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alabetes.

The vast majority of diabetes cases are type 2 diabetes, which is associated largely with older age and being overweight as well as family history. Older age and obesity also are risk factors for developing cancer, which means that people with type 2 diabetes are diagnosed with cancer more often than those in the general population.



Endocrinologist and diabetes expert Azeez Farooki

Having diabetes can complicate cancer treatment due to a number of factors.

At the same time, some treatments for cancer, including certain newer targeted therapy drugs, can spur the development of diabetes, especially in patients who already had a propensity toward developing the disease, although this effect is usually reversible.

<u>Azeez Farooki</u> is a Memorial Sloan Kettering endocrinologist who specializes in treating cancer patients who also have diabetes. We spoke with Dr. Farooki about what special considerations are taken into account when treating this group of patients.

A Disease of Blood Sugar

"Diabetes is a disease in which a person has increased levels of glucose, or sugar, in the blood," Dr. Farooki explains. "It can occur because the pancreas does not produce enough insulin — the hormone that allows glucose to be absorbed — or because cells do not respond to the insulin that is produced. Cells should normally take in sugar from the blood; if they don't, then high blood sugar or 'hyperglycemia' results."

The majority of people with type 2 diabetes are overweight, which often causes the body to become resistant to the effects of insulin. Type 2 disease may be treated with insulin injections, other hormonal injections, or oral medication. "But the cornerstone of therapy is weight control," he says, "by staying active, exercising, and carefully controlling the diet, especially by limiting the consumption of simple, low-fiber carbohydrates and sugars."

The short-term effects of not treating diabetes include frequent urination and severe thirst, fatigue, and recurrent infections. The long-term effects include loss of vision, kidney problems, heart disease, and nerve damage. "Cancer is also an under-appreciated long-term risk resulting from obesity, prediabetes, and type 2 diabetes," he adds.

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Effects of Chemotherapy

Chemotherapy is a common treatment for cancer patients, but its side effects can make it more difficult to keep blood sugar levels in check.

"Steroids are often given with chemotherapy to lessen nausea," Dr. Farooki says, "but we know that steroids can raise glucose levels pretty markedly. For this reason, diabetes treatments need to be adjusted, and insulin injections may need to be started, especially around the time that the steroids are given."

Steroids can also cause diabetes to arise, especially in people who already have risk factors for developing the disease.

For people with diabetes who take injectable insulin, determining the appropriate dose can also be a challenge. "Insulin is generally given before a meal, and that's done assuming someone's going to eat a full meal," Dr. Farooki says. "If a patient throws up or has diarrhea after eating because of their chemotherapy, they may not absorb the food, causing their blood sugar to drop too low."

Uncontrolled high blood sugar can also cause dehydration, as can vomiting associated with chemotherapy. "Thus, it is important to detect and prevent high blood sugar in this setting," he says.

In addition, he notes, patients who are not feeling well are more likely to eat so-called comfort foods, which tend to be high in carbohydrates and can negatively affect blood sugar levels.

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Other Complications

Dr. Farooki explains that cancer treatment can be more difficult for people with diabetes, because they tend to have more health problems before beginning their treatments. "Diabetic patients tend to be sicker," he says. "They have fewer reserves in their body to be able to fight against the various complications that may come up, such as infections."

New targeted cancer therapies offer treatment options for some patients, and these drugs generally cause fewer side effects than traditional chemotherapy. Nonetheless, several targeted drugs do affect blood sugar levels.

Dr. Farooki was part of a National Cancer Institute—sponsored task force that looked at this issue. The recommendations of the task force were published in the *Journal of Clinical Oncology* in 2012.

He explains that in patients who didn't previously have problems, blood sugar levels usually return to normal after treatment with these drugs has been completed, but that existing diabetes can be a barrier to starting these drugs, especially in patients who are participating in clinical trials with strict entry requirements.

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Treatment Decisions

Dr. Farooki notes that especially for patients whose cancer is advanced, controlling glycemic levels to the very strict levels aimed for in patients without cancer does not always need to be prioritized. "For these patients, the primary and immediate focus is on treating the cancer," he says.

"You don't want to deprive them of a potentially life-sustaining drug because you are concerned about their blood sugar being marginally high. However, we want to avoid very high blood sugars that can predispose to immediate symptoms such as frequent urination, dehydration, unintentional weight loss, and infection," he adds. "But the long-term effects of high blood sugar are of lesser concern. With advanced cancer, we've got bigger fish to fry."

Some research raises the possibility that using insulin itself to correct hyperglycemia may curtail cancer growth and progression. "Both diabetes and cancer are considered inflammatory diseases, and involve inflammation at the cellular level," he says. "It's possible that preventing hyperglycemia with insulin may have antiinflammatory and antiangiogenic properties."

Inflammation has long been associated with the development of cancer; blocking angiogenesis, the process by which tumors increase their blood supply in order to grow and spread, is a current focus of many cancer researchers.

On the other hand, since insulin is a growth factor, it has long been debated whether large doses of insulin could stimulate cancer growth.

In addition, some studies have indicated that metformin, an oral drug commonly used to treat diabetes, may provide oncologic benefits. "There's a lot of interest right now in studying this," he says.

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