for any violations. Some hospitals in Minnesota, which passed a law 5 years ago that imposes strict rules for releasing records, have banned external researchers—those not on hospital staff—from using their databases, Korn says. Having more health care systems put their databases off-limits, the AAMC letter warns, could "paralyze vital public health research." –JOCELYN KAISER

OBESITY RESEARCH

Pot-Bellied Mice Point To Obesity Enzyme

Words linking fruit and the human anatomy have long sweetened sonnets and love letters. But lately the term "apple-shaped" has gained renown on the pages of medical texts. People who carry excess fat around their waists—the so-called apple-shaped body type—are more prone to obesity-related maladies than their equally overweight but pear-shaped counterparts, who pack weight around their hips. Physicians have observed the connection for decades, but no one could explain it, let alone search for a therapy to right the scales.

Now on page 2166, researchers at Beth Israel Deaconess Medical Center in Boston suggest a reason for the disease–body type relationship, and a possible new target for treatment. The culprit is an obscure enzyme that works to recycle a steroid stress hormone called cortisol. Through delicate genetic engineering, endocrinologist Jeffrey Flier and his colleagues overexpressed the gene for this enzyme solely in the fat of mice. These rodents look and act a lot like overweight apple-shaped people: They eat more than normal mice and gain fat disproportionately around their middles. As adulthood sets in, the animals develop the early biochemical symptoms of heart disease and diabetes. Blocking the enzyme in people, the researchers suggest, might thwart obesity-related illnesses.

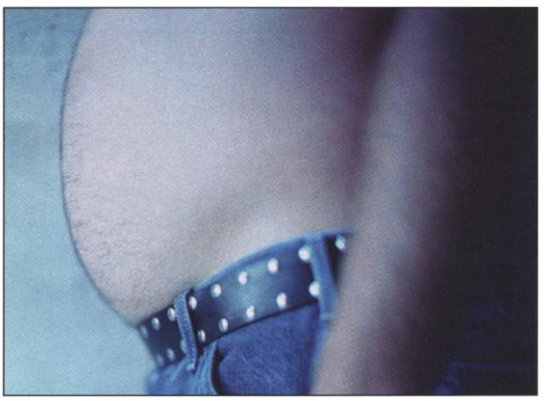
"This was really the first proof that manipulating steroid conversion in fat alone is enough to lead to all these abnormalities," says endocrinologist Stephen O'Rahilly of Addenbrooke's Hospital in Cambridge, U.K., who studies the genetics of obesity and diabetes. "I wish I'd done the experiment myself."

Inspiration for the study came indirectly from a rare illness called Cushing syndrome. Its sufferers have too much cortisol coursing through their bloodstreams and become diabetic and severely obese. For decades, endocrinologists hypothesized that common forms of obesity may represent very mild cases of Cushing syndrome. If so, most obese people should have higher than normal blood levels of cortisol—but researchers found that they don't and discounted the hypothesis.

The theory was resurrected by Paul Stewart of the University of Birmingham in Edgbaston, U.K., whose group found that people have pockets of high cortisol activity. The team compared stress hormone production in two types of fat in 16 patients undergoing surgery, most of whom were of normal weight. One sample came from underneath the skin, the other from adipose tissue in the abdomen. In the belly fat, the researchers found higher activity of an enzyme called 11β hydroxysteroid dehydrogenase type 1 (11β HSD-1), which regenerates active cortisol from its inactive form, cortisone.

Flier read a 1997 paper in *The Lancet* on the research and thought, "If we could make a mouse that overexpresses the enzyme only in fat, we could ask the question, 'Will that mouse get the apple-shaped body type and all its ill effects?' " he recalls. Visiting scientist Hiroaki Masuzaki engineered the mice; he linked a rat 11β HSD-1 gene to a promoter that turns on only in fat. The mice had 2.4 times more enzyme activity in their belly fat than did normal mice. Stress hormone levels in stomach fat tissue rose by 15% to 30%, but, as in most obese humans, bloodstream levels of the hormone were normal. As adulthood set in, the transgenic mice ate more, got fatter than normal mice, and carried the fat in their abdomens. Even when fed low-fat diets, the transgenics carried a spare tire that accounted for 37.9% of their total body fat compared with 27.5% in normal mice. The mice showed the hallmarks of early diabetes and hypertension: insulin resistance, renegade blood glucose levels, and other biochemical abnormalities. And a high-fat diet accelerated the pot-bellied rodents' downward spiral.

