Humans Made Early European Entry

An excavation in an underground cavern in northern Spain has yielded fossils and stone tools from human ancestors who inhabited the region at least 780,000 years ago, according to a new report. If that age estimate holds up, the discovery shows that the human colonization of Europe began about 300,000 years earlier than many researchers had assumed.

"The settlement of Western Europe probably occurred . . . at an early time in the evolution of the genus *Homo*," conclude Eudald Carbonell of the University of Roviri and Virgili in Tarragona, Spain, and his colleagues.

Beginning perhaps 1 million years ago, a succession of related *Homo* species, including Neandertals, evolved in Europe, the Spanish scientists assert. This European lineage eventually died out and was replaced by modern-looking humans who originated in Africa, they theorize.

Carbonell's group presents its findings in the Aug. 11 SCIENCE, along with a report on paleomagnetic dating of the site directed by Josep M. Parés of the University of Michigan in Ann Arbor.

"If the dating of the site is accurate, this is a fantastic discovery," asserts John J. Shea of the State University of New York at Stony Brook. "But the paleomagnetic dates need to be confirmed by a radiometric dating method."

The specimens come from a limestone cavern, called Gran Dolina, in Spain's Atapuerca Mountains. Exploration of a nearby cave has already produced 300,000-year-old Neandertal remains (SN: 4/10/93, p.228). The Gran Dolina project has unearthed 100 stone implements and 36 hominid bone fragments. Most stone artifacts had been chipped off larger stones and sharpened on one side, a rudimentary tool-making technique.

The fossils come from at least four individuals and consist largely of teeth, jaws, and parts of the braincase.

Comparison of the shape and size of the bones to those of other hominid specimens indicates that the Spanish site was inhabited either by an early form of *H. heidelbergensis*, a species already assigned to a 500,000-year-old German jaw, or a new and as yet unnamed *Homo* species, Carbonell's team contends.

Reversed polarity of the magnetic field in Gran Dolina's fossil- and artifact-bearing sediment places the finds at a minimum of 780,000 years old. They may date to as early as 1 million years ago, according to Parés, who plans to conduct further geological testing at the site in October.

"They've hit the jackpot with this new find," asserts F. Clark Howell of the University of California, Berkeley, who has visited the Spanish site and seen the hominid discoveries. Until now, he notes, many scientists thought that human ancestors lived on the Asian fringes of Europe for more than 1 million years before heading west about 500,000 years ago (SN: 2/11/95, p.85).

Both Howell and Shea suspect that rather than staying put, as the Spanish researchers propose, hominids filtered into and out of Europe between periods of extreme cold, beginning around 1 million years ago. Hominids that migrated from Africa later, not those at Gran Dolina, may have served as Neandertal ancestors, Howell proposes. — *B. Bower*

Inside the Gran Dolina site.

Sounding out a better way to deliver drugs?

Compared to their counterparts in the real world, physicians in the science fiction universe of *Star Trek* have it easy. When they need to administer a drug, they use a simple, hand-held device to shoot it through the patient's skin. No needles, no pain, no risk of infection.

Scenes like that may not be fiction for long. Low-frequency ultrasound can temporarily open up paths through usually impenetrable human skin, making it possible to introduce large, therapeutic proteins into the bloodstream, assert Robert Langer and his colleagues in the Aug. 11 SCIENCE. As a test of the technique, they successfully delivered insulin into diabetic rats and lowered the animals' blood sugar to normal concentrations.

"This could be our painless injections of the future," says Edith Mathiowitz of Brown University in Providence, R.I.

These results represent a significant advance in ultrasound-mediated drug delivery, a field that dates back more than 40 years. The barrier faced by investigators pursuing the idea has been the stratum corneum, a dense layer of dead cells that forms the outermost layer of skin. The walls of these cells consist of well-organized bilayers of fatty molecules called lipids. These lipids block all but the smallest molecules, which is why skin patches work for only a few drugs, such as nicotine.

To improve transdermal delivery, many investigators have tried using ultrasound with frequencies ranging from 1 to 3 megahertz to safely open channels through skin. Those experiments produced mixed results, and no one really understood why the technique worked when it did, says Langer of the Massachusetts Institute of Technology (MIT).

Langer, along with his MIT colleagues Samir Mitragotri and Daniel Blankschtein, recently put forward a model suggesting that ultrasound's effects on skin stem primarily from cavitation, the formation and collapse of gaseous bubbles. The bubbles come from gases, such as oxygen and carbon dioxide, dissolved in tissues, says Langer.

The key to making the technique effective, he and his colleagues thus argued, is to increase the amount of cavitation by lowering the frequency of the ultrasound to around .02 megahertz. The ultrasound-induced bubbles disrupt the stratum corneum's orderly lipid bilayers, creating "paths of minimal resistance," Langer explains.

In addition to their insulin work with rats, the researchers used the low-frequency method to deliver therapeutic doses of insulin, the immune system booster interferon-gamma, and the anemia drug erythropoietin across the skin of human cadavers, which Langer calls his field's "toughest model." Such large proteins are useless if taken orally and therefore have required injections.

The disruptions of the lipid bilayers produced by ultrasound seem to reverse quickly when treatment ends, says Langer. Though additional studies will be done to further establish safety, he hopes to start testing the technique on people within the year. —*J. Travis*