

John L. Couvaras, M.D. June 1, 2011

Ideas on Fat Metabolism and Blood Sugar control:

Observations about Insulin and the four counter-regulatory hormones.

Clinical Applications:

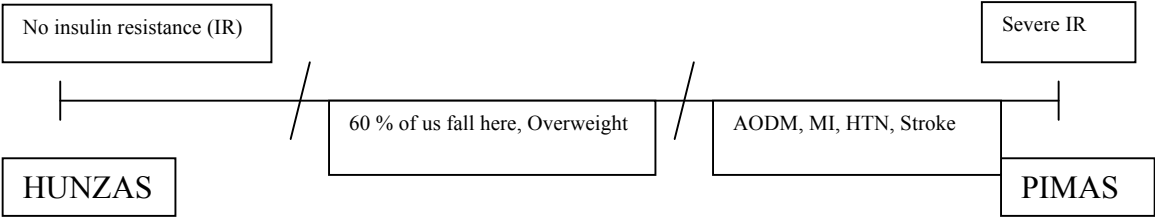
Polycystic ovarian patients, metabolic syndrome patients, adult onset diabetics (AODM) may be variants of a common theme. This common theme would be insulin resistance (IR). Before going further, I will outline the commonly understood classifications for diabetes and discuss their current medical objective in treating these patients. My approach is not to be used by Type I diabetics without close supervision and agreement with their doctor.

Diabetes:

- Type I: They make no insulin (I)  
Susceptible to diabetic ketoacidosis  
Typically onsets in young patients
  
- Type II: Hallmark is insulin resistance  
Typically called adult onset diabetes  
Use diet to try to control blood sugar  
Oral agents to increase insulin to control BS  
Add insulin when blood sugar control is poor.  
The aim is to control blood sugar (BS), and it is well documented that reducing the blood sugar reduces the risk of stroke and heart attack (MI).

**I am suggesting we try to achieve the same goal but focus on controlling insulin levels with lowered insulin and increasing insulin efficiency. Why? Fat cells store fat due to a constant low circulating level of insulin. If that insulin level can be reduced, fat cells cannot hang onto fat.**

Pre-clinical Insulin Resistance:



The syndrome of insulin resistance (IR) can be viewed as a progression of disease, from no insulin resistance to severe insulin resistance. At one end would be the Hunza's in Pakistan who live past 100, and the other end, at severe IR would be the Pima Indians. This group has adult onset diabetes in 95% of their people by age 13. The rest of us lie somewhere in-between. About 60% of us have strong family histories for

AODM, poly-cystic ovarian disease, heart attack, stroke, baldness, hypertension, obesity and peripheral vascular disease. In all these conditions, insulin resistance is implicated.

### What is Insulin Resistance?

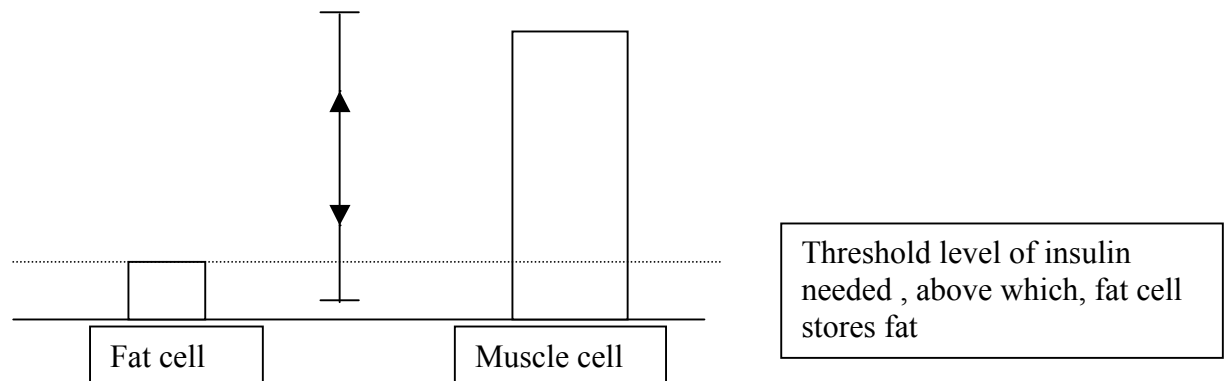
Insulin is a hormone formed in the pancreas and is used to push blood sugar into cells. At low levels, it keeps the fat locked up in the fat cell. Depending on our genetic and metabolic state, we may use insulin less efficiently. What this means is when we are young, one unit of insulin gave one unit of action. As we age, or get more insulin resistant, it may take 2, 3 or more units of insulin at the cellular level to get the same one unit of action. This higher level of insulin means resistance.

