Coase, however, determined that the farmer and the rancher could reach an economically optimal settlement regardless of the legal environment. Suppose the cattle regularly ate $1000 worth of corn, while erecting a fence on the rancher's land would cost only $100. If the government forced the rancher to assume liability, the rancher would build the fence. But even in the absence of government action, the fence would still get built, although the farmer would have to pay the rancher between $100 and $1000 to do so. In either case, both parties would be better off than if no fence had been built.

In the real world, of course, the rancher could set an unreasonable price because he bears a grudge against the farmer. Or, if erecting a fence were to cost more than the damage to the farmer's corn, the farmer might scheme to collect damages by deliberately planting corn near the property line. Such non-zero transaction costs significantly complicate dispute resolution. As a result, Coase concluded that policy-makers should act cautiously when forging legal rules that might increase transaction costs. This "Coase theorem" is now widely taught in law schools across the United States, and has played a significant role in the development of the discipline of law and economics. Coase's ideas had "a direct, immediate effect on...lawyers, who began thinking about legal rules from an economic perspective," says Harvard professor of law and economics Stephen Shavell.

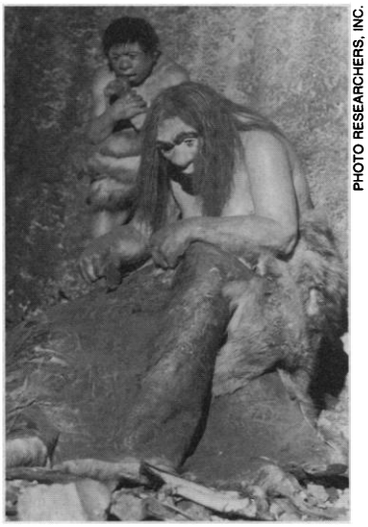
Outside of academic circles, Coase's influence is more difficult to assess. Political conservatives have used his theorem to argue against government interference in the economy, and at least two federal judges appointed by Ronald Reagan have been influenced by Coase's work. But conservatives are not alone in recognizing its value. "Regardless of how far you think the Coase theorem should take you in public policy, there's no denying that it's a seminal contribution to economics," says Lawrence Summers, a liberal Harvard economist now on leave at the World Bank.

Coase was vacationing in Tunisia last week, and wasn't reached with news of his Nobel for nearly 24 hours. The 80-year-old economist, described by a colleague as a man of "exceptional brevity and penetration," was characteristically brusque in his reaction. "What should one say about such an occasion?" he was quoted as saying in a university press release. "I'm interested only in promoting research." As if to prove it, Coase said he would use the nearly $1-million award to further economic research. "At my age, I'm not going to spend it on myself." ■ DAVID P. HAMILTON

Collagen: A New Probe Into Prehistoric Diet

Geochemists find that collagen may retain the memory of meals eaten thousands of years ago

Paris—STARTING WITH just a couple of chips of bone from the fossilized skull of a Neandertal, André Mariotti, a geochemist at the Marie Curie University in Paris, confidently announced last month that this early relative of man ate little other than meat. The reason for his confidence: a developing area of geochemistry that adds new meaning to the adage "you are what you eat."



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Neandertal. *A meat eater.*

Mariotti analyzed carbon and nitrogen isotopes in collagen extracted from 40,000-year-old Neandertal remains to determine the source of food that provided this protein's building blocks. The technique comes from ecology, where it has been used to establish the position of animals on the food web; Mariotti and his colleagues are the first to show that collagen isotope analysis can yield reliable data about ancient diets from fossils that are several tens of thousands of years old. Their results indicate that Neandertal man's dietary habits lay somewhere between those of the wolf and the fox—the wolf eats almost entirely meat but the fox gets some of its protein from occasional meals of fruits, grain, and even tree leaves.

