shown that the Ob protein is made by fat cells. They propose that some part of the body reads Ob levels the way a thermostat reads temperature and then tells the body to make the appropriate adjustments. If the levels are low, Friedman explains, this "lipostat" tells the body it doesn't have enough fat and needs to gain weight. If they are too high, the message is to eat less, burn more calories, and lose weight.

Mutant *ob/ob* mice make no Ob protein, and so, according to the model, their lipostats go unchecked, and they gain weight. But other obese mice, whose fat cells are making Ob protein, may be fat because their lipostats simply have a higher set point, requiring higher levels of Ob protein before they tell the body to lose weight. Injected doses of Ob protein may act in those mice like "virtual fat," fooling their lipostats into sensing that they are fatter than they are and triggering weight loss.

As a first step toward testing that model, researchers are searching for the target tissues for the Ob protein. At least one target seems to be in the brain; the Roche team reports that Ob protein injected directly into the brains of mice caused effects similar to those produced by injections into the bloodstream, but at a much lower dose. "We see reduced food intake and a loss of body weight," says Paul Burn, director of the Department of Metabolic Diseases at Roche. "That suggests the receptor for the Ob protein is localized in the brain." Many research teams are also hot on the trail of that receptor itself, which transmits the protein's message via a set of as-yet-unknown signals inside cells. Identification of the receptor "may eventually lead to novel drug targets within the signaling cascade," says Burn.

But while that research proceeds, all eyes are on the potential for Ob itself to be developed into a weight-loss drug. While the mouse studies are encouraging, "it is too early to be sure what the clinical implications will be," cautions Ruth Harris, a physiologist who studies obesity at the Pennington Biomedical Research Center of Louisiana State University in Baton Rouge. "A lot more work has to be done [on Ob protein levels in humans] to have a better understanding of the role it plays in obesity," she says.

Friedman readily agrees that much work must be done before considering the use of Ob in humans. "There is an orderly series of steps ... and that process has to be followed carefully," he says. "The next important step is to establish the safety of the protein in animals." Even if the early promise holds up, there is the matter of drug delivery. Because Ob is a protein, it can't be taken in pill form, as it would be destroyed in the digestive tract, and so would have to be injected, perhaps daily. But "for someone who is morbidly obese, it wouldn't be a problem for them to take an injection," says Larry Bellinger, a physiologist who studies obesity at Baylor College of Dentistry in Dallas.

If the Ob protein were to lead to a weight-loss drug, that would raise thorny questions about how such a drug should be used. If the mouse studies are an indicator, the drug might enable normal-weight people to become super-thin or allow fat people to drop pounds without changing their high-fat diets, which carry their own health risks. "That is a little scary because it could be abused," says Atkinson. "Maybe ... everyone will want to look like Twiggy."

Anyone concerned with how such a drug might be used or misused will have plenty of time to mull the issue over while researchers follow up these early results—and Amgen waits anxiously to see whether its $20 million investment will pay off.

–**Marcia Barinaga**

PALEOANTHROPOLOGY

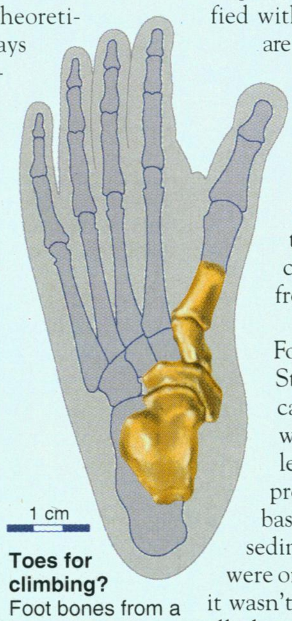
New Foot Steps Into Walking Debate

There's no doubt that our early ancestors walked on two legs—footprints left in the ground in Tanzania some 3 million years ago leave a firm record of their evolutionary strides. But anthropologists are in sharp disagreement over how much walking these creatures actually did. Did they spend their time wandering open savannas, or clambering up and down tree trunks in more wooded places? Because modern humans are fully grounded, and the apes we came from are not, researchers dearly want to know when the shift occurred.

With a report on the left foot of an early human forerunner, or hominid, that they've dubbed "Little Foot," anthropologists Ronald Clarke and Phillip Tobias of the University of the Witwatersrand Medical School in South Africa step into this debate—and onto the toes of some of their colleagues. On page 521 of this issue, the two researchers describe four bones they've found—probably from a hominid called an australopithecine that lived about 3.5 million years ago—that make up an arch running from the heel of the foot down to the beginning of the great toe. They are the first connected foot bones ever found from a single such creature.

