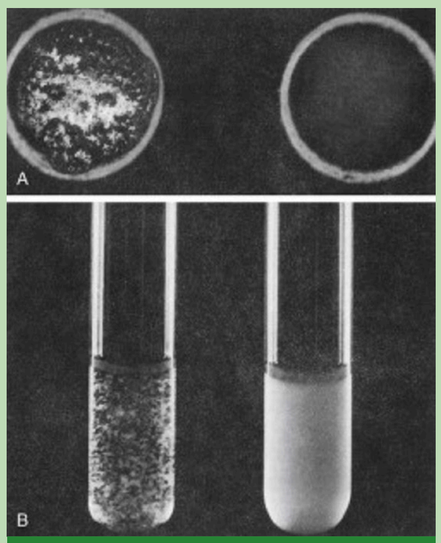
Blood and its various historical uses as a reagent

As microbiology and immunology developed, in the late 19th and early 20th centuries, blood and its components were found to be valuable tools for the isolation and identification of microorganisms and in the determination of the immune status of individuals.



Tube agglutination to detect *Salmonella*

Culture

Whole blood

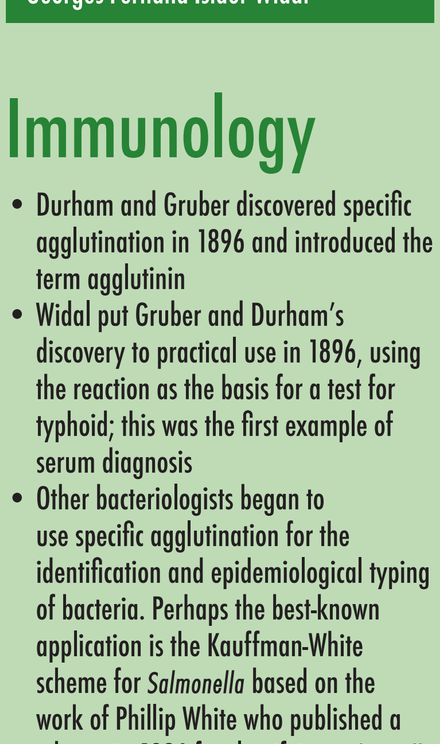
- Smeared blood agar was described by Pfeiffer in 1892 for the isolation of *Haemophilus influenzae* (aka Pfeiffer's bacillus).
- The haemolytic activity of streptococci was first noted in 1895 by Marmorek but it was Schöttmuller who introduced blood agar plates in 1903, that suggested the ability to haemolyse blood *in vitro* should be used in classification of streptococci
- Brown published a monograph in 1919 describing the haemolysis as Alpha, Alpha prime, Beta or Gamma.

