

Nobel prize in medicine for prostaglandin discoveries

A family of biologically active substances found throughout the body was the subject honored this year with the Nobel Prize in Medicine or Physiology. The first 1982 Nobel award to be announced went to Sune K. Bergström and Bengt I. Samuelsson of the Karolinska Institute in Sweden and John R. Vane of the British Wellcome Research Foundation Ltd. Their research on the hormone-like substances called prostaglandins has led to a variety of medical and veterinary treatments and is expected to have more and diverse applications in the future.

The Nobel committee cited Bergström for a "crucial breakthrough" in the 1960s when he purified and determined the chemical structure of several prostaglandins and showed that they are derived from such unsaturated fatty acids as arachidonic acid. Samuelsson, who had been a student of Bergström, was credited with a detailed description of arachidonic acid, clarifying the biological processes of prostaglandin formation and action and the discovery of various types of prostaglandin.

Vane was cited for discovering prostacyclin, a form of prostaglandin that affects blood platelets and may provide a means of preventing heart attacks. He also proved that the basis of aspirin's action in reducing fever, pain and inflammation is its inhibition of prostaglandin production.

Because prostaglandins are so widely distributed in the body and have so many different actions as local messenger chemicals, recent research has gone in many directions. More than 30 prostaglandins are now on the market or being tested clinically as drugs for human or animal use. The most promising applications are for fertility problems, gastric and cardiovascular therapy and bronchial asthma treatment.

Prostaglandins were discovered in the 1930s. The original observations were that a semen component thought to come from the prostate gland caused contraction of smooth muscles and affected blood pressure. Bergström started working on the purification of prostaglandin in 1945 and gradually discovered there were several types. In the 1960s methods of synthesizing prostaglandins speeded research progress by making increased amounts of prostaglandins available to researchers around the world (SN: 9/20/75, p. 188).

One of the first clinical applications was for inducing labor in pregnant women at term; a later application was for inducing abortion. Among the largest markets for prostaglandins is the livestock industry. In the breeding of horses, cows, sheep and hogs, the drugs are used to bring animals into heat synchronously. Another application of a prostaglandin is to delay the natural closure of a blood vessel in newborns requiring corrective surgery for a congeni-



Jerry Berndt/Harvard Medical School

Nobel prize winners Bengt I. Samuelsson, Sune K. Bergström and John R. Vane (left to right) got word of their award while in Boston for a scientific meeting celebrating the bicentennial of the founding of Harvard Medical School.

tal heart disease.

Drugs to counteract formation of prostaglandins are also in use. Such drugs can reduce menstrual pain (SN: 11/15/80, p. 312) or relieve pain caused by gallstones or kidney stones.

Encouraging clinical studies suggest prostaglandins will be useful for treating severe peripheral vascular disease by increasing blood flow. Some prostaglandins promote healing of gastric and duodenal ulcers and protect the stomach and small intestine from damage normally produced by such drugs as aspirin. Prostaglandins have also provided relief from asthmatic attacks (SN: 1/15/77, p. 40). But inhibitors of related substances, called leukotrienes

(SN: 6/16/79, p. 392), which in part generate the attacks, may eventually be the preferred treatment.

The prostaglandin called prostacyclin is being tested clinically to block platelet aggregation in surgery, such as heart bypass operations, where blood is circulated outside the body. It may eventually also be used to prevent obstruction of blood vessels, and thus prevent heart attacks (SN: 8/12/78, p. 104).

The full promise of prostaglandins with their array of biological effects has not yet been met. For the three Nobel prize winners, and the more than a thousand other scientists in the area, plenty of work remains. —J.A. Miller

Gossypol: All-purpose antimicrobial

Gossypol, a naturally occurring chemical constituent of cottonseed oil, has already received international attention as a potentially risk-free male contraceptive. Now, recent reports suggest that the compound has antimicrobial properties that may make it useful for combatting three of the world's major diseases: genital herpes, gonorrhea and Chagas' disease, a protozoal infection that is a leading cause of death in Central and South America.

Researchers at the University of Helsinki, Finland write in a recent issue of the *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY* (Vol. 142, No. 5) that gossypol can slow or even arrest the multiplication of herpes simplex virus type 2 (HSV-2) in laboratory cultures of human tissue cells. HSV-2 is the cause of genital herpes, for which there is no known cure. The researchers added doses of gossypol to cell cultures either before or after the cultures were inoculated with HSV-2. When added prior to inoculation, gossypol prevented viral infection. Added after inoculation, the substance slowed or halted the spread of viral infection and appeared to reduce virus-caused injury in cells already infected. In addition, the gossypol had no apparent side-effects on the tissue cells. Chinese scientists, investigating the compound's promise as a contraceptive, have also reported that gossypol has few, if any, ill effects on human subjects.

The Finnish workers also mention a second, yet-unpublished study in which they found that gossypol inhibits the growth of cultured gonococci, the bacteria that cause gonorrhea.

Elsewhere, a group of Argentinian researchers have investigated gossypol's effects on *Trypanosoma cruzi*, the protozoan parasite responsible for Chagas' disease. The researchers report in the Oct. 15 *SCIENCE* that gossypol retards the parasite's growth and motility, perhaps by interfering with the function of several metabolic enzymes. A similar mechanism has been proposed to explain gossypol's observed ability to inhibit metabolism and locomotion in human sperm, which make it a potent antifertility compound.

Chagas' disease strikes millions of Central and South Americans annually, and the drugs currently used to treat it are largely unsatisfactory, according to Thomas M. Trischmann of the School of Hygiene and Public Health at Johns Hopkins University. These drugs are ineffective against some strains of trypanosomal parasites and are sometimes toxic to patients.

Gossypol may prove the solution, but the evidence so far is slim, Trischmann points out. The Argentinians tested gossypol's effects on only one early stage of the parasite's life-cycle — not the later stage that infects human beings.

—R. Pollie