vitamin B complex deficiency unfortunately died a fortnight after the local condition had healed; the other patient recovered.

The impression has been gained that penicillin treatment gives the initial impetus to healing of phagædenic ulcers of several months duration; once healing has started, the subsequent course of events is controlled by the nutrition of the patient. It is to be noted that all our cases were ambulatory and all were under-nourished.

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Bacteriostatic Action of Sulphonamide Derivatives

WE have confirmed and extended the observations of L. K. Wolff and H. W. Julius (1939) that sulphanilamide acts on bacteria only when they are multiplying, that is, in the logarithmic phase of their growth. Taking into consideration the physico-chemical changes which are apparent in the environment of bacteria rapidly subdividing, more especially the rapid fall in potential which accompanies multiplication, we have looked for a reducing agent and have found that about the time when the sulphonamides begin to act *in vitro* a substance is produced which gives the *o*-dinitrobenzene test applied by Fearon and Kawerau (1943) to the recognition of dienol compounds. This substance is of the nature of, and may be identical with, reductone.

Reductone readily condenses with *p*-aminobenzoic acid, sulphanilamide, sulphapyridine and sulphathiazole to form coloured compounds. We have isolated these compounds in crystalline form by adding the appropriate aminobenzene derivative to solutions of glucose which have been heated with alkali and then made acid according to the method used by H. von Euler and co-workers (1933) for the preparation of reductone. On account of its solubility, the sulphanilamide - reductone compound has not yet been obtained pure; but the other derivatives have been separated completely from the added aminobenzene compound.

From a study of the properties of these reductone derivatives, we have arrived at certain conclusions as to the role of *p*-aminobenzoic acid in bacterial metabolism and the way in which it is supplanted by the sulphonamides. The *p*-aminobenzoic acid - reductone compound goes into solution readily at a *p*H of 7·5–8·0, giving a yellow solution in which it undergoes rapid hydrolysis, even at room temperature, setting free *p*-aminobenzoic acid and reductone. When completely hydrolysed the solution is colourless. The sulphapyridine and sulphathiazole compounds are much less soluble than the *p*-aminobenzoic acid compound, and hydrolyse slowly and incompletely. From these and other observations it is concluded that the function of *p*-aminobenzoic acid in bacterial metabolism is to condense with, stabilize and temporarily immobilize prior to utilization, reductone or compounds of the reductone type which play an essential part in the chain of metabolic reactions and which, without such stabilization, would, by reason of their reactivity, be either lost to the bacterial cell or toxic to it. If compounds of the sulphonamide type be presented to the cell, they compete with *p*-aminobenzoic acid for the reductone produced during metabolism, and form with it compounds which are not available for use by the micro-organism.

In support of this view the following are some of the experimental results which we have obtained:

(1) Growth of streptococci has been observed on supplying the *p*-aminobenzoic acid - reductone compound to a medium, deficient in energy sources, which otherwise failed to give growth.

(2) No growth has been observed when the sulphapyridine - and sulphathiazole - reductone compounds have been substituted in the above experiment.

(3) Bacteria can be shown to assimilate added *p*-aminobenzoic acid from their environment, especially during the most active phase of growth. At a later stage of growth they return it once more to the surrounding medium.

(4) Bacteria also assimilate and later liberate added sulphanilamide, sulphapyridine and sulphathiazole, but not so rapidly.

Full details of this work will be published elsewhere later.

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Mode of Action of Benzylamine Sulphonamide ('Marfanil')

THE antibacterial agent benzylamine-4-sulphonamide (I), which under the name of 'Marfanil' was supplied in quantity to Rommel's forces in North Africa, has given interesting results in Allied hands (cf. Mitchell, Rees and Robinson[1]). Organisms made resistant to sulphanilamide by growing them in contact with the drug were resistant to all other sulphonamides except 'Marfanil'[2]. Schreuss found that the antibacterial action of 'Marfanil' was not antagonized by *p*-aminobenzoic acid[3]. A possible reason for these differences from the sulphanilamide-like drugs is revealed by the determination of the basic strength.

Benzylamine sulphonamide, having the amino-group insulated from the benzene nucleus by a methylene group, should be a much stronger base than sulphanilamide and *p*-aminobenzoic acid, which were found to be very weak bases[4]. Following the procedure outlined in the previous communication[4], the negative log of the acidity constant (pKa) expressing the position of the equilibrium of the reaction

$$BH \rightleftharpoons B + H^+$$

(where B represents the base) was determined by potentiometric titration with the glass electrode in water at 20° C. (see table). Benzylamine-4-carboxylic acid (II), which stands in the same structural relationship to benzylamine sulphonamide as *p*-aminobenzoic acid does to sulphanilamide, was investigated also.