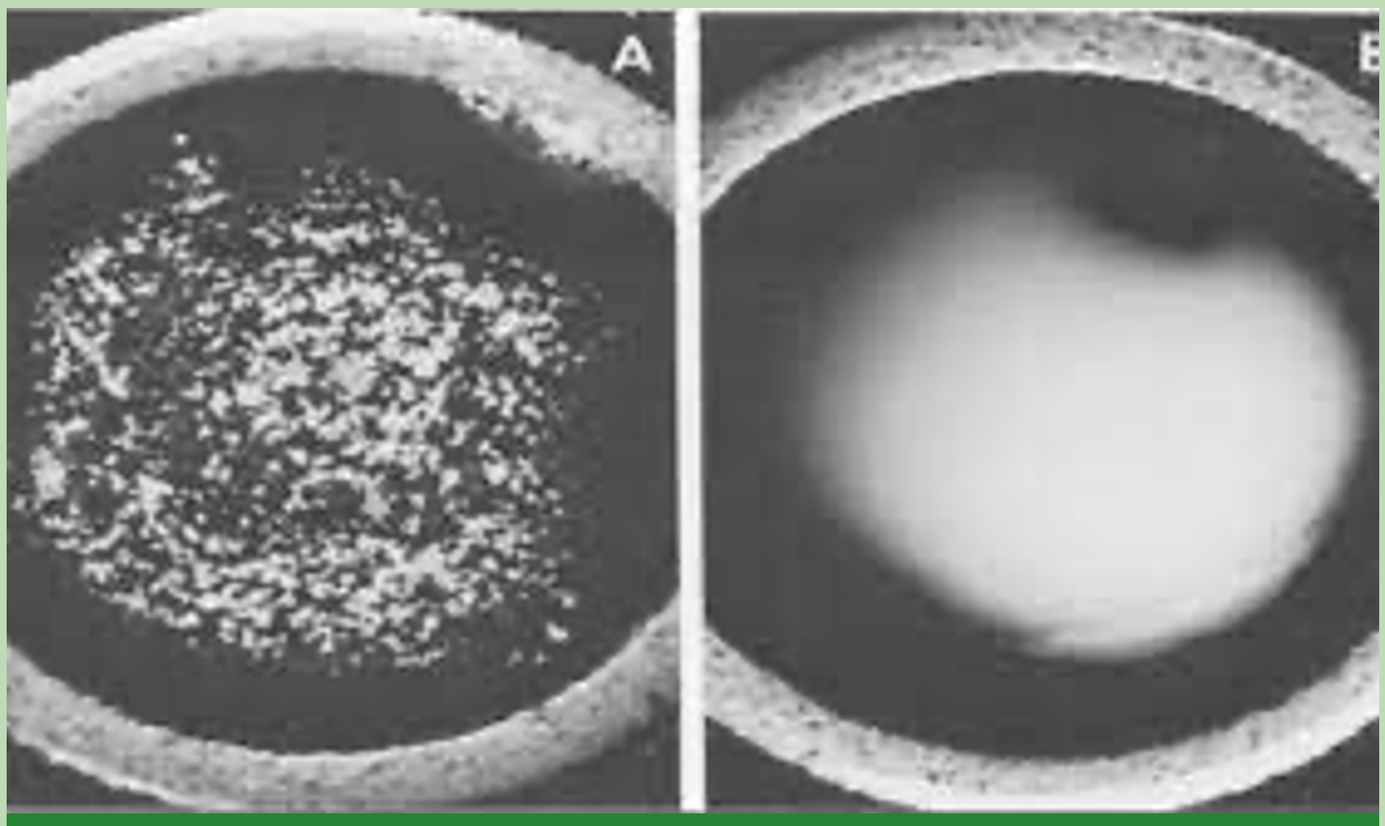
Serum

- Serum was also added to agar to enhance the growth of bacteria, but in the early 1920s Hiss found adding it to peptone water sugars made them more reliable for the identification of diphtheria bacilli.

Plasma

- Initially staphylococci were differentiated by the colour of their colonies: golden – *Staphylococcus aureus*, and white – *S. albus*. Although the ability of certain staphylococci to coagulate plasma was first described by Loeb in 1903, it wasn't until the early 1940s that a method for the detection of coagulase was given in laboratory handbooks.

