Pain: Placebo Effect Linked to Endorphins

The mystery of why sugar pills and other inert "medications" can sometimes produce almost instant relief of severe pain has now been partially solved: As a result of expectations aroused by such placebos, some patients seem able to subconsciously activate their body's own pain-suppression system, releasing the recently discovered proteins called endorphins (SN: 7/23/77, p. 59). Discovery of this link is likely to expedite research into some of the body's regulatory systems and lead to more efficient treatment of pain.

Long before medicine became a science, the power of placebos was well established: The earliest witch doctors found that if a patient really believed that a treatment — almost any treatment — would work, it often did. Modern researchers quantified this finding several decades ago, demonstrating that a remarkably constant fraction of their patients—about one-third—received significant pain relief through the use of placebos.

The common explanation of this phenomenon was that the patients benefited "psychologically," that only their perception and not the pain itself had changed. But then came discovery of several physiological changes — such as improvement of stomach ulcers — under the influence of placebos, and the search began to see whether these treatments actually triggered some intrinsic curative or analgesic.

In the case of pain, the opportunity to test this hypothesis came with discovery of endorphins — literally, "the morphine within" — released by the brain and the pituitary gland. These substances appear to be modulators of the signals between nerve cells and act specifically on the same nerve receptors that are affected by morphine and other opiates. They not only relieve pain but also appear to help control body temperature and affect consciousness (SN: 7/28/78, p. 38). They have been implicated in acupuncture (SN: 11/20/76, p. 324). The pain-killing action of both endorphins and morphine can be blocked by a drug called naloxone.

Using naloxone as the tool to detect the presence of endorphins, a team of researchers at the University of California at San Francisco set out to investigate the effect of placebos on 50 patients recuperating from wisdom tooth extractions. In a double-blind experiment, some patients received the usual postoperative treatment with morphine, while others received naloxone or a placebo. The patients then reported changes in their pain, using a ten-point scale (from "no pain" to "worst pain ever").

As expected, about one-third of the patients receiving placebos reported a significant reduction of pain. Members of this group who were subsequently given naloxone reported a significant increase in pain — bringing their pain back up to almost the same level as that reported by patients who didn't respond to a placebo in the first place.

Since naloxone has no known effect by itself on these patients, the researchers conclude that the observed effect in the placebo-responsive patients resulted from that drug's ability to block the action of endorphins. Thus the conclusion is that endorphins have been produced in response to placebo treatment.

In a paper to be published this fall in LANCET, authors Jon D. Levine, Newton C. Gordon and Howard L. Fields suggest a striking interpretation of this result: that "variability among patients in reported pain intensity for a given pathology is due to differences in endorphin activity." Endorphin activity may prove a useful measure of pain and of placebo effects, allowing greater precision than patient reports of sensation.

Additional findings suggest even more possibilities for exploration of the relationship between placebos and the body's natural pain-suppression mechanism. No one has ever been able to pin down just what sort of person, under what circumstances, responds best to placebos. Perhaps the most common factor in successful cases is stress: A person who has just experienced a traumatic interruption of marriage, for example, is more likely to respond to a placebo. The authors say that stress appears to have played a significant role in their experiment. Similar investigations with experimentally induced pain in a laboratory — lacking the stress of a clinical situation — had produced only ambiguous results.

Investigations into the yet-unknown mechanisms by which placebos can activate endorphins are well underway, and the San Francisco researchers plan to publish further results soon. These studies may well reveal significant information about poorly understood functions of the brain and pituitary.

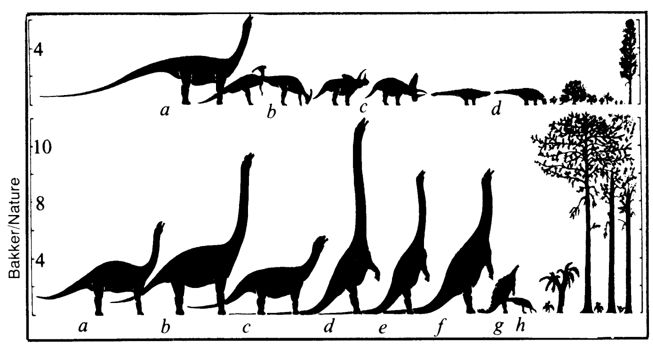
Levine summarized the potential impact for SCIENCE NEWS: "The importance of these results is that they shed new light on the body's own system for controlling pain. Further research along these lines should lead to more effective treatment of pain through a combination of methods, including drugs and psychological and physical treatment." □

Dinosaur tales: Flowers and a warm doom

Dinosaurs in their natural milieu provide a topic that will never yield to direct experimental investigation. Yet it's a tantalizing puzzle that continues to fascinate. How did those massive and powerful animals interact with their world? And why did they become suddenly (geologically speaking) extinct?

