



Hepatitis C HCCAP

The Hepatitis C-Diabetes Connection

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It has long been known that certain types of chronic liver disease and their treatment can cause problems with blood sugar (glucose) metabolism. However, with the discovery of the hepatitis C virus (HCV) in 1989, doctors soon recognized that the occurrence of diabetes mellitus (sugar diabetes) in patients with chronic hepatitis C was far greater than in patients with other types of chronic liver disease. Several studies have now confirmed what doctors have observed in their offices for the past two decades: hepatitis C increases the risk for the development of diabetes mellitus, especially type II disease.

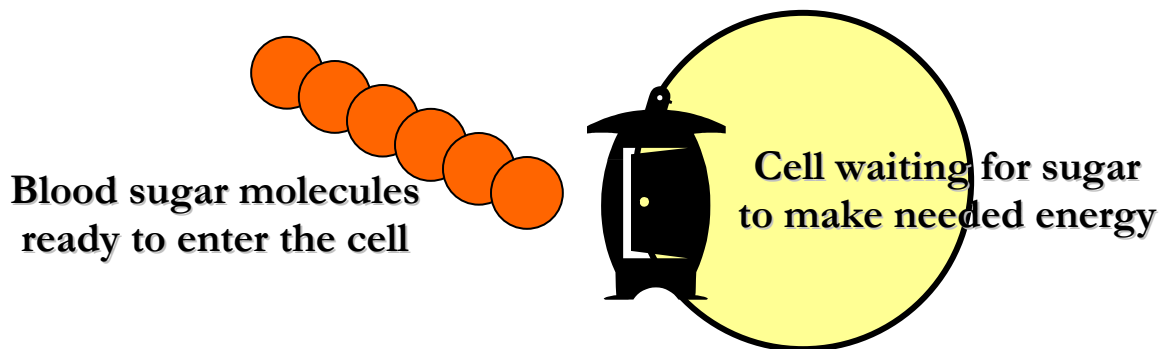
What is Diabetes Mellitus?

Diabetes mellitus (referred to as DM) is a metabolic disorder characterized by high blood sugar levels. There are two types of DM. Type I DM is caused by inadequate production of the sugar-regulating hormone insulin. Type I

DM is most often diagnosed in childhood or adolescence, which is why it is sometimes called juvenile diabetes. Type II DM is caused by ineffective action of insulin, a condition called insulin resistance. Type II DM used to be called "adult-onset diabetes," but with increasing rates of childhood obesity, children are now also being diagnosed with type II DM.

Insulin is the key to blood sugar control. It is produced by specialized cells in the pancreas and enables all the other cells of the body to absorb glucose and use it for energy. Think of insulin as the "sugar doorman" of your body's cells. Glucose cannot get into cells unless insulin (the doorman) lets it in (see figure). In type I DM, there aren't enough "doorman" (insulin molecules) to let the blood sugar into the cells. In type II DM, the "doormen" (insulin molecules) are there, but they don't always respond to the blood sugar molecules trying to get into the cells.

Insulin THE SUGAR DOORMAN



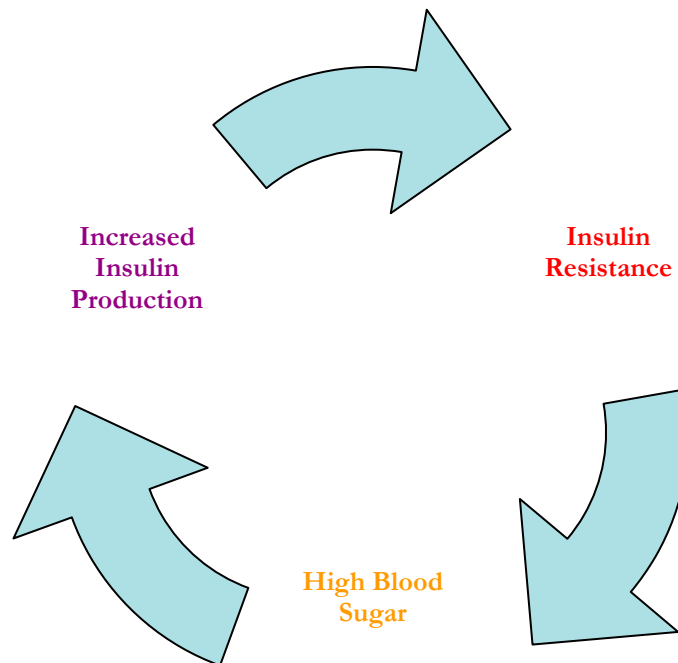
The hallmark of both types of DM is high blood sugar. Many people with type II DM do not have symptoms, or have only mild, vague symptoms such as thirst, frequent urination, hunger, and fatigue. However, the mild symptoms are misleading because diabetes is a serious condition. The potential long-term consequences of chronically high blood sugar are very serious and include kidney failure, heart disease, circulatory problems, infections, poor wound healing, and blindness.

