figuring out the gene response," says CTL's William Pennie.

Even though many researchers say that animals will never be replaced for conducting general investigations or checking a whole-body response to a potential toxicant, scientists are also enthusiastic about the potential of chip technology and in vitro tests for asking specific questions—with data from human cells, rather than animal models of disease. "We can now go into more depth," says toxicologist Sandra Coecke of ECVAM. "With in vivo tests, you ended up with kind of a black box." Indeed, Coecke and others feel that these kinds of new methods—once validated—could not only replace animals tests, they could be an improvement. —ERIK STOKSTAD

MEETING SOCIETY OF VERTEBRATE PALEONTOLOGY

The Stories Behind The Bones

DENVER, COLORADO—There's more to paleontology than fossils, as was shown here on 20 to 23 October at the 59th meeting of the Society of Vertebrate Paleontology (SVP). Genetics labs, for example, uncovered an Ice Age disease; a changing atmosphere was fingered as the force behind the evolution of mammals in North America; and dissecting modern animals has hinted at the reason dinosaurs had such big noses.

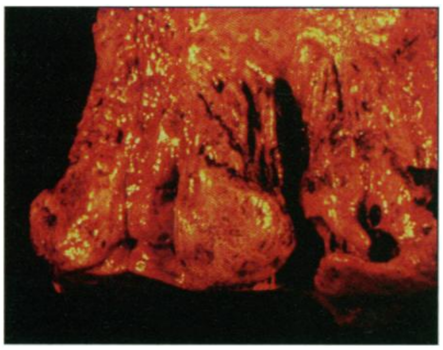
Ancient Tuberculosis Identified?

The world's deadliest infectious disease, tuberculosis plagues a third of all people on Earth, killing 3 million every year. Exactly how the scourge first got a toehold in our species has been a mystery, but at the meeting researchers made a controversial announcement that they had a clue—in the form of DNA from *Mycobacterium tuberculosis* dating back 17,000 years.

For decades, the traditional story of TB had it arising in Old World pastures. Cows and their bovine relatives carry strains of the mycobacterium that are closely related to the human form; people could have become new hosts for TB when they began herding cattle and handling meat and hides. That idea seemed to find support in the devastating epidemics that swept through Native American society when European colonists arrived in the New World. Native Americans, never having domesticated cattle, had apparently been spared the disease until then and thus had immune systems that couldn't cope with TB.

But in 1994, that notion collapsed with the discovery of *M. tuberculosis* in a 1000-year-old mummy in Peru—predating Columbus's arrival by 500 years (*Science*, 25 March 1994, p. 1686). Native Americans carried TB long before Europeans came on the scene, and the massive epidemics that followed the contact could have resulted from overcrowding, malnutrition, and bad sanitation.

So where did the New World TB come from? In the late 1980s Larry Martin, a paleontologist at the University of Kansas, Lawrence, and Bruce Rothschild, an expert on ancient diseases at the Northeastern Ohio Universities College of Medicine in Rootstown, looked for evidence of TB on bones from the New World's grazing animals. The disease can leave scars on bones in places where the immune system has walled off infected cells. Martin and Rothschild examined bones of bison, musk ox, and bighorn sheep from the Natural Trap Cave in Wyoming, dating back 15,000 to 20,000 years. They found the scars in abundance but couldn't say whether the animals suffered from TB or other lesion-forming diseases, such as brucellosis. Because the lesions looked more like those of TB than of other diseases, "we knew it was a likely diagnosis," says Martin. "But we knew we could be wrong."



CREDIT: B. ROTHSCHILD

Old scourge. TB appears to be to blame for these lesions on a 17,000-year-old bison bone.

The researchers suspected that they might be able to settle the issue by finding genetic material from the mycobacterium itself in the fossils. Natural Trap Cave gets its name from the way it is entered—by falling into the entrance and dropping 30 meters to the cave floor. Animals have been falling to their death in the cave for 100,000 years. During the Ice Age, these unlucky creatures would have crashed into a heap of snow on the cave floor and been freeze-dried. There was a chance, therefore, that some of their DNA could have survived until now.

