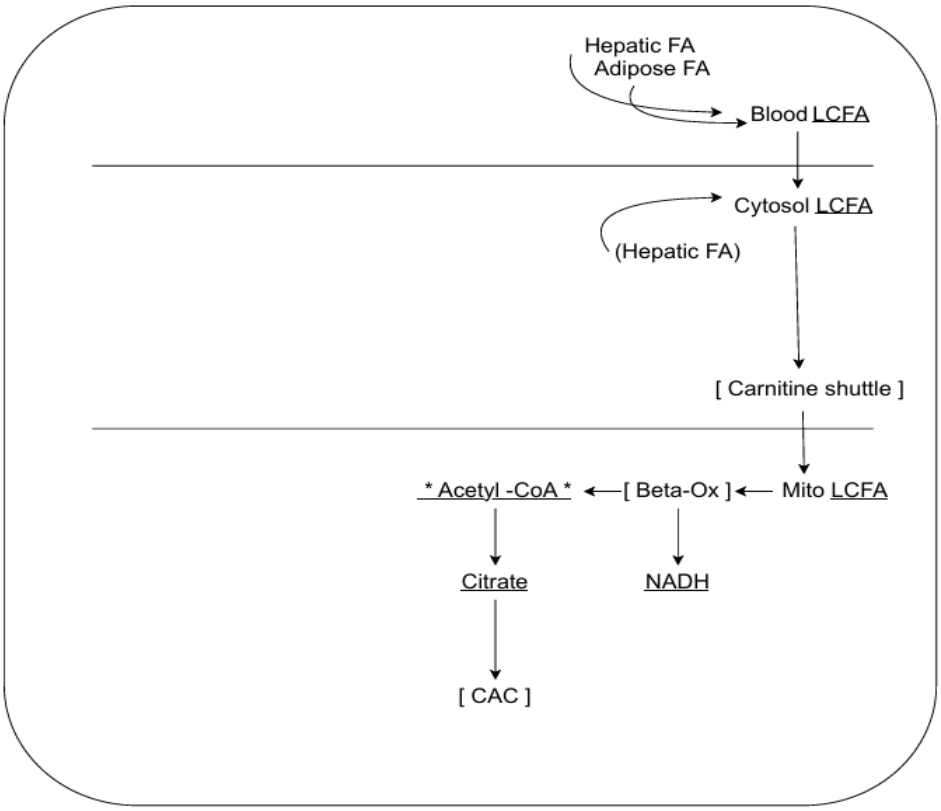
As you recall from your biochemistry course (years ago?!), Glucose is carried through the cell membrane into the Cytosol and flows right into Glycolysis. Follow the arrows in **Figure 2**, below. Glycolysis produces a little bit of ATP energy, but its main purpose is to break the Glucose down into Pyruvate, because it is Pyruvate that can penetrate into the Mitochondria and initiate the Citric Acid Cycle (CAC).

Figure 2



As you see as you follow the arrow from Mito Pyruvate to the right, an enzyme in the Mitochondria, PDH (Pyruvate De-Hydrogenase), converts the Pyruvate to Acetyl-CoA. The Acetyl-CoA flows right into Citrate, the first step of the Citric Acid Cycle. The CAC produces NADH, which then flows into the Electron Transport Chain (ETC), resulting in OXPHOS (Oxidative Phosphorylation), producing the bulk of the ATP for energy.

Figure 3

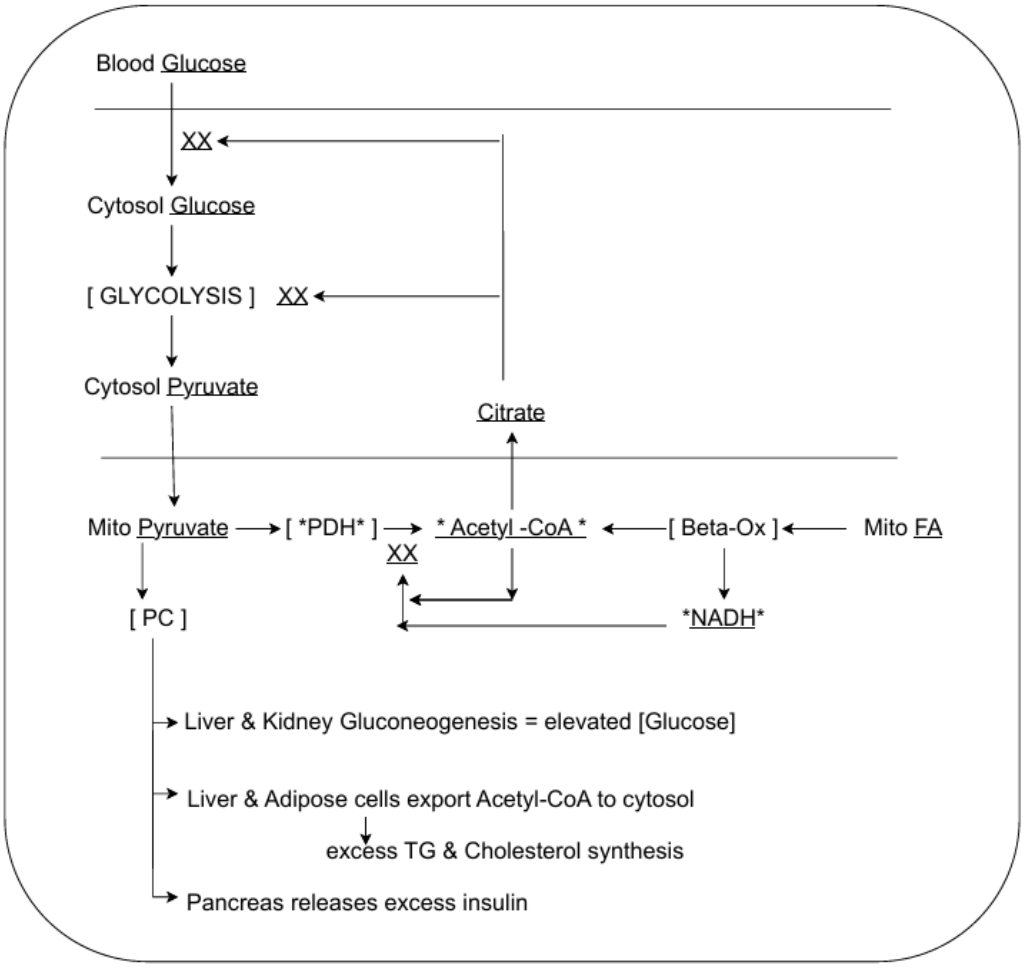


But in a Ketogenic Imbalance, that energetic flow is disrupted by the Randle Cycle inability to access Glucose energetics. FA are all that is available for energy production. Follow the arrows in **Figure 3**. FA are carried into the Cytosol where they are converted to a form that can then be carried by Carnitine into the Mitochondria. There, the FA undergo Beta-Oxidation to produce Acetyl-CoA. In a state of health, this Acetyl-CoA behaves just the same as the Acetyl-CoA derived from Glucose metabolism and enters the CAC.

However, with the excessive Beta-Oxidation of a Ketogenic Imbalance, there is a buildup of too much Acetyl-CoA and NADH, which blocks the energetic pathways of Glucose utilization in three places. For the first of those 3 blockages, look at the FA side of **Figure 4** --- where Beta-Ox is producing excess Acetyl-CoA & NADH. Follow the arrows from excess Acetyl-CoA and NADH and note how Dr. Randle uses these to block the conversion of Pyruvate (which came from Glycolysis of Glucose) to Acetyl-CoA by PDH. Inhibiting the enzyme PDH results is excess Pyruvate accumulating in the Mitochondria.

What happens to this buildup of Pyruvate that is blocked from moving toward CAC energy production? Look at the arrow down from Mitochondrial Pyruvate, representing its alternative pathway. Pyruvate is acted upon by the enzyme PC (Pyruvate Carboxylase), which allows the Pyruvate to flow into a CAC, not systemically, but only in certain tissues for specific potentially harmful functions, including (follow the arrow down to its 3 destinations) …

Figure 4



First, PC activates Gluconeogenesis in the liver and kidneys to maintain blood Glucose in the post-absorptive state, which can result in elevated blood sugar.

Second, in adipose tissue, the PC potentiates Lipogenesis, by exporting Acetyl-CoA from the Mitochondria into the Cytosol, where it is directed into excess synthesis of Triglycerides.

Third, in the pancreas, the PC potentiates "Pyruvate Cycling", which generates NADPH and other signaling molecules that stimulate Glucose-induced Insulin release, and potentially raise blood Insulin.

Summarizing the first of 3 mechanisms by which excess Beta Oxidation of fatty acids blocks Glucose energetics: Ketogenic Imbalance inhibits PDH of the Glucose energetic pathway, which allows excess Pyruvate to accumulate in the Mitochondria, thus over-activating PC action on the excess Pyruvate. The anti-metabolic effects include: inadequate energy from Glucose, elevated blood sugar, elevated blood Insulin, elevated Triglycerides in adipose and liver tissue and in the blood.

The second mechanism by which the excess Acetyl-CoA and NADH derived from Beta-Oxidation of FA blocks Glucose energetics involves an excess buildup of Citrate. Under normal energetics, Acetyl-CoA is converted directly to Citrate to enter the Citric Acid Cycle (as shown by the arrow down from Acetyl-CoA to Citrate in **Figures 2 & 3**). But when Beta-Oxidation results

in elevated Acetyl-CoA and NADH, the Citrate builds up in the Mitochondria and leaks back into the Cytosol, as illustrated in **Figure 4** by the arrow up from Acetyl-CoA to Citrate in the Cytosol.

