Ulcer drug may fight cancer . . .

Cimetidine (trade name, Tagamet) recently surpassed Valium as the world's largest-selling prescription drug. It is used to treat stomach ulcers, but now there are indications that it might also be used in the fight against metastasizing, or spreading, cancers, according to research reported in Washington at the recent meeting of the American Society of Clinical Oncology. The work was done by a team of researchers led by Michael E. Osband of the University Hospital in Boston.

The research is based on the activity of killer T cells and suppressor T cells. The immune system's killer T cells are supposed to reject tumors, but the immune systems of many cancer patients fail to do so. The reason the killer T cells fail to do their job, it has been suggested, is that the tumor stimulates the production of suppressor T cells that inhibit the activity of the killer T cells (SN: 11/18/78, p. 342). Osband and his colleagues suggested that if this is the case then the problem might be solved by suppressing the suppressor T cells in cancer patients. This would leave the killer T's free to go about their business.

But how do you suppress the suppressors? Osband and his co-workers knew that suppressor T's only become functional if they are activated in the body by histamine, and they knew that cimetidine fights ulcers by keeping histamine from activating the stomach to produce acid. With this in mind, they tested cimetidine's ability to block histamine activation of suppressor cells. When they found that this is the case, they tested cimetidine's ability to fight tumors by suppressing suppressor T cells. The researchers injected lung tumors into the footpads of mice and gave some of the mice cimetidine and some no treatment. Cimetidine significantly prolonged the survival of the treated mice over the control mice. The prolonged survival, say the researchers, was due to cimetidine's ability to suppress suppressor T cells and halt the spread of the lung tumors into the mice's lungs. Cimetidine may be able to halt metastasizing tumors in cancer patients by the same route, Osband and his colleagues conclude. But a cloud has now fallen over cimetidine. See next story. □

but synergisms could prove fatal

While gastric ulcers are not the leading cause of illness, cimetidine (Tagamet) is the world's largest-selling prescription drug. "It therefore appears Tagamet is being overprescribed," says University of Florida clinical pharmacist Leslie Hendeles. And this concerns him because there is a growing list of adverse interactions—some of which could prove fatal—being reported in patients who take the drug along with other medicines, most notably theophylline (frequently prescribed for asthma patients and persons with chronic lung diseases such as emphysema).

Hendeles and researchers from the University of Iowa reported on a theophylline-cimetidine interaction in the March 12 New England Journal of Medicine. "Cimetidine is a potent inhibitor of drug metabolism in the liver," Hendeles told Science News. While not highly toxic when taken alone, it can seriously slow the natural elimination of other drugs from the body, and thereby result in toxic buildups of the drugs at levels that could prove life-threatening.

The case described in NEJM involved a 15-year-old girl with chronic asthma. In determining an effective theophylline dose, blood-level concentrations of the drug were monitored during treatment: Blood levels should be higher than 10 micrograms per milliliter to be effective, but theophylline levels above 35 μg/ml could bring on seizures. And roughly half of all theophylline-induced seizures are fatal, Hendeles says.

The girl was prescribed a dose of theophylline adjusted to produce blood concentrations of 13 μg/ml. However, only two weeks after a local physician prescribed cimetidine for the patient, her blood levels of theophylline had nearly tripled to 36.7 μg/ml.

The body's ability to eliminate theophylline decreases by 60 percent after cimetidine is taken, a study showed last year. And as demonstrated by the asthma patient, that means a "severe, life-threatening" situation can develop for theophylline users within days of taking standard doses of cimetidine, Hendeles says. He adds that even some over-the-counter asthma remedies contain enough theophylline to produce toxicity in cimetidine users.

But cimetidine interactions are not restricted to theophylline. The drug reduces the body's clearance rate for Valium and for warfarin-like anticoagulants as well. In the latter case, unattended users could bleed to death. And the elderly face a special problem with cimetidine, even if they take no other drugs, Hendeles says. Because their bodies clear out the drug very slowly, toxic levels of the drug can build up, resulting in mental confusion and disorientation.

Cimetidine use in this country is still so new that a full list of its potential synergistic effects is not complete. Until it is, the role of preventing dangerous drug interactions may rest with physicians who keep up with their journals, alert community pharmacists and an informed public, Hendeles says. □

Fetus successfully treated in womb

One of the major problems with inherited, or inborn, errors of metabolism, is that by the time a child is born, he or she is already suffering damage resulting from the disease. Even prompt diagnosis and treatment right after birth may come too late to help the child. One means of assisting such a child would be to diagnose and treat the disease before the child is born. And this approach is being used successfully. In 1975 a fetus with an inherited defect in vitamin B_{12} synthesis was diagnosed and successfully treated by giving large doses of vitamin B_{12} to its mother during pregnancy (SN: 8/30/75, p. 121). Now a fetus with an inherited defect in biotin metabolism has been successfully diagnosed and treated by giving large doses of biotin to its mother during pregnancy, say Seymour Packman, Morton J. Cowan and Mitchell Golbus of the University of California at San Francisco, along with Donald Meyer of Santa Rosa Memorial Hospital.

In 1979, Debra Whitmore gave birth to a son who, on the basis of life-threatening symptoms, was quickly diagnosed for an inherited disorder that disrupts the metabolic process by which biotin is used in the body. Only massive injections of biotin saved him. In 1980, the woman became pregnant again, and this time it was known that the fetus she carried had a one-in-four chance of possessing the biotin disorder. Packman and his colleagues performed amniocentesis. The disease was detected, and the woman was given large amounts of biotin, in the hope it would pass through the placenta and be absorbed by the fetus. When the child (Nicole Whitmore) was born last December, she was free of the symptoms of biotin deficiency which her brother had shown at birth. Tests on Nicole, who continues to remain healthy thanks to ongoing biotin treatments, have confirmed that she indeed has the same biotin disease as her brother.

Packman and his colleagues foresee other fetuses with the same inherited disease receiving the same kind of treatment. They also anticipate that fetuses with an inherited inability to metabolize galactose might also be treated by giving their mothers large doses of galactose. The researchers will also be on the lookout for other inborn errors of metabolism that they might treat, provided the diseases meet certain criteria—are known to run in the family because a previous child has been affected by them, are diagnosed with amniocentesis and can be treated by therapies that will not harm the mother and have a good chance of helping the fetus. Such treatments are "going to be very high on the list of things we want to accomplish," Cowan told Science News. □