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Influence of Sodium Benzoate by Ingestion upon Urinary Excretion of Streptomycin.

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Bronfenbrenner and Favour[1] have reported that the oral administration of benzoic acid, which is converted by the liver into hippuric acid, reduces the degree and prolongs the duration of the urinary excretion of penicillin, administered by intermittent intramuscular injection, with the result that the serum levels of the compound are increased and longer sustained. Bohls, Cook and Potter[2] have also reported that intramuscular injections of alum-precipitated penicillin along with the oral administration of sodium benzoate resulted in high and prolonged serum levels due in part to the fact that the penicillin was more slowly excreted. Spaulding, Bondi and Early[3] have likewise observed that after the oral administration of single doses of 100,000 units of alum-precipitated penicillin along with 1.2 g of sodium benzoate, the serum levels were slightly higher and longer sustained than after the administration of penicillin alone; similar and somewhat better results were observed following the oral administration of single doses of 100,000 units of aluminum penicillin (not alum-precipitated penicillin) along with 2.4 g of sodium benzoate. These results have been ascribed to the effects of hippuric acid, resulting from the conjugation of sodium benzoate, in the selective excretion of penicillin by the tubules of the kidneys.

As in the case of penicillin, it is highly probable that the excretion of streptomycin by the kidneys is not only by filtration through the glomeruli but also by way of the renal tubules. In this connection, however, it does not appear that streptomycin is excreted by the kidneys in as high a degree as penicillin, with the suggestion that the compound is longer retained or undergoes more inactivation in the body following parenteral administration. Be that as it may, the effects of sodium benzoate upon the urinary excretion of streptomycin have not been previously reported upon and the results of experiments herein described indicate that the oral administration of sodium benzoate does not appear to reduce the urinary excretion of streptomycin with higher and longer sustained serum levels of the compound, as has been observed with penicillin.

In these experiments, single doses of streptomycin* dissolved in 2 cc of sterile saline solution were administered by intramuscular injection to adults of approximately the same body weight. At intervals of 1, 2, 3, 4, 6 and 24 hours thereafter blood and urine were collected for assay purposes, each specimen of urine being measured and the total excretion of streptomycin calculated on the basis of units per cc. Some individuals were given streptomycin alone, as controls, while others were given streptomycin along with sodium benzoate in tablets by ingestion. The first dose of the latter was administered 4 hours before the intramuscular injection of streptomycin, followed by 5 additional doses at intervals of 4 hours. All assays were conducted according to the method of Stebbins and Robinson[4] employing *Staphylococcus aureus* (S M strain).

The serum levels in 3 adult subjects (No. 1, 2 and 3) receiving single intramuscular injections of streptomycin alone in dose of 0.25 g (250,000 units) were 1.5, 3.0 and 2.5 units per cc, respectively, at the end of 6

[1] Bronfenbrenner, J., and Favour, C. B., *Science*, 1945, **101**, 673.

[2] Bohls, S. W., Cook, E. B. M., and Potter, R. T., *J. Ven. Dis. Inform.*, 1946, **27**, 69.

[3] Spaulding, E. H., Bondi, A., Jr., and Early, E., unpublished, personal communication.

* Streptomycin sulfate kindly supplied by the Abbott Laboratories, North Chicago, Ill.

[4] Stebbins, R. B., and Robinson, H. J., PROC. SOC. EXP. BIOL. AND MED., 1945, **59**, 255.

hours while the total urinary excretion of the compound over a period of 24 hours following its administration varied from 22 to 48% of the amount administered.

The serum levels in 3 additional adult subjects (No. 4, 5 and 6) following single intramuscular injections of 0.25 g (250,000 units) of streptomycin along with the oral administration of sodium benzoate in dose of 10 grains (0.65 g) for 6 doses totalling 60 grains (3.9 g) in subject No. 4 and 20 grains (1.3 g) for 6 doses totalling 120 grains (7.8 g) in subjects No. 5 and 6 were practically the same at the end of 6 hours, being 1.0, 2.5 and 2.5 units per cc, respectively. Furthermore, the total urinary excretion of streptomycin in these subjects was actually higher than observed in the 3 given streptomycin alone, having varied from 36 to as much as 75% of the dose of streptomycin administered.

In an additional experiment, 0.5 g (500,000 units) of streptomycin were given to each of 2 adult subjects (No. 7 and 8) by intramuscular injection. One of these (No. 7) served as a control while the second (No. 8) was given 20 grains (1.3 g) of sodium benzoate every 4 hours totalling 120 grains (7.8 g) in the period of 24 hours. The results were similar in that the serum level at the end of 6 hours (2 units per cc) in subject No. 8 receiving sodium benzoate was practically the same (2.5 units per cc) as observed in the control. In this experiment, however, while the control (No. 7) showed a total urinary excretion of 44% of the dose of streptomycin administered, subject No. 8 receiving sodium benzoate showed a total urinary excretion of only 30% of the dose of streptomycin injected, while the serum levels at the end of 2, 3 and 4 hours after injection were slightly higher than were observed in the control.

Summary. The results indicate, therefore, that the oral administration of sodium benzoate in tablets in dose of 10 to 20 grains (0.65 to 1.3 g) every 4 hours for 6 doses totalling 60 to 120 grains (3.9 to 7.8 g) along with single intramuscular injections of 0.25 and 0.5 g (250,000 and 500,000 units) of streptomycin does not appear to reduce materially the urinary excretion of streptomycin, and does not enhance or prolong the maintenance of the serum levels of the compound. It is to be emphasized, however, that these preliminary results are inconclusive and, in view of the clinical importance of the subject in relation to the administration of streptomycin, additional investigations are being conducted.

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Cultivation of African Sleeping Sickness Trypanosomes on Improved, Simple, Cell-Free Medium.*

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Progress in the investigation of many important aspects of African trypanosomiasis should be appreciably facilitated, it would seem, were it possible to grow the causative organism readily and in large quantities *in vitro*. Following the cultivation of the closely related *Trypanosoma brucei* by Novy and McNeal,[1] which acted as a notable stimulus, possible cultural methods for the human trypanosomes were investigated by Behrens,[2] Ponselle,[3] von Razgha,[4] Reichenow[5] and oth-

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[1] Novy, F. G., and McNeal, W. J., *J. Inf. Dis.*, 1904, **4**, 1.

[2] Behrens, C. A., *J. Inf. Dis.*, 1914, **15**, 24.

[3] Ponselle, A., *C. R. Acad. Sci.*, 1924, **178**, 1219.

[4] von Razgha, A., *Z. f. Parasitenkunde*, 1929, **2**, 55.

[5] Reichenow, E., *Z. f. Parasitenkunde*, 1932, **4**, 784.