"It is really the whole picture of what we refer to as the metabolic syndrome," says Flier, citing a term now in vogue in en-



Belt loosener. Activating an enzyme in fat gives mice a syndrome seen in apple-shaped people.

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ScienceScope

War's First Casualty The British government wants to stop publicizing the locations of U.K. labs working with genetically modified (GM) organisms. In October, the government's Health and Safety Executive (HSE) temporarily stopped releasing a list that pinpointed government, university, and commercial labs doing GM research on grounds that terrorists might use the list to locate ready sources of virulent superbugs. And last month, the HSE proposed to permanently strike labs working with potential bioweapons from the public list. If parliament agrees, the agency would release a sanitized version in January.

Observers disagree on whether the censorship is a good idea. "Any other position would be irresponsible," says Tom Loeffler of the Biotechnology and Biological Sciences Research Council, a grant-giving body. But because "GM organisms currently pose little more threat than existing ones," delisting the labs does little to improve security, says Alastair Hay, a bioweapons expert at the University of Leeds. Clever readers, he adds, can discover out what labs are doing by trolling through journals.

Wayward Brains? Scientists at the U.K.'s Institute for Animal Health (IAH) have come out swinging against two government-sponsored audits that conclude that they mixed up cattle and sheep brains in a high-profile study. The IAH had carried out a 4-year investigation into whether Britain's sheep flock was infected with "mad cow disease." But last October, an independent laboratory reported that sheep brain samples used in experiments actually came from cows, calling the study's results into question (*Science*, 26 October, p. 771).

The audits, made public last week, blame the fiasco on IAH's poor sample labeling and record keeping. But they produced "no clear evidence" for mistakes at IAH, argues institute chief Chris Bostock. The samples originally came from another government facility, he notes, meaning a mix-up or contamination could have occurred either before the IAH took custody or after it sent out the tissues for independent analysis.

IAH researchers complain that auditors spent just 1 or 2 days visiting their lab in Edinburgh, where much of the work was done, and did not interview the scientists who first worked with the samples. Says one IAH staffer: "Everybody is furious at the way this has been handled."

Contributors: Andrew Lawler, Richard A. Kerr, John Pickrell, Michael Balter

docrinology circles to describe the growing population of obese people at risk for diabetes and heart disease.

But O'Rahilly points out that no one can yet pin down 11β HSD-1 as the cause of the millions of cases of diabetes and heart disease. "You have to find out whether the level of metabolic disturbance in people correlates with the activity of this enzyme," O'Rahilly says.

Meanwhile, two recent clinical observations support the team's results: In April, Joel Berger's group at Merck Research Laboratories in Rahway, New Jersey, showed that a class of antidiabetic drugs now on the market suppresses 11β HSD-1 levels in fat cells. And Eva Rask of Umeå University Hospital in Sweden and Brian Walker of the University of Edinburgh, U.K., report that obese men express higher levels of 11β HSD-1 activity in fat tissue than do lean males, which begins to address O'Rahilly's concerns.

Flier and O'Rahilly both say they are aware of drug companies that have in hand, or are scrambling to come up with, potent inhibitors of the enzyme. Such compounds might be used to treat obesity by altering stress hormone levels in belly fat. "We have wanted to know for some time what properties of fat inside the abdomen make it different from fat outside the abdomen," says O'Rahilly. "If this enzyme explains it, that would be interesting indeed." **–TRISHA GURA**

Trisha Gura is a science writer in Cleveland, Ohio.

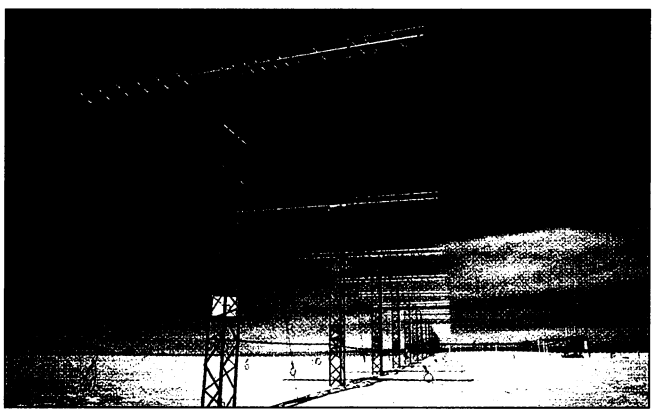
ATMOSPHERIC PHYSICS

Finding the Holes in The Magnetosphere

Just outside the protective cocoon of our atmosphere, a battle rages in space. A gas of electrically charged particles—the solar wind—traveling at hundreds of kilometers per second streams at us from the sun. All we have to guard us is Earth's magnetic field, but this shield is not impregnable. Every so often, particles and energy burst through, by means of a process called magnetic reconnection, causing displays such as the aurora borealis as well as magnetic storms that disrupt satellites, power lines, and communications. Researchers have puzzled for decades over how and where reconnection happens. Now physicists from the British Antarctic Survey (BAS) in Cambridge have developed a way to pick between two competing views of where reconnection occurs.