Testing is done to measure the insulin response or basal insulin levels, but in PCOS patients, this may only be positive in 30% of patients. There is a relationship of plasminogen activator inhibitor one (PAI-1) and inhibition of fibrin digestion and insulin resistance. In my practice, this is positive in 80% of PCOS patients. For this reason, I recommend measuring PAI-1 levels over insulin levels, and if elevated, adjusting metformin to titrate the PAI-1 levels to normal. Still, I am using low dose glucophage if the clinical picture of PCOS is present.

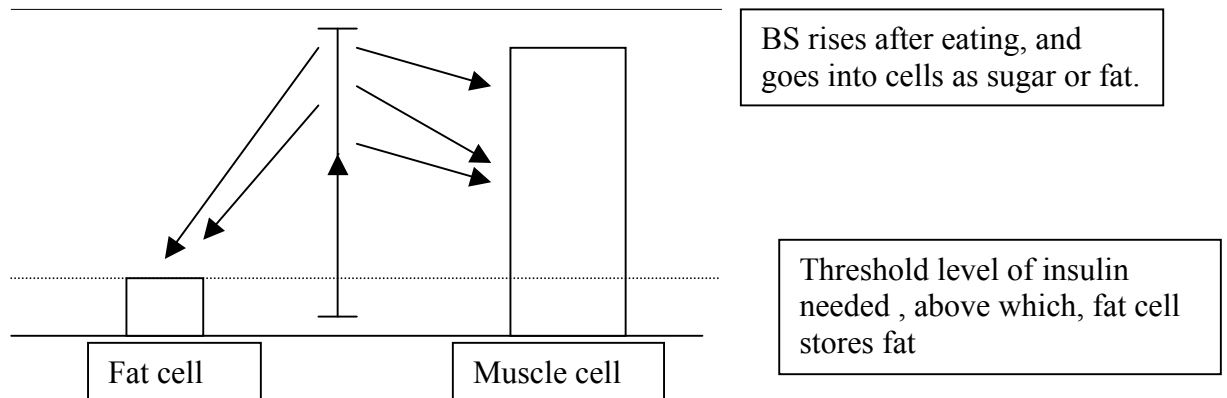
### FAT METABOLISM MODEL:

The model should apply to overweight people, men or women, as well as PCOS, or PCOS with overt signs of insulin resistance, or AODM patients and Adult onset Growth hormone deficient or insufficient patients. .

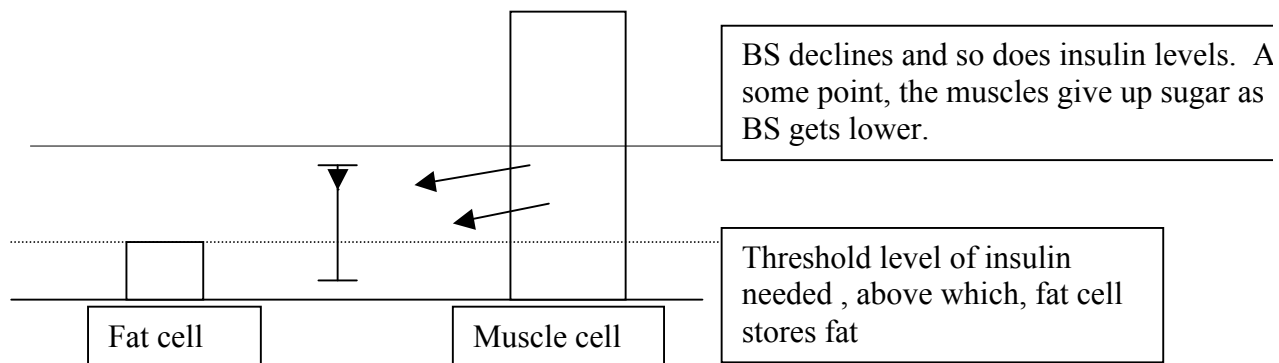
### Overview of sugar and fat storage.