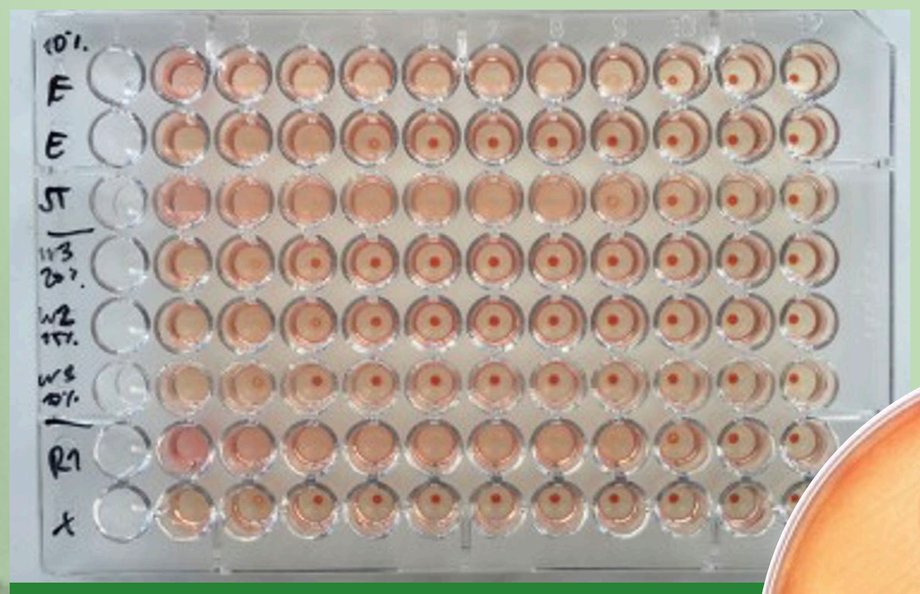

French physician
Georges-Fernand-Isidor Widal



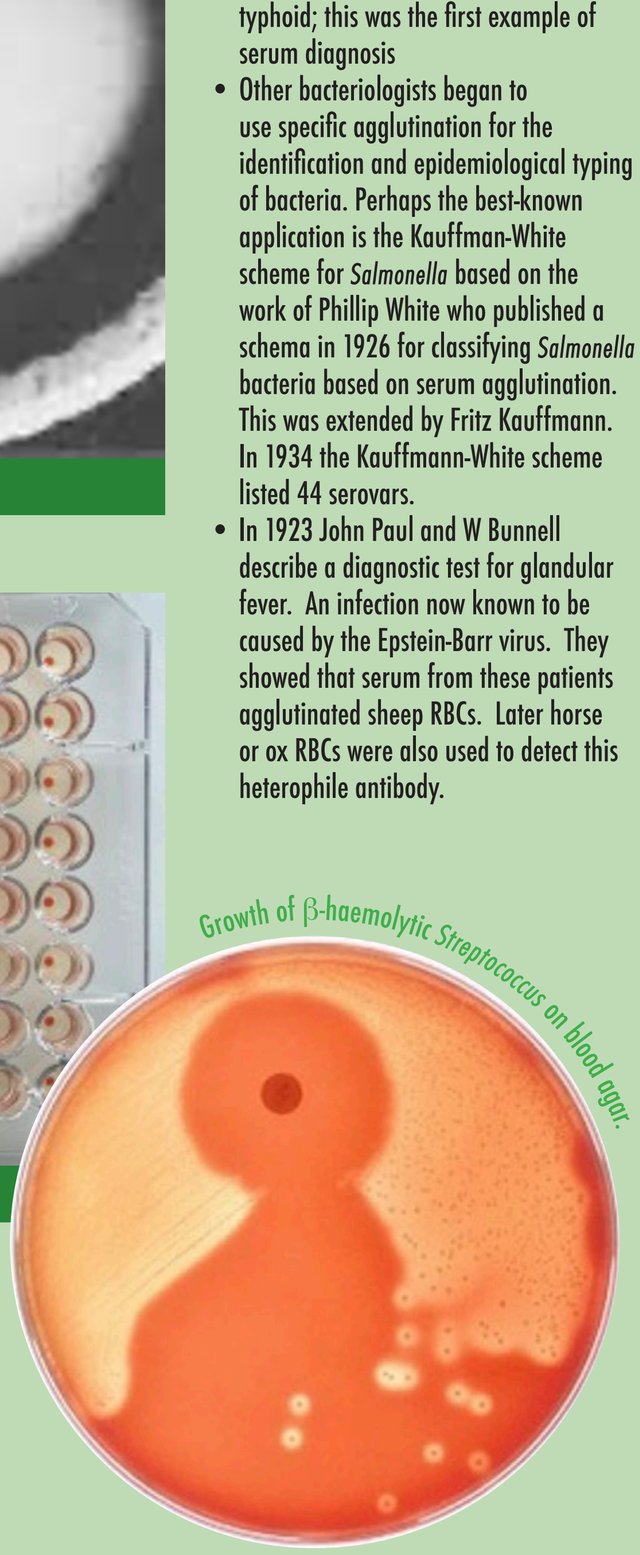
Slide agglutination to detect *Salmonella*

