Ulcer drug a cancer risk?

Since the ulcer drug cimetidine (Tagamet) was approved by the U.S. Food and Drug Administration four years ago it has become the world's largest-selling prescription drug in terms of dollar volume and is taken by millions of people. Yet cimetidine is a compound of many faces, it seems, and not all of them are flattering. For instance, while cimetidine can halt the spread of lung tumors in mice, it can also cause adverse, sometimes fatal reactions in patients if taken along with other medicines (SN: 5/23/81, p. 326). And now cimetidine has been associated as well with high levels of N-nitrosamines in the stomach, P.I. Reed of Wexham Park Hospital in Slough, Berkshire, England, and colleagues report in the Sept. 12 LANCET. N-nitrosamines are powerful chemicals that have been indicted as a cause of stomach cancer. So while cimetidine may cure ulcers, it may also increase the risk of stomach cancer, say the researchers.

Reed and his co-workers obtained stomach juice samples from 140 patients with stomach or small-intestine ulcers who had been taking cimetidine for periods ranging from one week up to 45 months and also from 267 control subjects (217 with stomach or small-intestine ulcers and 50 without ulcers). The researchers analyzed the levels of N-nitrosamines in the gastric juice samples from both cimetidine and non-cimetidine takers and compared them. They found the levels were significantly higher in those who took cimetidine, up to 100 times higher in some instances. Thirteen of the 140 patients, in fact, had N-nitrosamine concentrations equalling or even exceeding those of 23 stomach cancer patients, further suggesting that by raising N-nitrosamine levels, cimetidine might heighten the risk of stomach cancer.

Reed and his team then took gastric juice samples from 23 of the 140 patients up to 40 weeks after the patients had stopped taking cimetidine. The researchers then compared levels of N-nitrosamines in the samples taken from the patients while they had been getting treatment with those in the samples taken from the patients while they were no longer receiving treatment; they found no significant fall in N-nitrosamines. The results suggested that even after ulcer patients stop taking cimetidine they still have N-nitrosamine levels resulting from cimetidine treatment and thus may still be at a risk of stomach cancer.

Although Reed and his co-workers are not sure how cimetidine could increase the risk of stomach cancer via N-nitrosamines, they do suggest one possibility on the basis of available evidence. Cimetidine could reduce stomach acidity, which in turn could lead to the proliferation of bacteria and fungi in the stomach. These bacteria and fungi could then convert nitrates in the stomach (obtained from food and drinking water) into nitrites and then into N-nitrosamines.

More studies will have to be conducted, of course, before N-nitrosamine elevation due to cimetidine can conclusively be said to cause stomach cancer. However, stomach cancer, which is common in Japan but rare in Western countries, has been identified in a handful of British cimetidine users during the past several years. □

Women underrepresented in new drug trials

Food and Drug Administration regulations, because they restrict the use of young women as pharmaceutical research subjects, prevent an accurate evaluation of drugs, according to a new study reported in the Oct. 6 ANNALS OF INTERNAL MEDICINE.

Men and women respond different ways to different drugs. Yet, according to the authors of the study, only 50 percent of the 1,561 drugs listed in the 1981 *Physician's Desk Reference* were tested in young women. Only two of 17 pharmacokinetic studies published in the 1979 JOURNAL OF CLINICAL PHARMACOLOGY AND THERAPEUTICS used women as subjects, say the Pennsylvania State University and University of Texas researchers.

The average woman, because she weighs less than the average man, may need a smaller dosage of drug for optimum response. The opposite situation can also occur; for example, because the platelets from women aggregate more readily than the platelets from men, a higher dose of antithrombotic drug may be required, they say.

Current FDA guidelines proscribe administration of new drugs, not only to pregnant women, but to any woman who could potentially become pregnant. According to these guidelines, women can participate in large clinical studies only after completion of animal studies and small controlled trials. Participation in small trials is possible only after completion of dose-ranging studies. FDA regulations for dose-ranging studies specifically exclude women "of child-bearing potential."

Defenders of FDA policy argue that although women may benefit from more thorough testing, potential fetuses would not. FDA critics say that excluding women due to hypothetical pregnancy only postpones the eventual risk. Once a drug is on the market, side effects will appear throughout the general population. These victims, unlike research subjects, have not consented to the risk. □

New flu vaccine meets criticism

Despite assurances from government officials, this winter's super-potent influenza vaccine is causing a ripple of concern among members of the medical community. Some critics warn that there is no guarantee that the new vaccine will not produce side effects similar to those accompanying the swine flu inoculations in 1976.

The new vaccine is more than twice as strong as last year's vaccine, which was effective against only half of all prevalent flu viruses. Vaccine potencies were lowered in 1977 after 230 people died as a result of the federal inoculation program against swine flu virus. The higher antigen levels are more effective against viruses — and more likely to cause dangerous side effects.

The high-potency swine flu vaccine, designed to prevent a major epidemic, instead created a nightmare of pain, paralysis and litigation. More than 1,400 lawsuits, 63 million doses of unused vaccine, and numerous cases of paralysis are reminders of the epidemic that never happened.

Epidemiologist Edward Brink at Atlanta's Centers for Disease Control says that this year's vaccine has been tested and found safe at both high and low antigen levels. Only five percent of subjects experienced fevers; none contracted Guillain-Barré syndrome. Brink is reluctant to compare the potency of this year's vaccine with that distributed against the swine flu, saying that recent changes in unit classification prevent accurate comparison. He contends that the vaccine's restricted distribution — 18 million doses, as opposed to the 140 million doses of swine flu vaccine — will limit side effects. And only certain patients — those in whom the risks of flu complications are greater than the risks of vaccine side effects — are being inoculated.

Other experts counter that no signs of paralysis or neurological damage were seen anywhere in the swine flu testing program. Guillain-Barré syndrome, because it is so rare, appears only once a vaccine is widely distributed, they say. According to J. Anthony Morris, former chief of vaccine research for the Food and Drug Administration, "if the government really has an effective vaccine, they are being negligent in not distributing it to school children. But in fact, it is worthless. It's only being given to the chronically ill and the elderly because it is logistically easier; they are all either in nursing homes or hospitals. Plus, if an 85-year-old man dies, you won't hear much. If a seven-year-old child dies, it's a crime."

Unlike the swine flu program, this year's vaccination program will receive no federal funding. □