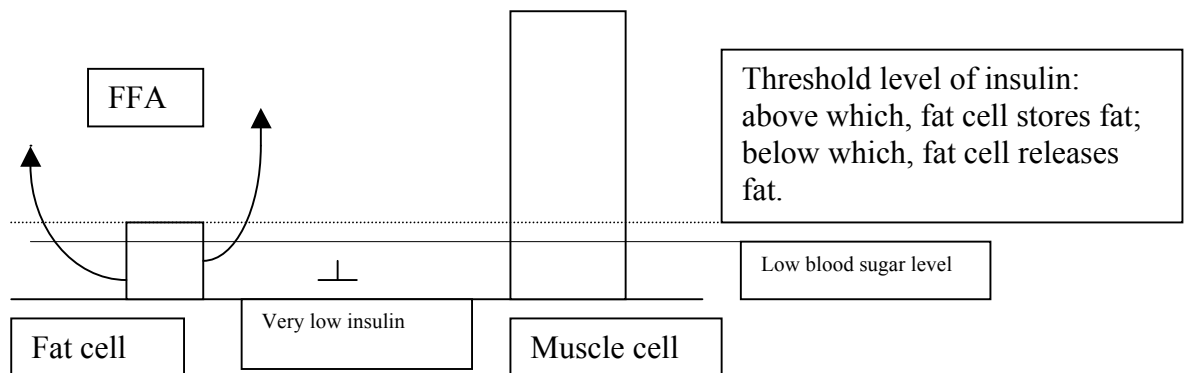
The bar graph above shows fat and muscle cells and the range of insulin levels that they need to function. Insulin range is represented by the I- bar between the cell bars.



After eating, BS rises, and (I) rises, pushing BS into fat and muscle cells as stored chemical energy.



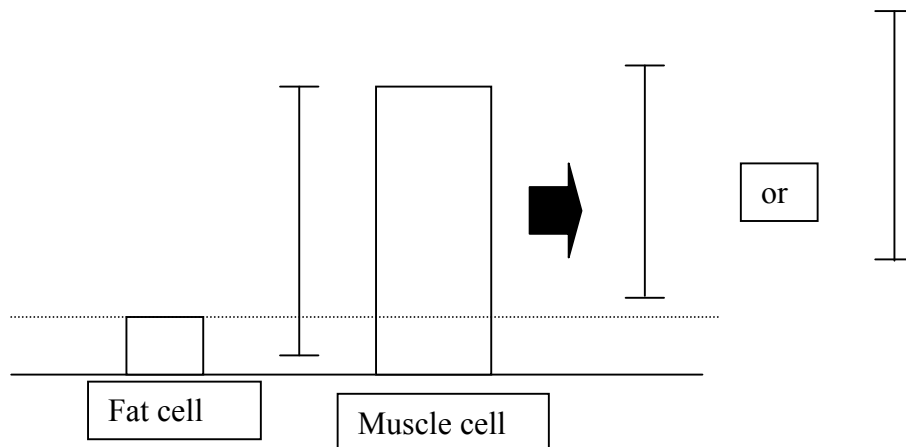
As BS decreases, so does (I). As BS gets lower, then muscles begin to release their sugar stored chemical energy.