From this excess Cytosol Citrate you see an arrow up into Glycolysis, blocking Glycolysis enzymes. Dr. Randle's inhibition of Glycolysis prevents Glycolysis from flowing through to Pyruvate and entering the Mitochondria for CAC energetics. (Instead, the blocking of Glycolysis results in the buildup of glycogen.)

The third mechanism by which Beta-Oxidation blocks Glucose energetics also results from the excess Citrate backed up into the Cytosol. Follow the arrow from Cytosol Citrate all the way up to the cell membrane. Citrate inhibits Glucose uptake into the cell via the Glucose transporters GLUT4 and hexokinase. So, you have now seen there are 2 ways the Randle Cycle blocks Glucose energetics before the Glucose pathway even reaches the Mitochondria. "Fatty Acids Rule".

Since the impairment of Glucose energetics by FA in a Ketogenic Imbalance is immediately devastating to health, activation of more Glucose utilization with a lower fat, higher carb diet (to remove the PUFA burden on Dr. Randle) clinically provides one means to regain cellular energetics.

Emphasis on the deleterious effects of PC as Pyruvate moves down the Glucose-deprived pathway: PC enzyme is critically important in coordinating Gluconeogenesis in the liver and kidneys, and in the balance between Lipogenesis and Lipolysis in adipose tissue, and in pancreatic Insulin release. In over-nutrition (particularly over-eating of fats, and especially PUFA) PC is increased in the pancreas to increase Pyruvate Cycling in response to chronically elevated liver and blood Glucose. In contrast, PC action in the liver is decreased by Insulin. During periods of over-nutrition, adipocyte tissue is expanded (= Tubby Tummy) with extreme expression of PC and other lipogenic enzymes in Ketogenic individuals.

In Ketogenic Imbalance patients there will be a significant deficiency of cellular energy. What little metabolic fire that does burn is very inefficient. The patient will typically show:

- a very low Respiratory Quotient, with low Carbon Dioxide production

- deficient ATP production

- excess conversion of Citrate into cellular fat (both in the liver and in adipose)

- high serum Triglycerides and Cholesterol

- steadily rising blood Glucose

This tendency to insufficient Glucose energetics is exacerbated by excess consumption of dietary fat, but of polyunsaturated fatty acids (both omega-6 and omega-3) in particular.

There is often also a hormonal component that predisposes to FA dominance, involving elevated Cortisol Stress and Estrogen Stress (and often a deficiency of the hormones that oppose Cortisol and Estrogen, including Testosterone, Thyroid, Progesterone, Pregnenolone, and DHEA).

GLUCOGENIC IMBALANCE: Now consider the "sweet" side of the Randle Cycle — the limiting of FA oxidation by Glucose.

By what mechanism does Glucose block FA oxidation in the liver, muscles, and other tissues? What is the metabolic breakdown in your patients with Glucogenic Imbalance?

PC enzyme is also a factor in this flip side of the Randle Cycle, the impairment of FA energetics. A deficiency of PC (the opposite of the excess PC activation needed to deal with

Pyruvate buildup in a Ketogenic Imbalance) causes excess Pyruvate conversion to Lactate. The Lactate can rise even to the point of Lactic Acidosis.

Under normal conditions, any excess Pyruvate is shunted into Gluconeogenesis by the PC-mediated conversion of Pyruvate. But in PC deficiency, excess Pyruvate is converted to Lactate instead. Since a key role of Gluconeogenesis is maintenance of blood sugar, deficiency of PC enzyme can lead to hypoglycemia.

Individuals on the Glucogenic side of this energetics imbalance not only need to avoid over-nutrition, particularly overeating on sugar/fructose, but must include in their diet or their supplementation regimen the catalysts that enhance PC function. Most important is Biotin. Other catalysts include Manganese, Zinc, and Magnesium.

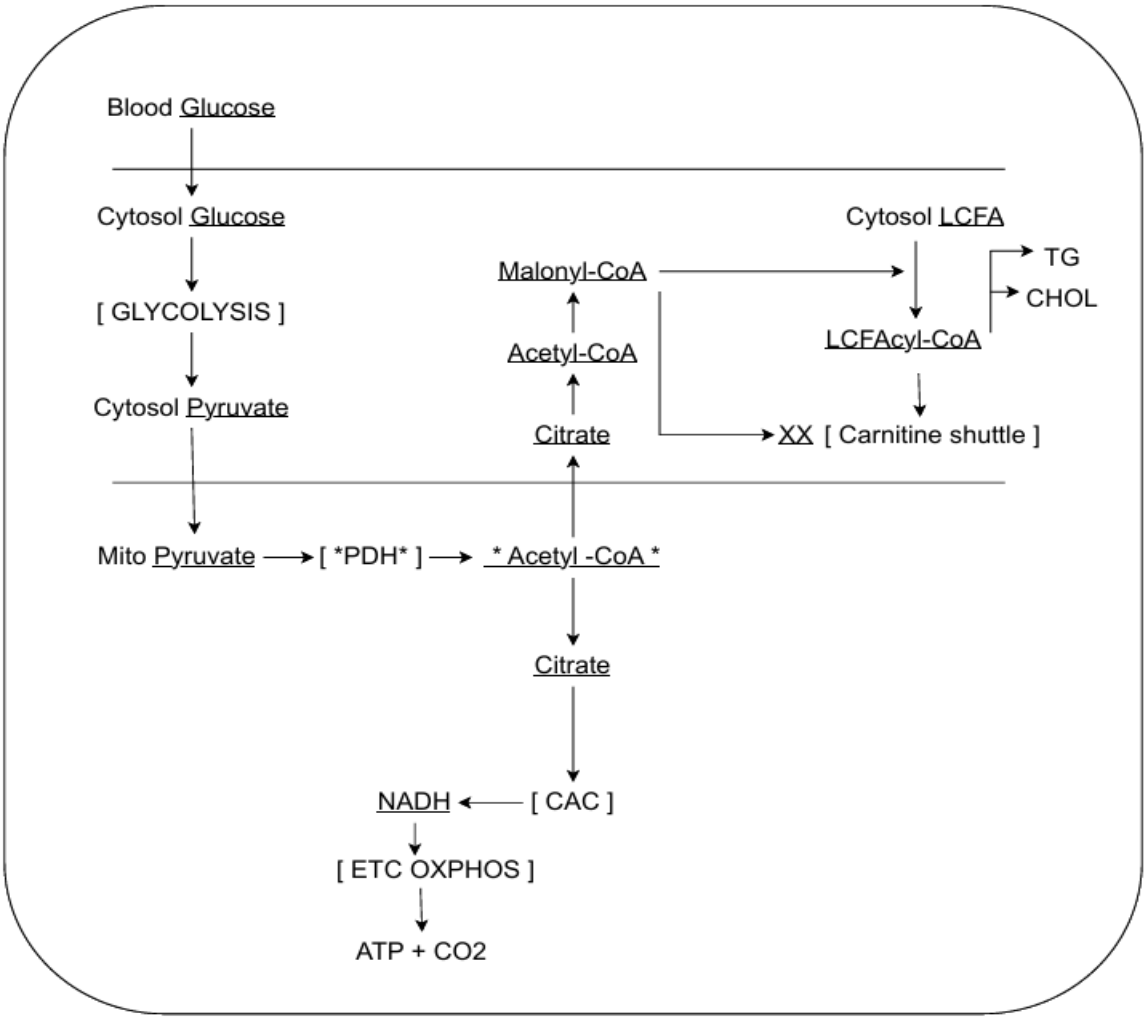
L-Carnitine can be an essential supplement for those with Glucogenic dominance. Carnitine is beneficial by several mechanisms. Carnitine's primary role is to carry FA into the Mitochondrial matrix for Beta-Oxidation to Acetyl-CoA. So, in that sense, Carnitine improves the efficiency and quantity of FA metabolism, thus flipping the Randle Cycle away from Glucose dominance.

However, the long-term effect of Glucose dominance is not only the inhibition of FA oxidation but a diversion of carbohydrate metabolism away from energy production and into lipid storage. Now, the Glucogenic individual is deprived of energy from FA metabolism but also intermittently deficient in Glucose energetics. Carnitine improves Insulin sensitivity and elevates Pyruvate De-Hydrogenase (PDH), which redirects Glucose down its energy production pathway and away from glycogen and fat storage. Carnitine buffers excess Acetyl-CoA away from the Mitochondria.

By improving and balancing liver function, Carnitine decreases the enzymes that indicate liver damage, ALT and AST, in patients with Metabolic-Associated Fatty Liver Disease. Carnitine causes decreased hepatic fat storage.

Refer to **Figure 5**: Any increase in blood Glucose, as after a meal in which carbs outweigh FA, stimulates Cytosol uptake of Glucose, particularly in the liver. Following the arrows down, you see the Glucose zips right through the Cytosol Glycolysis, happily producing huge quantities of Pyruvate, which glides right into the Mitochondria. Following the arrow to the right, you see PDH enzyme converts the mitochondrial Pyruvate into Acetyl-CoA, which (since there is no obstruction from excess Ketogenic FA Beta-Oxidation, and, as you see by the arrow down from Acetyl-CoA) flows right into Citrate and the Citric Acid Cycle.

Figure 5



The CAC produces NADH, triggering the Electron Transport Chain OX- PHOS. The cell dances with high energy. That same process occurs in tissues other than the liver, with the help of physiological quantities of Insulin. This is indeed the sweet side of Dr. Randle's Cycle.

