Infectious Diseases Linked to Heart Attacks?

Jay A. Glasel, Ph.D.
Managing Member
Global Scientific Consulting LLC

Over the past 50 years or more we have become used to thinking that the "conquering" of infectious disease is one of the triumphs of 20th century medicine. In the past few years clouds have appeared that darken this view. First, a worldwide resurgence of multiple drug-resistant tuberculosis was recognized. Then came the understanding that a remarkable bacterium, *Helicobacter pylori*, is the causative agent for most cases of chronic nonspecific gastritis and has a role in the pathogenesis of duodenal ulcer disease and most cases of gastric ulcer.

More recently, a number of epidemiological studies linking chronic bacterial infections (even with *H. pylori*!) to coronary heart disease (CHD) have been reported. As usual, such studies only indicate the possibilities of new risk factors for disease. It's up to basic research to link cause and effect.

Very recently, some progress has been made along these lines. Using a mouse animal model, reports linking infection with a genus of bacterial parasite, *Chalmydia*, to inflammatory heart disease have begun appearing (see references below). The way in which *Chalmydia* infections may be linked to CHD is fascinating and illustrates how knowledge from several scientific disciplines can contribute to understanding disease.

To set the stage: *Chalmydia* are intracellular parasites found in many vertebrates, including humans. They are 250 to 500 microns in diameter and contain DNA and RNA. Their infections can be treated with antibiotics. Infection with one species of *Chalmydia*, *C. trachomatis*, is responsible for a variety of sexually transmitted diseases while another, *C. pneumoniae*, causes various respiratory tract infections. Unfortunately, like *H. pylori*, *Chalmydia* infections are very common: most people can expect to experience at least one during their lifetime.

Now some immunology enters the story. It has been known for more than a decade that inflammatory heart diseases and dilated cardiomyopathy (DCM, a common cause of progressive heart disease, heart failure and death) can be reproduced in mice by immunizing them with myosin, a protein found in heart muscle. Such immunization produces an autoimmune myocarditis, an inflammatory condition that frequently precedes DCM in humans.

Myosin is a very large protein, made up of six peptide chains (two heavy chains, and two pairs of different light chains) but it was found that immunization with just a small peptide portion (13 amino acid residues long) of a heavy chain induces severe myocarditis in mice. From the knowledge of the identity of the sequence of amino acids in this peptide that is important in producing heart inflammation, it was a simple matter to find, via a computer database search, that a similar sequence exists in a small, myosin-unrelated,

protein present in *C. trachomatis*. The next step was to see if immunization with the *Chalmydia* protein induced heart inflammation. It did: the *Chalmydia* protein induces an autoimmune response similar to that of the myosin peptide. As antigens, the two unrelated proteins mimic each other.

Although this opens up a new avenue of research on heart disease, much more work needs to be done before the knowledge can be used clinically. For example, not everyone with present or past *Chalmydia* infections has or gets heart disease. Genetic, and perhaps environmental factors must come into play that make certain individuals susceptible to autoimmune responses leading to inflammatory disease.

Perhaps as the century closes out, our conquest of infectious diseases will appear more modest.

References:

Bachmaier K, et al, "Chalmydia Infections and Heart Disease Linked Through Antigenic Mimicry," Science 283 1335-1339(1999)

Bachmaier K, et al, "Generation of Humanized Mice Susceptible to Peptide-Induced Inflammatory Heart Disease," Circulation, 99 1885-1891(1999)

Quinn TC, et al, "Epidemiologic and Microbiologic Correlates of *Chalmydia trachomatis* Infection in Sexual Partnerships," Journal of the American Medical Association, 276 1737-1742(1996)

Libby P, et al, "Role of Infectious Agents in Atherosclerosis and Restenosis," Circulation, 96 4095-4103(1997)

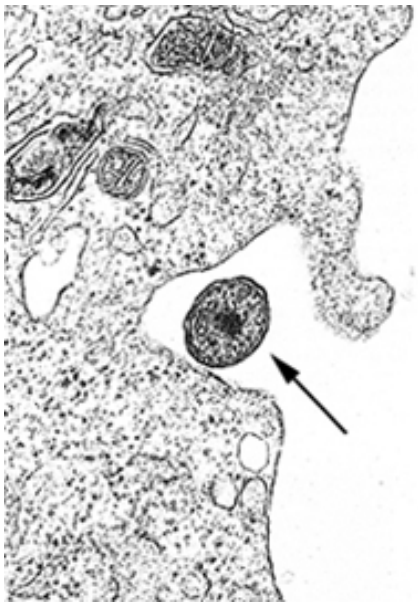

Figure 1. *Chalmydia* (arrow) infection of human tissue.