

Low cholesterol and heart attacks

Although high levels of cholesterol in the blood are a well-accepted heart attack risk factor, scientists disagree over whether or not a low-cholesterol diet can prevent heart attacks (SN: 5/31/80, p. 343; 6/7/80, p. 357). And now the ability of anti-cholesterol drugs to prevent heart attacks also appears questionable, according to a team of World Health Organization scientists. In fact, the anticholesterol drug under study — clofibrate — may increase the risk of death from heart attack and other causes. These findings, the scientists report, are “totally unexpected.”

H. Geizerova of the Institute for Clinical and Experimental Medicine in Prague, Czechoslovakia, and other WHO investigators conducted a clinical trial between the late 1960s and the mid 1970s to determine if the drug clofibrate could reduce blood levels of cholesterol and, in turn, protect against heart attacks. Approximately 5,000 men with high levels of serum cholesterol received clofibrate for an average of 5.3 years, while two other groups of 5,000, one with high levels of blood cholesterol and one with low levels of blood cholesterol, received a placebo (an olive oil capsule) for a comparable period.

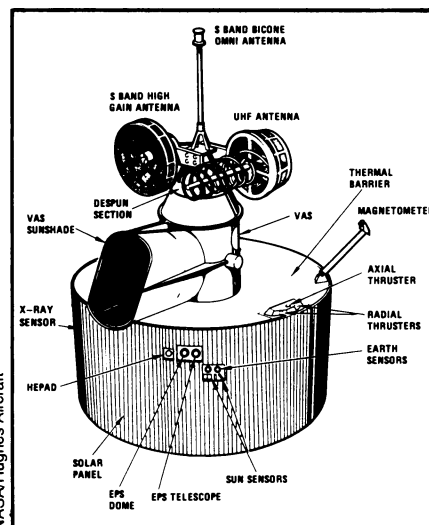
In 1978, the researchers reported a 25 percent reduction in nonfatal heart at-

tacks among the clofibrate-receiving subjects compared with the control subjects with high levels of cholesterol. There was, however, no significant difference in the number of fatal heart attacks between the two groups. Moreover, a significantly higher number of deaths from a variety of causes was found among the clofibrate subjects compared with the high-cholesterol control group, implying that clofibrate was not only ineffective against fatal heart attacks but dangerous as well.

Now, in a four-year follow-up study reported in the Aug. 23 LANCET, the researchers find that the group who received clofibrate still shows a higher number of deaths from a variety of causes, including heart attacks, than does the high-cholesterol control group. In addition, deaths from causes other than heart attacks are higher among subjects who received clofibrate than among the low-cholesterol group. “The implications that there may be a continuing adverse effect on the treated men after leaving the trial is serious,” the researchers write.

The researchers suggest that clofibrate might act by producing a persistent loss of tissue cholesterol over a period of years, thus impairing cell function. This suggestion is supported by earlier findings of a higher number of noncardiovascular deaths among subjects whose blood levels of cholesterol were lowered by a low-saturated-fat, high-polyunsaturated-fat diet than among control subjects. □

GOES-D launched to measure atmosphere



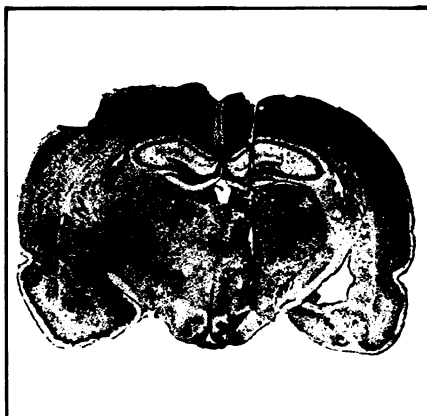
On Sept. 9, the first geostationary satellite able to take vertical readings of atmospheric moisture and temperature was launched for the National Oceanic and Atmospheric Administration. Like its predecessors in the Geostationary Operational Environmental Satellite series, GOES-D will remain continually over one spot on earth and will provide visible-light and infrared photographs of developing weather patterns every 30 minutes. Unlike other GOES satellites, however, the newcomer will also measure temperature and moisture at various levels in the atmosphere. Because storms develop vertically in the atmosphere and are fed by moisture and heat, such measurements will allow weather forecasters to track storms as they develop. Similar instruments on other satellites, such as the polar-orbiting series, do not provide information frequently enough to be useful to meteorologists. Initially, the instrument will be used on an experimental basis. □

