Narcotics: How they kill pain

Up to a year ago, pharmacologists and biochemists knew pathetically little about the action of narcotics upon the brain. Then Candace B. Pert and Solomon H. Snyder of the Johns Hopkins University School of Medicine reported that narcotics bind to rat brain tissue, especially to tissue toward the front of the brain (SN: 3/17/73, p. 167). Exactly what opiates do in nervous tissue to produce their painkilling effects, however, remains to be determined.

Now British researchers report in the March 1 NATURE that narcotics may well produce their analgesic effects by keeping the E class of prostaglandins from stimulating cyclic AMP. Prostaglandins act as local chemical messengers between cells. Cyclic AMP regulates activities within cells. Prostaglandins and cyclic AMP are known to interact in various situations (SN: 9/2/72, p. 148).

The investigators, H. O. J. Collier and A. C. Roy of Miles Laboratories Ltd. in Buckinghamshire, England, say that the concentrations of narcotics that inhibit prostaglandins' stimulation of cyclic AMP in brain tissue probably correspond to the concentrations that produce painkilling effects in animals and people. Moreover, they say, the relative potencies of the narcotics used are consistent with their affinity for rat brain tissue, as reported by the Maryland scientists.

When the E class of prostaglandins are given to animals or people, they cause pain—pain that opiates are used clinically to lessen. Reports have also appeared on the antagonism between morphine and E prostaglandins in some preparations of intestinal tissue. So Collier and Roy decided to see whether morphine might inhibit some biochemical process of E prostaglandin production or action in homogenized rat brain tissue.

In five of their experiments, adding the prostaglandin known as PGE_1 to brain tissue increased cyclic AMP formation 1.4 to 2.7 times, compared with cyclic AMP formation in brain tissue that did not receive the prostaglandin. In five experiments, morphine inhibited the stimulation by PGE_1 of cyclic AMP. The potency was high and dose-related. When the amount of PGE_1 used to stimulate cyclic AMP formation was reduced tenfold, the effectiveness of morphine was raised. Methadone (the narcotic substitute used to get addicts off the hard stuff) and heroin likewise inhibited the stimulation by PGE_1 of cyclic AMP formation.

Interestingly, one of the drugs that shows promise as a heroin antagonist, naloxone (SN: 4/15/72, p. 251), antagonized the inhibitory effect of morphine on the stimulation by PGE_1 of cyclic AMP.

Stimulation by E prostaglandins of cyclic AMP formation in brain tissue, the authors believe, was probably due to the activation of adenyl cyclase, a cell membrane that is responsible for the synthesis of cyclic AMP in cells.

Collier and Roy therefore propose: "The ability of the opiates to inhibit the stimulation by E prostaglandins of cyclic AMP formation in rat brain homogenate, presumably by inhibiting stimulation of a neuronal adenyl cyclase, represents a biochemical mechanism that could account for the analgesic and allied efforts of these drugs." □

Serious defoliant damage in Vietnam

Between 1961 and 1971, the U.S. military dropped more than 100 million pounds of herbicides on an area slightly larger than Connecticut. The purpose of the missions was to strip away foliage in the dense forests of Vietnam for the detection of Vietcong, and to a lesser degree for the destruction of crops in the Central Highlands.

In 1970, a nationwide debate took place over the extensive use of chemical herbicides in Vietnam, and culminated in a request by Congress that the National Academy of Sciences assess the physiological, psychological and ecological long-term effects of the sprayings. The study was conducted by 17 scientists from the United States, Sweden, Great Britain and South Vietnam. Results were recently presented to the Senate Armed Service Committee. Briefly, they conclude that while ecological damage is "extensive," there is "no conclusive evidence" that herbicides cause birth defects in humans.

The committee concludes that the Vietnamese people have survived the 4,561 defoliation and 858 crop destruction missions very well. It was unable to find any evidence of direct damage to human health, though there were numerous secondhand reports of deaths among the Montagnard children. Due to the problem of security, the scientists were unable to visit the people in the highlands. Instead, they relied on "intensive interviews" with Montagnard informants who reported a variety of respiratory disorders among the people living in or near sprayed areas, and a high number of deaths among children after spraying.

