Hormone Therapy: Issues of the Heart

At the close of a woman's childbearing years, her body undergoes hormonal changes that render her more vulnerable to a number of degenerative conditions, especially heart disease and osteoporosis. Drug therapy can slow or forestall that vulnerability.

However, the recipe of hormones most commonly prescribed in the United States may not fill the bill—at least in lowering heart risks, several new studies indicate. That's troubling, maintains veterinarian Kent Hermsmeyer, who coauthored two of the studies, because heart disease kills three out of every four postmenopausal women.

Hormone therapy delivers estrogen to make up the shortfall that occurs with menopause. To prevent the rise in breast cancer risk that typically develops when women receive estrogen alone, physicians often prescribe a combination that contains a second hormone—usually a synthetic form of progesterone.

The new studies suggest that this duo's heart benefits depend on the form of progesterone used.

Hermsmeyer's team at the Oregon Regional Primate Research Center in Beaverton gave estrogen daily to 18 rhesus monkeys whose ovaries had been removed to simulate menopause. Six also got natural progesterone, while another six monkeys received the synthetic medroxyprogesterone acetate (MPA), the most widely prescribed progesterone for postmenopausal U.S. women.

After 4 weeks, the researchers injected the animals with two chemicals released by blood platelets, simulating a heart attack. In monkeys receiving MPA and estrogen, this injection provoked an unrelenting constriction in the coronary artery, cutting off blood flow. Unless treated within minutes, the animals would have died, says Hermsmeyer. This chemical challenge produced the same result in animals that had received no hormone therapy.

Monkeys that had been treated with estrogen alone or together with natural progesterone quickly recovered normal blood flow without drug treatment. The researchers report their findings in the March NATURE MEDICINE and the March 1 JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY.

"The big surprise," Hermsmeyer says, is that "MPA poses such a huge risk. This is a really dangerous drug."

J. Koudy Williams of Wake Forest University's Bowman Gray School of Medicine in Winston-Salem, N.C., was less surprised by the findings. He says new data from his team's experiments on monkeys show that MPA can "obliterate the beneficial effect of estrogen [therapy] on the progression of coronary artery atherosclerosis."

Peter Collins of the National Heart and Lung Institute in London and his colleagues saw similar effects in 16 women with coronary artery disease. Participants in their study received two hormone replacement therapies, each for several weeks. The therapies contained estrogen plus natural progesterone or MPA.

The women exercised on a treadmill until tests showed they were experiencing reduced blood flow to the heart. They could exercise significantly longer when natural progesterone was part of the hormone therapy. "There appeared to be a negation of the beneficial effects of estrogen by MPA but not by natural progesterone," concludes Collins. He plans to present these data in a few weeks at the American College of Cardiology's annual meeting.

As far as MPA is concerned, "there's enough data accumulated to give us pause," Williams argues. In terms of heart disease protection, "it's worse than no treatment at all."

Endocrinologist JoAnn E. Manson of Harvard Medical School in Boston disagrees, arguing that the relevance of these "intriguing" studies remains uncertain. Yet they do "underscore a need for more research on different forms of progesterone," she adds.

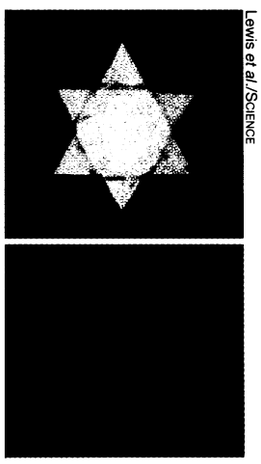
Indeed, Williams' newest data indicate that some synthetic progesterones—such as nomegestrol acetate, widely used in Europe—do not erase postmenopausal estrogen's benefits. —*J. Raloff*

Bacteria give new meaning to 'computer bug'

A team of researchers has devised a scheme to use a light-sensitive protein made by a saltwater bacterium as the basic component of an optical computer. In an optical computer, information zips around as photons of light rather than as electrons. The protein, called bacteriorhodopsin, converts light energy into electric energy quickly and efficiently.

Bacteriorhodopsin is an attractive material for optical computers because it exists in two stable forms, one purple and one yellow. Shining two lasers of different wavelengths alternately on the protein flips it back and forth between the two colors. Several groups have used bacteriorhodopsin as computer memory and as the light-sensitive element in artificial retinas.

Aaron Lewis and his colleagues at the Hebrew University of Jerusalem impregnated a plastic film with equal concentrations of the purple and yellow forms of bacteriorhodopsin. As they report in the March 7 SCIENCE, they then illuminated the film with two lasers, modifying the light using an array of lenses with focal properties that differ slightly for the two wavelengths. Along the edge of an object placed above the film, the two lasers produced shadows slightly displaced from one another, creating a narrow region where the relative intensity of the two wavelengths varied.



Lewis et al./SCIENCE

A paper cutout star casts a shadow on a plastic film infused with light-sensitive bacteriorhodopsin and illuminated by two lasers (top). The edge of the shadow leaves a faint, but distinct, image (bottom).

That varying intensity altered the relative concentrations of the purple and yellow forms of bacteriorhodopsin.

In the system devised by Lewis and his colleagues, high concentrations of yellow represent negative values, high concentrations of purple indicate positive, and an equal amount designates zero. Because the state of the film can be quickly switched by light, it could, in principle, form the working element of an optical computer that would have an immediate electronic output.

The device operates under a digital "trinary logic system," says Robert R. Birge, a chemist at Syracuse (N.Y.) University and director of the W.M. Keck Center for Molecular Electronics. In analog environments, the scheme also provides "the capability to both add and subtract."

One of the main disadvantages, Lewis and his colleagues say, is that the experimental setup is complex and expensive—a significant obstacle to making a practical device. Also, few commercially available lasers produce the wavelengths of light that most efficiently stimulate bacteriorhodopsin. —*C. Wu*