"Its a very exciting result," says Henry Schwarcz, a geologist at McMaster University in Hamilton, Ontario, who is one of the small band of people using geochemical techniques to study ancient diets. Schwarcz has analyzed 10,000-year-old human fossils from France with the aim of seeing if people then were eating fish. Nothing as old as a Neandertal had been tested reliably, he says.

The key measures for paleodietary studies are the nitrogen-15 and carbon-13 levels in animal organic remains—usually in bone collagen, which can survive long after everything else has turned to dust. N^{15} gives clues to the position of an animal in the food web: There is more N^{15} in carnivores than in herbivores, and more still in carnivores that eat carnivores. Ecologists have worked out empirical rules for this isotope enrichment but do not fully understand how it arises. At least part of the explanation, however, is that N^{14} is excreted preferentially in urea, leaving a higher level of N^{15} behind in the body; animals that eat other animals will get a double dose of this enrichment.

C^{13} ratios directly reflect corresponding isotope ratios in plants at the base of the food web and give a host of clues about the types of plants in the diet. The environment (marine or terrestrial) in which the plant grows and the type of photosynthetic pathway—C_3, C_4, or CAM—all affect isotope ratios.

Putting N^{15} and C^{13} together it is often possible not only to distinguish between herbivores and carnivores but to tell whether a carnivore ate fish or meat or whether, in a savanna environment, a herbivore was a browser (eating C_3 shrubs) or a grazer (eating C_4 grasses).

The chief difficulty faced by Mariotti and his colleague, Herve Bocherens, in trying to push the use of these techniques far back in time is that collagen, although more durable than most other animal remains, does break down—the older the specimen, the harder it gets to extract sufficient quantities and the harder it is to be certain that the key isotope levels have not changed. To tackle the Neandertal, Mariotti teamed up with Jacques Paul Borel and Georges Bellon, two physicians from the University of Rheims who specialize in collagen diseases. Together, they were able to refine a method of identifying collagen by its amino acid spectrum, and then succeeded in extracting the protein from some 400 bone samples of fossils of reindeer, auroch, horse, marmot, hyena, wolf, and fox—as well as Neandertal—found at Maurillac, a famous cave site north of Bordeaux.

First results were encouraging: although the amounts of collagen extracted were often only about 2% of those found in modern

animals, measurement of N^{15} levels placed all the animals in their expected positions on the food web. That gave the researchers confidence that their placement of the Neandertal between the wolf and the fox was correct, although Mariotti stresses that study of one Neandertal does not imply that all were carnivorous. C^{13} analysis ruled out the possibility that this Neandertal, at least, traveled to the coast and ate fish.

With this first success, Mariotti is now optimistic that archeologists and paleoanthropologists will be convinced that isotopic studies can provide a window on an important aspect of prehistory. That, he hopes, will make museum curators less hesitant to yield bits and pieces of Neandertals and early Homo sapiens sapiens for analysis.

Schwarcz for one is not so optimistic, however. "Wishful thinking," he says. In particular, he notes, "Curators are very unwilling to allow specimens to go for destructive testing...the availability of bones to do this kind of work is very rapidly diminishing as the American Indian movement insists that ancient remains be re-buried." For North America, it seems, the new field of isotopic paleodietary studies may have arrived too late. ■ ALEXANDER DOROZYNSKI and ALUN ANDERSON

Alexander Dorozynski is a free-lance journalist living in Paris.

On the Trail of the Errant T Cells of Multiple Sclerosis

Patients with multiple sclerosis (MS) are victims of a mutiny in their own immune system. The disease results when the white blood cells that normally help to ward off diseases by destroying foreign cells turn on the body, attacking a vital tissue in the nervous system and triggering a patient's slow decline into paralysis. Researchers had expected that the mutinous army of cells would be highly diverse, consisting of a varied array of so-called T cells. But according to a report in the 15 October *Proceedings of the National Academy of Sciences*, only a specific set of T cells seems to be taking part in the mutiny. In that case, the researchers argue, putting down the rebellion might turn out to be easier than had been thought.

