

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 tis-

sue. 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 PGE₁ 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 PGE₁ of cyclic AMP. The potency was high and dose-related. When the amount of PGE₁ 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 PGE₁ 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 PGE₁ of cyclic AMP.

Stimulation by E prostaglandins of cyclic AMP formation in brain tissue, the authors believe, was probably due to the activation of adenylyl 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 adenylyl cyclase, represents a biochemical mechanism that could account for the analgesic and allied effects of these drugs." □

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

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