At its highest efficiency (= with Dr, Randle at the controls), this Glucose-burning pathway can enhance its own action by clamping down on any intrusion by FA metabolism. The mechanism involves some of the Citrate derived from Glucose being shuttled back into the Cytosol (as shown by the arrow up from Acetyl-CoA in **Figure 5**), and reversed into Acetyl-CoA there. The Cytosol Acetyl-CoA then produces Malonyl-CoA. This is a neat little trick because Malonyl-CoA (follow the arrow down) blocks the action of Carnitine to carry FA into the Mitochondria. Glucose reigns supreme.

However, Dr. Randle must be careful to remain ever watchful. While the Glucose-derived Malonyl-CoA prevents futile and harmful oxidation of Cytosol fatty acids, it also favors (follow the arrows far to the right of the flow chart) FA esterification into Triglycerides and Cholesterol. When these FA are rerouted into esterification, we have one mechanism for Metabolic-Associated Fatty Liver Disease.

The Randle Cycle now becomes sickeningly sweet, as this process occurs not only in lipogenic tissues such as the liver and adipose, but also in the heart and skeletal muscles. This imbalance occurs in individuals in whom Glucose uptake is over-stimulated, either by excess Insulin, or by other mechanisms that drive patho-physiological Glucose metabolism in Glucogenic Imbalance (such as excess AMPK (Adenosine Mono-Phosphate Kinase) activation).

When this Glucogenic Glucose dominance exists chronically, the long-term effects become metabolically programmed, such that not only is FA oxidation inhibited, but the focus shifts toward Glucose storage into lipids rather than on Glucose oxidation for energy**. So in a sense, the end-result of Glucogenic Imbalance is similar to Ketogenic Imbalance, as both deprive the cells of Glucose entry into the Mitochondrial ETC to drive high energy OXPHOS.**

One way to conceive of the difference between Glucogenic and Ketogenic Imbalances, is that Ketogenic Imbalance is typified by a gross overutilization of FA energetics, which severely blocks Glucose utilization by 3 mechanisms, the most significant being suppression of PDH, with compensatory over-activation of PC.

In contrast, Glucogenic Imbalance is associated with incomplete and inefficient FA oxidation associated with PC deficiency, which elicits an attempted compensatory response by increasing Glucose uptake. The problem there is that the attempted Glucose utilization further blocks the already inefficient FA energetics. In both Glucogenic and Ketogenic Imbalances you see a deficiency of Glucose utilization as the most energy-efficient fuel.

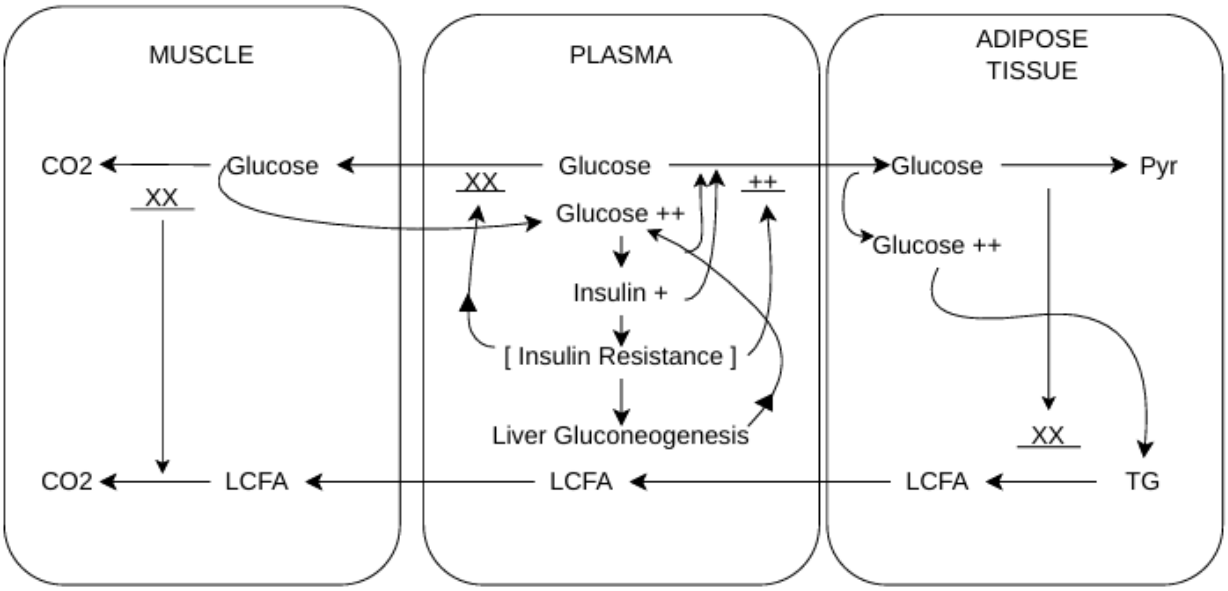
Our model of Glucogenic/Ketogenic Imbalance involves PC enzyme on both sides of the coin. The Ketogenic individual initially produces excess PC to handle the Pyruvate accumulation derived from Beta-Oxidation inhibiting PDH, thus blocking Pyruvate conversion to Acetyl-CoA. The excess PC activated in response to the elevated Pyruvate provokes Insulin release and promotes excess Lipogenesis.

But, in a later phase of Ketogenic Imbalance, chronically high Insulin causes Insulin Resistance, which in turn suppresses PC. The elevated Triglycerides and Free Fatty Acids now released by Lipolysis from adipose tissue further impair pancreatic beta-cell function and PC expression. This Phase 2 Ketogenic individual now shows elevated Glucose, elevated Insulin, marked Insulin Resistance, and elevated Triglycerides and Free Fatty Acids.

Ketogenic Phase 2 develops concomitantly with increasing Insulin Resistance. In Phase 1 the buildup of excess Pyruvate as PDH is inhibited causes a frantic over-activation of PC, with the resulting low energetics and specific strain on hepatocytes, adipose cells, and pancreatic beta cells --- all of which lead to Insulin Resistance.

In Phase 2, after years of steadily progressing Insulin Resistance, Insulin reaches a level that cripples PC. The increase in blood lipids, the Tubby Tummy, the load on the liver-adipose axis, the inability to burn FA, and the fatty deposits in the liver and muscles all accelerate, but by a somewhat different mechanism. Mitochondrial energetics of both FA and Glucose is limited; Metabolic-Associated Fatty Liver Disease is likely now medically diagnosable; Type 2 Diabetes and Metabolic Syndrome are just over the horizon.

Figure 6



Look at **Figure 6**, illustrating Ketogenic Imbalance after it has reached Stage 2 of somewhat advanced Insulin Resistance. The illustration is not as complex as it appears. To follow the arrows, begin at the very heart of the matter --- at Insulin Resistance as it appears in the middle of the PLASMA section. Follow the arrows from there …

First, note the arrow running from Insulin Resistance down to Liver Gluconeogenesis. The Gluconeogenesis excess pumps out rising Glucose, then, as you see, the arrow from Gluconeogenesis runs up to Glucose ++, indicating a major rise in hepatic cell Glucose. The most immediate effect of the increased liver Glucose is shown by the down arrow from Glucose to an additional increase in Insulin, which flows through to Insulin Resistance, then onto more Gluconeogenesis, which, as the arrow shows, continues an upward push on hepatic cell Glucose = a vicious cycle.

You also see arrows going up to the left and up to the right from Insulin Resistance. The arrow up to the left shows that Insulin Resistance blocks Glucose transport from plasma into muscle, thus further increasing blood Glucose. As a side note, look at the Glucose in the muscle cell. Since this is a Ketogenic Imbalance, Doctor Randall is blocking its energetic pathway. That same blockage of Glucose utilisation occurs in the liver cells themselves, which further causes their Glucose level to rise, leading to more Insulin and Insulin Resistance, thus potentiating the vicious cycle.

The arrow up to the right from Insulin Resistance shows not an **XX**, but rather a ++. The double + indicates that Glucose movement into Adipose Tissue is facilitated. The Glucose really has nowhere else to go since Insulin Resistance blocks its entry into muscle. Now you also see Glucose ++ in the Adipose Tissue. Follow the arrow from the elevated Adipose Tissue cellular Glucose. It points directly to increased Lipogenesis of Triglycerides = MAFLD.

In contrast to this Ketogenic Imbalance progression into PC exhaustion Phase 2, the Glucogenic individual is initially and always PC deficient. The Imbalance is exacerbated by a high fructose diet and by a high carb to protein ratio in the diet. The lack of PC activity causes accumulation of Pyruvate (just as high Pyruvate was typical of the Ketogenic individual), which can be subsequently converted to Lactate by LDH enzyme (= analogous to an Anaerobic Imbalance).

With inadequate PC, the elevated Lactate, along with glucogenic amino acids (which are deficient in an inadequate protein diet), cannot be converted to Oxaloacetate for entry into the CAC. With low Oxaloacetate there is inadequate Gluconeogenesis. That is one reason for the hypoglycemia common in Glucogenic individuals in its early stage.

Insufficient Oxaloacetate leads to liver failure to oxidize the Acetyl-CoA derived from Fatty Acids via Beta-Oxidation. The deficiency in Oxaloacetate also impairs CAC activity, affecting the various CAC intermediates needed for many biosynthetic pathways.

