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Discoveries about fat show how obesity kills

By DANIEL Q. HANEY
Associated Press

Research into the biology of fat is turning up some surprising new insights about how obesity kills. The weight of the evidence: It's the toxic mischief of the flesh itself.

Experts have realized for decades that large people die young, and the explanation long seemed obvious. Carrying around all those extra pounds must put a deadly strain on the heart and other organs.

Obvious but wrong, it turns out. While the physical burden contributes to arthritis and sleep apnea, among other things, it is a minor hazard compared to the complex and insidious damage wrought by the oily, yellowish globs of fat that cover human bodies like never before.

A series of recent discoveries suggests that all fat-storage cells churn out a stew of hormones and other chemical messengers that fine-tune the body's energy balance. But when spewed in vast amounts by cells swollen to capacity with fat, they assault many organs.

The exact details are still being worked out, but scientists say there is no doubt this flux of biological cross-talk hastens death from heart disease, strokes, diabetes and cancer — diseases that are especially common among the obese.

"When we look at fat tissue now, we see it's not just a passive depot of fat," said Dr. Rudolph Leibel of Columbia University. "It's an active manufacturer of signals to other parts of the body."

The first real inkling that fat is more than just inert blubber was the discovery 10 years ago of the substance leptin. Scientists were amazed to find that this static-looking flesh helps maintain itself by producing a chemical that regulates appetite.

ROUGHLY 25 different signaling compounds — with names like resistin and adiponectin — are now known to be made by fat cells, Leibel estimates, and many more undoubtedly will be found.

"There is an explosion of information about just what it is and what it does," Dr. Allen Spiegel, director of the National Institute of Diabetes and Digestive and Kidney Diseases, said of fat. "It is a tremendously dynamic organ."

Fat tissue is now recognized to be the body's biggest hormone-producing organ, and its sheer volume is impressive even in normal-size people. A trim woman is typically 30 percent fat, a man 15 percent. That is enough fuel to keep someone alive without eating for three months.

The fat cell's main job is to store our excess calories as fat. When people

grow obese, their fat cells swell with fat and can plump up to three times normal size. As very overweight people get fatter still, they may also layer on many more fat cells.

THE PROBLEM is the volume of chemicals these oversize cells churn out, said Dr. George Bray of Louisiana State University. "The big cell secretes more of everything that it secreted when it was small. When you get more of these things, they are not good for you."

Many scientists are trying to learn exactly what these excess secretions do that is so harmful. By far the biggest single threat of obesity is heart disease. Someone with a body mass index over 30 has triple the usual risk. Scientists can visualize many ways that fat cells' chemical flood contributes to heart attacks, heart failure and cardiac arrest.

For instance, it has long been known that weight increases blood pressure. Once doctors thought this was a matter of physics, the force needed to push blood through the more yards of blood vessels that nourish the extra flesh.

But now it is clear that fat can trigger high blood pressure by making blood vessels narrow in several chemical ways. For instance, it produces a substance called angiotensinogen that is a powerful constrictor. At the same time, it stimulates the sympathetic nerves to

squeeze the circulatory system. And that may just be the beginning.

"It's a very complicated system, and the more we learn about it, the more complicated it becomes," said Dr. Xavier Pi-Sunyer, head of obesity research at St. Luke's Roosevelt Hospital Center in New York City.

One of the clearest hazards of over-filled fat cells is their influence on the body's production and use of insulin, the hormone that instructs the muscle to burn energy and the fat cells to store it. Oversize fat cells blunt the insulin message, in part by leaking fat into the bloodstream. So the liver must compensate by making more insulin and other proteins.

SCIENTISTS NOW understand that increasing insulin levels — part of a condition called insulin resistance — are particularly harmful. They can directly damage the walls of arteries and lead to clogging.

Fat cells churn out a variety of proteins that cause inflammation, too. These may be especially destructive to the gunky buildups in the arteries, causing them to burst and triggering heart attacks and strokes.

These inflammatory proteins and other fat-driven chemicals, such as growth hormones, may also contribute to one of the less appreciated consequences of obesity — cancer.