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## Science and the sources of pain

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Chronic pain is no small problem for thousands of Americans. They take analgesics, sedatives or tranquilizers. They seek out chiropractors, acupuncturists or even miracle workers. Often they are not helped, at least over the long run, and become depressed. Some even commit suicide.

These hard facts were brought home last week at a pain seminar, held at the annual meeting of the American Society of Anesthesiologists in Washington. The reason that so many people aren't getting relief from pain is that clinicians still aren't sure what pain is and how to treat it.

Does pain consist of a stimulation of peripheral nerves, or of central nervous system nerves? Does it have its origin in the brain or in another organ of the body? Pain can be anything that the brain or body sees as noxious. Or pain can describe a single sensation.

Since pain is often diffuse, clinicians are rarely able to measure it scientifically. So they have to rely, to a large degree, on patients' descriptions of where they hurt. "An alert and cooperative patient can help us pick out his pain fibers," reports Hubert L. Rosomoff, a neurosurgeon with University of Miami School of Medicine. However, many patients, while cooperative, aren't particularly sensitive to pain sites, or their pains just don't lend themselves to accurate description. Prime examples are abdominal pains or organic pains caused by tumors. In such cases clinicians have to use other strategies for tracking down pains.

One physician is using a multipronged technique to zero in on pain sites. First a patient is given a placebo (an injection of salt solution near the purported pain site). If the placebo brings pain relief, he is fairly sure that the source of the pain is psychological. If the placebo doesn't bring relief, he concludes that the pain is physiological and tries blocking nerve fibers near the pain site. If the blocking helps, he is assured that the source of the pain is in the fibers. But if the blocking doesn't help, he will test an organ for pain. If the organ doesn't turn out to be the pain site, he will try the central nervous system. The physician asked not to be identified, to avoid any possibility of the publicity jeopardizing his research procedures.

Using this strategy, he has been successful at diagnosing pain sites that other physicians had misdiagnosed or had not been able to pinpoint. Of 100 patients for whom no cause of their pain could be found, 75 percent turned out to suffer from pain in the sympa-

thetic nerves. The sympathetic nerves control sweating, vasoconstriction and other autonomic nerve functions. They are not normally associated with pain since pain usually travels along nerves responsible for feeling (sensory nerves). The other 25 percent of the patients suffered from pain whose origin was organic, psychosomatic or of the central nervous system.

Even if clinicians manage to diagnose the site of pain, it doesn't necessarily mean that they're able to treat patients effectively. "We're still shooting very much in the dark with drugs that were used centuries ago," says Rudolph H. deJong, an anesthesiologist and pharmacologist with the University of Washington School of Medicine. Electrode stimulation of nerves in the spinal cord for low back pain, Rosomoff asserts, "is probably not worth a blessed thing in its present state of development." It's tricky making holes in the spinal cord to relieve pain, Kenneth L. Casey, a neurologist and neurophysiologist with the University of Michigan, points out, because nerve fibers may grow back in

the hole and cause pain once more. "The central nervous system," he laments, "is not a Swiss watch."

The most disconcerting aspect of pain treatment, the seminar speakers concur, is that a 70 percent success rate is reported for nearly all new pain treatments. But as more and more experience is gained with these treatments, the 70 percent success rate falls off for many of the treatments. The initial 70 percent success rate appears to be due to the enthusiasm of the clinician who believes he has found a great new cure and transmits his enthusiasm to his patients.

The pain picture isn't all glum, though. Recent studies have shown that specific pain fibers exist, and that their activity can be modified in the central nervous system by other nerve fibers or by impulses from the brain. So Casey is doing research to see whether drugs or electrical stimulation that act on the brain might control pain via the central nervous system. "We need to do more work on animals before trying these techniques on patients," he says. □

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## Hormones linked to birth defects

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Oral contraceptives have changed population patterns and birth rates almost single-handedly in most of the world's industrialized nations. The pill has many advantages over other forms of birth control, but it has come in for much criticism, too. Physicians and researchers have linked the pill to blood clots, migraine headaches, elevated blood pressure, liver tumors, diabetic effects and cervical cancer, among others. And the list is still growing.

