A scientist whose work with the blood coagulation system led to effective treatments for people with hemophilia is the recipient of the ninth annual Bristol-Myers Squibb Award for Distinguished Achievement in Cardiovascular/Metabolic Research. Earl W. Davie, PhD, professor of biochemistry at the University of Washington in Seattle, received the award May 12, 1999, at a dinner in New York, NY. The prize carries with it a $50,000 award and a silver medallion.

In research that spanned more than 4 decades, Dr Davie hypothesized, elucidated, and defined the blood clotting system. His work began as a graduate student, when he showed that the digestive pancreatic protein trypsinogen was converted into an active enzyme called trypsin when a single peptide bond was cleaved. This study served as a model for the coagulation process proposed by Davie and his collaborator, Dr Oscar Ratnoff. As a young researcher at Case Western University in Cleveland, Ohio, Dr Davie studied the blood of people with rare clotting disorders. He discovered that blood that would not clot on its own would clot when combined in a test tube with the plasma of a person with normal blood. From this, he predicted that blood that did not clot lacked certain factors that were the signals for coagulation.

In 1962 and 1964, Drs Davie and Ratnoff published their theory that coagulation was the result of a series of sequential actions in which proteins in blood plasma are activated from a dormant state. The final result is the production of a fibrin clot at the site of the injury.

During the second half of the 1960s and the 1970s, Dr Davie and another collaborator, Dr Kazuo Fujikawa, isolated and purified most of the plasma proteins involved in the sequential cascade of events that is the blood clotting system. They also identified the peptide bonds involved in the cleaving process that activates each factor. With the advent of recombinant DNA technology, Dr Davie collaborated with Dr Dominic Chung in cloning and sequencing the genes for each factor. During this process, they sequenced the full-length gene for hemophilia B. They demonstrated that the variation of even a single nucleotide could result in a severe clotting disorder.

When Drs Davie and Chung cloned and sequenced the genes for more than a dozen other clotting proteins, they paved the way for the mass-production of these proteins in mammalian cells. These proteins, used as clotting factors, treat both hemophilia A and B. These clotting factors made by recombinant technology are also safer than factors made from pooled blood products, which can be contaminated with viruses such as HIV and various forms of hepatitis.

In recent research, Dr Davie has focused on understanding the mechanisms that trigger, regulate, and unclot blood. In collaboration with postdoctoral fellow Dr Evan Sadler, Dr Davie purified, partially sequenced, and cloned another plasma protein, called the von Willebrand factor, which is involved in formation of the platelet plug that forms at the site of injury. With Dr Jose Lopez, he cloned specific receptors on the surfaces of platelets. These receptors bond to von Willebrand factor. This research enabled Dr Davie to determine how clotting occurs only at the site of a vascular injury. He showed that platelets normally flow freely in the blood system; however, they adhere to the site of any injury, where they are activated by thrombin. This activation signals that the platelet surface is available for blood coagulation. The platelets attract a host of clotting factors to the surface of the injury, which explains the phenomenon of site-specific clotting.

Dr Davie received his undergraduate chemistry degree in 1950 and his PhD in biochemistry in 1954, both from the University of Washington. He joined the faculty of Case Western University in 1956. In 1962, he became an associate professor biochemistry at the University of Washington, achieving his full professorship in 1966, and he was chairman of the biochemistry department from 1975 to 1984. Dr Davie is a member of the American Academy of Arts and Sciences and the National Academy of Sciences and a foreign member of the Royal Danish Academy of Sciences and Letters. He has received the International Prize of the French Association of Hemophiliacs, the Stratton Medal of the American Society of Hematology, the Distinguished Achievement Award of the American Heart Association, and an honorary medical degree from Lund University in Sweden. He has served on numerous editorial boards and national and international panels. Since 1980, he has been associate editor of the journal Biochemistry.

Winners of this award are selected by an independent, peer-review selection committee composed of administrators of current Bristol-Myers Squibb unrestricted cardiovascular research grants. The first winner of this prize, Robert F. Furchgott, PhD, won a Nobel Prize in Medicine and Physiology earlier this year.

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1999 Bristol-Myers Squibb Cardiovascular Metabolic Research Award: Earl Davie, PhD, Defined the System of Blood Coagulation
Ruth SoRelle

Circulation. 1999;100:332
doi: 10.1161/01.CIR.100.4.332

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/100/4/332

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