Over time, there also develops a later stage of Glucogenic Imbalance. Just as in Stage 2 of Ketogenic Imbalance, Stage 2 Glucogenic dominance eventually causes Insulin Resistance. HOW, you wonder, can an imbalance of Glucose energetics associated with falling blood sugar and inhibited hepatic Gluconeogenesis of Glucose develop into Insulin Resistance with its characteristic rising sugar levels? Your thinking is right on target --- it makes no sense --- except that there is another factor involved …

What happens to all those Cytosol LCFA in liver, adipose and muscle cells whose entry into Mitochondria blocked by Dr. Randle's use of the Malonyl-CoA trick to close the gate to Beta-Oxidation? As you have seen, much of the LCFA stuck in the Cytosol are synthesized into excess Triglycerides &/or Cholesterol. But the rest of those FA undergo pathological oxidation (= analogous to a Dysaerobic Imbalance). Ultra-destructive free radical damage ensues.

The long-held theory that Insulin Resistance results from decreased/insufficient Mitochondrial FA oxidation is now demonstrated to be inaccurate. It was hypothesized that unoxidized FA are inhibitors of Insulin signaling. However, more recent studies show that neither increasing nor decreasing FA metabolism induces or mitigates Insulin Resistance.

Now, the opposite theory has gained acceptance, namely, excessive rather than deficient FA oxidation is the culprit. In research models of metabolic overload (food intake unmatched by physical activity), lipid-induced Insulin Resistance occurs only when there is prior partial oxidation of FA, with an accumulation of incompletely oxidized lipid intermediates.

It is these accumulated incompletely oxidized fats, accompanied by the ROS (Reactive Oxygen Species) secondarily generated, that create the Insulin Resistance.

As our model of Glucogenic and Ketogenic Imbalances demonstrates, a dietary overload of either sugar (fructose) or fats (particularly polyunsaturates) will lead to continuous production of ROS, with damage to the Mitochondria and Cytosol. It is the ROS production that actually precedes the onset of Insulin Resistance, rather than resulting from it.

After Insulin Resistance develops in a Glucogenic Imbalance, you see that Stage 2 Ketogenic and Glucogenic Imbalances are remarkably similar. They both show …

- Insulin Resistance
- deficient PC enzyme
- rising Triglycerides &/ or Cholesterol (in the blood &/**OR** within cells)
- deficient energetics, with low CO2 & ATP production
- MAFLD
- ascending Type 2 diabetes ----- Metabolic Syndrome

By late-stage G/K Imbalance, a differential analysis can only be made with Nutri-Spec Metabolic Imbalance testing. ----- However, there is one surprising feature of Glucogenic individuals. Even after they have become Insulin Resistant, they can eat a surprisingly high amount of fructose without the blood Glucose spiking high --- and --- these individuals will still often suffer attacks of reactive hypoglycemia. Though the blood sugar never drops low, it can fall precipitously from moderately high to low normal. Weakness, dizziness, orthostatic failure, and brain fog can be episodic.

The Randle Cycle can be understood as the mechanism of what is called "Metabolic Flexibility", which is the ability to switch to and from FA and Glucose metabolism based on differences in food intake and changes in exercise level.

Some researchers suggest that Glucose intolerance and Insulin Resistance may be a protective mechanism developed to prevent Glucose toxicity. From the practical dietary perspective, the key to a proper diet plan for Ketogenic patients is to very definitely increase the carbohydrate intake, but it is absolutely essential that the increase in carbs be accompanied by an even greater decrease in dietary fat intake, with particularly strict avoidance of polyunsaturated oils.

It is interesting to note that both in fed and fasted states, it is the same molecule, Citrate, that creates the signal in the Cytosol. It signals to the Cytosol the ongoing Mitochondrial oxidation of either Glucose or FA. Rising and falling Citrate in the Cytosol keeps the cell continuously apprised of its need for either Glucose or FA.

The Clinical Picture in Glucogenic/Ketogenic Imbalances

How is the Glucogenic/Ketogenic deficiency in oxidative metabolism evident clinically? Far and away the most common symptom presented is fatigue. The next most common symptom is emotional duress of some type; and the third most common symptom is lowered resistance to infection. But, what are the objective clinical indicators?

The test results include:

- Breath Rate
- Breath Hold Time
- Pulse Rate
- Saliva pH & Urine pH
- Specific Gravity
- Low Body Temperature
- [Glucose]

What is it about these particular clinical entities that reveals the presence of Glucogenic/Ketogenic problems? Most of these tests relate specifically to three things:

- deficient oxidative energetics
- abnormal **carbon dioxide** levels
- abnormal serum pH

Here is a simple way to picture what is going on. If Glucogenic/Ketogenic means low energy production, what would you expect to find when you look for the normal end-products of energy production? Decreased energy would mean decreased **end-products** of energy production. And what is the major end-product of energy metabolism? **Carbon dioxide**. So, Glucogenic/Ketogenic patients, being low in energy production, tend to have low carbon dioxide levels in their blood, in the interstitium, and intracellularly.

Carbon dioxide is the major constituent of saliva determining its pH. That is why the adjusted saliva pH is the keystone of your Unified Acid/Alkaline Analysis.

Your Ketogenic patients are low in carbon dioxide both quantitatively and qualitatively. What we mean by that is they are quantitatively low in CO2 because of quantitatively low energy production. They are qualitatively low in CO2 because they are particularly deficient in carbohydrate energy production (which produces CO2 as its major end-product) and relatively high in fat metabolism (which produces very little CO2). The deficiency of carbohydrate metabolism also leaves Ketogenic patients with a somewhat elevated serum pH.

Your Glucogenic patients are, like Ketogenic patients, quantitatively deficient in CO2 because of an overall inadequate energy production. However, the Glucogenic patient is qualitatively high in CO2 because carbohydrate metabolism predominates over fat metabolism. The deficiency of fat metabolism in these Glucogenic patients leaves their serum pH somewhat decreased.

Because of the continuous compensation that Glucogenic and Ketogenic patients must make to their abnormal carbon dioxide and pH levels, there are no **absolute** generalizations that can be made with respect to their test results. Instead, it is necessary to define Glucogenic/Ketogenic Imbalances in terms of abnormal **ratios** of the saliva pH in comparison to the Breath Hold, Breath Rate and Pulse Rate (as per your Nutri-Spec Unified Acid/Alkaline analysis).

The detailed physiology behind these ratios is beyond the scope of discussion in this chapter. A complete explanation would include an in-depth look at:

- changes in Respiratory Quotient

- changes in hemoglobin's ability to carry carbon dioxide

- altered ability of hemoglobin to carry oxygen vs. delivering oxygen

- the changes in carbon dioxide fixation associated with changes in fatty acid levels in the blood

- changes in oxygen fixation associated with changes in sterol concentration in the blood

- renal loss of chloride ions

- the ability to handle pyruvic and Lactic Acids with enzymes such as pyruvate carboxylase

- AMPK (Adenosine Monophosphate Kinase) in liver-adipose axis communication

- Malonyl-CoA activity as a switching station between cellular Glucose & fatty acid energetics

- Long Chain Fatty Acid Acyl-CoA opening the gate to fatty acid energetics

- GLUT4 pulling Glucose into cells

- PPAR-alpha & PPAR-gamma as the Master Regulator of mitochondrial lipid metabolism

The beauty of the NUTRI-SPEC system is that you can effectively use all this physiology clinically without getting your PhD in biochemistry. (If you think you really must understand all these technicalities, feel free to write or call NUTRI-SPEC with your questions.)

Again, the adjusted saliva pH is critical in your Unified Acid/Alkaline Analysis because it is such a strong indication of aberrant CO2 plus carbonic acid levels. CO2 plus carbonic acid is, in turn, a direct indication of the patient's Respiratory Quotient – the direct indicator distinguishing whether the patient is metabolizing predominately fats or carbohydrate at the moment.

Also critical to your Unified Acid/Alkaline Analysis is the relationship between the Breath Rate and the Breath Hold Time. Add the Urine pH, and those 3 analytes give you a reliable indication of abnormal serum pH. (You will use these analytes again as you determine Acid/Alkaline Imbalances.)

The Specific Gravity reflects certain end-products of metabolism. Since the Glucogenic patient is weaker in fat metabolism than in acidic carbohydrate metabolism, while the Ketogenic patient is weaker in carbohydrate metabolism than in alkaline fat metabolism -- it follows that Glucogenic Specific Gravity tends to be higher than the Ketogenic.

There are several other common clinical findings in Glucogenic/Ketogenic Imbalances that are not part of your Unified Acid/Alkaline Analysis …

Blood sugar regulation is a critical problem in your Glucogenic/Ketogenic patients. Your Glucogenic patients are your classic reactive hypoglycemics. Their blood Glucose may never go extremely low, but the rapid rate of blood sugar drop can precipitate a hypoglycemic episode --- with extreme fatigue or weakness, and often brain fog. In contrast, Ketogenic patients are suffering from dysinsulinism, Insulin Resistance, and ultimately may develop Type II diabetes.

In the early Stage, before they become Insulin Resistant, your Glucogenic patients show extreme Insulin sensitivity. Sugar is very quickly pulled out of the blood stream to either be stored as fat or pushed through the Krebs Cycle to produce energy. Unless these patients have the capacity for a strong Sympathetic compensation to their Glucogenic Imbalance, their blood and brain sugar may sometimes crash.. There are seemingly no limits to the physical, mental, and emotional hypoglycemic symptoms these patients can experience.

Your Ketogenic patients have likely developed Insulin Resistance. Many of them produce tremendous amounts of Insulin in a desperate attempt to push the sugar out of the blood and into the tissues, but to no avail. The chronically high Insulin levels in these patients sets off a chain reaction of biochemical and endocrine disasters. Liver function is compromised; blood pressure begins to elevate (--- some studies estimate that more than 65% of all blood pressure problems are at least partly associated with elevated Insulin levels and poor glycemic control); balance is lost in many other hormone systems, and the patient begins to age prematurely.