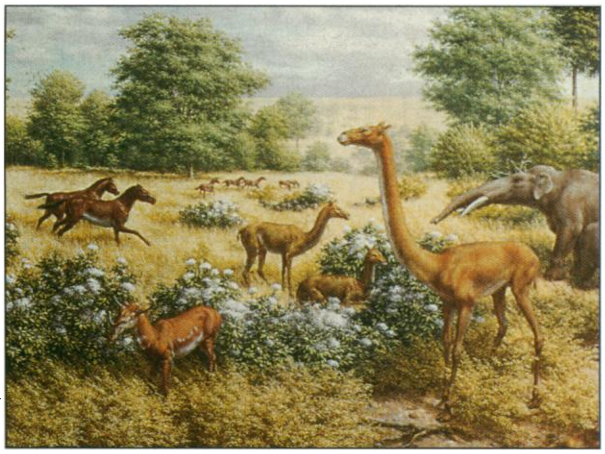
Rothschild and Martin extracted some of the bone tissue from a lesion on a 17,000-year-old bison. They sent samples to labs in Israel and England, each of which used the polymerase chain reaction to amplify any fragments of genes. As Martin explained in his talk, both teams identified genes belonging to *Mycobacterium*. Although the timing of human arrival in the Western Hemisphere is still under intense debate, Martin says, "my suspicion is that tuberculosis was waiting for humans when they came."

Based on the talk, however, other researchers are skeptical. "They didn't put all their ducks in a row," contends Ross MacPhee of the American Museum of Natural History in New York City. Many species of mycobacteria live in the soil, he points out, and they might have gotten into the cave and contaminated the bison material. Contamination has proven to be a big headache for scientists who study ancient DNA, yet Martin and Rothschild didn't present any control tests that could have ruled it out—for example, testing the bones of animals that don't get TB for the presence of the mycobacterium. "The result is really interesting, so why didn't they go that extra step and knock out the ambiguity?" asks MacPhee. According to Martin, his team will soon present data that address this issue.

If Martin and Rothschild are right, New World TB must have come from the Old World, when some infected mammals crossed the Bering Land Bridge and then infected the early Americans who hunted them. And if people in the New World picked up the disease from hunting, rather than farming, maybe the same goes for the Old World, too. The two researchers note that their scenario resembles current theories that trace AIDS in humans to hunting chimps and monkeys. "It shows that even for the most sophisticated side of medicine, it's useful to know what happened 17,000 years ago," says Rothschild.

Where Have All the Browsers Gone?

Two artist's conceptions, common in Earth history texts, tell the story. One portrays North America 20 million years ago in the early Miocene, showing a mix of grassland and trees, with many sorts of hoofed mammals, or ungulates, craning their necks to browse on leaves. In the second,



When food was plentiful. Browsers dominated North America 20 million years ago in the early Miocene.

showing the landscape of the last few million years, most of the browsers are gone, and many of the animals—horses, bison, and other grazing ungulates—have their heads to the ground, chewing up the grass. Why did the mammals of North America go through such a drastic shift? The explanation, many researchers think, is blowing in the wind: a drop in atmospheric carbon dioxide since the Miocene, which could have affected the vegetation that the big herbivores depended on. At the meeting, Brown University paleontologist Christine Janis offered a new scenario for how this CO_2-driven change in North America's ecosystems might have taken place: by gradually starving the plants the browsers ate.

Many researchers think the shift was abrupt. Isotopes found in ancient soils and in the fossil teeth of horses show that between 8 million and 6 million years ago, plants that use a photosynthetic system known as C3 declined, while those that use a system called C4—tougher species such as crabgrass—suddenly became dominant in North America and elsewhere. C4 plants do better than C3 plants in low levels of CO_2, suggesting that the declining levels of atmospheric CO_2 triggered their spread. The grazing ungulates, equipped with high-crowned teeth, could grind down the hardy C4 plants. But many of the low-crowned browsers, adherents say, couldn't handle life on the new grasslands and went extinct (*Science*, 28 August 1998, p. 1274).

Janis and her co-workers, John Damuth of the University of California, Santa Barbara, and Jessica Theodor at Brown, decided to test that idea by taking a close look at the fossil record. "It has to be better examined, instead of just [being] asserted," says Janis. They tallied instances when hoofed mammals evolved into new species or went extinct over the past 20 million years, noting whether the animals were browsers, grazers, or those with a mixed diet. Nowhere in their database could they find a pulse of extinctions that coincided with the shift from C3 to C4 plants.

The pattern they found instead was distinctly different. Before 18 million years ago, browsers made up the majority of ungulate species at just about every site where Janis and her colleagues looked—in some places reaching levels as high as 80%. The browsers then started a slow, steady decline that carried on for millions of years, through the C3-C4 transition and into more recent times.