And while the foot shows some humanlike traits, such as a weight-bearing heel obviously adapted to bipedalism, Tobias says its long, flexible big toe is perfect for grabbing onto tree limbs and, along with some other traits, it "virtually settles the argument" that our ancestors at that time were still partly in the trees.

"I find it conceptually and theoretically a very compelling paper," says Randall Susman of the State University of New York, Stony Brook, long an advocate of arboreal ancestors. "The back part of the foot around the ankle joint is very human, but as you get out toward the toes, they get more and more apelike." Elwyn Simons of Duke University in North Carolina, who recently viewed the bones, says that "it's very important because all the other foot bones [found up to now] didn't really show as clearly the climbing ability."



Toes for climbing? Foot bones from a human forerunner.

Critics, however, react to Little Foot as if they've been kicked. "Their conclusion is patently absurd," says Owen Lovejoy of Kent State University in Ohio, a champion of early unabridged bipedality. The australopithecine hip, knee, and spine have been adapted for an upright life, he says, and to ignore all that evidence in favor of one foot joint "is mechanically and developmentally naive."

Anthropologists such as Susman and Lovejoy have been "butting feet"—as one onlooker calls it—over this issue for more than a decade. Susman's camp, for instance, has argued that curved fingers and toes from *Australopithecus afarensis* (the species identified with the famous "Lucy" skeleton) are "arboreal hooks" much like those seen in modern apes. Lovejoy and several colleagues have countered that the pelvis and other anatomical traits show that such early hominids were already grounded, and that any apelike traits they still carried were unused baggage from their evolutionary past.

Into this debate now steps Little Foot—more properly known as Stw 573 for the Sterkfontein cave in South Africa in which it was found. The creature was at least 3 million years old, and probably as much as 3.5 million, based on geologic dating of the sediments in the cave. The bones were originally excavated in 1980, but it wasn't until last year that Clarke put all the pieces together. He found an ankle bone (talus), some foot bones, and the first part of a big toe. "All jointed perfectly together when you held them one against the other," Tobias recalls.

One of these joints in particular—the

joint between the metatarsal and the medial cuneiform, which makes up the ball of the foot—reveals features that Tobias says almost certainly indicate time spent in the trees. "That joint, in modern humans, is remarkably flat, permitting little rotational movement," Tobias notes, "whereas in apes it is highly curved." This, he says, allows the big toe to abduct—to rotate inward like the human thumb rotates in relation to the rest of the fingers. An abductable big toe can grasp things like branches, which is a useful trait if you're frequently up a tree.

This line of reasoning is really what's up a tree, says Lovejoy. He argues that the Sterkfontein foot bones pretty much mirror what he's seen in various *A. afarensis* foot bones at Hadar—a site in Ethiopia that's produced an abundance of *afarensis* fossils—and yet when he has reconstructed the ball joint from these bones, he's found that it allows no rotation and little motion of the big toe. Therefore, he contends, the anatomically similar Little Foot would have the same constraint. Tobias, however, counters that the Sterkfontein foot bones are the first articulated bones that appear to be from a single australopithecine. Therefore, he says, information derived from them is much more compelling and illuminating than extrapolations from composites of fossils, which is how many researchers describe the Hadar bones.

Still, Lovejoy says, even if Little Foot's big toe could rotate, it wouldn't prove that the hominid actually used it as a climbing toe. "You can't expect an animal that has recently evolved bipedality to no longer have any anatomical characters that aren't also found in modern-day apes," he says.

Here Susman vehemently disagrees. If a bone is shaped to perform a task, he says, that's what it must be doing—an inactive bone will be reshaped during a single lifetime of disuse. He points, as evidence, to changes in the bones of people confined to bed for years. Because Little Foot's great toe appears well adapted to climbing, he concludes, the hominid probably did spend a good deal of time doing just that.

This, says anthropologist William Kimbel of the Institute for Human Origins in Berkeley, California, cuts to the heart of the argument, which is less about bones and more about philosophy. "What's driving most of the differences are more philosophical views about how to interpret morphology and its relationship to adaptation," he says. And until anthropologists can thrash out the issue of whether apelike bones necessarily mean an apelike pattern of locomotion, no fossil is likely to ever change any researcher's mind. Directly confronting this issue with Little Foot, he says, will be a step in the right direction.