"Although these reports did not come from medically qualified observers, the committee considers it to be important that this matter be pursued at the earliest opportunity," says Philip Handler, president of the National Academy of Sciences, in a statement that prefaces the study.

In addition to physiological damage, the spraying also had adverse psychological effects, turning the Vietnamese people against the United States. But contrary to what might be expected, the herbicide missions were less an emotional issue among the peasants than among the urban intellectuals. The people in the countryside feel that the herbicides were merely one among many bad occurrences that resulted from the war, while for the urban dwellers the herbicide missions became an emotionally charged symbol for many apprehensions and distresses, but especially those for which Americans could be blamed.

Adverse effects on vegetation are largely confined to those plants that were in direct contact with the chemical agents. Most of the chemicals disappear from the soil before the next crop comes up. However, among the vegetation that received direct spraying, the damage is extensive. Particularly vulnerable were mangrove trees and inland tropical forests that received over three-fourths of all sprayings.

Mangrove trees are economically important to the Vietnamese as a fuel source and as a spawning place and food source for fish. According to the study, about 260,000 acres or 36 percent of the mangrove trees were destroyed by the spraying missions, and that "under present conditions of use and natural growth, it may take well over 100 years for the mangrove area to be reforested." Handler states that massive reforestation program could restore the forest in approximately 20 years if sufficient money and seed resources could be made available.

Inland forests received the brunt of the herbicide attacks. And though, the study states that losses in merchantable timber are "extensive and serious," committee members do not agree on the degree of damage suffered. In fact, three panel members, biologist Paul W. Richards of the University College of North Wales, botanist Pham-Hoàng-Hô of the Faculty of Science in Saigon and behavioral scientist Alexander H. Leighton of the Harvard School of Public Health, disassociate themselves from the study's final assessment of inland damage and feel the estimate should be higher. (The committee's estimated damage is 500,000 to 2 million cubic meters of

merchantable timber.)

The dispute arises largely over the method used to assess the damage. Because much of the inland forests are still under Vietcong control, assessment rested almost entirely upon interpretation of aerial photographs. The criticism is that the photographs alone are inadequate for measurement of damage, especially beneath the dense canopy of tropical forests.

If the Alaska pipeline leaks?

Environmentalists fighting to stop the trans-Alaska oil pipeline have expressed two main worries: Will increased activity of men and machines permanently damage the permafrost that underlies the peat topsoil and will inevitable oil spills spell instant disaster for the fragile tundra biome? The tentative answer, according to a review article in March 1 NATURE, is a qualified "no."

When trucks drive over the "active layer" of topsoil that freezes and melts to a depth of 35 to 60 centimeters each year, they leave deep ruts that some early observers feared would turn long, thin stretches of the tundra into a bog. Research has now shown that regeneration of vegetation and disappearance of the ruts depends on the region involved. In wet areas, regeneration is completed in five years; in dry areas, the process may take 20 years. Nevertheless, repeated traffic could erode the peat too much.

To identify the possible effects of oil spills, carefully controlled experimental spills have been made in the Mackenzie Delta area of northwest Canada, in amounts equivalent to 1,950 barrels per acre. Evaporation of the oil—as much as 15 percent within the first 16 hours after application—apparently removes some of the most lethal constituents of the petroleum and helps counteract the heating effect of a blackened surface, by absorbing heat during vaporization. All lichens and mosses, with one exception, were killed; but higher plant species, including sedge and willow, recovered pretty well. Total plant recovery was as high as 55 percent after one growing season following a spill and temperature rises were not enough to melt permafrost.