One common finding in both your Glucogenic and your Ketogenic patients is ketones in the urine. Your Ketogenic patients tend to go into ketosis very easily because they are so deficient in carbohydrate metabolism that they are over-dependent on beta oxidation pathways that produce ketones.

The Glucogenic patient may also show ketones, but for the opposite reason. Glucogenic patients tend to be overly carbohydrate dependent for what little energy they can produce, and thus they tend to run a low blood sugar very quickly. It does not take much for the blood sugar to drop low enough that they struggle to inefficiently produce what energy they can from fat, thus going into ketosis.

So – Ketogenic patients can show ketones most anytime; Glucogenic patients will show ketones when in the post absorptive state, i.e. when they have not eaten in many hours or when their only food has been predominantly carbohydrate, which they either oxidize or store as fat very quickly.

The body temperature is low in both these imbalances for the simple reason that the metabolic rate of energy production is low. Thus, the production of body heat is low.

Bilirubin is also a common finding. Bilirubin in the urine is conclusive evidence that your patient's diet is either too low in protein and saturated fat, or too high in sugar (fructose) or polyunsaturated oils.

Finally, we cannot put enough emphasis on the connection between Glucogenic/Ketogenic Imbalances and emotional problems. Radical fluctuations in brain sugar levels as well as brain neuro-transmitter levels are typical of Glucogenic and Ketogenic patients. These fluctuations in brain function can be totally debilitating to certain individuals. Furthermore, the hormonal component of this pair of metabolic imbalances can trigger extreme depression or anxiety.

Excessive utilization of FA (as we see in Ketogenic, Dysaerobic and some Glucogenic Imbalances) results in an increase in the Mitochondrial NADH/NAD ratio, which is by definition a reductive (not oxidative) state, indicating inefficient OXPHOS energy production in proportion to the energy consumed by the metabolic pathway.

In summary: ROS production, and an elevated NADH/NAD ratio (indicating Reductive Stress) via Beta-Oxidation are typical of inefficient FA energetics. This inefficient energetics (particularly typical of Ketogenic and Dysaerobic Imbalances) is exacerbated by fasting and by excess calcium.

Weight Gain

Weight gain is common in both Gluco and Keto Imbalances. Both are marked by dysregulated Lipogenesis and Lipolysis. Both Glucose and FA tend to be stored as adipose rather than directed efficiently through the CAC and ETC to produce ATP and CO2. Surprisingly, the key to reducing fat deposition from inefficient Randle Cycle control is not the low carb, increased protein diet recommended by both doctors and dietitians.

In fact, the key to weight loss is increasing the percentage of calories from carbs (Glucose) relative to fat calories (and particularly deleting polyunsaturated fatty acids from the diet). Fasting as a means to increase “fat burning” is not only a failure, but counterproductive. Drugs purported to mobilize and metabolize fatty acids are also ineffective.

A study by Purnell confirms the importance of the Randle Cycle in controlling energetics and in benefiting glycemic control as well. Subjects on an ad-lib low fat, high carbohydrate diet lose weight and, therefore, may have even greater improvement in the metabolic disturbances of the Insulin Resistance syndrome. The primary causative role of dietary fat, via the Randle Cycle, in Insulin Resistance, is emphasized.

Hoehn, et al. shows that neither acute nor chronic upregulation of mitochondrial fatty acid oxidation has any net effect on whole body energy expenditure or weight loss. To illustrate: administering AMPK increases fatty acid oxidation, but that increase in “fat burning” results in zero change in energy expenditure, zero change in body weight, zero change in percent body fat, and does not prevent Insulin Resistance. The increase in FA oxidation is accompanied by an equal decrease in Glucose metabolism (as per the Randle effect), and so there is no weight loss.

The study confirms that the common weight loss diet plan decreasing carb intake and/or using various drugs or supplements to increase “fat burning” are of no benefit whatsoever. The only weight reduction comes from decreasing Caloric intake to create a negative energy balance.

Truswell's work demonstrated the benefits of a higher carb eating plan on restoring healthy blood lipids, even cases of extremely high cholesterol and Triglycerides. The only non-responders are those consuming sugar as an extraordinary percentage of carb calories.

In the first few weeks after an increase in dietary carbohydrates, there is a moderate increase in fasting Triglycerides but not Cholesterol. But over the long-term, the Triglycerides return to or near the original level. Elevated fasting Triglycerides are only observed in humans ingesting more than 35% of their calories from Sucrose, or greater than 20% from Fructose (since Fructose is more lipogenic than Glucose/Dextrose).

Furthermore, the elevation in Triglycerides from a high sugar diet generally occurs when there is also a high-fat intake. Even in individuals with Type 4 Hypertriglyceridemia, reduction in dietary carbohydrates is not recommended since that implies a higher percentage of energy from fat. Only in a certain percentage of subjects, reduction of high Fructose and Sucrose intake will lower Triglycerides. But the general statement can be made that high carbohydrate intake can be associated with lower plasma Cholesterol and often lower plasma Triglyceride levels.

Type 2 diabetics are those in whom the medical profession most rigorously enforces a low carb diet. Yet, Brunzell and Odell demonstrate that there is improved Glucose tolerance with high carbohydrate feeding, and that increasing the percent of carbohydrate compares favorably with the drugs prescribed for Insulin Resistant diabetics.

These studies confirm that research was done as far back as 1935 showing that reducing carbohydrate intake, which has long been standard medical advice for diabetic individuals, actually decreases carbohydrate tolerance. Conversely, increasing dietary carbohydrates, while maintaining constant calorie intake, actually improves carbohydrate tolerance. Many studies now show that carbohydrate tolerance is improved by increasing carb intake in both normal subjects and diabetics.

Brunzell et al tested both non-diabetic and diabetic individuals ranging from 91% to 163% of ideal body weight. All subjects ingested a balanced diet (as has been conventionally recommended by the medical paradigm) of 40% fat, 45% carbohydrate and 15% protein, vs. a high-carb diet of 85% carbohydrate, 15% protein and 0% fat. Fasting Insulin, fasting Glucose, and Glucose tolerance tests all significantly improved on the high-carbohydrate diet in both normals and diabetics, whether they were underweight or overweight.

The Magnitude of the Problem

You will find G/K to be the most common of the Five Fundamental NUTRI-SPEC Imbalances. However, many patients will test as having Electrolyte Stress or Anaerobic/Dysaerobic Imbalance superimposed upon, and perhaps hiding, a G/K Imbalance.

But, the fatty liver is there in perhaps half your adult patients, and the Metabolic-Associated Fatty Liver underlies all that ails them. The liver cannot efficiently access energy substrates for energetics, either quantitatively starving the mitochondria, or qualitatively creating a mitochondrial Electron Transport Chain that breaks down, producing toxic anti-metabolites. The liver and adipose tissue are not coordinated in mobilizing fatty acids for energy, yet may easily store dietary fatty acids in fat cells. Abdominal weight gain is an almost certain sign of fatty liver. Another indication of Glucogenic/Ketogenic Imbalance is hepatic diversion of sugars away from energetics and down the pathways to Cholesterol and Triglyceride production.

Do you have any patients who:

1. suffer from **fatigue**? You undoubtedly have countless patients who lack the power to meet the routine demands of life -- perhaps pushing themselves with stimulants.

2. are **under weight or over weight**? You could build an entire practice helping people achieve their ideal weight.

3. have **high or low blood sugar**? The typical American eats over 140 pounds of sugar per year. This works out to be (believe it or not) fully 20% of the caloric intake from sugar. No wonder most of your patients are riding the blood and brain sugar roller coaster with a fatty liver.

4. suffer from **anxiety** or **depression**? H elp these people get off their SSRIs and Benzo drugs!

5. are showing the effects of **premature aging**? The breakdown of body structure and function resulting from deficient mitochondrial energetics is evident in your patients in many ways – as fatigue, as joint deterioration, as memory loss, loss of muscle mass, loss of skin tone, loss of bone density, loss of libido, and the list is endless. Vital Reserves are depleted.

[Be aware that G/K Imbalance begins in childhood, even though testing children will most often reveal a more obvious Anaerobic/Dysaerobic Imbalance. When testing children, one modification of your Unified Acid/Alkaline Analysis is required: If the child's Exhalation Breath Hold is less than 2 0 seconds, then count it as 20 seconds.]

The inhibition of Glucose energy production and a dominance of the inefficient and somewhat toxic FA oxidation in either Glucogenic or Ketogenic Imbalance is an early feature of heart disease. Use of the word "toxic" in the literature describing FA dominance alludes to several anti-metabolic and inflammatory pathways. FA oxidation results in the production of Reactive Oxygen Species (ROS), which are responsible for oxidative free radical damage, and ultimately Reductive Stress and premature aging – via both the Exogenous Inflam-Aging and Endogenous Inflam-Aging pathways.

Furthermore, excess FA oxidation leads to the elevation of proinflammatory cytokines, as well as the inflammatory products of eicosanoid pathway production, including prostaglandins, leukotrienes, and thromboxane.

The severe abnormalities of carbohydrate metabolism, including diabetes, Cushing's Syndrome and starvation/fasting, are associated with high plasma concentrations of FA. This FA dominance (or as originally termed by Randle, "the fatty acid syndrome") shows that FA dominance or FA metabolic inefficiencies, create the state of Insulin Resistance.