Insulin Resistance

Type II DM is caused by insulin resistance. With insulin resistance, the pancreas produces plenty of insulin, but the body is resistant to its actions. In fact, most people with insulin resistance produce abnormally high levels of insulin in an attempt to compensate for the

body's sluggish response to it. High levels of insulin cause even greater insulin resistance, setting up a vicious cycle (see figure). Blood sugar levels increase when the cells of the body are unable to absorb and use it.

Insulin influences not only sugar metabolism but fat metabolism as well. Therefore, people with insulin resistance often also have abnormal levels of blood fats. Triglycerides and LDL (a dangerous fat) are often abnormally high, and HDL (the good cholesterol that protects against heart disease) is too low. Because insulin resistance causes abnormal fat metabolism, it is a risk factor for fatty liver, a condition wherein excess fat is present in the liver cells. Fatty liver has been linked to accelerated progression of liver scarring in people with chronic viral hepatitis.



Chronic Hepatitis C and Type II Diabetes Mellitus

Up to 1/3 of patients with chronic HCV develop type II DM. People with chronic HCV have at least a 2-fold greater risk of DM compared to both the general population and people with other liver diseases. Several studies have examined the prevalence of DM in people with HCV compared to those with hepatitis B. The results consistently show that the incidence is markedly higher among people with HCV. Age greater than 40 years, obesity, a family history of diabetes, race/ethnicity (increased risk for African-Americans, Hispanic-Americans, Native Americans, Asian-Americans, and Pacific Islanders), and extensive liver fibrosis increase the risk for the development of type II DM in people with HCV, just as they do in people without HCV. For example, among people with HCV, a family history of diabetes increases the risk of developing DM 16-fold, and cirrhosis increases the risk by 13-fold.

The Inflammation Link

Chronic viral hepatitis causes persistent inflammation in the liver. Inflammation is the body's normal response to injury, infection, or tissue damage. The purpose of the inflammatory process is to destroy or wall-off the invading agent and injured tissue. While inflammation helps heal injuries and rid the body of short-term infections, chronic inflammation can cause significant tissue damage. Liver scarring (fibrosis) that develops with chronic viral hepatitis is the result of ongoing inflammation caused by long-standing liver infection. In other words, chronic hepatitis causes an ongoing inflammatory state in the liver.

Numerous studies have shown that chronic inflammatory states such as chronic hepatitis may lead to insulin resistance and vice versa.

Many experts believe this is the key link between chronic hepatitis C (CHC) and diabetes. People with chronic hepatitis C, even those with stage 0 or 1 fibrosis, often have evidence of insulin resistance on biochemical tests. Insulin resistance promotes fibrosis. The severity of insulin resistance correlates with the degree of fibrosis in people with hepatitis C. The precise mechanisms underlying this relationship between insulin resistance and liver fibrosis are being actively studied by researchers.

Liver Transplantation

A significant number of patients with HCV undergoing liver transplantation develop DM after transplant, most frequently type II disease. While all patients undergoing liver transplantation are at somewhat increased risk for new-onset DM because of the medications needed to prevent rejection of the new liver, patients with HCV are at higher risk than people receiving a new liver for other causes. Since viral infection of a transplanted liver is almost universal in patients undergoing liver transplant for HCV, the viral factors that lead to DM act on transplant patients as they do on other people with chronic HCV.