Hypothalamic link with GI tract

The link between the hypothalamus of the brain and the gastrointestinal tract, while real enough, has always been a strange one. Why, for instance, are proteins that are commonly found in the gastrointestinal tract also detected in the hypothalamus (SN: 1/27/79, p. 57; 1/19/80, p. 41)? Part of the answer may lie in the increasingly apparent control of the hypothalamus over the GI tract, according to a report in the Sept. 5 SCIENCE by Barry L. Tepperman and Mark D. Evered of the University of Western Ontario.

The peptide hormone gastrin is secreted by the lower part of the stomach when it is full of food. Gastrin then travels into the bloodstream and acts on the upper part of the stomach to stimulate the production of gastric acid. Gastrin is also one of the gut proteins recently found in the hypothalamus. So Tepperman and Evered attempted to determine if gastrin in the hypothalamus might influence gastrointestinal function.

They injected gastrin into the hypothalamus of rats and measured gastric acid secretion from the animals' stomachs. Gastrin consistently caused gastric acid secretion to double or triple 15 minutes later. In contrast, the injection into the hypothalamus of other proteins common to the gut and brain did not increase stomach



Injection of gastrin in rat hypothalamus (arrow) caused secretion of gastric acid.

gastric acid output. Hypothalamic gastrin, therefore, appears to influence stomach gastric acid secretion, whereas other gut proteins in the hypothalamus do not, Tepperman and Evered conclude.

The researchers believe that hypothalamic gastrin influences the gut by acting as a neurotransmitter or neurohormone on the vagus nerve (which connects hypothalamus and stomach). When they severed the vagus nerve in rats, hypothalamic gastrin did not increase stomach gastric acid output. □

Keeping protein destroyers in check

Bodily functions ranging from digestion to conception to the immune response depend on enzymes with a destructive capacity. The protein-cutting enzymes are useful for prompt, irreversible initiation of particular physiological processes. But when the enzymes get out of control, they can degrade body tissue, causing such diseases as emphysema, arthritis and muscular dystrophy.

Protein-cutting enzymes, which are called proteases, are held in check by molecules that inhibit their action. James C. Powers of Georgia Institute of Technology said at the recent meeting in Las Vegas of the American Chemical Society that 10

percent by weight of proteins found in human blood plasma are protease inhibitors. For diseases caused by an imbalance of proteases and their inhibitors, a dose of extra inhibitor may become the most appropriate treatment.

Animal studies have now demonstrated the effectiveness of several chemically synthesized inhibitors in countering emphysema, Powers reports. In emphysema lung material is progressively destroyed by a protease released from white blood cells. An inhibitor called α_1 -PI normally protects the lung from such digestion. But a small number of people are genetically deficient in the inhibitor, and in a much larger number smoking has inactivated α_1 -PI.

Powers and colleagues have synthesized chains of amino acids that can substitute for the natural inhibitor. They bind at the same position on the enzyme (called elastase) that destroys the lung material elastin. One effective inhibitor is a chloromethyl ketone ($\text{CH}_3\text{OCOCH}_2\text{CH}_2\text{CO-Ala-Ala-Pro-ValCH}_2\text{Cl}$). Powers also reports inhibition by a trifluoroethyl ester of a nitrogen-containing peptide chain.

"Synthetic elastase inhibitors have considerable potential for the treatment of emphysema," Powers says. The ketone described above is orally active in protecting rats from experimentally induced emphysema. A related inhibitor has been shown effective in hamsters by other researchers. Although no toxic effects have been observed, Powers remains doubtful that those very reactive compounds will survive the stringent safety requirements for human pharmaceuticals.

"It is likely, however, that many future drugs will be irreversible enzyme inhibitors," according to Powers. He points out that at least one common medicine — aspirin — already falls into that category. Aspirin permanently inactivates an enzyme involved in prostaglandin biosynthesis. Another inhibitor is being used in Europe for treating a disease in which protease leaks from the pancreas into plasma. Squibb is testing a reversible protease inhibitor as treatment for hypertension.