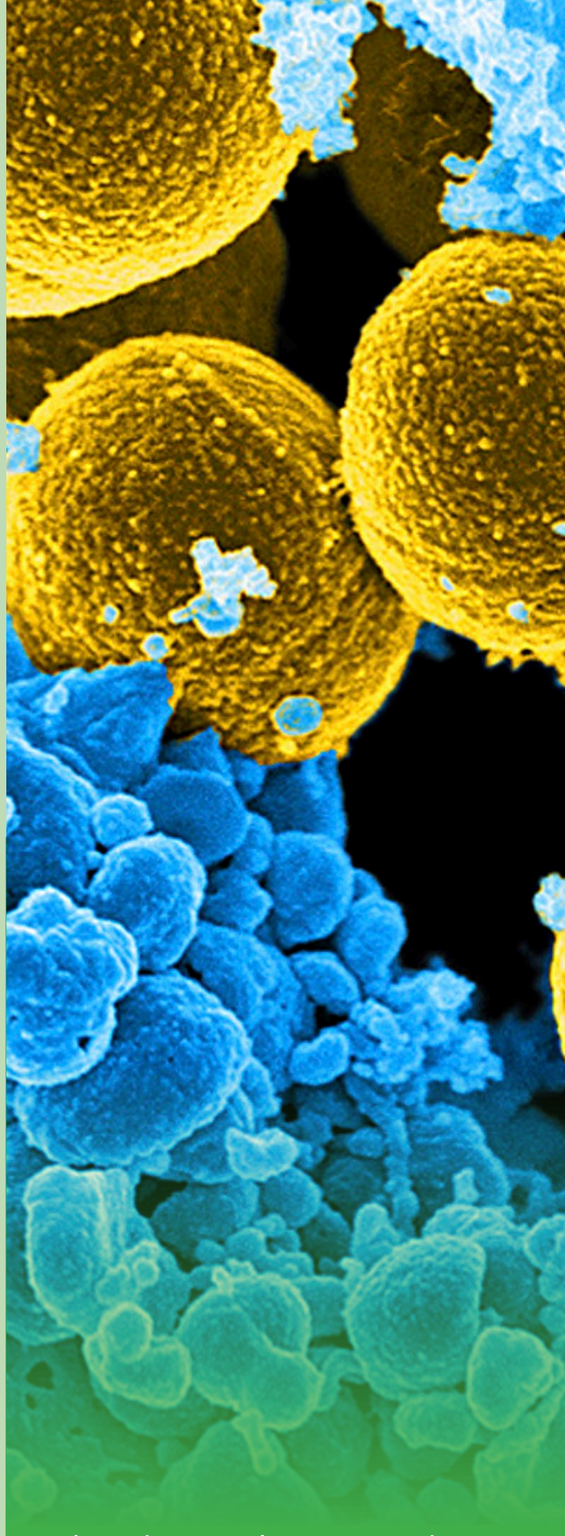
Immunology

- Durham and Gruber discovered specific agglutination in 1896 and introduced the term agglutinin
- Widal put Gruber and Durham's discovery to practical use in 1896, using the reaction as the basis for a test for typhoid; this was the first example of serum diagnosis
- Other bacteriologists began to use specific agglutination for the identification and epidemiological typing of bacteria. Perhaps the best-known application is the Kauffman-White scheme for *Salmonella* based on the work of Phillip White who published a schema in 1926 for classifying *Salmonella* bacteria based on serum agglutination. This was extended by Fritz Kauffmann. In 1934 the Kauffmann-White scheme listed 44 serovars.
- In 1923 John Paul and W Bunnell describe a diagnostic test for glandular fever. An infection now known to be caused by the Epstein-Barr virus. They showed that serum from these patients agglutinated sheep RBCs. Later horse or ox RBCs were also used to detect this heterophile antibody.


Haemagglutination assay plate


German bacteriologist
August von Wassermann


Growth of β-haemolytic Streptococcus on blood agar.


Colourised scanning electron micrograph of *Staphylococcus aureus* (yellow).

Since the beginning of the 20th century, lysis or agglutination of red blood cells has been used as indicators in diagnostic investigations:

- In1906, using the complement fixation test of Bordet and Gengou, the German bacteriologist August von Wassermann and others developed the first serological test for the diagnosis of syphilis. The lysis of red cells indicating the absence of treponemal antibodies
- Todd in 1932 demonstrated that titres of anti-streptolysin O (ASO) were raised in Rheumatic Fever. In the ASO test lysis of sheep RBCs indicated the absence of antibodies
- The haemagglutination and the haemagglutination inhibition assays were developed in 1941–42 by American virologist George Hirst for quantifying the concentration of viruses or antibodies
- In 1967 Stewart and colleagues described a haemagglutination inhibition assay for the detection of rubella antibodies
- The single radial haemolysis assay, in which sheep RBCs are labelled with a virus and complement and added to agarose and serum added to wells cut into the agarose, was initially described for influenza antibodies, and was adapted in 1975 for measuring IgG antibodies to rubella

Blood Lines:
A Resource Not To Be Taken In Vein
Produced by the IBMS History Committee for Congress 2023