New evidence now has been published linking the pill to birth defects. Epidemiologists from the New York State Department of Health at Albany report in the Oct. 3 *NEW ENGLAND JOURNAL OF MEDICINE* a possible link between exposure during pregnancy to hormones produced outside the body and limb malformations in offspring. Dwight T. Janerich, Joyce M. Piper and Donna M. Glebatis studied 108 cases of babies born with limb-reduction malformations (the absence of an entire or part of a limb) and 108 normal babies. The mothers were matched by age and race for more valid comparison. Among the mothers with malformed children, 14 percent had been exposed to exogenous hormones (produced outside the body) during pregnancy, while only 4 percent of the mothers of normal babies had been similarly exposed.

The exposure took one of three forms: the unintentional use of birth control pills after pregnancy had occurred; the administration of estrogens or progestogens as supportive therapy

for one of a number of reproductive system disorders, or the administration of hormones during a certain type of pregnancy test.

One puzzling fact emerging from the study is that in 11 of the 15 cases of malformations following hormone exposure, the mothers received the hormones orally (not by injection) and the affected babies are all males. This indicates, Janerich told *SCIENCE NEWS*, that hormones taken orally during pregnancy may have a sex-specific effect on the growing fetus, that is, cause deformations in male babies but not female. Hormones were injected into four women who later gave birth to malformed children of both sexes. Janerich does not know at this point how or why sex-specific effects could be occurring, but one possible answer suggested to him by a colleague is that oral hormones are derived chemically from testosterone, a male hormone, while injectable hormones are not. The converted male hormone may have a residual effect.

The team made these findings after studying New York state birth certificate information recorded between 1968 and 1973. The study was part of an ongoing congenital malformation surveillance program sponsored by the New York State Department of Health. The records show 145 limb reduction malformations occurred in New York during the five-year period, but the team was able to locate and interview only 108 mothers. Limb-reduction defects are fairly rare, occurring only

once in every 4,000 births, but the incidence has been rising in recent years. This is to be expected, the team reports, if in fact oral contraceptives are one cause, since their use has increased during the same period.

Janerich emphasizes that the defects are rare, that "the vast majority of pregnancies in which these drugs are used do not result in defective offspring," and that there may be a maternal predisposition to the malforming effects of hormone exposure. Janerich also emphasizes that the results, although significant, are preliminary at this point, and it cannot be stated with certainty that exposure leads to birth defects until more research is completed, including laboratory tests.

But physicians can modify some of their procedures in the meantime, Janerich says. First of all, pregnancy tests in which hormones are administered should be avoided, he says. A physician sometimes gives a large dose of estrogen or progesterone to a woman who has missed a menstrual period. If the period commences soon after the administration of the hormones, the woman is not pregnant, but if the period does not begin, she often is, and the fetus is exposed to the hormones during the crucial early stages of its development. There are many alternative pregnancy tests available and one of these should be used, Janerich says. A spokesman for the U.S. Food and Drug Administration told SCIENCE NEWS that that agency's drug bureau has reviewed hormonal pregnancy tests and an order withdrawing them from the market is expected soon.

Second, a physician should not prescribe birth control pills for a woman until he is sure she is not already pregnant. And third, physicians might be more careful about administering hormone therapy. These treatments are used "in many instances where a rationale is not well established," Janerich says, including preventative treatments for a problem that occurred during an earlier pregnancy but not the current one.

