

NOTES

PARA-AMINOSALICYLIC ACID IN THE METABOLISM OF BACTERIA

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Received for publication February 18, 1949

Several reports have demonstrated that *p*-aminosalicylic acid, "PAS" (4-amino-2-hydroxybenzoic acid), strongly inhibits the growth of *Mycobacterium tuberculosis* (human and bovine strains) *in vitro* and, in animal experiments, *in vivo*. High dilutions of PAS (about 0.25 mg per 100 ml) inhibit the *in vitro* growth of tubercle bacilli. All other bacteria so far tested (including other species of mycobacteria) are inhibited only by much higher concentrations, such as 100 mg per 100 ml or more. This extreme specificity of PAS for tubercle bacilli is still unexplained.

When it was reported that the *in vitro* action of PAS against tubercle bacilli was antagonized by *p*-aminobenzoic acid (PABA), experiments were run to determine what role PAS might play in the metabolism of other bacteria. The work was not completed, but preliminary results of considerable interest were obtained.

With the synthetic media and the methods of Roepke *et al.* (*J. Bact.*, **48**, 401, 1944), it was found that in the case of two mutant strains of *Escherichia coli*, nos. 273-384 and 1861-460, which ordinarily require added PABA to support growth in a synthetic medium, PAS could be substituted for PABA. The amounts required to obtain the same amount of growth varied from approximately 6 to 25 times as much, depending upon the time at which the growth was determined, the pH and constituents of the medium, and other conditions. Samples of PAS recrystallized to eliminate possible traces of the more soluble PABA gave the same results as the original material. Therefore it is very probable that the lack of action of small amounts of PAS against most bacteria is due to the fact that PAS can be utilized in a manner similar to that in which PABA is utilized.

These results do not explain the fact that low concentrations of PAS inhibit the growth of tubercle bacilli or that this inhibitory action is antagonized by PABA. At present it is only possible to say that tubercle bacilli apparently utilize PABA in such a fashion that the insertion of a hydroxyl group in the molecule adjacent to the carboxylic group produces a strongly inhibitory action on growth. The same substitution has little or no effect on other bacteria. Much more work must be done to provide a fuller explanation of the antitubercular action of PAS.

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