# Metformin and Risk For Vitamin B12 Deficiency

Metformin (brand names Glucophage, Glucophage XR, Fortamet, Riomet, Glumetza, and others) is a popular and highly effective oral diabetes drug used to help manage Type 2 diabetes. This drug works by lowering the amount of glucose made by the liver and by making the body's cells more sensitive to insulin. Metformin also has some other beneficial effects in that it may help lower blood lipid, or fat, levels (cholesterol and triglycerides) and can, in some people, promote a small amount of weight loss.

Metformin can be used with other diabetes pills and with insulin. Side effects of taking metformin are relatively rare, the most common being bloating, nausea, and diarrhea, all of which are temporary. Some people shouldn't take metformin, including people with kidney disease, liver disease, or congestive heart failure, for example, because of an increased risk of a potentially fatal condition called lactic acidosis.

In recent years, there's been some concern over the risk of vitamin B12 deficiency in people who take metformin. Vitamin B12 (also known as *cyanocobalamin* or *cobalamin*) plays many important roles in the body, such as keeping your blood cells and nervous system in tip top shape. There's also some evidence that vitamin B12 may help prevent heart disease and possibly even Alzheimer disease (the jury is still out on this one). This vitamin is found primarily in animal foods, such as beef, seafood, eggs, and dairy products, which is why some vegetarians are at risk for a B12 deficiency. Elderly people are often at risk for deficiency as well, due to problems with absorption from the gastrointestinal tract. Symptoms of B12 deficiency include certain types of anemia, neuropathy, memory loss, confusion, and even dementia.

So, why would taking metformin possibly put you at risk for a B12 deficiency? According to some studies, between 10% and 30% of people who take metformin on a regular basis have some evidence of decreased B12 absorption. Researchers aren't quite sure why this happens. In a study recently published in the October 9 issue of the journal *Archives of Internal Medicine,*155 Chinese people with Type 2 diabetes taking metformin were identified as having a B12 deficiency, regardless of factors such as age or body weight. The study found that the longer a person had been taking metformin and the higher his daily dose of the drug, the greater his risk of developing B12 deficiency.

The authors of the study advocate consideration of vitamin B12 deficiency screening for people who take metformin. While this screening isn't routine, it's worth it to have a talk with your health-care provider to see if you're at risk for deficiency, especially if you've been taking metformin for several years or take a high dose. Also, if you have any of the symptoms of B12 deficiency mentioned above, particularly those related

to neuropathy (numbness, pain, or tingling in your hands or feet), be sure to let your physician know. He or she can check the level of vitamin B12 in your blood.

Vitamin B12 deficiency can be treated with either oral, injected, or inhaled forms of B12. Some people, such as strict vegetarians or the elderly, may need to take supplements or receive injections on a regular basis. B12 is found in most multivitamin supplements, so it doesn't hurt to take a multivitamin as a safeguard. However, avoid taking a B12 supplement unless your doctor has prescribed them. Too much vitamin B12 may be harmful, and B12 can also interact with certain medicines. Always let your health-care team know about all medicines and supplements that you're taking at each visit.

## Lactic Acidosis

The buildup of lactic acid in the bloodstream. This medical emergency most commonly results from oxygen deprivation in the body's tissues, impaired liver function, respiratory failure, or cardiovascular disease. It can also be caused by a class of oral diabetes drugs called biguanides, which includes metformin (brand name Glucophage).

Another biguanide called phenformin was pulled from the market in the United States in 1977 because of an unacceptably high rate of lactic acidosis associated with its use. Concerns about lactic acidosis also delayed the introduction of metformin to the U.S. market until 1995, despite the fact that it had been widely used for years in other countries.

There have been reports of lactic acidosis occurring in people taking metformin, and the U.S. Food and Drug Administration estimates that lactic acidosis occurs in 5 out of every 100,000 people who use metformin for any length of time. However, this risk is much lower than it was in people taking phenformin, and it is not clear whether the episodes of lactic acidosis associated with metformin have actually been due to metformin use. In fact, the lactic acidosis could have been explained by the person's diabetes and related medical conditions. Nonetheless, diabetes experts recommend that metformin not be used in people with congestive heart failure, kidney disease, or liver disease. They also recommend that it be discontinued (at least temporarily) in people undergoing certain medical imaging tests called contrast studies.

Symptoms of lactic acidosis include feeling very weak or tired or having unusual muscle pain or unusual stomach discomfort.

## Neuropathy

Damage to nerves. In people with diabetes, neuropathy is generally caused by high blood sugar levels, but there are other possible causes of neuropathy, such as a B

vitamin deficiency, injury, some drugs, and cancer.

Excess glucose from the blood can infiltrate the nerves, interfering with their function by disrupting the electrical impulses they carry. Depending on which nerves are affected, neuropathy takes two main forms: sensory neuropathy and autonomic neuropathy.

Sensory neuropathy affects the sensory nerves, the nerves responsible for sensation throughout the body. It most commonly affects the feet, legs, hands, and arms. The symptoms may include numbness or a loss of sensation, coldness, tingling, burning, and extreme sensitivity to touch. Sensory neuropathy, especially in the feet, can cause people to be unaware of an injury, which, in conjunction with poor wound healing, can set the stage for a foot ulcer.

Autonomic neuropathy affects the nerves that control the involuntary functions of the internal organs. Depending on the exact nerves affected, autonomic neuropathy can cause the following problems:

- When it affects the cardiovascular system, autonomic neuropathy can cause heart attack, rapid heartbeat at rest (when you are sitting or lying down), very high blood pressure during exercise, and a condition called *orthostatic hypotension.* (Orthostatic hypotension is caused by damage to the nerves that control contraction of the blood vessels. It is characterized by a drop in blood pressure when a person stands up or sits up from a lying position, causing weakness or dizziness.) Autonomic neuropathy can also cause the nerves to the heart to fail to speed up or slow down the heart rate in response to exercise.
- When the nerves controlling the stomach are affected, a condition known as diabetic gastroparesis may result. In this condition, the movement of food through the stomach is slowed or even stopped, which can cause nausea and vomiting. In addition, by disrupting the timing of food absorption, gastroparesis can seriously disrupt blood sugar control.
- Autonomic neuropathy can affect the bladder, making it difficult to tell when it is full, sometimes leading to urinary incontinence.
- It can cause sexual dysfunction, especially in men. Nearly half of all men with diabetes develop impotence. In some cases, this may be caused by damage to the nerves affecting blood flow to the penis.

Maintaining near-normal blood sugar levels can help prevent and treat both sensory and autonomic neuropathy. For painful sensory neuropathy, your doctor may recommend a number of pain relievers, such as aspirin, acetaminophen, or one of the nonsteroidal anti-inflammatory drugs. Pain may also be relieved by tricyclic antidepressants such as amitriptyline or anticonvulsants such as gabapentin (brand name Neurontin). Other, nonmedical treatments such as biofeedback, guided imagery, and meditation may also be helpful to some people.

One of the most promising new treatments for painful sensory neuropathy is an over-

the-counter cream, sold under various brand names, that contains capsaicin. Capsaicin, found naturally in red peppers, has been used for centuries as an herbal pain remedy. Research shows that it depletes substance P, a neurotransmitter responsible for signaling pain, in the peripheral nerve endings (those in the feet, hands, legs, and arms). Studies show that it may relieve symptoms in about half of people taking it. The rest either show no improvement or, in a few cases, worsening of their symptoms. Speak with your doctor before trying this or any other over-the-counter pain product.