

### Vanished sea leaves climatic legacy

A map of Asia during the Oligocene period, 30 million years ago, is a mix of familiar and foreign, like a picture of one's face taken at birth. The broad cartographic features are recognizable, but the heart of the continent holds a strange sea, the Paratethys, which stretches from the Mediterranean to Siberia.

Since the Oligocene, the Paratethys has shriveled, leaving tiny geographic remnants that include the Black, Caspian, and Aral Seas. The disappearance of that once great body of water has also made a lasting mark on the Asian climate, according to new computer simulations.

Past studies have tended to link the emergence of today's climate in Asia to the birth of the Tibetan Plateau during the last 30 million years. In this scenario, the rise of the plateau redirected wind patterns, drying out central Asia and strengthening the south Asian monsoon. These studies ignored the role of the shrinking Paratethys.

Now, French researchers have assessed the various factors by using a complex atmospheric computer model to simulate the Asian climate in the Oligocene period and in the present. They tested the influence of the Paratethys and the Tibetan Plateau separately and together.

In the April 24 *NATURE*, Gilles Ramstein of the Laboratoire de Modélisation du Climat et de l'Environnement in Gif-sur-Yvette and his colleagues report that the shrinking sea played just as important a role as the rise of Tibet. As the sea disappeared, it removed a large source of water from central Asia, helping both to dry the region and to enhance temperature extremes between summer and winter. At the same time, it intensified Asia's monsoon rains. — *R.M.*

### Debate smolders over cause of ice ages

During the last 2 million years, Earth has endured more than 20 ice ages of various lengths. The standard explanation for these periodic freezes involves rhythmic variations in the planet's orbit and tilt, but this theory has come under fire in recent years from researchers studying a Nevada cave called Devils Hole (SN: 10/10/92, p. 228). Now, a team of scientists contends that their findings have exorcised the specter of Devils Hole by confirming the orbital theory.

The debate centers on the timing of the last interglacial period, the short warm spell sandwiched between the last ice age and the next-to-last one. Dating of calcium carbonate layers in Devils Hole suggests that the last interglacial started more than 150,000 years ago—a time that doesn't fit the orbital hypothesis. Summer sunlight then was not strong enough to melt the giant ice caps and end the glacial epoch.

R. Lawrence Edwards of the University of Minnesota in Minneapolis and his colleagues attacked the problem with a dramatically improved version of an old dating technique that relies on the radioactive decay of uranium-235 to protactinium-231. They rechecked the ages of previously dated coral from Barbados that grew during the last interglacial, when Earth was warm and sea levels were higher than they are today.

The new coral dates confirm that sea levels were high 126,000 to 121,000 years ago, when summer sunlight grew most intense in the far northern latitudes, the scientists report in the May 2 *SCIENCE*. These results, they argue, back up the orbital explanation of the ice ages.

That conclusion gets a cold reception from Isaac J. Winograd, a researcher at the U.S. Geological Survey in Reston, Va. Winograd lauds the protactinium dating technique but objects that the new study reanalyzed coral samples already known to support the orbital hypothesis. To address the issue thoroughly, says Winograd, Edwards should redate other corals that show sea levels rising far earlier or later than orbital theory would predict. — *R.M.*

### Deciphering the grapefruit juice effect

Some dozen different studies have shown that drinking grapefruit juice appears to increase markedly the potency of several commonly prescribed drugs, including sedatives and medicines for high blood pressure. There have even been reports of patients who unwittingly overdosed when they used the citrus libation to wash down a prescribed pill.

Researchers have now traced grapefruit's effect to a decrease in a critical drug-degrading enzyme in the small intestine, they report in the May 15 *JOURNAL OF CLINICAL INVESTIGATION*.

The components of the juice that suppress this enzyme, known as CYP3A4, remain unknown. If identified, however, they might be added to certain drugs to lower the effective doses, says gastroenterologist Kenneth S. Lown of the University of Michigan Medical School in Ann Arbor. Indeed, notes Lown, who led the study, because this enzyme plays a role in "metabolizing one out of every three drugs," the unexpected finding could have broad applications.

His team admitted 10 healthy men to a hospital for a 12-day trial. Each volunteer was put on a diet entirely devoid of fruits and vegetables. Beginning on day 6, the men received 8 ounces of grapefruit juice with each meal.

The scientists already suspected that this juice worked by inhibiting the ability of CYP3A4 to break down drugs, but because the body often compensates by ratcheting up its production of an affected enzyme, they expected the grapefruit effect to diminish with each succeeding glass of the juice.

To "our shock," Lown observes, the opposite occurred.

On days 4, 6, and 11, each man took 10 milligrams of felodipine, an antihypertensive drug whose effect is enhanced by the juice (SN: 2/9/91, p. 85). When the pill was swallowed after the first glass of juice, concentrations of the drug in each man's blood more than tripled over those measured 2 days earlier. By day 11, and the men's 16th glass of juice, drug concentrations had climbed to more than four times the initial values. Moreover, though intestinal amounts of CYP3A4 initially varied widely among the men, after 6 days of drinking the juice, all exhibited similar low enzyme concentrations—and should reflect an equal response to the drug. — *J.R.*

### Dieting impairs reaction time

Women who diet become a tad less quick at the switch.

That's what Mary J. Kretsch of the U.S. Department of Agriculture's Western Human Nutrition Research Center in San Francisco and her colleagues reported last month at the Experimental Biology '97 meeting in New Orleans.

The group recruited 25 premenopausal women, each initially weighing in at around 190 pounds, for a 21-week-long trial during which the center supplied all of the women's meals. After a 3-week baseline period, 14 women began dieting, eating only 50 percent of the calories needed to maintain their initial weight. They finished this regime with 3 weeks on a diet to maintain their new weights. Throughout the study, the other 11 women consumed as much of the available food as they desired.

Eight times during this nearly 5-month trial, the scientists administered a battery of cognitive tests to the women. Only simple reaction time—how quickly a volunteer could hit the space bar after spotting a particular image on a computer screen—distinguished the dieters, Kretsch's team found.

The weight-loss group experienced a reaction slowdown that began in week 5 and didn't stop when weight loss ended. Surprisingly, Kretsch notes, the reaction time fell at a somewhat faster rate during the maintenance dieting phase. Nondietering women, in contrast, exhibited no change in reaction time.

Overall, the dieters' reactions slowed by 11 percent. "Even though this change seems small, it might be enough, when you're driving, to cause an accident," Kretsch worries. — *J.R.*