**BS continues to decline and so does insulin levels. At some point, the BS is so low, the insulin level falls below the fat cell threshold, and the fat cell can not hold onto the fat. It releases free fatty acids, (FFA)**

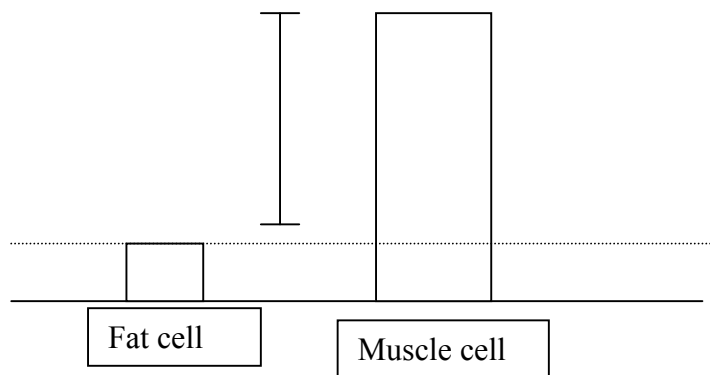
When BS is very low, the fat cell is triggered to release its chemical energy, fat. This process should be seamless---similar to when the electricity (muscle energy) gives out, the un-interrupted power supply (fat energy) kicks into action.

**With IR, the insulin needed to get the same unit of action is higher. This shifts the insulin curve somewhat higher.**



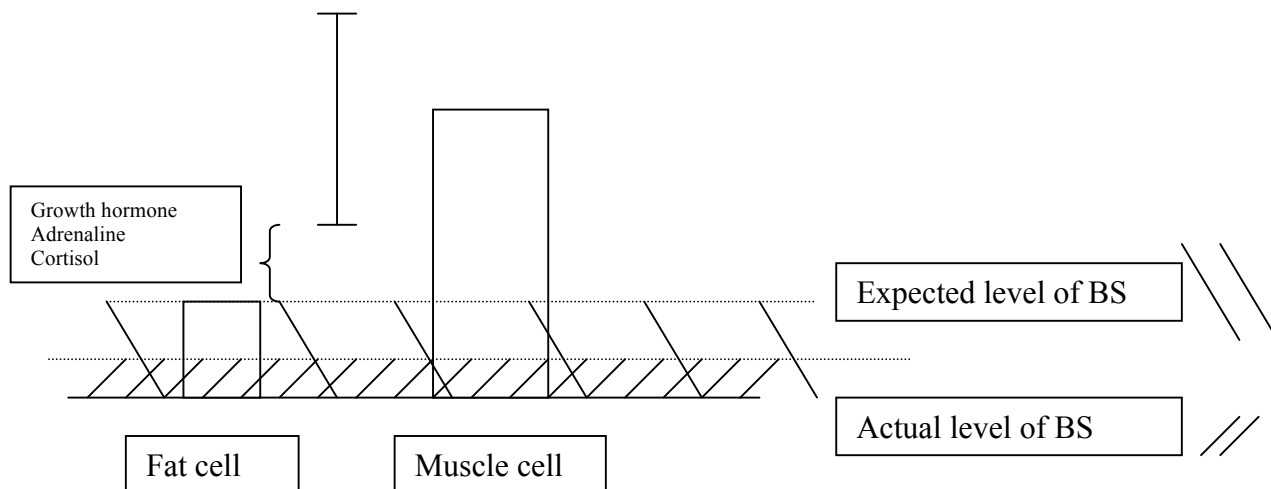
What this means is the fat cell does not get the signal to release the fat. Also, as IR gets worse, the level of insulin is higher for a given load of food. This keeps the insulin elevated longer.

Now what happens:



Any calorie eaten that is not burned at that time is stored, and if it is stored in the fat cell, it remains stored. This begins the slow weight gain in one's 30s. As IR worsens, the baseline level of (I) may get higher for longer.

When BS drops due to high (I) levels, **the low point of circulating insulin is still higher than the fat cell threshold**, but the blood sugar is low.



**The body will alarm and panic with low blood sugars**, since the brain and the red blood cells will only use glucose for fuel. **The body releases four counter regulatory hormones to increase BS.** These are glucagons, growth hormone, cortisol, and adrenaline. I

Glucagon does 80% of the heavy lifting or crude control.. It tends to regulate or counteract insulin's effects on blood sugar. The drug Actos, or pioglitazone, is a glucagon-like receptor stimulator and has been noted to effect modest weight loss. In recalcitrant weight loss cases, I have found it to be helpful, especially when the insulin response to glucose is exaggerated, or it is difficult to achieve ketosis with lowered carbs.

