of endogenous morphine-like materials parallels that of the opiate receptors. Hughes says that it seems possible that the brain does possess a pain suppressive system and that enkephalin plays a role in it.

There is additional evidence in favor of the hypothesis that opiate receptors are actually receptors for an endogenous neurotransmitter. When Snyder and Pert separated brain tissues into subcellular fractions, they found the receptors in the fraction containing synaptic membranes. These are the membranes located around nerve synapses—the region of contact between neurons through which nerve impulses are transmitted—and they are the logical site for location of receptors for neurotransmitters. Receptors for the neurotransmitters acetylcholine and norepinephrine, for example, are located at the synapse. All these observations support the hypothesis that the endogenous morphine-like material is a neurotransmitter, although, according to Hughes, enkephalin and the opiate receptors are found in certain smooth muscle preparations; consequently, its function may not be restricted to brain.

Studies of the receptors itself are not only yielding information about how opiates interact with their receptors but they are also providing a more efficient approach for designing potent analgesic drugs that have no addictive potential. Despite the fact that opiates are very effective pain-relievers, their use is limited because they produce euphoria and are addictive.

Some opiate antagonists completely prevent all the effects of opiates. For this reason they are useful in treating overdoses of heroin because they reverse its effects within minutes. They may also be useful for treating heroin addicts because the narcotic does not elicit a "high" in the presence of antagonist and should no longer be attractive to the addict. Other antagonists, however, retain some of the usual effects of opiates. The idea is to design a drug for therapeutic use that still relieves pain effectively but which has just enough antagonist activity to prevent the addictive effects. The drug pentazocine is one example of an agent with such mixed properties.

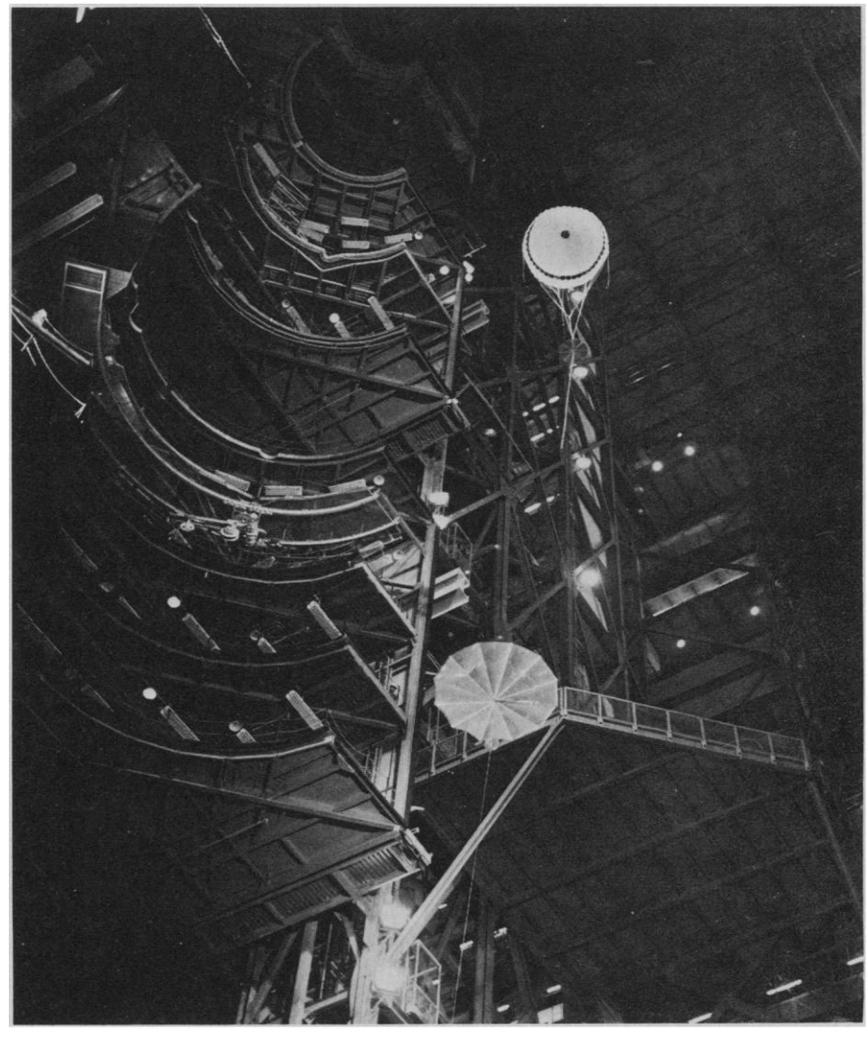
Predicting what chemical features will produce the desired characteristics is difficult. Screening the drugs in animals is both time-consuming and expensive, and the results may not be borne out in human trials. But differences in the way sodium ions affect the binding to receptors of the three classes of agents—that is, opiates, complete antagonists, and drugs with mixed properties—appears to provide a method for distinguishing between them.

Sodium ions increase the binding of antagonists but decrease the binding of opiates by receptors. Based on this effect, Snyder and Pert devised what they call the sodium response ratio. This is the ratio of the concentration of the test drug that inhibits by 50 percent the binding of labeled naloxone (a pure antagonist) in the presence of sodium to the comparable concentration in the absence of sodium. The assay is convenient because the test drug need not be labeled.

In the presence of sodium, opiates should have decreased potency in preventing the binding of naloxone; that is, more drug should be required to give 50 percent inhibition and the ratio should be much greater than one. Drugs that are predominantly antagonists should have the same capacity to inhibit the binding of naloxone whether sodium is present or not; for these the ratio should be equal to one. And those drugs with mixed characteristics should have ratios greater than one but less than those of the more potent opiates. When Snyder and Pert tested a variety of drugs with known pharmacological properties, the ratio values they found agreed well with those predicted. Although this test should be valuable in screening for agents with mixed properties, additional testing in animals and humans will be required to determine whether they have the right mix of effects.

It's Not Mars, But It's Still a Big Drop

The Viking spacecraft is scheduled to be launched this week toward a July 1976 rendezvous with Mars. The lander, which is to be dropped into the uncertain atmosphere of the red planet, was put through its paces earlier this year at the world's largest indoor parachute test facility, the huge Vehicle Assembly Building at Cape Canaveral.—A.L.H.



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