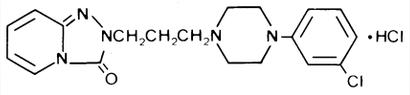
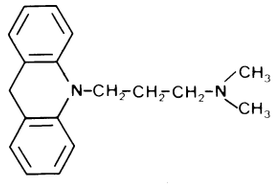
NOVEL ANTIDEPRESSANT: TRAZODONE



TRICYCLIC ANTIDEPRESSANT: IMIPRAMINE



is trazodone (Desyrel™). Duncan P. Taylor of Mead Johnson Pharmaceutical Division in Evansville, Ind., says this drug blocks serotonin uptake very selectively. Over a four-week period, administration of the drug to rats also produced a significant loss of serotonin, but not other, receptors. Taylor suggests the loss of serotonin receptors is responsible for the drug's clinical antidepressant action.

The most important difference between the tricyclics and the new generation of antidepressant drugs, which includes mianserin (Organon), iprindole (Wyeth), zimelidine (Astra), fluoxetine (Lilly) and viloxazine (ICI), is the absence of side effects. Taylor says the tricyclics' side effects are largely due to their binding to a variety of receptors, including those for the neurotransmitter acetylcholine. Some of the novel antidepressants are expected to reach the U. S. market in the next two to three years. □

Third interferon cloned

The last of the three types of human interferon has been produced in bacteria, yeast and mammalian cell culture through recombinant DNA methods, David Goeddel of Genentech, Inc. reported in San Francisco at the International Congress for Interferon Research. The new product, immune interferon (also called gamma interferon), was identified by its anti-viral activity, acid and detergent sensitivity and inactivation by antibodies to the natural human material, which is produced in the body by white blood cells. The laboratory-produced interferon is much needed in research because immune interferon, the smallest of the three types, has been the most difficult to isolate. Previous studies using limited amounts of material suggest immune interferon is more active in fighting cancer cells than are the leukocyte and fibroblast forms. Goeddel reports there is a single human gene for immune interferon, and the gene appears to have a signal sequence and at least one intervening sequence. The Genentech research on immune interferon is funded by the Japanese companies Daiichi Seiyaku Co., Ltd. and Toray Industries, Inc., which will share exclusive rights for the product in Japan. □

'Giga-seal' view of membrane channels

A new technique that allows scientists to analyze single channels in cell membranes is rapidly spreading from one physiology laboratory to the next. Developed last year by German scientists Erwin Neher and Bert Sakmann of the Max Planck Institute for Biophysical Chemistry in Göttingen, the method was in use in 10 laboratories six months ago and is used in 30 to 50 labs currently, Neher estimates. After its description in Los Angeles at the recent meeting of the Society for Neuroscience, the technique's use is expected to spread even more rapidly. It may soon replace the long-time reliable tool of neurophysiologists, the intracellular electrode, for examining how ions pass across cell membranes and how hormones, neurotransmitters and drugs modify these currents.

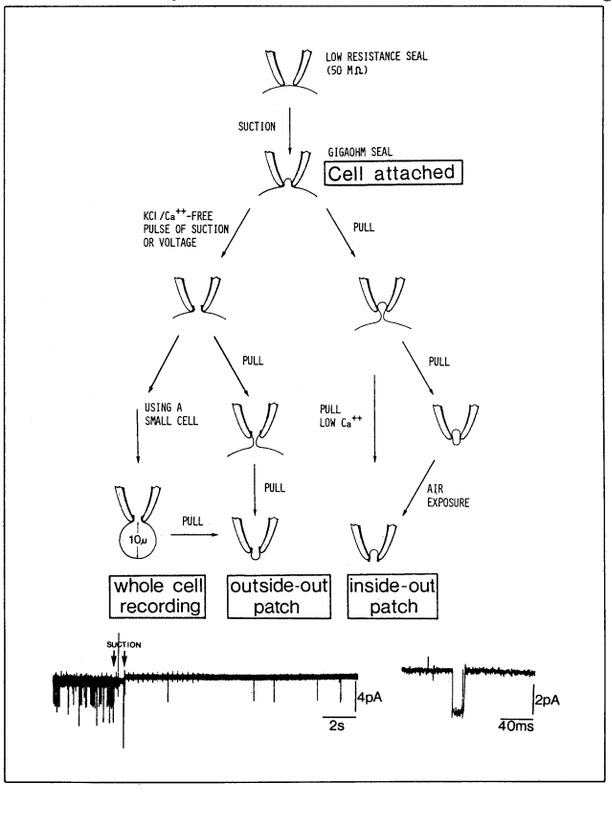
A tight seal between a membrane and the tip of an electrode is the basis of the new technique. A small, heat-polished glass pipette is placed against the outside of a cell membrane and suction is applied to pull the membrane slightly into the pipette, which is used as an electrode. The contact has a very high resistance, 10 to 100 gigaohms, and so the scientists call it a "giga-seal." The tight seal produced by suction reduces the background "noise" of electrical recordings, increasing the sensitivity of the technique by a factor of 100 to 1,000, Neher says.

With the giga-seal, Neher and colleagues have observed 10 to 15 types of membrane channels open and close. They have successfully described the characteristics of the calcium-dependent potassium channel, a pore found in many cell membranes but whose characteristics have baffled electrophysiologists. Anyone who does electrophysiology should be able to pick up the new technique, Neher told SCIENCE NEWS, and he expects the scientists to find it simpler than now-standard procedures.

Because giga-seals are mechanically stable, they can be used to isolate patches of membrane for electrical study, as well as for examining membranes of an intact cell. By simple manipulations Neher can obtain a membrane patch a few microns square either inside-out or outside-out across the electrode tip. With these preparations scientists can have the membrane separate solutions of any composition they choose. They then can record the current passing through its channels.

"As a byproduct of our technique, we found a very gentle way to penetrate cells," Neher says. "For intracellular recording we make a seal, then break the patch and so have access to the inside of the cell." This procedure is easier than penetrating the cell with a microelectrode, because it does not create a leak. "You can use cells as small as you want," Neher says. "You can easily record from a cell 10 microns in diameter."

A requirement for smooth surfaces is the major limitation of the technique. The electrode tip must be flawlessly clean, solutions must be filtered and some cells must be enzymatically treated, removing surface coating material, to provide a smooth membrane. "We have obtained giga-seals on nearly every cell type we have tried," Neher and collaborators say in a recent article in PFLUGERS ARCHIV (Vol. 391, p. 85, 1981). Successful preparations already include more than 20 cell types. Among them are neuroblastoma and leukemia cell lines, spinal cord cells, cerebellar cells and fibroblasts in tissue culture; blood cells; cells from adrenal gland, heart, liver and pancreas; and enzyme-treated muscle fibers and ganglion cells. □



Sensitivity of signal is improved by slight suction (applied at center of top row of recording). Opening and closing of single channels can be detected (bottom row, larger scale than above).