The other three hormones are the fine tuning for blood sugar regulation. During unstressed conditions, Growth hormone does about 16% of the work, followed by cortisol, 3% and adrenaline 1%. In non-diabetic cases, low GH or its metabolite, IGF-1 (insulin like growth factor-1) can explain the majority of common symptoms such as insidious weight gain, especially central weight gain, afternoon fade, early morning wakening, and labile moods. Addressing onset of adult onset growth hormone deficiency can be life transforming. In 2010, I have discovered 31 AOGD patients, prompting my supporting endocrinologist to wonder how I was finding so many of these patients. They were simply my infertile and miscarrying patients.

The next hormone in the daisy chain is cortisol. It is a stress hormone but is is one of the best mobilizers of fat into circulation. Unfortunately, after mobilizing it from the periphery it tends to place fat on people centrally, especially around their waist. Cortisol ages a person, thins their skin, breaks down elastin, and stiffens the arteries. The early morning wakening between 2-4 am has been believed to be a sign of depression, but I have correlated this with a high AM fasting cortisol. I believe this is simple compensation during 2-4am, when blood sugar is declining and growth hormone is not spiking adequately. The cortisol attempts to raise sugars, but will induce wakening and heat generation and interrupt the deep sleep needed to release more growth hormone.

This pattern is self reinforcing, with declining GH over time and with age. Without adequate GH, basal metabolic rate will decline. This is associated with slow weight changes, and we have been working on improving GH release through a variety of lifestyle alteration. In a person suffering from obesity they often have coexisting depression. The drops in blood sugar, or “hypoglycemia” occur throughout the day, and the episodic cortisol release affects a person’s moods. As cortisol rises, one feels good, but once it drops, the person feels depressed. Carbohydrates are known to stimulate serotonin release in the brain, and this can add to the addiction to carbohydrates.

Eating carbohydrates affects moods:

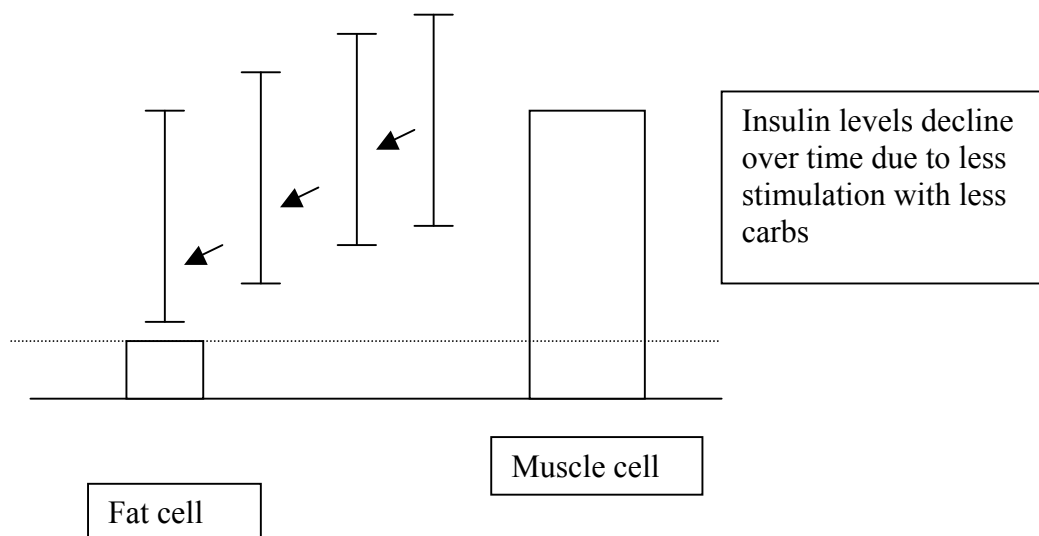
- 1.) raises BS quickly, thus shutting off the anxious-nervousness of adrenaline
2. Raises serotonin , thus makes one feel better, like taking prozac
3. Raises cortisol temporarily, thus makes one feel better.