There have been related reports on hormones and birth defects by other investigators during the past year. James and Audrey Nora from the University of Colorado Medical Center at Denver refer in an editorial in the same issue of the medical journal to some of their own work. They found that defects of the spinal cord, intestinal tract, heart, throat and lungs and kidneys may also be associated with hormone exposure during pregnancy. Both groups emphasize the preliminary nature of the work thus far, and the need for laboratory and epidemiological studies before a positive link can be forged between hormones and birth defects. □

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## Science, secrecy & grant applications

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Scientists who fear piracy of their original research designs by unscrupulous colleagues have a new worry: A U.S. appeals court has ruled that Federal research grant applications must be made public under the Freedom of Information Act. Up to now, grant-awarding agencies have kept the proposals confidential. Some grant officials regard the ruling as a threat to the system of peer review by which grants are parceled out. They foresee theft-wary researchers submitting proposals so devoid of detail that review committees will be forced to blindly fund projects, giving investigators and institutions with established reputations the edge.

However, the decision by the U.S. Court of Appeals for the District of Columbia in September overturned that part of a lower court's ruling a year ago which also would have made the summary statements ("pink sheets") and site visit reports prepared by these review committees public information. The earlier decision ordered the Department of Health, Education and Welfare to surrender all documents relating to 11 National Institute of Mental Health grant projects involving drug treatment of hyperactive and learning-impaired children to the Washington Research Project, a nonprofit public interest group.

HEW appealed the decision, arguing that "ideas are a researcher's 'stock-in-trade'"; that to release research applications submitted in confidence would amount to revealing "trade secrets"—a category of information specifically exempted from disclosure under the 1966 Act.

The Washington Research Project disputed that research designs could be considered trade secrets because "secrecy is antithetical to the philosophical values of science and is notably absent from the structures by which modern scientific research is carried out." To wit: collaborative projects and elaborate communications networks. Even proposals submitted for Federal funding are reviewed by competitors who "consciously or unconsciously assimilate useful ideas from other proposals into their own work," the group contended. "If the work of one scientist is used by another to reach a desired result more quickly, the gain to society will be substantial."

In the end, the decision making research proposals public hinged on the legal definition of "trade." "It defies common sense to pretend that the scientist is engaged in trade or commerce," concluded Judge Carl McGowan in his opinion. "This is not to say that the scientist may not have a

preference for or an interest in non-disclosure of his research design, but only that it is not a trade or commercial interest. To the extent that his interest is founded on professional recognition and reward, it is surely more the interest of an employee than of an enterprise." He noted that profit-making "enterprises" aren't eligible for grants under HEW regulations.

The decision renders all types of grant applications—initial, continuation, supplemental and renewal—subject to disclosure under the FOI Act. Rejected grant proposals are presumably also included, although the court was not explicit on this point. The summary reports and site visit reports written by the review panels of experts who pass on the scientific merits of proposals were ruled exempt from the Act because they are primarily evaluative in nature and hence considered part of the internal deliberative process of the agency. HEW voluntarily discloses the purely factual information in these documents regardless.

The issue of public access to research protocols could go into a third round of legal proceedings if either side decides to appeal to the Supreme Court. In any case, the Association of American Medical Colleges, which filed a friend-of-the-court brief supporting HEW in the appeals suit, is already lobbying in Congress for legislation that would exempt grant applications from disclosure. President Ford on Oct. 17 vetoed a bill that would have amended the FOI Act to make government records more accessible. □

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## Ancient fossil mammal

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A vertebrate paleontologist from Harvard made a find so lucky recently that the others on the expedition wouldn't believe it at first. Searching through mountains near Billings, Mont., last summer and "feeling futile," Charles R. Schaff found a pile of bleached bones. Half of them were exposed from weathering and the other half were encased in soft, gray shale, but Schaff knew immediately what he had discovered. From a small tooth with three prominent cusps laying neatly exposed, he determined that the animal was a triconodont ("three coned tooth"), a small carnivorous mammal that lived among the dinosaurs 100 to 120 million years ago.

Triconodont skulls and teeth have been found before, but Schaff, expedition director Farish A. Jenkins Jr. and Harvard's zoology museum now have the oldest fossil mammal skeleton ever found in North America. □