Dickerson builds cytochrome c model.

seven-step scheme of earliest evolution.

Though remote, this early evolutionary process was critical for the development of the rest of life, for it started with an atmosphere that contained little or no oxygen, 3.5 billion years ago, and ended with the development of multicelled organisms in an oxygen-rich atmosphere 1.2 billion years ago. Thus, the evolving bacteria and algae not only laid the genetic foundation for the higher forms of life to come, but were responsible for changing the atmosphere to make their development possible.

The research into such an early process is possible only because barely changed descendants of even the most primitive organisms still exist. The first bacteria, whose descendants are typified by the organism that causes gangrene, were able to obtain energy only through the inefficient method of fermentation. The first big improvement on this process occurred about 3.0 billion years ago with the evolution of "sulfur" bacteria, which contained the first cytochrome enzymes and could conduct photosynthesis using the hydrogen sulfide then present in the atmosphere. These were followed by bacteria that could utilize more energetic sulfate molecules. (Their descendants are found today in sewage.)

The next big step was development of the Krebs cycle, the respiration process that produces the universal "energy currency" of life—the ATP molecule. The beginning of green plants, as we know them, then came with the development of microorganisms with the ability to use water instead of a sulfur compound in photosynthesis. These were the ancestors of blue-green algae, and over the next hundreds of millions of years they slowly produced our present oxygen-laden atmosphere. Cytochrome c was fundamental to both the new respiration and photosynthesis processes.

But then comes a missing link. A unique class of bacteria is thought to have evolved that were capable of both nonsulfur photosynthesis and oxygen respiration based on the Krebs cycle. Such an organism would have evolved from bacteria that had to derive energy from the sun, through photosynthesis, and would have led to the final great stage of bacterial evolution—the organism that could rely solely on oxygen respiration. These oxygen respirers, which evolved some 1.8 to 1.4 billion years ago, were able to extract 19 times more energy from the same amount of food as the primitive fermenting bacteria.

The pace of evolution was by then able to speed up considerably, to produce nucleated cell organisms some 1.4 to 1.2 billion years ago and eventually multicelled organisms about 1.2 billion years ago. At this time, the plant and animal kingdoms began to diverge. Later stages of evolution have been well understood.

An important conclusion Dickerson derives from this scheme is that respiration evolved from photosynthesis, with the electron-transporting enzymes being the part common to both systems. Cytochrome c, for instance, occurs near the end of the transport chain, delivering an electron to an oxidase molecule in respiration, and to a chlorophyll molecule during photosynthesis.

Though Dickerson's research has involved analysis of samples taken from present living organisms, fossil and geological records corroborate his findings. Fossil spheres resembling blue-green algae have been found in South African rocks 3.1 billion years old. This means that a relatively short period of less than 1.5 billion years may have elapsed between the condensation of the earth and the emergence of life at the bacterial level, Dickerson concludes.

Several reports have been published of this decade-long project, and one of the most recent and comprehensive appears in the JOURNAL OF MOLECULAR BIOLOGY, (vol. 110, p. 473). □

Heart attacks and testosterone

Despite the well known fact that men are more susceptible to heart attacks than women are, at least before women go through the menopause, scientists haven't been able to produce any hard data explaining why. Now some tough evidence is finally being served up by researchers at Georgetown University Medical Center in Washington. The culprit? The male steroid hormone testosterone.

A thrombus is a blood clot that forms inside a blood vessel and obstructs it, often leading to a heart attack or a stroke. An ingenious method was developed in 1973 to produce in rats experimental arterial thrombi that are similar to those that occur naturally in humans. A long plastic loop is inserted into the abdominal aorta, a major artery. With the passage of time, platelets in the blood start to bind together to form a thrombus and obstruct the blood vessel—a natural response to this foreign object in the cardiovascular system. The Georgetown investigators used this technique to study the effects of testosterone on thrombosis and thrombosis-caused death.

They found that young male rats have twice the thrombus size and thrombosis death rate of young female rats. However, the size and death rate increase comparably in older male and female rats. These results dovetail with the clinical situation where young men are more susceptible to heart attacks than young women are, yet where thrombosis increases with age for both males and females.

Assured that the rats' susceptibility to thrombosis was comparable to the human situation, they next tested the effects of testosterone and a female estrogen on thrombosis and thrombosis deaths in rats. One group of male and female rats received injections of testosterone, then thrombi were induced in them. Another group of male and female rats received injections of an estrogen, then thrombi were produced in them. Still a third group of male and female rats served as controls (received no injections prior to thrombus induction). The testosterone markedly increased the rates of thrombus formation and increased the death rate from thrombosis more than fourfold in both male and female rats. This result strongly indicts testosterone as a causative or conspiratorial agent in thrombosis and thrombosis-caused deaths. In contrast, the estrogen treatment did not exacerbate thrombosis or thrombosis death rates in either male or female rats. In fact, it even decreased thrombus weights in the majority of male rats.

Finally, the researchers studied the effects of an antitestosterone agent in both male and female rats submitted to experimental thrombosis. This agent, Flutamide, significantly decreased thrombosis death rates in both male and female rats when they received it along with testosterone. Specifically, of the rats treated with testosterone alone, 62.5 percent of the males and 34.3 percent of the females died. When the antitestosterone agent was given with testosterone, 33.3 percent of the males and 16.7 percent of the females died.

"Our results provide for the first time significant experimental evidence for an association between sex and age and the development of arterial thrombosis," the Georgetown team explains in the June 24 NATURE. Very clearly, the male hormone testosterone is a high risk factor, they conclude.

They hope that their findings will give impetus to the search for antitestosterone agents that would not feminize men yet still offer them protection against heart disease. □