Adrenaline makes a dieter irritable, confused, angry, and “drives one to find food”. This makes a person a difficult dieter, if they are on a calorie restricted diet. Additionally, the nervousness from the adrenaline is removed once they eat something, especially carbohydrates, and this creates an addictive behavior pattern.. If a patient has the interrupted sleep pattern between 2-4am, and note they are hot AND sweaty, it is likely they are calling for adrenaline.

### How to use our metabolism to our advantage.

The key is to control the insulin and in weight loss it is to keep it as low as possible to allow the fat cells to get into discharge mode. I have gathered some simple rules to follow.

- 1.) **Change the composition of what you eat.** Less carbohydrates means less (I) stimulated which means lower insulin rise and over time, lower basal (I) levels.

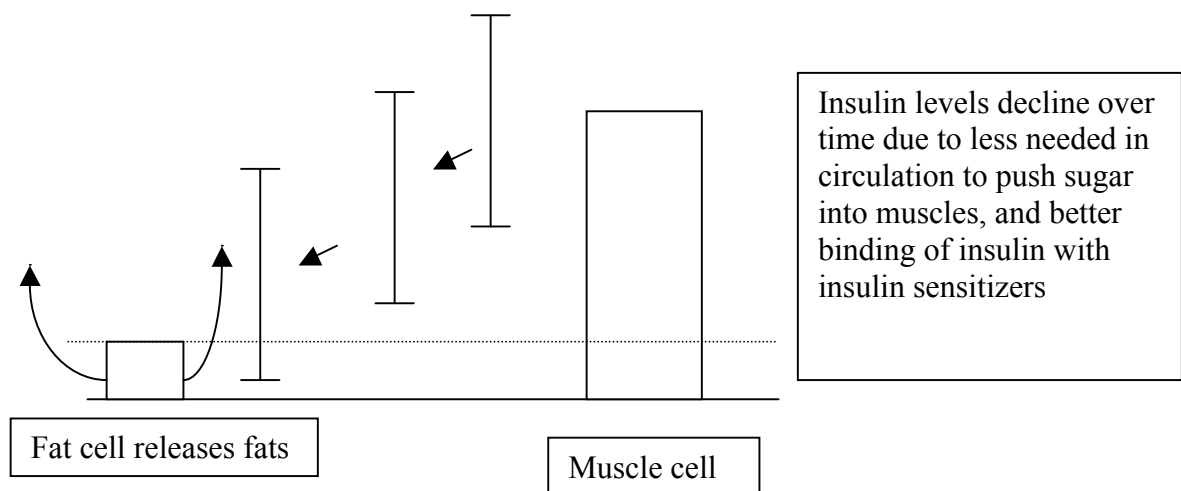


2.) **Exercise regularly, at a minimum, 25 minutes every day and between 4-8pm.** This is not meant to burn up excess calories, but gets the muscles to bind (I) better and to stimulate more GH/IGF-1 . We need to know that as we age, and especially if we develop adult-onset diabetes, our muscles bind (I) less efficiently, thereby needing higher levels of circulating (I) to get the same effect. This exercise is more than enough to get the muscles to bind (I) at 100% for 24-36 hours.

3.) Insulin sensitizers-glucophage(metformin), Actos, or an amino acid called N-acetyl cysteine. Actos works at a different mechanism than metformin, but Actos tends to keep fat around the abdomen. Actos stimulates the Glucagon receptor to regulate insulin and blood sugar levels.

Glucophage does:

- 1.) decreases liver formation of glucose, less glucose means less insulin.
- 2.) Decreases intestinal uptake of carbohydrates.  
(For this reason, the diarrhea associated with it. If one reduces the carbs, the diarrhea is limited.)
- 3.) Increases insulin binding to skeletal muscles.