"It seems," the article concludes, "that the tundra can probably cope with occasional, acute pollution from oil spills," and that local ecology is resilient enough to recover naturally, suggesting the desirability of no "further interference." But the question of how low-intensity, chronic pollution may affect the Alaskan environment remains unanswered. □

On helping the less developed nations

The world of 1994, envisions Roy Amara, president of the Institute for the Future in California, will embody rejuvenated cities, increased ecological concern and socially rather than economically motivated development. Yet, he predicts, there will still be a conspicuous absence of much-needed ways to share the wealth—to equitably allocate income and other kinds of wealth among the nations and peoples of the world.

As thousands of scientists at the annual meeting of the American Association for the Advancement of Science discussed the questions and answers of their fields, several groups confronted the problems of applying science and technology where there essentially is none: in the underdeveloped regions of the globe. There have certainly been successes—a favorite example at the meeting was rural China—but many of the participants agreed that for some of the neediest regions the difficulties are huge, and that much of the current effort is at best being misdirected.

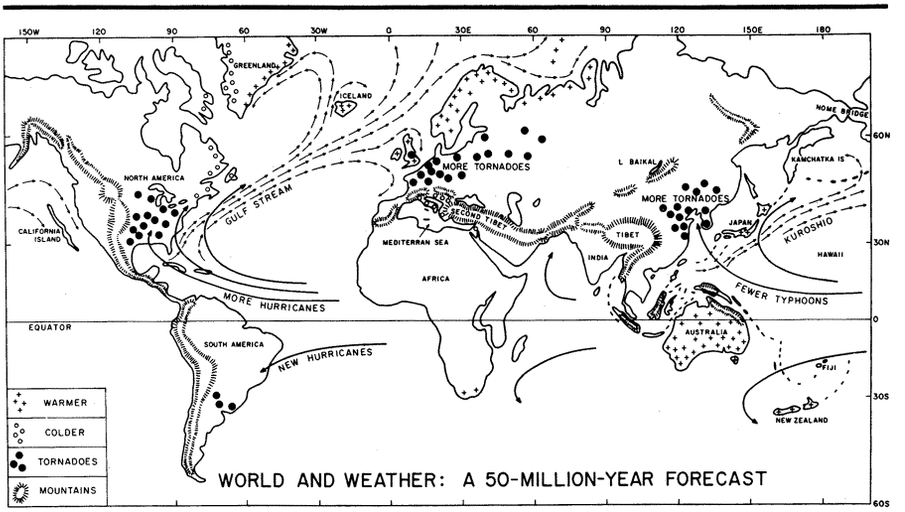
A major problem with rural development, says Uma J. Lele, who has been analyzing some 3,000 programs in Africa for the International Bank for Reconstruction and Development, is that the emphasis is often on the simple, direct import of technology, rather than on development of ways to help technology become involved with the population, particularly through social understanding. A plan to breed more compact cattle in Kenya to conserve grazing land, for example, hit a snag when planners failed to deal with the herdsmen's desire for larger herds of bigger cattle, even though undernourished.

In fact, says University of Maryland economist Irma Adelman, some of the most highly-touted goals of outside developers—increased political participation and a larger share of the national wealth for the poor—often backfire completely. A study of 12 years of development efforts in 43 countries, she says, suggests that the initial impact of such plans on these two areas is to decrease both. Many of the common elements of economic redevelopment schemes, such as tax changes and even land redistribution, make little difference by themselves, and need to be part of an overall plan that will support them.

In the least developed areas, Adelman says, economic development efforts may work in reverse, with the income of the poorest 60 percent of the people actually decreasing significantly, and only the top five percent going up. "In these countries," she says, "the path toward sustained economic growth is eventually blocked, unless either the country is sufficiently large or redistributive policies are sufficiently important to generate an internal market for growth."

Corporations, points out international business consultant Charles S. Dennison, are often more maneuverable than governments in implementing such programs, but as one development planner pointed out at the meeting, "the number of corporate people in any country who are interested in development is distressingly small." □

A look ahead: 50,001,974 A.D.



U. of Chicago

Radical changes on the earth due to 50 million years of continental drift are predicted by three University of Chicago paleoclimatologists *(see p. 176).*