SEROLOGICAL DIAGNOSIS OF TYPHOID FEVER: A review of the limitations of the Widal test

Michael A. Borg

Typhoid fever remains an infectious disease of major importance worldwide. Even in developed countries, sporadic outbreaks continue to occur, often localised around a single origin - an asymptomatic carrier or an infected foodsource particularly shellfish. The ever increasing ease of international travel has resulted in more imported typhoid cases. The severity of presentation, potential life-threatening complications as well as the serious side-effects of the antibiotics used in its treatment necessitate prompt and accurate diagnosis.

The only definite diagnostic investigation remains the isolation of Salmonella typhi from samples of blood, bone marrow, faeces, bile and urine. Nevertheless serological tests are still commonly requested in the form of the Widal reaction. Very often the request is for a combination of this investigation together with the Weil-Felix test for typhus and the Brucella agglutination test as the febrile agglutinin titration (sometimes incorrectly referred to as the B.S.R.).

The Widal test measures the specific antibody titre of the patient's serum to typhoid antigens by haemagglutination (1). Recently enzyme immunoassay (EIA) (2) and latex agglutination (3) systems have become available as alternative methods. The antigens tested against are the O (somatic) antigens resident within the cell wall structure; the H (flagellar) antigens prepared from the bacterial flagellae and the Vi (virulence) antigens originating from the capsule surrounding the cell wall.

Somatic (O) agglutinins are IgM in nature and appear early in the disease; diagnostic levels are usually reached by the beginning of the second week. Occasionally, however, they are undetectable till a number of weeks into the course of the illness. IgG antibodies to flagellar (H) antigens reach maximum levels by the third week and may persist for months if not years.

The O and H antigens form the basis upon which the Salmonella genus is divided into species level. Salmonella typhi having O; 9, 12 and H: d antigens forms part of Group O: 9 (D1) in the Kaufmann-White classification scheme. This group has O antigens 9 or 12 common to at least 89 serotypes amongst which is the S. berta subgroup (4). This subgroup, which includes S. enteritidis, is much more commonly isolated than typhi particularly from cases of salmonella food poisoning. Although serum titres to O antigens from non-typhoidal salmonellae occur only at a low level, the possibility of cross-reactivity to these far commoner species should always be borne in mind when interpreting a positive Widal result (5). Cases have also been described where cross seroreactivity has occurred with salmonellae belonging to serogroups other than 0:9 (6).

Documented false positive reactions have alternatively been the result of anamnestic reactions in non-typhoidal fever states as well as due to immunological disorders particularly active chronic hepatitis (7), rheumatoid arthritis (8) and ulcerative colitis (8). Finally a past history of typhoid vaccination would render inconclusive any positive result especially the H titre.

The Widal test is also prone to false negative values. A defect in antibody production, infection of a site such as the synovial cavity which is apart from the reticuloendothelial system or early treatment with ampicillinor chloramphenicol (9) can all have a profound inhibitory effect on agglutinin production.

The Vi test has been used in the past to detect asymptomatic typhoid carriers. However the difficulty in preparing

M.A. BORG
M.D., M.Sc.(Med) (Lond)
Dept. of Microbiology
St. Luke's Hospital

bacterial suspensions of uniform agglutinability together with the presence of this antibody in sera from healthy individuals (10) has led to a decline in its popularity.

A four fold rise in titre between the first and second week is generally considered to be highly suggestive of typhoid. However there is practically no consensus in the interpretation of a single Widal test taken within the first few weeks of illness. Knowledge of the prevalent titres in the healthy population of the area is helpful in determining significance or otherwise. Schroeder (5) suggests an O antigen titre of 1:100 as the lower limit of relevance. Hoffman et all (11) claim sensitivity levels of 96% using as low a titre as 1:20 as their diagnostic criterion. However, the general opinion seems to be that in a previously unvaccinated individual, O antigen titres must be at least 1:320 to be regarded as significant. (12,13).

The importance of an elevated H titre is normally accepted to be much less. These agglutinins are often extremely variable and can rise as a nonspecific response to other infections. Therefore they have only a minor role in the serological confirmation of typhoid fever. This view however has been disputed by Brodie (14) who suggests, from his investigation of the 1964 Aberdeen outbreak, that H antibodies can sometimes be more useful in diagnosing typhoid than the O.

In conclusion, the Widal test is non-specific, difficult to standardise and problematic to interpret. A negative result does not in any way exclude typhoid fever (15). The titre of the agglutinins to the O antigen has the only meaningful value and even this can be present in significant levels in the absence of S. typhi infection. The test should not be used as an easy way out instead of a thorough clinical examination and appropriate bacteriological cultures which remain the mainstay of diagnosis. It must never be the sole basis upon which a notification of typhoid fever is issued nor does it have any value in the diagnosis of non-typhoidal salmonella gastroenteritis and food poisoning.

Faced with these deficits and the major improvements in cultural techniques, a number of diagnostic laboratories have ceased to perform the Widal test as a standard investigation, relying solely on the isolation of S. typhi from the appropriate clinical samples. Where it continues to be available, its limitations and deficits should be clear to all and sundry if a load of incorrect diagnoses is to be avoided.

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