The work—by Halina Offner, Arthur Vandenbark, and their colleagues at the Oregon Health Sciences University and the Veteran Affairs Medical Center in Portland, Brian Kotzin and his colleagues at the University of Colorado Health Sciences Center in Denver, and other collaborators at Xoma Corporation in Santa Monica and Berkeley, California—bears out a similar finding made last year by David Hafler and his colleagues at Harvard Medical School and Brigham and Women's Hospital (see *Science*, 25 May 1990, p. 1016). And because it parallels results in animal models of MS, it may brighten prospects for a treatment strategy that is already showing promising results in animals and has recently moved into limited clinical trials.

Offner and her colleagues searched through white blood cells from MS patients, looking for the T cells capable of recognizing—and hence attacking—myelin basic protein. That protein is a major component of myelin, the nervous system tissue that degenerates in MS. They found that a large number of these cells carried the same T-cell receptor, a surface protein that enables T cells to recognize their targets. That might not sound surprising: All the errant cells home in on the same protein, after all. But an antigen as complex as myelin basic protein would ordinarily be attacked by a wide array of T cells, bearing a variety of different receptors.

The researchers have no ready explanation for this surprising specificity, but they nonetheless think it bodes well for potential therapies. "The good news," Vandenbark says, "is that there is a strong enough bias in T-cell receptor use that you can treat with one or a few agents" to try and check the autoimmune response. The Oregon group's strategy is to inject part of the same T-cell receptor protein found on the harmful cells. In theory, the injected protein elicits another immune response, this one directed at the disease-causing cells. And that, in turn, might quell the autoimmune attack on myelin basic protein and relieve some symptoms of the disease.

Offner, Vandenbark, and their colleagues have started to work out the strategy in animals, where they say it does appear to reverse the progression of the disease. More recently, they have also begun testing the treatment for toxicity in 11 human patients. At the very low doses used so far, they see no clinical improvement, but the injected protein does seem to be evoking a protective immune response.

But that therapeutic approach may not suffice, says Howard Weiner, a member of the Harvard group that saw a similar restriction in the array of T cells responsible for the human disease. He notes that myelin basic protein may not be the only component of myelin under autoimmune attack in MS. The destruction of myelin proteolytic protein (PLP), he says, may also account for some of the disease's symptoms. And while the array of white blood cells attacking myelin basic protein may be limited, Weiner says, that might not be true for the cells responding to PLP. In that case, stimulating a specific immune response against PLP-reactive cells might prove difficult.

And even the cells attacking myelin basic protein may not be as uniform as the Vandenbark team's results seem to show, according to Hafler, the leader of the Harvard group. "Their findings confirm to some degree the major point of our finding: that the T-cell receptor repertoire for cells reactive to myelin basic protein is restricted," he says. But the Harvard team found that while the autoimmune cells in any one patient may bear one type of receptor almost exclusively, the specific kind of receptor may vary between individuals. That variability would mean that each individual would have to be tested for receptor type before the appropriate therapy could be administered, says Hafler.

Vandenbark and colleagues don't know whether the discrepancy between their results and the Harvard group's earlier findings is due to differences in the two subject groups or in the researchers' analytical techniques. But the Oregon group does agree that receptor typing would have to be done for each individual before therapy. "If the approach does work in humans," says Vandenbark, "we would have to know the biases [toward specific T-cell receptors] for each patient."

And it's surely too early to rule out other therapies, Hafler adds. He, Weiner, and their colleagues are exploring a sort of hair-of-the-dog-that-bit-you approach to autoimmune disease, in which patients are fed the very proteins that triggered the autoimmune response in the first place (see *Science*, 5 April, p. 27). Somehow, the proteins—myelin basic protein or PLP, in the case of MS—seem to summon a set of "suppressor" immune cells, which limit the autoimmune response. But only full-scale clinical trials, says Hafler, will show whether either their approach or the Oregon strategy offers any real hope in the fight against MS. ■ MICHELLE HOFFMAN