Fossil and geological records allow for structured speculation. Recently two novel ideas have been set forth. The first is from Robert T. Bakker, who is well known for his advocacy of the warm-blooded dinosaur (SN: 4/8/78, p. 218). He now suggests that the initial development of flowering plants was, at least in part, a direct result of dinosaur feeding habits. The eventual demise of the dinosaurs was the result of a short period of climatic warming, according to new information and a reappraisal of older data by Dewey M. McLean of Virginia Polytechnic Institute and State University. McLean warns that a modern warming trend, from human use of fossil fuels, over the next century or two threatens to initiate a Mesozoic-like period of worldwide extinctions.

Charles Darwin called the origin of flowering plants an "abominable mystery," because they seemed to appear abruptly without a clear hint of ancestry. Bakker now proposes that a swift change in dinosaur feeding behavior opened ecological opportunities for the rapid spread of those plants. An animal's height is most important in determining its selective pressure on vegetation, Bakker says. Tall animals, like a giraffe, will eat leaves, buds and fruit, but will rarely kill an adult plant. Short animals, however, concen-



Jurassic dinosaurs (lower line) can stretch to nibble higher leaves than dinosaurs of the later Cretaceous period (upper line). Vertical scale is in meters.

trate on annuals and seedlings, and thus depend more on continuous regeneration of cropped land.

Bakker sees two major shifts in feeding behavior during dinosaur evolution. In the Late Triassic, prosauropod dinosaurs, with long necks, long hindlimbs and powerful tails, became predominant over the earlier short-necked, short-limbed, big herbivores. That shift from low browsing to high browsing corresponds with one major vegetation shift. Later, at the beginning of the Cretaceous period, there is fossil and footprint evidence for new groups of big, low-browsing ornithischian dinosaurs. Intense low browsing favors plants that can rapidly regenerate cropped foliage and colonize areas laid bare by herbivores, Bakker says in the Aug. 17 NATURE. Flowering plants fit that bill. Bakker says that, once acquired, the life-history strategy of flowering plants gave them a competitive advantage in many habitats, beyond those subjected to dinosaur feeding.

Thus, angiosperms prosper, although dinosaur feeding has not been a problem for 65 million years. The dinosaurs became extinct along with an estimated 75 percent of the animal species alive at that time. McLean suggests in the Aug. 4 SCIENCE that a slight, but critical, increase in temperature disrupted sperm production in those species.

In McLean's scenario shallow seas over the continents receded late in the Mesozoic, reducing the marine algae population. Because those organisms are major consumers of atmospheric carbon dioxide, the gas built up in the atmosphere and, in a "greenhouse" effect produced a warming of the earth. The warming, in turn, raised the temperature of the ocean, reducing the amount of dissolved carbon dioxide and further contributing to the temperature rise. Large animals have a low ratio of surface to volume, and thus the biggest suffered most from the warming trend.

McLean has assembled a variety of evidence for that explanation. Many marine algae species do disappear from fossil records at the end of the Mesozoic. Rocks of the period show isotope and carbonate compositions consistent with warming and carbon loss from the oceans. Dinosaur eggs became progressively thinner-shelled and fragile as the time of extinction neared. (Among some modern birds, elevated temperatures cause thin-shelled eggs.) Finally many eggs are found unhatched; thus they may never have been successfully fertilized.