Insulin Resistance is characterized by decreased Glucose uptake and abnormal lipid metabolism. It is the path to Type 2 Diabetes, the metabolic disorder associated with obesity, fat deposits in the liver, adipose and muscles, and many secondary inflammatory states, and eventual failure of pancreatic beta-cells. The relationship between Insulin Resistance and lipid deposits in tissues indicates that these lipids are both markers and mediators of metabolic dysfunction, especially in skeletal muscle. Exercise is the main means by which Glucose is disposed of.

Exercise and Glucogenic/Ketogenic Imbalances

Glucogenic/Ketogenic patients' mitochondrial energetics will improve much more quickly if they exercise intensely. Effective exercise will do much to stimulate the under-efficient metabolic pathways and to inhibit the over-reactive metabolic pathways. Conversely, the wrong form of exercise will greatly exacerbate these patients' fatigue.

Here is the story in a nutshell. Partial pressure of carbon dioxide (PCO2) is influenced by two things – by blood flow rate and by metabolic rate. Increasing the blood flow or decreasing the metabolic rate both have the effect of decreasing PCO2 of the interstitial fluid.

Now, think about this – both Glucogenic and Ketogenic patients have decreased metabolically produced CO2. Anything that further decreases PCO2 in these patients makes them feel rotten. This explains why so many Glucogenic/Ketogenic patients tend to be such slugs – moaning and groaning at even the thought of physical activity. Part of the reason may be that the increased blood flow and the increased Breath Rate blow off of CO2 **as physical activity is initiated** briefly further decreases the already too low PCO2 in these patients.

If you can get these patients off the couch long enough to do some exercise intense enough to increase energetically-produced CO2, you will give them a **double** shot of vitality – the exercise increases the CO2 levels short term as the immediate mitochondrial effect of the exercise itself, **plus**, a regular exercise program increases the CO2 long-term by increasing the metabolic rate.

There is more. You must be very specific in your exercise recommendations for these patients. Only high-intensity, short-duration exercise will maximize the metabolic response to a regular workout regimen. A combination of sprint interval training and heavy strength training will yield a persistent elevation of metabolism and CO2 production. Low-intensity, long-duration exercise will only further decrease glycemic control, and disastrously, further slow the metabolic rate.

Low intensity, long-duration exercise is perceived by the hypothalamus and brain stem as a relentless stressor. The physiological survival protective mechanism is pushed into defensive mode. Metabolic control centres sense that if the punishment does not let up, there will be a long-term disaster. So to conserve vitality, metabolism is deliberately slowed. The thyroid in particular is inhibited, and all mitochondrial energetic pathways are down-regulated.

The slower metabolic rate is adopted as the new normal. The individual becomes ever more physically and mentally sluggish, and the increasingly deficient cellular energetics accelerates the ageing process. One particular adaptation is the conversion of fast twitch Type 2-B muscle fibres into slow twitch Type A fibres. That is a devitalizing degeneration that happens as part of the typical ageing process anyway, and now the low-intensity, long-duration exercises such as jogging, treadmill self-abuse, and all the other health club counterproductive "cardio" equipment accelerates the loss of Vital Reserves.

One fascinating benefit of exercise <u>of sufficient intensity</u> (NOT long-duration!) is that it acts as a "peacekeeper" in the battle between Glucose and FA. Essentially, <u>exercise increases AMPK</u> (Adenosine Mono-Phosphate Kinase) in skeletal muscle tissue, which in effect disarms both the Randle Cycle Glucose inhibition of FA, and the FA impairment of Glucose.

Thus, in response to high-intensity, short-duration exercise, both sides of the Randle Cycle operate maximally and in perfect balance. AMPK overrides any Glucogenic or Ketogenic Imbalance. However, the AMPK capacity to improve Glucose oxidation even in the presence of Glucogenic or Ketogenic Imbalances is diminished by a high-fat diet, or by any significant intake of polyunsaturates, or by fasting.

In cardiac and skeletal muscle, inhibition of FA energetics by Glucose also implies an upregulation of Glucose uptake. That process is demonstrated by infusing Glucose before exercise. The acute exposure to Glucose causes Hyperinsulinemia and inhibits FA oxidation.

But some degree of FA utilization is essential under the stress of (non-physiological, anti-metabolic) prolonged exercise. However, metabolism-enhancing intense exercise demands that muscles decrease FA oxidation and increase Glucose utilization during the high energetic output.

So in that sense, infusion (or ingestion) of Glucose before exercise (especially in Ketogenic individuals) can be beneficial, particularly for high-intensity short-duration exercise**.**

In the absence of intense exercise-induced energetic demand, flooding the Randle Cycle with dietary Glucose on top of excess dietary FAs causes considerable damage to Mitochondria already in an Ketogenic FA-dominate state. The increased Glucose load force-feeds electrons from Glucose into the ETC, which is already inhibited by FA dominance. The excess calorie supply, not matched by energy demand, will exacerbate the back-up of electrons in the Electron Transport chain, and result in massive ROS production and Mitochondrial damage. The beneficial effects of physical activity and muscle exercise protect Mitochondria from such damage.

Consider now the benefits of high-intensity exercise (NOT fitness industry contrived "cardo" workouts on maintaining and regaining heart health, and how myocardial capacity relates to the Randle Cycle …

To illustrate, the healthy heart at rest predominantly relies on Mitochondrial oxidation of FA (60-90%) and of Glucose and Lactate (10-40%) for the generation of ATP. But as per the Randle Cycle, the contribution of each substrate to cardiac ATP production varies to an extreme depending on exercise, diet, and fasting.

In heart failure, this metabolic flexibility is compromised and in the failing heart, the ability to oxidize FA is decreased, while the glycolytic conversion of Glucose to Lactate increases (= Anaerobic Imbalance). But the shift toward Glucose energetics is an attempted compensation that actually results in greater inefficiencies/deficiencies of FA energetics. In essence, the failing heart is "energy starved". The levels of both ATP and creatine phosphate are chronically low.

The failing heart ultimately ends up demonstrating the Warburg Effect, with excessive reliance on Glucose producing Lactate and a very small amount of ATP via Glycolysis --- rather than going through the entire CAC and ETC to produce large quantities of ATP through OXPHOS. This Anaerobic Imbalance, the increase in Glycolysis and its partial uncoupling from Glucose oxidation during cardiac hypertrophy and failure, are indications of the Warburg Effect (glycolytic Lactic Acid-producing "cancer metabolism") occurring in the diseased heart.

Anerobic Glycolysis is one part of attempted compensation by a failing heart, and another is directing energetics through the Pentose Phosphate Pathway as an attempt to maintain essential protein synthesis in heart cells.

The diversion into the Pentose Phosphate Pathway is also typical of cancer metabolism, the same pathway by which cancerous cells proliferate via nucleotide synthesis. It may be that the increase in Glycolysis and diversion into the Pentose Phosphate Pathway are more to support cardiac anabolic processes (attempts in repair and regeneration) instead of sustaining energy metabolism.

While AMPK stimulation by exercise overrides Randle Cycle imbalances in muscle tissue, epinephrine achieves the same effect in the heart. A healthy epinephrine stress response (not overdone and not prolonged enough to create a chronic condition of Sympathetic Imbalance adrenergic stress) inactivates the antagonistic mechanisms that Glucose and FA express toward one another. Heart muscle energetics is improved. Particularly, the ability of FA to suppress Glucose is blocked and the increase in heart function introduced by epinephrine is sustained primarily by Glucose utilization.

Think how critical is your Nutri-Spec system of testing and balancing the autonomic nervous system. Both Parasympathetic Failure Imbalance and Sympathetic Stress Failure Imbalance must be addressed concomitantly with Gluco/Keto Balance, to maximize myocardial Vital Reserves.

The need for epinephrine to maximize myocardial function brings into question the use of beta-blockers and calcium channel blockers to control hypertension in heart failure patients. Inhibiting epinephrine's beneficial effect on the myocardium may partially explain the increased mortality in heart patients taking calcium channel blockers.

Dietary Recommendations

Of all the five Nutri-Spec Imbalances, Glucogenic/Ketogenic is the one most self-inflicted. In other words, it is the imbalance that is most associated with the miserably inadequate diet and sedentary lifestyle that typifies most of your patients. It is thus the imbalance that is most totally responsive to diet and exercise, but also the one most easily sabotaged by your patients' self-destructive lifestyle choices. The two essential functions most intimately and directly associated with Glucogenic/Ketogenic Imbalances are the maintenance of glycemic control and the maintenance of ideal pH (particularly the systemic pH).

Is your Glucogenic/Ketogenic patient your ally or your adversary in achieving metabolic balance and restoring essential function? Think of it this way. Since your average patient consumes 140 pounds of sugar each year, if your patient testing G/K shows loss of glycemic control – you can be certain that patient is guilty of sickening (literally) sugar intake.

Furthermore, in people who have an inborn tendency to either a Glucogenic or Ketogenic predominance in their metabolism, even the "ordinary" grotesque sugar intake of the average person is enough to push them into a devastating state of imbalance.

Decreasing the percentage of Fructose in the diet is vital for Glucogenic patients. Eliminating Fructose in favor of lower glycemic index carbs is critical for Ketogenic patients. The emphasis for Glucogenic/ Ketogenic patients is not on high protein, but on **frequent** protein. It is essential that these patients' protein intake be divided approximately equally over 2 or 3 feedings. And, it is most essential that the Glucogenic patient **never** eat a meal that is predominately carbohydrates.