One strain of bacteria, *Pseudomonas aeruginosa*, causes hemorrhagic pneumonia by doubly inducing an imbalance of elastase and its inhibitor. The bacterium produces elastase to break down lung tissue and also inactivates the body's natural inhibitor. Powers has designed an inhibitor to that bacterial elastase.

An imbalance between the protease that breaks down collagen and its inhibitor is suspected of being responsible for arthritis and chronic pulmonary fibrosis. A protease-inhibitor imbalance is probably involved also in the muscle tissue degradation characteristic of muscular dystrophy. In that case the protease is still unknown. The challenge to the chemists is to continue custom-synthesizing inhibitors as researchers identify more and more proteases out of control. □

Inexpensive proposal to aid global ills

1978 U.S. SPENDING (Net)

Spending priorities	\$ (Billions)	% More Than Spent on ODA
Official development aid (ODA)	\$ 4.8	
Flowers, seeds and potted plants	5.0	104
Barbershop, beauty parlor and bath services	5.9	123
Spectator amusements	7.4	154
Pets, cable TV, lotteries, camping, photo studios and film processing	7.6	158
Watches and jewelry	9.3	194
Nondurable toys and sports supplies	11.7	244
Cleaning, polishing and misc. household supplies	16.4	342
Tobacco products	17.9	373
Radio, TV, records and musical instruments	19.5	406
Alcoholic beverages	30.9	644

Selected personal-consumption choices made by individuals contrasted with government expenditures to aid developing nations.

With the buying power of the American dollar seeming to diminish daily, protectionist strategies — spend the dollar at home, not abroad — now prevail. But spending more to aid the economies of developing nations is probably a much better remedy to America's long-term fiscal woes, says the Overseas Development Council in a new study. And the investment in developing economies need not break the pocketbook. ODC's recommendation for near-term U.S. spending increases — roughly \$3.07 billion in fiscal year 1981 — represents but a fraction of America's annual discretionary spending.

"Three quarters of the world's people live in the developing world, where even such basic needs as food, shelter, health, education and jobs are not met," says Father Theodore M. Hesburgh in his introduction to "The United States and World Development: Agenda 1980" (published for the Overseas Development Council, whose board Hesburgh heads). "A false dichotomy has been drawn in recent years between those who say that meeting these 'basic needs' is the most important objective and those who say that reform of the international economic system must take place before any other development progress is possible," Hesburgh says. "The question is not which ... to pursue, but rather how to pursue them both."

How and where science and technology might be harnessed to provide for these interrelated goals — basic needs and a restructuring of the world's developing economies — was tackled at a United Nations conference in Vienna last year (SN: 8/18/79, p. 126). Hesburgh, the U.S. ambassador to those negotiations, donned a slightly different hat this week to explain how fostering development of those goals — with money, policy changes or R&D — will also benefit the donor. For example, he said that any long-term solution to domestic U.S. problems — such as energy, unemployment or the economy — must involve the developing world.

Not only is the developing world the fastest growing market for U.S. exports —

up 18 percent a year over the past decade to total 38 percent of all 1978 U.S. exports — but one of the major sources of strategic materials for the United States (including 82 percent of its tin, 56 percent of its aluminum, 45 percent of its cobalt and 39 percent of its tungsten).

While the United States vocally supports economic efforts to aid developing nations, its annual expenditures amount to only 0.10 percent of its GNP, among the lowest in the developed world. Bearing in mind that the United States, particularly the Congress, has adopted a tight-pocket posture over foreign aid, "Agenda 1980" offers inexpensive short-term proposals for bolstering the economies of developing nations. □

Sex and violence: Pornography hurts

Sexual attacks against women — our newspapers, magazines, novels, movies and television shows are full of such incidents. Considering the long history and continued prevalence of this kind of violence, it might seem that little can be done to curb it. But the situation may not be so bleak. Social scientists are beginning to pinpoint the many factors associated with violence, and the National Institute of Mental Health recently has concluded that an understanding of the conditions that lead to sexual attacks against women should be a major goal of research. Some of that research was presented last week in Montreal at the annual meeting of the American Psychological Association.

Pornography and its possible role as a causative factor in eliciting violent behavior against women is one of the many areas currently being investigated. And the findings contradict much previous research. Ten years ago, the Presidential Commission on Obscenity and Pornography concluded that there was no relationship between exposure to erotic pres-

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