Various climatic studies have claimed that current global temperature is on the upswing. McClean warns that the world may arrive inadvertantly at a critical threshold, triggering an accelerated warming beyond people's capacity to control it or adapt to it: "A sudden climatic warming could potentially impose on us conditions comparable to those that terminated a geologic era." □

NAS: Soviet-American science in peril

Intensifying the crescendo of U.S. scientists' indignation over the recent political trials of their Soviet colleagues Yuri Orlov, Anatoly Shcharansky and Sergey Kovalev, the National Academy of Sciences' Committee on Human Rights last week urged "scientists the world over to petition Soviet authorities for the release of these three men." Although there are, of course, many others suffering similar plights globally, the committee observed in their formal statement, "these three have captured the attention of the world scientific community by their independence of thought, their courage in the face of inevitable adversity and their personal integrity."

Sentenced last May, to seven years in prison and five years' exile within the USSR, Orlov, who is a high energy physicist, was convicted of anti-Soviet agitation, a vague, catch-all charge often leveled at Soviet dissidents and refuseniks (persons who are refused a visa to Israel). Recently, Orlov's judicial appeal was rejected. Shcharansky, a cyberneticist who has made distinguished contributions to the theory of decision making, is planning to appeal his 13-year sentence (three years in prison plus ten at hard labor) for treason and espionage. His case in particular attracted the supportive but apparently vain efforts of President Carter and members of Congress. Sergey Kovalev, sentenced almost three years ago to seven years at hard labor plus three years' exile, was convicted of anti-Soviet agitation for illegally circulating THE CHRONICLE OF THE LITHUANIAN CATHOLIC CHURCH.

Perceiving these and many other cases like it in the USSR and other countries as unmerciful abuses of human justice, many U.S. scientists pointedly expressed their sentiments last week by refusing to attend the 14th International Congress of Genetics. Of those Americans specifically invited to participate, more than 60 percent declined to go, according to Mark S. Mellman, director of the Committee of Concerned Scientists, headquartered in New York. This organization of about 4,000 American scientists has views on this issue essentially identical to those expressed by the NAS committee, Mellman told SCIENCE NEWS.

Besides decrying the fates of the three Soviet scientists, the two committees stress that their attempts to incite scientists' support stop short of advocating a uniform, collective boycott of the USSR. This is in recognition, Mellman said, "that [continued] interactions themselves can be helpful to the refusenik and dissident scientists." Furthermore, as the NAS Committee on Human Rights statement reads, "It is precisely because the response of U.S. scientists is so individualistic that continued Soviet-American scientific relations are in peril. Scientific exchange programs can be negotiated and organized, but individual participation cannot be commanded." □

Seeking the ocean crust in Iceland

Iceland is one of the few spots where the Mid-Atlantic Ridge, the birthing place of the Atlantic Ocean floor, reveals itself above water. Seismic profiles of Iceland differ radically from those of continental masses, resembling instead the seismic reflections characteristic of the ocean crust. Molten lava churning beneath Iceland's surface, which stokes the furnace of the country's geothermal energy resources, inflicts physical and chemical wounds on surrounding deep volcanic rock much like those changes occurring beneath the ocean floor.

Drilling into the ocean floor may reveal much about the composition, evolution and movement of the basaltic layers of the crust. Drilling into Iceland's analogous crust may reveal some of the same information. And Iceland is several thousand meters, and hundreds of thousands of dollars, more accessible.

During the past two months, 26 researchers from Iceland, Great Britain, Canada, Germany, Denmark and the United States have drilled 1,920 meters into the Icelandic crust near Reydarfjordur, about three times deeper than the *Glomar Challenger* has penetrated the ocean crust. Combined with samples from a 1,300-meter-high cliff near the drill site, researchers have a continuous core record more than 3,000 meters deep, representing the past 12 million years. In addition, the cores show 100 percent recovery of the rock drilled; 50 to 70 percent is par for deep sea drilling.

The project, coordinated by Jim Hall of Dalhousie University in Halifax, means "the day of land drilling is dawning," according to University of Washington researcher Roy Wilkens. "We hope this can be a bridge between what the *Challenger* is able to do and deeper drilling." Though Wilkens cautions that strict comparisons to the ocean crust must be made cautiously because the Icelandic crust was not formed under the same conditions as oceanic crust, the Icelandic borehole is already answering many questions.

For example, preliminary studies indicate that the abrupt change in seismic velocity between the two volcanic layers of the crust represents changes which occurred in the lower layer after its formation, rather than a difference in the way the two layers were formed. Such direct comparisons between geological and geophys-