THE SIGNIFICANCE OF SMALL-FLAKING AGGLUTININS IN THE DIAGNOSIS OF ENTERIC FEVER.

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The original method of diagnosing enteric fever by the estimation of the agglutinins contained in the serum was concerned only with the agglutination of bacilli into large snow-like flakes.

This served its purpose exceedingly well until the advent of anti-typhoid inoculation on a large scale, when it became necessary to await the results of at least three agglutination tests before a definite diagnosis could be made with regard to any case of suspected enteric fever.

Certain workers have now questioned the soundness of this method of diagnosis in the case of an inoculated person, but whether they prove their point or not, it must be admitted that the present method is a tedious affair and a speedier one would be to the advantage of all concerned.

A considerable amount of work has been done on the use of small-flaking agglutination as a means of diagnosing an enteric infection in an inoculated person.

Until recently this small-flaking agglutination method, or to give it its right name, "the qualitative receptor analysis," could only be used by the experimentalist who had ample time and facilities for employing a somewhat elaborate technique which involved the use of a living emulsion of a particular strain of Bacillus typhosus. Now, however, Gardner has
published some work which suggests that good results can be obtained with a formalized emulsion of B. typhosus made up according to definite instructions. This special emulsion could be made, standardized and issued from the Royal Army Medical College, and the idea of this article is to summarize the salient features of the subject for the benefit of those officers who might like to increase the volume of evidence for or against this method of diagnosis, and who have not themselves the opportunity of referring to the periodicals in which the work has been published.

Weill and Felix described two forms of B. proteus which, from the character of their colonies, they described as "H" (hauch = hazy) and "O" (ohne hauch = clear) forms.

The "H" form was visualized as possessing two antigens or "receptors," one of which was heat-labile and the other heat-stable, whilst the "O" form had only one "receptor," and that a heat-stable one. Diagrammatically the forms might be represented thus:

![Diagram](http://example.com/diagram.png)

Further investigations satisfied these workers that similar forms and receptors occurred in other bacilli, including the typhoid group of organisms.

Incidentally the usual form, which one meets with in everyday life, and which one uses in making up the ordinary agglutinating emulsions, is the "H" form.

Now these receptors each produced in rabbits corresponding agglutinins which could be distinguished from one another by the fact that they agglutinated each in its own fashion, that is to say, the agglutinins corresponding to the heat-labile receptors agglutinated in large flakes, and the agglutinins corresponding to the heat-stable receptors in small granular flakes. These agglutinins have been designated in consequence the "large-flaking" and the "small-flaking" agglutinins.

The significance of this experimental and somewhat theoretical work is that Felix asserts that the serum from an enteric fever case develops both large-flaking and small-flaking agglutinins, whilst the serum from an inoculated person develops only the large-flaking agglutinins.

Here then is a means of distinguishing between the serum of an infected man, whether inoculated or not, and a normal inoculated man; the serum of the infected man will contain small flaking granular agglutinins, the other will not.
The demonstration of the small-flaking agglutination is made by means of the Widal test, in which Gardner's special typhoid emulsion replaces the ordinary agglutinating emulsion in common use. The tubes must be left in the water-bath for twenty to twenty-four hours and the final reading is made with the aid of a watchmaker's glass.

The large-flaking agglutination is demonstrated by the ordinary Widal test, which requires no explanation.

When using this small-flaking agglutination method, it is important to remember that one can only diagnose a case as "enteric fever," and this term must include a Gaertner infection as well as the typhoid and paratyphoid fevers. The reason for this is because the enteric group of organisms have a common heat-stable receptor, though their heat-labile receptors are specific, consequently the sera of enteric patients will have a small-flake agglutinin common to the group, and a specific large-flake agglutinin. Now Gardner's special typhoid emulsion will only react with the small-flake agglutinins, consequently agglutination of Gardner's emulsion by a suspected serum can only indicate that the patient is infected by one of the enteric group of organisms.

Though somewhat incomplete this diagnosis of enteric fever is of considerable value to the military hygienist, especially if it can be made without delay.

One more point: there is a great temptation to those who like to get their scientific ideas neatly arranged and docketed to try to connect up Felix's "H" and "O" forms and his large-flaking and small-flaking agglutinins with Arkwright's well-known "rough" and "smooth" colonies, and his floccular and granular agglutinins.

A study of the literature on the subject leads one to the conclusion that there are few points of contact in the work of these investigators, although superficially they appear to have much in common.

While Felix's statement that inoculated persons never develop the small-flaking agglutinins is open to doubt and requires further proof, it seems probable that the amount of these agglutinins the inoculated man could produce would be so much less than the amount produced by an enteric case that no real difficulty should be encountered in this respect.

One more word about Gardner's emulsion—it is a specially prepared typhoid emulsion, but theoretically it could be made just as well with a para B or a Gaertner bacillus, since the essential part is the non-specific heat-stable receptor which is common to all three organisms.

REFERENCES.

FELIX, A. (1924). Journ. of Immunology, ix, No. 3.