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## Overweight Children: Living Large

By Alice Park

High cholesterol. Soaring blood pressure. A fatty liver. Dangerously elevated insulin levels. Even a first-year medical student could recognize the signs of a middle-aged patient struggling with weight problems and diabetes and probably heading for a heart attack.

And in most cases, that med student would be right. But increasingly, the same deadly mix of problems is appearing in a startlingly younger population: teens and adolescents barely through their second decade of life. While the obesity epidemic is starting to show signs of waning, doctors are bracing for the more lasting legacy it leaves behind--a cohort of kids who are getting sick earlier or, at the very least, are a whole lot likelier to develop serious problems later. "We are seeing conditions that we as pediatricians are not used to seeing in children," say Dr. Seema Kumar of the Mayo Clinic in Rochester, Minn. "And we are seeing these a lot more."

The comparative novelty of such early-onset diseases makes them particularly tricky to treat, since extensive studies on the long-term consequences of childhood obesity just don't exist yet. But doctors know enough from work on adults to be worried. Overweight people of any age are at risk of not only better-known ills like cardiac disease but also arthritis, joint damage and sleep apnea. Adults who were overweight as children have nearly twice the risk of dying from any cause in their 70s than are adults who were of normal weight as youngsters. Early evidence also suggests that heavier children are even 35% more likely to develop cancer in their later years. "If you are a fat kid, you know you're in trouble," says Dr. Robert Lustig, a pediatrician at the University of California, San Francisco, "and you know you need to do something about it now and not later."

Of all the ills overweight kids risk (see chart), the two that may be the most complex--and thus earn a lot of new research attention--concern breakdowns in the function of the liver and pancreas. Mess with these organs, and you mess with some very fundamental metabolic systems that govern how well the body recruits and uses energy--a systemwide disruption that causes systemwide harm.

To understand the damage that obesity can do, investigators first have to understand the very dynamics of fat, and that knowledge has been slow in coming. The accepted wisdom had long been that we're all born with a fixed number of fat cells, and gaining or losing weight is simply a matter of filling or emptying them. But things are more complicated than that. As children develop, they continue to add fat cells to their body--at least until a certain age. Scientists don't yet know if kids who eat more food accumulate more cells, but studies in the 1960s pointed in that direction. However many fat cells you have, it becomes increasingly hard, as that fat bank grows, to pare it down, even in adulthood.

And far from being inert, excess fat, researchers now know, is actually an active participant in the body's biological ballet--particularly if it's visceral fat, which can surround and even suffuse organs like the liver. Relatively shallow subcutaneous fat, which sits just under the skin, imposes a weight burden on the body but remains biologically dormant--more a repository for energy than anything else. Visceral-fat cells can secrete hormones and cytokines that help control inflammation and guide energy use by all the body's other cells. Normally this regulation of cellular fueling is maintained by a well-balanced relay of metabolic signals. As food calories are absorbed, the pancreas secretes insulin, which prompts the liver to convert sugars into fat. Fat cells then release leptin, a hormone that puts the brakes on eating. Leptin does this by passing along the message that the body is satisfied with the deposit of calories it has received.

Overloading the body with too many calories and keeping insulin levels high short-circuits this loop and can lead to insulin resistance and Type 2 diabetes, in which organs no longer respond to changing insulin levels. The result: a brain and body that are constantly hungry and in need of more food. Disrupting the insulin threshold usually takes decades--which explains why this form of diabetes was generally more common in adults over age 30 and why the more genetically driven Type 1 diabetes was more prevalent among children. Before 1994, only about 5% of school-age children with a diabetes diagnosis had Type 2, but today anywhere from 30% to 40% of diabetic kids are told they have Type 2. And use of insulin-controlling medications to treat the disease in children rose 150% from 2001 to 2007.

Even more alarming to doctors are the changes that excess weight can wreak on the liver. It's this organ, after all, that orchestrates the breakdown and distribution of fats and sugars from the diet. When too much of either comes in, the liver starts to keep some of the excess for itself, converting sugars from soft drinks and the ubiquitous high-fructose corn syrup into fat that remains within its tissues.

Many overweight children already show abnormal levels of liver enzymes, and fully one-third suffer from fatty liver, a condition in which the organ becomes streaked with fat. "I worry about the outcome of these children 10 to 20 years from now," says Dr. Miriam Vos, a pediatrician and liver expert at Emory University. "In adults, we know that 3% to 5% of those with fatty-liver disease will progress on to cirrhosis or to an advanced stage where you might need a liver transplant." While not all cases reach such a dangerous state, Vos notes that in about 23% of children with fatty-liver disease, excess fat can lead to inflammation and scar tissue in the organ--the first signs of trouble.

During the early stages of these liver changes, however, there is hope. Vos' work shows that just as fat can be recruited into the liver, it can also be coaxed out, as long as the child eats properly and stays active enough to keep calorie input in line with what's burned off. Kumar says the key to reversing liver abnormalities--not to mention all the additional burdens excess fat places on the heart, bones and other organs--is to detect signs of weight gain in kids early. "We don't want to get to the point where children are so overweight, they have trouble moving," she says. "If that happens, we've lost the battle." As any parent of an overweight child knows, in the war on obesity, every battle counts.



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