The actual **quantity** of protein recommended for your Glucogenic/Ketogenic patients is not that great, and in fact, may be no more protein than they are currently consuming. The problem with too many people is that they consume 80% or more of their daily protein intake in one meal – the other meals being predominately starches, "salads", and other low nutrient density foods. The minimum protein requirement for Glucogenic/Ketogenic patients is little different than you recommend to your other patients.

Defining protein foods as meat, fish, poultry, eggs, and cheese, you can follow this quantitative rule: **Estimate your ideal body weight and divide that number of pounds by 15. That gives you the number of ounces of protein food you need to consume daily.** To illustrate: If your ideal weight is 150 pounds, divide the 150 by 15 and get 10. You need 10 ounces of meat, fish, poultry, eggs, or cheese (with 2-3 eggs being the equivalent of 3 ounces of meat) daily. That means five ounces of protein twice daily, or 3 ½ ounces of protein 3 times daily.

As regards the specific needs of Glucogenic or Ketogenic patients, not all proteins are created equal. Protein foods can be grouped according to their purine (adenine and guanine) content.

- High purine foods include organ meats — sardines, herring, and anchovies — meat extracts, gravies or broth.

- Moderate purine proteins include meat, fish, poultry, and sea food

- Low purine proteins include eggs and cheese

Glucogenic patients thrive on high purine foods and moderate purine foods. They will feel exceptionally well if they have a meal that includes a high purine protein on a regular basis. They will be nowhere near their best physically or mentally or emotionally if their protein sources are predominantly eggs, cheese, or milk.

Your Ketogenic patients will not feel well on high purine proteins, and should avoid them. They will do well enough on moderate purine proteins, but will be at optimal function if at least one meal a day features eggs or cheese.

There are non-protein foods that are also high in purines:

- dried beans, peas, lentils, and peanuts

- oatmeal and wholegrain wheat bread and cereal

- mushrooms, asparagus, cauliflower, and spinach

Glucogenic patients do well emphasizing the above foods in their diet. Ketogenic patients can handle them without major problems, but should place a higher emphasis on carb foods such as rice, quinoa, buckwheat, winter squash (butternut, acorn, pumpkin), and sweet potatoes.

Potatoes are problematic for several reasons, and should not be a large part of anyone's eating plan.

An additional note is required on beans, peas, lentils, and peanuts. Theoretically, they should be particularly good for Glucogenic individuals. But the truth is, they are a problem for everyone, and for several reasons. First, they contain lectins that are somewhat toxic to many people, causing agglutination of body fluids (--- Electrolyte Stress blood clumping). Second, almost all the beans are very high in isoflavones, which are estrogenic. Another problem is that many of the beans contain goitrogens that inhibit thyroid function (and lima beans and chickpeas/garbanzos are the worst).

Turning our attention to carbs, we can say that if the facts just presented on carbohydrate foods are taken into consideration, there is not really much else you and your patients need to be concerned about regarding starchy foods. Yes, the Glycemic Index is important, but if adequate protein is included at the meal (which automatically includes adequate fat), even high glycemic carbs such as rice will not rock the glycemic boat too much, as long as the portions are not too high. Another consideration regarding carbs is the distinction between those that are high in amylose starch and those that are high in amylopectin. But again, if the meal contains adequate protein, and the carb portions are not excessive, those distinctions from one carb to another are not clinically significant.

Sugar? The problem is all about **fructose** ("fruit sugar"). White refined granulated sugar is a dimer = exactly 50% Glucose/dextrose (the blood sugar and brain sugar essential to meet energetic demands), and 50% anti-metabolic fructose. Fructose places an immediate stress on both Glucogenic/Ketogenic and Anaerobic/Dysaerobic control, and, it devastates the gut microbiota.

"But wait!", your patients will exclaim, "Isn't fruit 'natural sugar'?" The truth is, there is no such thing as natural sugar, in the sense that there is no such thing as unnatural sugar. Both dextrose and fructose exist (in small quantities) in nature. But all the fruits your patients eat are unnatural in the sense that they are agribusiness-created hybrids --- quantitatively outrageously high in sugar far exceeding anything that ever existed in nature. And more than 50% of fruit's

grotesque sugar content consists of fructose. So, not only do fruits provide nearly 100% of their calories as sugar, but they are a greater metabolic assault than refined sugar. (The only popular fruits with less than the 50% fructose offered by the sugar bowl are plums and apricots. Pears have the highest fructose content. And honey is devastatingly high in fructose.)

The undeniable metabolic truth is that a fructose molecule is a fructose molecule, regardless of its source. The victimized liver cannot distinguish between fructose from high-fructose corn syrup, from a candy bar, or from an organically grown apple. Fruit should be regarded just as any other sugary dessert — as a dessert or special treat item that should be consumed in only small quantities and only on occasion.

Dietary fats are a far more critical consideration than carbohydrates. The first rule, and the consideration that far outweighs all other considerations regarding dietary fat is that all individuals, regardless of Metabolic Imbalances, must strictly avoid polyunsaturated oils. These HOHUM PUFAs include soy, canola, corn, safflower, sunflower seed, pumpkin seed, walnut, and peanut oils, and all other vegetable/seed oils. That also includes nuts, and nut butters.

Nutri-Spec has often posed the question, which is more damaging to health span and life span, dietary intake of sugar, or of polyunsaturated oils? Fructose and HOHUM PUFAs are both immediately devastating to, and long-term accelerators of, INFLAM-AGING. If we had to pick one as more as more destructive than the other, we might lean toward the HOHUM PUFAs, but really, avoidance of both fructose and HOHUM PUFAs, plus the rule of adequate protein at each meal, covers at least 90% of what anyone needs to EAT WELL - BE WELL.

If polyunsaturated fats are the Number One destroyer of health span and life span, what about other types of fats? First, consider the ever-popular omega 3 fatty acids. Do they live up to their hype? They absolutely do not. The one clinical benefit derived from omega 3 oils is that they block the damage done by the omega 6 oils — the HOHUM PUFAs described above. The omega 6 oils are destructive by two mechanisms. They cause a tremendous amount of oxidative free radical damage, and, they are the mother substance for the entire family of eicosanoid inflammatories, including prostaglandins, leukotrienes, and thromboxane.

Suppose an individual suffers arthritis or premenstrual syndrome or migraines or any of the other countless symptoms associated with eicosanoid pro-inflammatories. If that person supplements with either alpha-linolenic acid, or (to a certain extent) with fish oils, there will be a clinically significant improvement in the inflammatory symptoms. That is why the omega 3 oils are such an easy sell for the health food industry. People do feel temporarily better with supplementation.

But as just stated above, the second disruptive effect of omega 6 oils is the direct oxidative free radical damage they cause. Unfortunately, omega 3 oils cause even greater oxidative catabolic tissue damage. But, while the symptomatic improvement from omega 3s blocking the eicosanoid inflammatory pathway are immediate, the oxidative damage done by omega 3s takes months and years to show clinical significance. Note that particularly sensitive to omega 3 oxidative inflammatory damage is brain tissue. The EPA and DHA in fish oil (which is now (alarmingly!) added to baby formulas) are most catabolically damaging, and many of them are already rancid when taken as supplements. Alpha-linolenic acid (as found in flax oil) is not nearly as damaging. However, anyone who follows the EAT WELL – BE WELL dietary recommendation gets plenty of alpha-linolenic acid in the diet, with no supplementation needed.

What about saturated fats in the diet? Good or bad? As Porta and Hartroft showed many decades ago, and highlighted in no less than The Lancet, in its 1965 series on Healthy Longevity (ironically at just the time when agribusiness was beginning to promote margarine and other soy oil products as the keys to heart health, and protection against the purported damage of saturated

fats), **health is directly proportional to the dietary ratio of saturated fats over polyunsaturated oils**.

Particularly beneficial are the short-chain saturated fats in butter or ghee. Also especially beneficial are the medium-chain saturated fats in coconut oil. The long-chain fatty acids, which in meat, fish, poultry, and eggs means predominantly stearic acid and palmitic acid, are the raw materials from which (along with Cholesterol, which they usually accompany) we make tissue membranes and hormones. If there is any problem with excess long-chain fatty acids it is that the over-fattening of livestock for meat shifts the ratio of fatty acids to a relative decrease of stearic acid and an excess of palmitic acid. To maintain a higher level of stearic acid it is best to avoid the fattier cuts of meat and poultry and pork.

A cautionary note about chicken, turkey, and pork: Agribusiness has converted an extraordinary source of protein and healthy fats into a disaster. How? Commercial chicken and turkey houses are designed to fatten up the birds as fast as possible. Hormones and antibiotics are used, which is a separate issue, but our main point here is that chicken and turkey are force fed processed soy meal as almost their entire diet. The result? Instead of the fat in poultry being predominantly saturated fat along with some monounsaturated fat, it is extremely high in — you guessed it — soy oil. Chicken and turkey are so high in omega 6 HOHUM PUFAs that they should be absolutely minimized in the eating plan. The same caution applies to soy- and corn-fed pork.

The ideal meats are fish, and even better, the meat from ruminants --- the grazing animals, beef, lamb, bison and venison. Why ruminants? Their fat (assuming grass fed, not feed house stuffed) is especially high in stearic acid. Stearic acid has significant anti-inflammatory benefits.

The fat in cheese and milk and butter and cream is quite interesting. There is a phenomenon referred to in the research literature as, "the milk fat paradox."

