Shutting off plaque's lifeline of blood

Plaques, the gummy, blood vessel deposits that are central to heart disease, are usually considered just artery-clogging lumps. However, plaques often contain living cells in need of nutrients. New, minuscule blood vessels appear near plaques to provide those supplies.

A study of mice now shows that drugs known to curb vessel growth seem to starve plaques, suggesting a tantalizing way to battle heart disease. The compounds are already being tested as weapons against cancer.

In a report in the April 6 CIRCULATION, researchers describe a study of 47 mice that were bred to have a humanlike susceptibility to plaque formation. Their food mimicked the diet consumed by people in the United States. When the mice were 20 weeks old, the researchers pulled 10 out of the group and measured the plaque that had accumulated in each animal's aorta, the large artery leading out of the heart.

For the next 16 weeks, some of the remaining mice received alternate-day doses of drugs that inhibit new vessel growth. Ten received a protein called endostatin, and 15 got a synthetic compound called TNP-470. Twelve other mice received inert injections.

Compared with the mice analyzed earlier in the experiment, all these mice had more plaque—three times more in the case of the untreated mice. However, the mice getting TNP-470 showed a more modest 60 percent increase, while those given endostatin experienced plaque growth of only 28 percent, says study coauthor Karen S. Moulton, a cardiologist at Brigham and Women's Hospital and Children's Hospital, both in Boston.

"It's a very intriguing study," says Jan L. Breslow, a cardiologist at Rockefeller University in New York. "It suggests that one can limit the growth of large plaques through angiogenesis inhibition."

Angiogenesis, or new blood vessel growth, is currently an area of intense research. Scientists suspect that heart muscle damaged in heart attacks might be salvageable if angiogenesis can be harnessed to feed blood to those areas.

In contrast, other researchers want to stifle blood vessel formation in order to cut off nutrient supplies to tumors.

The explanation proposed for the drugs' effects on plaque is complex. Beyond limiting nutrients available to plaque's fat and collagen cells, endostatin and TNP-470 may shrink plaque by hampering the activity of roving immune cells called macrophages, Moulton says.

These cells normally react to plaque-caused lesions on a vessel wall by bundling up cellular debris in the area, recruiting other cells, and performing various housekeeping duties. However, in a blood vessel chronically abused by excess cholesterol, residues of cigarette smoke, or high blood pressure, macrophages may do more harm than good, Breslow says. In particular, macrophages induce vessel growth that could nourish plaque cells and provide an avenue for additional cells that may swell the plaque, Moulton adds.

The greatest danger of plaques arises when they rupture, attracting platelets that can form blood clots. The largest plaques aren't always the ones that rupture, so physicians don't know which plaques to watch.

Thus, a broad preventive approach that thwarts angiogenesis may work, Moulton says. "Shutting off the portal of entry of inflammatory cells may slow [plaque formation] down," she says.

Ironically, if angiogenesis-promoting and angiogenesis-inhibiting drugs become available for human use, many patients might be candidates for both: one to reverse heart-muscle damage and the other to limit plaque growth. Angiogenesis stimulants last only a short time, whereas the angiogenesis inhibitors seem to work for months, at least in mice. These "different kinetics" may avert the conflict, Moulton says. —*N. Seppa*

Radiation helps break down toxic waste

The legacy of the Cold War lies buried underground. At sites across the United States, hundreds of concrete, steel-lined tanks hold toxic mixes of radioactive metals and nonradioactive compounds—organic and inorganic—left over from production of nuclear weapons.

As millions of gallons of hazardous chemicals stew, scientists know little of what is occurring in these cauldrons. A new finding may explain how the wastes decompose and how they produce dangerous gases.

High-energy gamma rays, produced copiously by the radioactive decay of waste elements such as cesium and strontium, can activate common minerals also found in the tanks. These activated particles help organic compounds break down and form gases faster than they otherwise would, according to the recent study.

George Adam Zacheis and Kimberly A. Gray of Northwestern University in Evanston, Ill., and Prashant V. Kamat of the University of Notre Dame (Ind.) report their findings in the April 8 JOURNAL OF PHYSICAL CHEMISTRY B.

Information from such studies will help resolve safety questions and "ultimately feed into ways to process the waste," says Donald M. Camaioni, a staff scientist at the Pacific Northwest National Laboratory in Richland, Wash. He works on tank-waste safety programs at the Hanford Nuclear Reservation near Richland. With 54 million gallons of waste in 177 containers, Hanford is the largest nuclear-waste storage site in the United States and the one with the most cleanup problems (SN: 12/20&27/97, p. 410).

The recently demonstrated breakdown of organic compounds makes the waste less hazardous, but the gases generated create a serious problem for underground tanks. So far, scientists haven't found ways to prevent the gas from being produced.

Hydrogen gas builds up in the tanks at Hanford, says Camaioni, but vents allow it to escape, relieving the pressure and the danger of the gas igniting.

Kamat, Gray, and Zacheis conducted their study on a simple system including aluminum oxide, or alumina, a major component of tank wastes. They coated nanometer-size particles of the mineral with the organic pollutant hexachlorobenzene and exposed the powder to gamma rays. They monitored the decomposition of hexachlorobenzene with infrared and ultraviolet spectroscopy and extracted the breakdown products for analysis.

When an alumina particle absorbs high-energy radiation, "it starts a whole series of events," says Kamat. The gamma rays excite electrons in the particle, causing them to migrate. This movement separates positive and negative charges. The charged alumina surface strips chlorine atoms off the hexachlorobenzene.

Normally, organic contaminants in very low concentrations do not decompose by themselves, says Kamat. They need a catalyst like alumina to help them along. "This is the first study to look in a more mechanistic way at how alumina promotes degradation," he says.

Researchers have largely overlooked reactions taking place on particle surfaces, Camaioni notes. "It has only recently been appreciated that you can excite particles [with radiation] to do chemistry on absorbents."

Whether this particular process occurs in underground storage tanks remains unknown, but Kamat says that based on the composition of the waste, "my personal opinion is that some of this is occurring."

Camaioni says that Hanford scientists have not done studies that would indicate whether the new findings are relevant to the stored nuclear wastes. —*C. Wu*