Chronic Hepatitis C and Type I Diabetes Mellitus

Whereas the link between chronic hepatitis C and type II DM is now firmly established, the possibility of an association between CHC and type I DM remains a topic of debate among experts. Case reports of new-onset type I DM among patients with CHC have appeared in the medical literature. Most of the reports involve patients on interferon-based therapy. However, no clear link has been established between interferon-based therapy and the development of type I DM. Nonetheless, some experts speculate that the seemingly rare development of new-onset type I DM in

people with CHC may be an autoimmune phenomenon promoted by the presence of high levels of interferon. Patients with CHC are known to have an increased risk for certain autoimmune disorders.

Management of Type II Diabetes

Type II diabetes is often called non-insulin dependent diabetes (NIDDM) because insulin is generally not needed to control blood sugar levels. Remember, the problem with type II DM is not lack of insulin but rather insulin resistance. Diet is the key to management of type II DM. Foods are made up of three main components: proteins, fats, and carbohydrates (“carbs”). Carbohydrates include simple sugars, which are concentrated in foods we usually think of as sugary such candies, desserts, sweet syrups, fruits, and fruit juices. But there are also complex carbohydrates, substances that the body breaks down into simple sugars. Foods rich in complex carbohydrates include such items as breads, pastas, and potatoes. Controlling type II DM requires controlling your carbohydrate intake while maintaining a healthy, well-balanced diet. Many resources are available to help you learn to manage your diet and control your blood sugar. Your doctor may recommend that you take a class or consult with a nutritionist to help you. People with chronic liver disease may need to make special adjustments to their diet to ensure that their liver health is being addressed along with maintaining blood sugar control. Be sure to discuss any major changes in your diet with your doctor before making the change.

Weight loss is another key factor in the management of type II DM for those who are overweight at the time of diagnosis. Excess body weight and insulin resistance go hand-in-hand. Approximately 90% of people with type II DM are greater than 120% of their ideal body weight. Therefore, one aspect of overcoming insulin resistance is weight reduction for people with excess pounds. With

weight loss, insulin resistance is reduced, helping to break the insulin resistance-overproduction cycle.

Exercise is another key factor in the management of type II DM. For those trying to lose weight, the combination of diet and exercise is far more effective than dieting without exercise. Exercise, no matter what form it takes, burns calories – the basis of weight loss. But exercise has other benefits in addition to weight reduction or maintenance. Regular exercise has been shown to help reduce insulin resistance. People with type II DM who exercise regularly tend to have lower levels of insulin (indicating less insulin resistance) than those who do not exercise.

Daily monitoring of blood sugar levels is an essential part of gaining and maintaining control over type II DM. Most of the testing is done at home with a small glucose testing machine. Periodically, blood work is done to check the average glucose level over a period of months, blood fat levels, and kidney function. Other blood work may be added according to specific needs.

Depending upon the situation, oral medication may be prescribed to help control blood sugar levels. These medications are known as anti-hyperglycemic agents (hyperglycemia is the medical term for high blood sugar). Anti-hyperglycemic agents are not insulin, but are medications that help reduce insulin resistance and thereby improve insulin sensitivity. Many different types of anti-hyperglycemic agents are available. Doctors make recommendations based on individual circumstances including liver health. Some people who lose excess weight and begin to exercise regularly may eventually be able to discontinue anti-hyperglycemic medications. However, you should never discontinue taking any of your medications without first discussing it with your doctor.

While insulin is not generally used for maintaining blood sugar control in type II DM, it is sometimes prescribed in special circumstances. Insulin may be used as a “last resort” if the maximum doses of oral anti-hyperglycemic agents, diet, exercise, and weight loss fail to bring about consistent blood sugar control. Other circumstance such as a sudden illness, injury or surgery, or pregnancy may also necessitate the use of insulin for a limited period of time.

The bad news about type II DM is that it is currently a life-long condition with no known cure. But the good news is that controlling type II DM is largely in your own hands. It is often difficult to make the kind of lifestyle changes necessary to gain control over type II DM, but the payoffs in terms of your liver health and overall health make the effort most definitely worthwhile.