Consider how agribusiness, teamed up with the pharmaceutical industry, "proved" that eating saturated fat and Cholesterol is dangerous. They took little bunny rabbits that have zero saturated fat or Cholesterol in their natural diet, and stuffed them full of feed high in palmitic acid and Cholesterol. Sure enough, these cute little critters developed atherosclerosis and succumbed to cardiovascular disease. But here is what is interesting about milk fat. It has the same high content of saturated fat and the same high content of Cholesterol, yet when you stuff bunny rabbits or human beings with milk fat, there is no inflammation, and there is no atherosclerosis and there is no cardiovascular disease!

Why not? As it turns out, the long-chain saturated fatty acids in milk are not stearic acid and palmitic acid. Both stearic and palmitic acids have an even number of carbons in their fatty acid chain. But the two dominant saturated fatty acids in milk fat are just as long, and just as saturated, but contain an odd number of carbons in their fatty acid chain. These odd-chained fatty acids are not only not inflammatory in any quantity, but they are actually anti-inflammatory.

Getting back to EAT WELL – BE WELL as it applies to Glucogenic/Ketogenic Imbalances…

How do the Glucogenic and Ketogenic ideal diets differ? It is not at all complicated. Both imbalances need to strictly avoid fructose and HOHUM PUFAs. The Glucogenic individual should emphasize the high and medium purine proteins, while the Ketogenic should emphasize the low purine proteins. Quantitively speaking, both G and K individuals can use the body weight divided by 15 rule to select the quantity of protein. But, the Ketogenic patient should consider that as the ideal, while the Glucogenic should consider that amount of protein as the minimum. So, if you look at the perfect dinner plate for a Glucogenic individual and a Ketogenic individual the difference is the Glucogenic patient will have a slightly larger portion of protein, and a little smaller portion of carbs. Both imbalances should eat freely of non-starchy vegetables.

Ironic, isn't it, that a high carbohydrate, low protein, and ultra low fat diet is the diet is still promoted as ideal by major sectors of both the medical/pharmaceutical establishment and the natural food industry? Is it any wonder that people living according to the common wisdom of our day are falling into Glucogenic/Ketogenic Imbalance in such high numbers?

Additional evidence supporting Glucogenic/Ketogenic Imbalances in the etiology of gall bladder problems comes from a study (2) in which thirty-eight women were put on an ultra low fat, low protein, high carbohydrate diet which was also low in calories, for the purpose of weight loss. Those conducting the study were surprised at two things: 1) how little weight the women lost in a period of eight weeks, and, 2) that thirteen out of the thirty-eight women developed gall stones within the eight week period.

"Wait a minute!" you exclaim, "How can it be that gall bladder problems are associated with excess starches, when everyone knows that the gall bladder relates specifically to fat metabolism, and that gall bladder problems are caused by excess fats?"

You are absolutely correct. One purpose of the gall bladder is to assist in the digestion and assimilation of fats. When the gall bladder is over-loaded with excess fat (particularly PUFAs) you will have gall bladder problems – **and** these patients will test as having a Dysaerobic Imbalance. But, please understand that while the **purpose** of the gall bladder relates to fat, the **functioning** of the gall bladder depends upon normal metabolism (as does every other organ in the body). E xcess starch consumption with low fat intake causes stagnation of bile acid flow, thus the formation of stones. Meanwhile the high carb + inadequate protein regimen is also leading to fatty deposits in the liver (Metabolic-Associated Fatty Liver Disease).

This gall bladder connection shows up in your NUTRI-SPEC testing very often as **bilirubin** appearing in your patients' urine. In fact, when you see bilirubin in a patient's urine who is not Dysaerobic you can bet the farm you have found either Glucogenic or Ketogenic Imbalance.

Something else regarding dietary recommendations that you will notice immediately upon using NUTRI-SPEC is how quickly some of your Glucogenic/Ketogenic patients respond, both in terms of improving their test results and improvement in symptoms – but **only** if they are following the dietary recommendations.

Largely associated with the production of carbon dioxide as a metabolic end-product, we find (as explained above) that Glucogenic patients tend to be somewhat acid at the systemic level. Ketogenic patients tend to be alkaline. Watson (from whose observations our Glucogenic/ Ketogenic paradigm is derived) showed that aberrations in serum pH were more directly correlated with patients' symptoms than any other quantifiable factor. Foods and nutrition supplements that increased the systemic pH were immediately beneficial for Glucogenic patients and devastating for Ketogenic patients. Acidifying foods and supplements had the reverse effect. And the effect, as you will happily find, can be immediate.

In summary, note that while your Glucogenic and Ketogenic Imbalances represent opposite phases of a diphasic metabolic control system, they both have one thing in common – **sugar handling stress**.

Quite simply – some people succumb to a 140 pound annual sugar assault by getting stuck in a Glucogenic rut. Others react to the overwhelming sugar load with a Ketogenic metabolic response. This is the NUTRI-SPEC key concept of **biological individuality** displayed quite clearly. The same metabolic stressor can result in the exact opposite metabolic response in two different people. Never lose sight of the fact that if your patient is Glucogenic or Ketogenic, the perfect supplement regimen can only take the patient so far if the relentless stress of the 140 pound sugar load, along with the anti-metabolite HOHUM PUFA devastation, is not removed.

One final consideration regarding dietary recommendations concerns the dietary intake of Cholesterol. You will note that your Glucogenic patients tend to have elevated serum Cholesterol. This is due to poor utilization of fats associated with the excess dependence on Glucose for energy. Without benefit of the knowledge obtained through NUTRI-SPEC you might jump to the conclusion that your Glucogenic patients should avoid high Cholesterol foods. Nothing could be further from the truth. We have a paradox here in that the very foods that Glucogenic patients need most to normalize their metabolism and thus lower their Cholesterol levels are the foods that are rich in Cholesterol.

This same dietary paradox applies to your Dysaerobic patients as well. Among your Dysaerobic dietary recommendations are such high Cholesterol foods as dairy fat and eggs, while your Glucogenic patients thrive on ruminant meat, fish, and regular servings of high-purine organ meats. Glucogenic and Dysaerobic Imbalances are your two NUTRI-SPEC imbalances most often associated with elevated Cholesterol, and the dietary recommendations for both include the essentiality of a high dietary Cholesterol intake.

In Summary: One important take away from your understanding of the Randle Cycle is that the battle for supremacy between Glucose and FA can swing in one direction or the other in response to nothing more than food selection. A high-fat meal, particularly high in polyunsaturated oils, will exacerbate a Ketogenic Imbalance. In contrast, a high-carb meal, provided it is somewhat low in fat and particularly low in polyunsaturated fatty acids, will inhibit the suppressing effect of FA on the metabolically more efficient Glucose energetics. The ideal meal for a Ketogenic patient is high carb, with a small serving of ultra-lean beef, bison, or fish, or eggs, or cheese.

From a dietary plan standpoint, Ketogenic individuals need to increase carb intake while simultaneously decreasing dietary fat, with particular emphasis on eliminating polyunsaturated oils. Glucogenic individuals also need a steady supply of carbohydrates/dextrose in the diet, but carb intake must be quantitatively small to avoid an overload of Glucogenic energetics that further derange FA metabolism. For that reason, the carb intake must be accompanied by a small but consistent intake of good saturated fat (particularly fat from ruminants, which includes beef, lamb, cheese, eggs, coconut oil, and butter. But the emphasis must be on the lower carb to protein ratio (with high adenine organ meats being at least an occasional part of the eating plan.). As with those who are Ketogenic, strict avoidance of polyunsaturated oils is essential.

By suppressing Glucose energetics, both a high-fat diet and fasting contribute to metabolic inflexibility, which is defined as a failure to adapt metabolism to transitions from the fasted to fed state. Such is a characteristic of Insulin Resistance in both Ketogenic and Glucogenic Imbalances.

Summary of Glucogenic/Ketogenic Imbalances:

GLUCOGENIC	KETOGENIC
1) Over-dependence on glucogenic energy production	1) Over dependence on ketogenic energy production
2) Deficient ketogenic energy production	2) Deficient glucogenic energy production
3) Low carbon dioxide levels	3) Low carbon dioxide levels
4) Serum pH decreased	4) Serum pH increased
5) Urine Specific Gravity elevated	5) Urine Specific Gravity low
6) Body temperature low	6) Body temperature low
7) Blood sugar decreased or erratic	7) Blood sugar increased
8) Blood fats elevated (especially Cholesterol)	8) Blood fats elevated (esp. Triglycerides)
9) Fatigue	9) Fatigue
10) Depression/Anxiety	10) Depression/Anxiety
11) Bilirubin in urine = gall bladder dysfunction with gall stone formation	11) Bilirubin in urine = liver overload
12) Urinary chloride retention normal to high	12) Urinary chloride retention poor
13) Pyruvate carboxylase enzyme decreased = hypoglycemia, increased pyruvate to lactic acid, increased Fatty Acid to & from liver	13) Pyruvate carboxylase enzyme increased or decreased = increased [GLUCOSE], Insulin, Gluconeogenesis, Lipogenesis
14) Dietary starch/sugar excess with respect to protein and saturated fat; PUFA excess	14) Dietary sugar and fat excess with respect to carbohydrate; PUFA excess.
15) Fatty liver associated with excess Glucose utilization = increased fatty acid synthesis and fatty liver	15) Fatty liver associated with poor Glucose utilization, resulting in glycogen storage up to its limit, then, conversion to fat
16) Premature aging associated with free radical peroxidation of fatty acids, and with Advanced Glycation End-Products	16) Premature aging associated with inefficient mitochondrial energetics, and Advanced Glycation End-Products

Chapter 14: GLUCOGENIC/KETOGENIC BALANCE REFERENCES

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