4) Now what about those **carbohydrate addictions? I give short term welbutrin** to boost serotonin, and block the need to take carbohydrates to stimulate serotonin. Once the growth hormone is improved, this seems to diminish these addictions

## What should I eat?

For people with insulin resistance/metabolic syndrome, they don't tolerate carbohydrates well. The Atkin's or ZONE diets, both seek to reduce carbohydrates to ultimately reduce insulin levels.

In theory, the ZONE would work better on a younger person, 25 or less, who has not gotten too overweight, nor having early insulin resistance. The Atkin's induction phase uses 20-30 grams of carbohydrates a day to reduce the insulin levels and in the 30-plus year olds, this helps to get them into ketosis and pull insulin levels down quickly. The quick ketosis also helps to cut their appetite, and makes it easier to adhere to the diet. The problem with curbing appetite with severe calorie restriction and ketosis is the body will signal a starvation state and this will interfere with fat loss. Atkins promoting weight loss with low carbs but not concerning about calorie restriction, but over the short term, moderate calorie restriction should still be a consideration.

- My rules:
- 1.) calories of protein/fat to 1200-1400 cal/day
  - 2.) Look for hidden carbohydrates in vitamins, etc, restrict carbs.
  - 3.) Aim for 1-2 pounds/week weight loss, preferably 1 pound/week.

Extreme calorie restriction will trigger starvation mode after two weeks and will force the body to burn up protein to make glucose to feed the brain and red blood cells. After two weeks of ketosis, the brain will agree to splitting its energy needs between glucose and fats, 55%/45%. Muscles can always use glucose or fats. Red blood cells will never use anything but glucose as a fuel source. For this reason, the body needs a certain level of glucose, and it will make up the difference by breaking down muscle protein to glucose.

**Protein and fat are not very insulin stimulating. As long as the insulin levels are low, the fat cells remain in release or discharge mode, unable to hold on to the fat, unable to put any fat into storage; even in the face of excess calories.** The excess calories in circulation will be made into ketones. This is mostly done by the liver ramping up its ability to chop up fats into ketones but this takes 1-2 weeks. For this reason, the triglycerides and cholesterol in low carb dieting patients will always be very high in the first 3-5 weeks, but after this, the levels should come way down. If this does not happen after 5-6 weeks of ketosis, then lipid metabolism should be evaluated.

These ketones come out in the urine. They indicate the level of fat burning, as well as the level of hydration and exercise and glycogen depletion.. The process is supposed to be a controlled burn, and I recommend patients keep their fasting AM urine ketone sticks to be (small). If one is moderate ketones, they can drink more water or take a spoon of peanut butter, or small handful of

peanuts. Exercise is a key component to keeping one in ketosis. Avoiding alcohol, especially in the early stages is imperative.

A final precaution:

Low carbohydrate dieting has been maligned plenty over the years. It didn't mesh with balanced dietary principles which held that weight loss was simply a matter of less calories in versus more calories out. In addition, the early studies of low carb dieting reported that cholesterol and triglyceride levels were elevated, and the diet itself clashed with the recommendations of the American Heart Association to reduce fats, and red meat.

In certain patients, low carbohydrate dieting has been associated with an increase in kidney stones, and the high protein diet could tip an individual with higher uric acid into a gout attack. I have heard of a patient having severe potassium depletion when on this diet. In this extreme case, I could not determine how this could have happened unless the patient had a potassium losing kidney disorder, or was undiagnosed diabetic. If she was diabetic who was insulin dependent, then the diet may have made her ketosis too extreme and she could have lost the potassium in her urine along with the ketones.

As with any diet, one should use caution, have realistic expectations, and consult their doctor before starting.

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My low carb milk recipe:

- One pint of heavy cream from Trader Joe's
- 6-8 ounces of regular cream cheese
- 5 packets of Splenda
- dash of vanilla extract

Microwave the cream cheese for 45 seconds and chop into quarters and mix in a blender, half full with hot water—6-8 minutes, till good and blended.

Pour the heavy cream into empty gallon container, and add the cream cheese mixture. Add the five packets of Splenda and dash of vanilla.

Shake and chill.

**The entire gallon of faux milk has 8 or less grams of carbohydrates.**