Janis agrees that the ultimate spur for this mammal overhaul must have been the fall in CO_2 concentrations, but says the changes started many millions of years before the C3-C4 shift. Atmospheric levels of carbon dioxide have been declining for the past 50 million years. This long-term atmospheric change exerted its effects gradually, she proposes, as the leafy C3 plants the browsers depended on produced less food, and many of the browsers gradually went extinct. The C3-C4 transition certainly didn't help matters, but it came after CO_2 had already been declining for at least 10 million years. "The transition was at the end of a long progression," says Janis.

The work "is a wonderful demonstration that the decline of browsers and the evolution of grazing morphology is probably not directly related to the spread of certain types of grass," says Tony Barnosky, a paleobiologist at the University of California, Berkeley. But Barnosky thinks forces other than the CO_2 decline could have played a role. The early Miocene saw a period of volcanism in the western United States, and the dusting of ash would have made plants hard to chew and digest. The rough stuff would have been a challenge for the low-toothed browsers, eventually starving them, but the high-toothed grazers could have coped. Whatever the mechanism, Barnosky says, "the decline of browsers seems to have an environmental trigger, but the gun was a much bigger—and earlier—one than the C3-C4 shift."

Dinosaur Air Conditioning

Dinosaurs evolved some pretty bizarre anatomy, from the ridge of plates along a *Stegosaurus*'s back to the fantastically long tail and neck of *Apatosaurus*. But for Larry Witmer, a paleontologist at the Ohio University College of Osteopathic Medicine in Athens, dinosaurs' coolest feature was hidden from view—specifically, up their noses. In most vertebrates, the nasal cavity is the smallest part of the skull, he explains. Yet in several groups of dinosaurs, the nasal cavity expanded to gigantic proportions. Indeed, a small child could climb inside the nasal cavity of the long-faced, beaked *Triceratops*. "There must be something pretty important going on to devote half the skull to that," Witmer says. The answer, it appears, was to keep dinosaurs, and especially their puny brains, from frying.

To figure out what dinosaurs used their noses for, Witmer has spent the past few years engaged in something he calls the DinoNose Project. Muscles, mucous membranes, and blood vessels can all leave marks on a fossil, in the form of grooves, shelves, canals, and other structural features. To interpret the structures of dinosaur skulls, Witmer and his co-workers have studied the anatomy of living animals that have big, unusual noses, looking at the way their soft tissues shape their bones. And because dinosaurs are closely related to today's alligators and birds,

Cool nose, cool brain. *Triceratops* was one dino that may have paid through the nose for AC.

Witmer's group studied the heads of these animals as well, identifying the structures they could have inherited from a common ancestor. With this knowledge, Witmer is beginning to make some inferences about what dinosaur noses probably looked like and what they did—work that is winning admiration. "This is some of the most exciting and innovative research being done in vertebrate paleontology," says Greg Erickson, a paleontologist at Brown University.

The noses must have been up to something important, Witmer says, because they were suffused with a huge amount of blood. In his talk at the SVP meeting, for example, he reported that his group identified three separate blood supplies to the noses of ceratopsians,

CREDITS: (LEFT TO RIGHT) *THE AGE OF MAMMALS*, A MURAL BY RUDOLPH F. ZALLINGER/PEABODY MUSEUM OF NATURAL HISTORY, YALE UNIVERSITY; A.J. COPLEY/VISUALS UNLIMITED each of which formed big networks of capillaries. Based on the pattern of impressions in fossilized bone, he suggests that the blood vessels were embedded in mucous membranes lining the walls of the nasal cavity.

What's more, the mucous membranes themselves were apparently extensive. In another talk, a DinoNose collaborator, Scott Sampson of the University of Utah, Salt Lake City, pointed out a number of ridges in the ceratopsian schnozz that probably supported curtains of cartilage; these in turn may have served as scaffolding for layers upon layers of mucous membranes. Yet the most obvious function of noses—smelling—probably wasn't responsible for their size. Smelling takes place at the rear of the nasal cavity, while all the extra space and blood supply is found at the front end of dinosaur noses.

