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# George Fernand Widal (1862–1929): Serologist and clinician-scientist

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Translational medicine targets the application of laboratory science to the practice of clinical medicine. A popular buzzword in today's medical lexicon, its origin can be traced to late 19th century clinician-scientists such as George Widal. Trained in the tradition of bedside medicine in Paris during a time of landmark discoveries by the likes of Pasteur, Widal's emphasis on relating laboratory observations to patient care made a lasting impact on the trajectory of medical progress.

**A PROMISING BEGINNING** George Fernand Isidore Widal was born in 1862 into a Jewish family in Dellys, Algeria. The son of a distinguished doctor who served as the medical inspector of the army, Widal followed in his father's footsteps and began his studies at the University of Paris. He was a star undergraduate who placed first when competing for a coveted position of *Interne des Hôpitaux*, or assistant physician. Beginning at the age of 22, he lived the life of an intern, with morning rounds on an astounding 80 patients, a 75-minute quick luncheon, long afternoons spent in the laboratory and evening hours consumed with seeing patients and writing up his research. The hard work paid off; he obtained his doctorate four years later, publishing a thesis on *Streptococcus* as an aetiologic agent in puerperal fever, endocarditis and erysipelas. By supplementing clinical observation with revelations from microscopic pathology and bacteriology, he emerged as one of a small group of scientists with the novel idea that many different diseases could be caused by a single organism.


**THE NAME THAT STUCK** Widal is best known for the diagnostic test that bears his name – the Widal agglutination test for typhoid fever. Eberth was the first to describe a bacillus implicated in typhoid fever in 1880, and Widal found that by adding Eberth's bacillus to the serum of a patient, agglutination would occur if the diagnosis proved to be typhoid. He presented these findings to the Medical Society of the Hospitals of Paris on 26 June, 1896 and published a description of the test a few months later in the 14 November issue of *The Lancet*. His conclusions: *"Here is a simple and rapid process which can be employed by everyone, necessitating no lab material. All that is necessary is to have at one's disposal pure cultures of Eberth's bacillus, a microscope, and a few drops of serum or even only one drop of the blood of the patient."*

Widal was not the first to describe the phenomenon of agglutination, which had been previously demonstrated by Charrin and Roger. In fact, animal studies by Gruber had suggested its utility in testing for typhoid, and to this day, controversy surrounds who should receive credit for the test, sometimes referred to as the 'Gruber-Widal reaction', or simply, 'the agglutination reaction'. It found worldwide acceptance, as it differentiated typhoid from mimicking conditions like tuberculosis, typhus or pneumonia. Additionally, it was used to screen populations and identify carriers during epidemics. Extension of his research allowed Widal to be instrumental in the immunisation of the French army against typhoid fever during World War I.

**PATHOPHYSIOLOGY** Widal understood the importance of the pathophysiologic basis of disease, and was a true clinician-scientist possessed of keen observation and laboratory skills. For example, in order to define the phenomenon of shock, known at the time as 'Widal's haemoclastic crisis', he meticulously described changes in the blood, noting decreased numbers of white blood cells and aberrations in coagulation. He later observed similar haematologic changes in a sheep trader who developed severe asthma attacks whenever he was exposed to the animals, and this allowed him to link allergy and asthma to the development of anaphylactic shock. He postulated that the underlying pathophysiology involved an influx of biological particles into the bloodstream, as the same phenomenon could be reproduced with extrinsic proteins or in haemolytic anaemia caused by pathological products released into the circulation. This led to the clinical application of desensitisation as treatment, and his work in serology earned him eponyms such as the Hayem-Widal type of idiopathic acquired haemolytic anaemia and the Widal-Abrami test for paroxysmal haemoglobinuria.

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Widal also investigated pathophysiologic changes in kidney disease, emphasising the importance of functional changes over anatomical classification. By studying a patient who maintained a constant blood urea level for several weeks and then had alterations in urea levels with dietary modification, he was able to conclude that blood urea levels were linked to diet. He established the prognostic significance of this biomarker, equating the prognosis of a patient with a level above 200 with that of cancer. He also found that salt deprivation reduced oedema, while reversion to a normal diet caused it to reappear, a finding independently arrived at and corroborated by German physician Hermann Strauss. Widal applied this to patient care by recommending salt restriction as treatment for nephritis-related oedema. However, his varied research work was not universally admired, one critic actually lamenting that *"…his laboratory work in the later phases of his career was of a desultory [disconnected] character; he showed extreme keenness in many directions, but can hardly be credited with any ordered researches"*.

**ACADEMIC HONOURS** Widal was well-loved by his students, patients and friends, treating them *"with bluff cordiality and laughing bonhomie which was his manner"*. He was equally effective as a clinician and lecturer as he was a researcher. He rose rapidly through the academic ranks, being named *Professeur Agrégé* at the age of 32 (the title given to a member of the group of doctors from whom professors were chosen), Professor of Internal Pathology at 48 and Chair of Clinical Medicine at 56. At the Hôpital Cochin, his meticulously planned lectures were immensely popular. One of his students wrote that he was a complete master of his material and that he lectured without notes. His astonishingly penetrating eyes would allow him to understand almost infallibly which part of his exposition needed to be repeated in order to leave a firm impression on his students. In 1917, Widal was awarded the 'Grand Cross of the Legion of Honour', France's highest civilian honour, and in 1919, he won membership in the prestigious *Académie des sciences*.

**LASTING IMPACT** Not much is recorded about the personal life of the man described as stout, handsome and rather large-headed. It is known that he was married, but details about his wife are scant. They did not have any children. His colleague Weissenbach noted that Widal had a broad general culture and was interested in all the manifestations of the human spirit. He was fascinated with history, especially the life of Napoleon, which is in line with Widal's reputation as a proud French patriot.

Following Widal's death from a cerebral haemorrhage in 1929, his colleagues erected a statue at the Hôpital Cochin in memory of this great serologist whose agglutination test stands as a lasting testament to one of medicine's original prophets of translational research.

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