The work "seems to provide strong evidence for one [model] rather than the other," says space plasma physicist Stan Cowley of the University of Leicester, U.K. Finding a recipe for picking between the two models is an "important step," agrees physicist Ray Greenwald of Johns Hopkins University's Applied Physics Laboratory in Laurel, Maryland.

The solar wind is no steady breeze. Violent events in and around the sun, such as flares and coronal mass ejections, can whip up the wind to gale force. And because it is made up of charged particles, the solar wind carries the sun's magnetic field with it. As it nears Earth, our magnetosphere diverts the solar wind around our planet like river water around a bridge pier. But sometimes the two magnetic fields don't just rub together: They hook up, creating an entry point for the particles and energy to pour into the magnetosphere.



Looking up. The British Antarctic Survey's SHARE radar scans the skies over Halley research station in Antarctica.

Researchers still don't understand reconnection events well enough to predict when and where they will happen. Theoretical models have divided them into two principal camps. Supporters of the "subsolar" theory hold that the action takes place at the point closest to the sun, the "nose" where the magnetosphere bears the full brunt of the solar wind. The rival "antiparallel" camp, meanwhile, believes that any point where the sun's and Earth's fields are in direct opposition—typically well away from the "nose"—is fair game for reconnection. "It is debated at every meeting," says Greenwald.

A team from BAS decided to settle the matter. A key difference between the two theories is that, under particular seasonal and solar wind conditions, the antiparallel model predicts that two reconnection points will always be created, whereas the subsolar theory produces only one. Finding reconnection events, which may be just a few thousand kilometers wide and last only a few minutes, is hard for the handful of spacecraft currently surveying the vast magnetosphere. But Richard Horne and his BAS team realized they had just the tool for the job: ground-based radar.

Horne and his colleagues have spent years monitoring Earth's ionosphere, the plasma layer that forms the uppermost tier of the atmosphere. Because reconnection events cause disturbances in the ionosphere, the BAS researchers realized that the radar data they had collected might contain "footprints" of past reconnections. The team searched back through years of data from radar stations close to the poles, the best places to monitor the ionosphere. Data collected from Goose Bay in Newfoundland and Stokkseyri in Iceland on a December day in 1997 showed two distinct ionospheric disturbances signaling reconnection events. Neither took place close to the spot nearest the sun favored by the subsolar model. The results, to appear this month in the *Journal of Geophysical Research* (Volume 106, p. 28995), show "clear evidence in favor of the antiparallel theory," Horne says.

Researchers caution that one example doesn't clinch the case. Reconnection events may appear "all over the place," Cowley says, perhaps with one model dominating the other. Greenwald agrees that more observations are needed. The BAS team has since identified three more double events and has submitted a second paper to the *Journal of Geophysical Research*. In time, these results should help solve what Cowley calls "the fiendishly difficult problem" of understanding in full how magnetic reconnection works. **–ANDREW WATSON**

Andrew Watson is a writer in Norwich, U.K.

PALEONTOLOGY

Paring Down the Big Five Mass Extinctions

BOSTON—The five largest extinctions of the past half-billion years seemed immutable milestones on the path to modern life. Ever since researchers fingered a huge impact to explain the most recent of them, the one that ended the age of the dinosaurs 65 million years ago, the rest have also borne the tinge of doom. But now a pair of paleontologists say that two of the Big Five just don't measure up. Instead, Richard Bambach and Andrew Knoll of Harvard University argue, the losers should be demoted to "mass depletions": plunges in diversity caused by still-mysterious failures to produce enough new species.

Doubts about the legitimacy of the Big Five—those that came late in the Ordovician and Devonian periods and at the ends of the Permian, Triassic, and Cretaceous—began with the same sort of data first used to identify them. As they reported last month at the annual meeting of the Geological Society of America (GSA) here, Bambach and Knoll

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