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Effect of Purines on Sensitivity of *Acetobacter suboxydans* Assay for p-Aminobenzoic Acid.

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It has been demonstrated that *Acetobacter suboxydans* requires p-aminobenzoic acid as a growth essential.¹ The p-aminobenzoic acid requirement of this organism forms the basis of a microbiological method for its determination.²

We have observed that when the casein hydrolysate employed in the basal medium for the above assay method is treated with Darco G-60 charcoal (10% of weight of casein) at pH 2.5 for one half hour, growth response to lower concentrations of p-aminobenzoic acid is variable and generally subnormal. Of a variety of compounds examined for ability to increase growth at lower concentrations of p-aminobenzoic acid the purine bases* adenine, guanine, and xanthine were found to be effective. Not only was the quantity of growth increased, but the sensitivity of the *Acetobacter* response to p-aminobenzoic acid was increased considerably. While in the absence of purines the test organism responds to 0.01 μ g of p-aminobenzoic acid, the presence of purines brings about readily measurable growth with 0.001 μ g per culture. The purines are without effect in the absence of p-aminobenzoic acid or when p-aminobenzoic acid is supplied in amounts above 0.03 μ g per culture, indicating that they are not essential for growth but act instead as growth accessories.[†]

¹ Lampen, J. O., Underkofler, L. A., and Peterson, W. H., *J. Biol. Chem.*, 1942, **146**, 277.

² Landy, M., and Dicken, D. M., *J. Biol. Chem.*, 1942, **146**, 109.

* Eastman Kodak chemicals were used.

[†] Purine bases have been found to exhibit growth factor activity for *Lactobacilli* and under certain conditions are interchangeable with p-aminobenzoic acid in promoting growth of *Lactobacillus arabinosus* and *Lactobacillus pentosus*.³ While no such interchangeability can be demonstrated in the case of *A. suboxydans*, our data definitely indicate a relationship between purines and p-aminobenzoic

The results of a typical experiment are given in Table I.

Adenine possesses the greatest activity and 150 μ g per culture can generally replace the combination of the 3 purines. Results with the 3 bases have, however, been more uniform

TABLE I.
Effect of Purines on Growth Response of *Acetobacter suboxydans* to p-Aminobenzoic Acid.

μ g p-aminobenzoic acid per 10 cc culture	Without added purines	Adenine, guanine, xanthine, 50 μ g of each per 10 cc culture
—	97	94
.0005	97	91
.001	97	89
.003	97	82
.005	97	75
.007	96	69
.010	95	61
.012	93	59
.014	92	53
.016	87	50
.018	83	49
.020	73	47
.025	52	43
.030	45	42
.035	40	39
.040	38	36
.045	33	32
.050	31	30
.100	23	23

Basal medium and test conditions were as reported by Landy and Dicken,² with casein hydrolysate treated as described in text. Growth was measured in the Evelyn Photometer at 660 m μ .

and in the absence of detailed information on the purine requirements of this organism it seems desirable to employ all 3 purines. Hypoxanthine was not available for test. The pyrimidine base uracil exerted no effect on

acid both for growth and for reversal of sulfonamide bacteriostasis.⁴

³ Snell, E. E., and Mitchell, H. K., *Arch. Biochem.*, 1942, **1**, 93.

⁴ Landy, M., Larkum, N. W., and Oswald, E. J., in press.

growth under these test conditions.

Parallel assays on bacterial extracts with and without purines in the basal medium yielded values in agreement within $\pm 15\%$. The possibility exists, however, that unless purines are present in the basal medium, un-

knowns rich in purines and containing p-aminobenzoic acid will give high assay values. It is therefore recommended that adenine, guanine, and xanthine be incorporated in the basal medium used for p-aminobenzoic acid assay.

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The Bone Marrow in the Five-Day Treatment of Syphilis.

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A study* of the 5-day treatment of syphilis¹ made by the Department of Medicine of the Albany Medical College made it possible, at the suggestion of Dr. L. W. Gorham, to investigate the effect of intensive arsenical therapy on the bone marrow. The patients, who had primary or early secondary syphilis, were given 0.24 g of Mapharsen in 2000 cc of 5% glucose in 12 hours by the intravenous drip method daily for 5 days. Every patient was studied exhaustively before and after treatment, and watched during treatment for signs of individual idiosyncrasy to the drug. As is well known, the administration of arsenicals to patients who have idiosyncrasies to such drugs may result in dermatitis (sometimes exfoliative), toxic hepatitis, leukopenia, secondary thrombocytopenia, aplastic anemia or hemorrhagic encephalitis. No such reactions occurred.

In addition to other laboratory tests made by the Department of Medicine, a sternal marrow puncture was performed before and after the treatment. Reticulocyte counts and 500 cell differential counts were made on the marrow samples. The reticulocyte count in the marrow of 14 cases showed no significant change after treatment. Differential counts on the 14 patients showed that in 6 patients the number of segmented neutrophils in the

marrow was slightly lower after treatment, in 6 cases it was slightly higher after treatment, and in 2 cases there was no change. Moreover, there was no significant change in the number or type of nucleated red cells present in these marrows, nor was there any significant change in the cellularity of the 2 marrow samples from each patient. In short, after the 5-day treatment of syphilis, in patients having no individual idiosyncrasies to arsenical drugs, there was no demonstrable change in the bone marrow. These results are reported because of the present great interest in intensive arsenical therapy.

Three of the 14 patients had a left shift in the Schilling index of the peripheral blood, although the total leucocyte count was within normal limits. These patients had a corresponding increase in neutrophilic band forms and metamyelocytes in the bone marrow. The other 11 had normal peripheral blood pictures and the differential counts of their marrows were within the range of "normal" marrow found by other investigators.²

Summary. The intensive arsenical therapy used in the 5-day treatment of syphilis produces no demonstrable effect on the bone marrow of patients who have no individual idiosyncrasy to arsenical drugs. Cases of primary and secondary syphilis in which there is no change in the peripheral blood picture have a distribution of cell types in the bone marrow which is within the normal limits of variation.

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¹ Hyman, H. T., Chargin, L., Rice, J. L., and Leifer, W., *J. A. M. A.*, 1939, **113**, 1208.

² See table in Scott, R. B., *Quart. J. Med.*, 1939, **8**, 127.