Reprinted from
Antimicrobial Therapy
THE ULTIMATE REFERENCE
antimicrobe.org

Development of the Complement–Fixation Test: Jules Bordet

By Janet Lee

Jules Bordet was born in 1870 and was raised in Brussels, Belgium as the second son of Charles Bordet, a primary school teacher. Bordet became interested in chemistry and eventually enrolled in the medical program at the Universite Libre de Bruxelles at the age of sixteen.

Six years later, Bordet graduated medical school, during which he performed research on adaptation of viruses to vaccinated organisms in the *Annales de l'Institute Pasteur*. For his work, Bordet received a grant from the Belgium government in 1894 to join the Pasteur Institute under the mentorship of Elie Metchnikoff, the Ukrainian zoologist who was a leading pioneer in cellular immunology.

Upon arriving in Paris, Bordet set to work on in vitro experiments to test a previous observation, or the "Pfeiffer phenomenon". This observation showed that bacteriolysis would result when serum taken from an immune animal was introduced into a non-immune animal. Bordet saw that Pfeiffer's phenomenon applied in vitro, when serum from an immunized animal was microbicidal against a cholera suspension. However, microbicidal activity was eliminated when the serum was heated to fifty-five degrees centrigrade, although agglutination remained unaffected. Furthermore, the heated serum regained its killing ability when fresh serum from non-immune animals was added. From these experiments, Bordet concluded that there were two factors responsible for the bacteria killing—a heat-stable sensitizing factor or antibody, and a heat-sensitive non-specific substance that acted only on a sensitized target. This non-specific substance was later named "complement" by German bacteriologist Paul Ehrlich. Bordet's experiments set the basis for humoral immunity: a highly ironic outcome viewed from the perspective as Metchnikoff's protégé.

Bordet astutely recognized a parallel between his experiments involving bacteriolysis and previous hemolysin experiments involving the agglutination of erythrocytes. In 1898, Bordet demonstrated the universality of Pfieiffer's phenomenon by discovering that red blood cells added to blood serum resulted in hemolysis of the red blood cells if complement was present in the serum. However, if the red blood cells were added after bacteriolysis, hemolysis did not occur since the free complement was already bound to antigen-antibody complexes.

Bordet developed complement fixation tests as a serodiagnostic tool for detection of antibodies to determine if a person was exposed to a particular agent. This became valuable for pathogens which not easily culture from clinical specimens. August von Wassermann adopted the complement-fixation test for the diagnosis of syphilis (the Wasserman test). Additional complement-fixation tests were developed for typhoid fever and fungal infections.