Pain killer abuse spells renal damage

Overuse of non-prescription drugs that contain more than one active ingredient to kill pain can severely damage the kidneys, a governmental panel announced last week, as members urged that "serious consideration" be given to restricting such compounds to prescription use only.

Occasional use of the products, which typically combine aspirin with a second pain reliever, seems harmless, said the scientists convened by the National Institute of Health in Bethesda, Md., to review 30 years of international studies on the topic. But pain sufferers who go beyond the manufacturer's recommendation, and ingest more than 10 tablets per day for three years or more, seem to increase their risk of kidney damage and possibly some cancers of the urinary tract.

Roscoe R. Robinson, a nephrologist at Vanderbilt University in Nashville, Tenn., who chaired the panel, says he is reluctant to specifically name the brands in question because specific formulations are subject to change. But most of such compounds in the United States combine aspirin (or other forms of the chemical family "salicylates") with the pain-killer acetaminophen. The kidney damage seems to stem from an interaction between these compounds, he says. Other chemicals often added to cold and hay fever remedies, including caffeine, antihistamines and decongestants, seem to play no part in the interaction.

"Right now, the evidence suggests that if you have pain, you can get the same relief from aspirin or acetaminophen alone that you get from a mixture of the two drugs," he says. "There doesn't seem to be any synergistic benefit, but there does seem to be synergistic harm to the kidney." The mechanism of damage is still unclear. But one theory, based on animal data, suggests that breakdown products of acetaminophen decrease the kidney's production of an enzyme that usually protects against aspirin's damage to cell proteins.

Drug producers objected to the panel's conclusions. "The findings should be interpreted with great caution," Jerry Parrott, of the Bristol-Meyers Company in New York City told SCIENCE NEWS. Most of the epidemiological studies the panel reviewed were from other countries, he says, and involved combinations of aspirin and phenacetin, a drug no longer used in U.S. products (SN: 8/28/82, p. 137). In addition, he claims, it is difficult to distinguish in the studies between damage actually caused by the analgesics and damage caused by an underlying illness that might lead patients to overuse the painkillers.

Michael Dunn, a nephrologist from Case Western Reserve University in Cleveland, said panel members felt justified in including phenacetin data in its review because more than 90 percent of phenacetin is broken down in the body to yield acetaminophen. He agreed that very few cases of kidney failure in the United States can be linked to abuse of analgesics — an estimated one new case per million persons per year, but estimated that the medical costs of caring for such patients may total more than $40 million a year.

"The manufacturers argue that removing such a compound from the market would be something like taking away cars because some people speed," says Dunn, adding that the analogy might be a good one if — and only if — the mixture drugs proved more effective than single compounds in relieving pain. "But there doesn't seem to be any evidence of that," he says. *— D. Franklin*

Clot-buster clicks in human trials

Tissue plasminogen activator (t-PA) marches on. The natural clot dissolver, which holds promise in mitigating the effects of a heart attack, has scored victories in the first two studies reporting on its use in humans.

Most heart attacks are associated with a clot that forms in one of the arteries delivering blood to the heart muscle itself. Clot formation can result in death of muscle beyond the clot, jeopardizing the function of the entire organ. At the American Heart Association meeting last year, researchers reported that t-PA administered within an hour of the onset of a heart attack saved heart tissue in dogs (SN: 11/26/83, p. 340).

Last week Johns Hopkins University researchers announced successful use of t-PA derived via recombinant DNA methods on a handful of heart attack victims at Baltimore City Hospitals. And researchers from Washington University in St. Louis and the University of Leuven in Belgium describe using t-PA collected from a cultured tumor cell line in the March 8 NEW ENGLAND JOURNAL OF MEDICINE. The t-PA broke up clots in six of seven tries.

The activator binds to fibrin, the basic framework of a clot. Plasminogen, an enzyme, binds to the complex and is activated to break up the clot. Two other clot busters are currently under evaluation, but they can cause spontaneous bleeding and allergic reactions. Tissue plasminogen activator only works at clots and does not seem to cause allergic reactions. In addition, t-PA clears the body within a matter of minutes rather than hours or days, so a patient can be operated on without the fear of excess bleeding. What remains to be seen is if t-PA can be administered quickly enough in an average hospital setting, if breaking up clots is beneficial to heart health in the long run and if t-PA can be supplied economically. *— J. Silberner*

EPA to limit, then ban EDB in citrus

The Environmental Protection Agency last week proposed interim limits on the levels of ethylene dibromide (EDB) that will be allowed in citrus fruits and papayas. Expected to go into effect within 30 days, the rule would limit levels of the carcinogenic pesticide (SN: 10/8/83, p. 229) to 250 parts per billion (ppb) in whole fruits. This translates into an allowable residue of just 30 ppb for the edible portions. The interim ceiling, which applies to both domestic and imported produce, lasts only through Aug. 31; after that, no EDB residue will be allowed on these fruits.

EPA's administrator, William Ruckelshaus, says, "Our purpose is to get EDB out of the American diet in as orderly a way as possible." He notes, "The fact that the domestic use of EDB has virtually ceased means that our sole remaining concern for American dietary exposure lies with imported citrus." Fruit sampled by the agency over the past month turned up evidence of EDB contamination in imported fruit as high as 2,200 ppb in the edible portions.

"In our view these levels, if they are representative and are continued over time, would pose an unacceptable health risk," Ruckelshaus says. However, he adds, "I want to remind everyone that the risks associated with exposure to EDB are chronic risks that accrue over a long period of time. EDB does not present an acute short-term health risk."

Acceptable alternatives for fruit-exporting nations affected by this proposal — primarily Caribbean countries — are limited to fumigation with methyl bromide or cold treatment (see p. 153) at this time, EPA says. In fact, Ruckelshaus notes that there are already three ports where cold treatment is now available to handle citrus fruit entering this country. Moreover, because there is already some question about methyl bromide's safety — long-term toxicology tests are currently underway in this country and in the Netherlands — cold treatment "may be ultimately the way to go," Ruckelshaus says. Though gamma irradiation of produce has been proposed (SN: 3/3/84, p. 138), Ruckelshaus pointed out at a news briefing "that it is not possible to have such technology approved and on line in those [affected fruit exporting] countries before our tolerance expires Sept. 1."

The remaining primary use for EDB—as a leaded-gasoline additive to keep lead from building up on engine parts — may also see an early phaseout. Though use of leaded gasoline is currently slated to end by the mid-1990s, EPA's Joseph Cannon says his agency is considering an accelerated phaseout. Details are expected to be made public this summer. *—J. Raloff*