–Lori Oliwenstein

Lori Oliwenstein is a science writer in Los Angeles.

MEETING BRIEFS

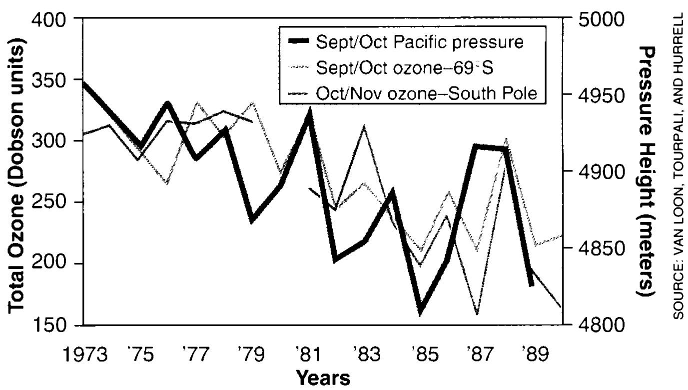
At Quadrennial Geophysics Fest, Earth Scientists Think Globally

BOULDER, COLORADO—The study of Earth is by nature a global endeavor, but only every 4 years do geophysicists come together from the four corners of the world for a general assembly of the International Union of Geodesy and Geophysics (IUGG). The 6000 scientists who gathered here for 2 weeks earlier this month had thousands of talks and posters to choose from, including two addressing a suitably international concern: ozone loss.

A Stratospheric Whodunit

Earth scientists are used to tracing far-flung connections. A calming of the trade winds in the equatorial Pacific can mean a wet winter in the southeastern United States; the eruption of a volcano in the Philippines can temporarily slow the ongoing warming of the globe.

At the IUGG meeting, meteorologists Harry van Loon and James Hurrell of the National Center for Atmospheric Research in Boulder, Colorado, unveiled another long and unlikely seeming chain of connections. Their proposed linkage stretches from the warm surface of the tropical Pacific Ocean, through the atmosphere at midlatitudes in the Southern Hemisphere, to the icy stratosphere over Antarctica. And that's where it may have left its mark, by allowing a warming of the tropical sea surface 15 years ago to set the stage for the notorious Antarctic ozone hole.



Down, down, down. Springtime ozone over two sites in Antarctica started to decline around 1980, when a Southern Hemisphere pressure oscillation *(red line)* weakened, suggesting a link.

Van Loon and Hurrell haven't pinned down all the links in this chain. And they have only circumstantial evidence for its involvement in ozone destruction: hints, says Van Loon, that "something drastic" happened to the chain around 1980, when the ozone hole first appeared. Other climate researchers aren't sure the chain is as long or as potent as Van Loon and Hurrell suggest. But they are intrigued by some of the individual links and say that following such connections, especially in the poorly understood Southern Hemisphere, should help tease apart the tangled threads of global change.

Clues to the connection come from records of atmospheric pressure gathered over many decades at weather stations in the Southern Hemisphere. There meteorologists long ago identified a pressure seesaw that operates on a 6-month cycle in mid and high southern latitudes. Driving the oscillation are differences in the response of the mainly ocean-covered middle latitudes and the Antarctic continent to seasonal changes in solar heating. Because atmospheric pressure differences spawn winds, this semiannual oscillation (SAO) drives changes in the strength of the vortex of winds that swirls around the Antarctic in the winter and early spring. The vortex creates the stratospheric cauldron where humanmade chemicals, icy clouds, and sunlight combine to destroy ozone.

Around 1980, Van Loon and Hurrell found, the SAO began weakening, with serious consequences, they suggest, for the stratospheric ozone over Antarctica. Meteorological data showed that the net effect of the weakening was to strengthen the Antarctic vortex in the spring and delay its annual breakup by a month or two, Van Loon says. That would have intensified the cold within the vortex and given the spring sunshine extra time to drive ozone-depleting chemical reactions—and 1980 is just when the ozone hole started to become obvious.

By the same token, when the SAO temporarily returned to near normal in 1988, weakening the vortex, the hole shriveled, registering some of its smallest ozone losses of the decade. "If I'm right," says Van Loon, the weakening of the SAO "is a necessary but not sufficient condition for the ozone hole."