Witmer thinks dinosaur noses helped keep their brains cool. He notes that all the big-nosed dinosaurs had big bodies as well, and for them, heat must have been a problem, because in big animals the ratio of surface area to body mass is much lower than that for smaller animals. As a result, even if dinosaurs didn't have a fast-burning metabolism like that of mammals, the bigger ones must have been unable to shed heat fast enough from the skin to keep their body temperatures from rising to dangerous levels. The brain in particular could have been damaged by such high temperatures, as everyone knows from the occasional tragic stories of teenagers dying from heat-related "brain attacks" after playing sports in summertime.

Witmer proposes that dinosaurs relied on their noses, with their vast networks of blood vessels, to get rid of excess heat. The vessels were probably in contact with the air in the nasal passages and could have wicked heat from the brain. This would be analogous to what happens in mammals, such as the gazelle, that live in hot climates. These animals have veins just under the skin on their head, which cool the blood as they release heat to the air. Rather than traveling straight back to the heart, this cooled blood takes a detour, flowing through a mesh of veins surrounding the brain. These veins run alongside the arteries bringing warm blood from the body's core. The cool veins absorb the heat from the arteries and carry it away from the brain. "Big animals get a big benefit from heat exchange," Witmer says. "It would allow the core temperature to rise while keeping the brain cool."

All this does not rule out other roles for the big noses of dinosaurs. For example, they may have helped attract mates, although Witmer's group has yet to study that possible function. Says Sampson, "We have yet to come up with the final word." –CARL ZIMMER

Carl Zimmer is the author of *At the Water's Edge*.

BIOMEDICAL RESEARCH

NIH Eyes Sweeping Reform Of Peer Review

Authors of a reform proposal say their goal is not to make radical changes but to create a system that can be "continually evaluated by outside experts"

Like Lewis Carroll's White Queen, who could believe "as many as six impossible things before breakfast," scientists who analyze the National Institutes of Health's (NIH's) peer-review system often find themselves torn between conclusions that are, at the very least, contradictory: The cornerstone of NIH's success has been its peer-review system, in which small committees of nongovernment scientists, known as "study sections," judge the scientific merit of about 40,000 grant applications a year; *or,* NIH peer review too often amounts to error-prone, turf-conscious nitpicking by obsolete study sections that reject novel ideas out of fear, ignorance, and self-interest.

NIH officials and many researchers today seem to believe both. As a result, NIH is now in the midst of a major drive to refurbish the system—updating it to fit today's biomedical science, setting standards of behavior to improve peer reviewers' manners and methods, and creating a mechanism to ensure that peer review will adapt as science evolves in the future.

In the most dramatic reform proposal so far, a blue-ribbon panel headed by National Academy of Sciences president Bruce Alberts wants to completely restructure the array of study sections operated by NIH's Center for Scientific Review (CSR), which pass judgment on about three-quarters of NIH grant applications (*Science*, 30 July, p. 666).

But the changes that will finally emerge, after they are refined and tested over the next 2 or 3 years, may be considerably less sweeping than the Alberts panel blueprint. "I don't think it's going to be as radically different as some people have said," says NIH director Harold Varmus. "Peer review basically works pretty well now. We don't want to make abrupt changes that could be threats to the system."

The Alberts panel's proposals, if not radical, certainly look pretty startling. Currently, more than 100 CSR study sections are clustered into 19 "Integrated Review Groups" (IRGs), focused mostly around scientific disciplines such as "Biochemical Sciences" and "Cell Development and Function." Instead, in what it calls the "first draft" of its report, the Alberts panel proposes reconstructing the system around 21 reorganized IRGs—16 centered on disease or organ systems and five focused on basic research areas whose application to specific disease areas cannot be predicted.

Basic research that "more directly underlies clinical or applied studies" on specific

What's Wrong With NIH Peer Review?

[illegible]

"I have been on study sections and have seen members who clearly lacked expertise review proposals and grade proposals in a biased, or self-serving, or bad scientific manner." —Louis Gerstenfeld, Boston University Medical Center

"I have seen the results of ideas being stolen [by peer reviewers]. Who will be believed, the experienced peer or the new investigator?" **—unsigned**

"Under the present 'culture,' which focuses on fault finding and amplification of minor errors and discouraging innovative research, nearly all NIH funding has gone into confirming, reconfirming, and reinventing what is already known, by individuals of very little insight or talent." **—unsigned**

"Every one of us has received reviews that clearly misstated facts, indicated that the reviewer failed to read the proposal thoroughly, or were filled with unsupported assertions of opinion. Such poorly performed reviews, which are, I believe, all too common, undermine confidence in the system." —unsigned