staphylococci, but in no instance were inhibiting substances demonstrated.

Randall, Price, and Welch (*2*) have suggested the use of *Bacillus subtilis* as a test organism in assaying penicillin in various body fluids by a modification of the dilution method of Rammelkamp (*1*). This organism was proposed because of the ease with which it may be cultivated, the sharp reproducible end-points said to be obtained, and because its use obviates the employment of washed erythrocytes as required in the Rammelkamp technic. These investigators did not state, however, whether or not serum obtained from patients before the administration of penicillin inhibited their test organism.

The data presented in this paper would indicate that the results of any assay of serum for an antibiotic, using *Bacillus subtilis* as the test organism, are open to question, unless, prior to the administration of the antibiotic, the serum has been tested for the presence of natural inhibiting antibodies.

Summary: Sera from 35 normal persons who had received no previous medication were tested for inhibiting substances against *Bacillus subtilis* and *Staphylococcus aureus*. Thirty of the sera (85 per cent) inhibited *Bacillus subtilis* in dilutions varying up to 1:32, but in no instance was *Staphylococcus aureus* inhibited. The data presented would indicate that *Bacillus subtilis* is not a suitable organism for use in the assay of antibiotics in the presence of serum.

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Preliminary Studies on the Absorption and Excretion of Streptomycin in Dogs

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Pharmacologic studies on three lots of streptomycin, ranging in potency from 105 to 500 units/mg., were done on 14 male and female dogs. The animals were starved or fed a liquid diet for 24 to 48 hours prior to administration of streptomycin. They were divided into four groups. Only the dogs in Group 1 were anesthetized, and these experiments were acute. Intravenous (saphenous vein) administration was employed in Groups 1 and 2. The intramuscular (gluteal) route was used in Group 3 and oral administration (stomach tube) in Group 4. Urine samples were collected by catheterization from all dogs of Group 1, from one dog of Group 3, and from two dogs of Group 4. All other urines were collected via the metabolism cage.

Plasma volumes and streptomycin levels were calculated from haematocrit determinations. By our method of assay (*3*), using a paper disc-agar plate, neither plasma nor urine in a twofold dilution with a 0.2-M phosphate buffer exerts an inhibitory effect on the test organism (*Bacillus subtilis*).

Results

In general, the rates of disappearance of streptomycin from the blood of anesthetized and unanesthetized dogs (Groups 1 and 2) following intravenous injections of 100,000 to 210,000 units were comparable. Only 18 to 29 per cent could be accounted for in the plasma during the period of 3 to 18 minutes postinjection. After 4 to 5 hours about 3 per cent could be detected in the plasma. The low total recovery of streptomycin (16 to 20 per cent of the amount injected) from the urines of the dogs in Group 1 may be due to the short experiment, or to anesthesia, since 45 to 65 per cent was recovered from the urines of Group 2. Approximately 35 to 55 per cent of the streptomycin injected was probably destroyed or inactivated. These results are in agreement with those found in humans (*1, 2, 4*). The purity of the three lots of streptomycin used apparently did not alter the results.

In Group 3, the highest plasma levels were 7.2 and 2.7 per cent of the injected amounts (100,000 units). These were reached after 1 and 1½ hours, respectively. After 5½ hours only a trace to 0.8 of one per cent could be detected. Therefore, the maintenance of plasma levels was no better with intramuscular than with intravenous injection. Only about 20 to 40 per cent of the stretopmycin administered could be recovered in the urines of this group.

In Group 4, streptomycin in doses from 210,000 to 420,000 units per dog could not be detected in the blood during the 24 hours following oral administration. The recovery in the urine of one dog of this group of 3.9 per cent of the drug administered, and lesser amounts in the others, indicates that streptomycin was absorbed to a small extent. The small percentage recovered in the urine is in agreement with the observations made on humans (*1, 2, 4*).

Summary

Streptomycin varying in potency from 100 to 500 units/mg. has been administered to 14 dogs intravenously, intramuscularly, and orally in amounts of 100,000 to 420,000 units.

High blood levels of streptomycin were observed after parenteral administration and 23 to 65 per cent was excreted in the urine of normal dogs. After 4 or 5 hours only small amounts were detected in the blood.

The maintenance of blood levels was no better with intramuscular than with intravenous administration.

Following the oral administration of as much as 420,000 units of streptomycin, it could not be detected in the plasma, but up to 3.9 per cent was recovered from the urine.

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The Activity of Streptomycin in Experimental Syphilis

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The striking therapeutic response following the treatment of syphilis with penicillin prompted the investigation of the action of streptomycin in experimental syphilis.[1]

Herrell and Nichols (*1*) have recently reported the results of the treatment of four cases of syphilis with streptomycin. Improvement was noted, but relapses occurred even after the administration of 10,000,000 units over a period of 10 days.

The technique employed in the present study will be described subsequently in full (*2*). A brief summary follows. Suspensions of rabbit testes infected with the Nichols strain of *T. pallidum* were employed to infect rabbits by intracutaneous injections in the clipped skin of the back. Commencing within three days, intramuscular injections of streptomycin or crystalline penicillin G[2] were made every four hours for four days. When lesions developed at the site of inoculation, their syphilitic nature was confirmed by dark-field examination for spirochetes. All other rabbits were kept for four months, at which time a suspension of the popliteal lymph nodes of each rabbit was injected intratesticularly in two rabbits. If the testes of these rabbits remained normal, the donor rabbit was judged to have been cured. The streptomycin preparations employed had potencies of 158 units/mg. to 229 units/mg.

A total of 79,000 units of streptomycin per kilogram of body weight protected one out of three rabbits. The three rabbits that received 650,000 units/kg. were also proved to have been cured. In another experiment, the lymph node transfers have not yet been made from the rabbits that have remained free of local lesions, but in the case of other rabbits that have been infected by the technique described above, lymph node transfers have not changed significantly the results obtained by reading the dermal lesions. In this experiment, none of the four rabbits in each of the groups that received 748,000 units/kg. and 374,000 units/kg. developed lesions. Of the four rabbits that received a total of 187,000 units/kg., three failed to develop chancres. A total of 93,500 units/kg. did not protect any of the four rabbits in this group. All control rabbits in each experiment developed typical lesions.

The smallest amounts of streptomycin that cured any of the rabbits when administered in divided doses during four days was 79,000 units/kg. (375 mg./kg.) in one experiment and 187,000 units/kg. (817 mg./kg.) in another. A similar effect was obtained with 147 units/kg. (0.088 mg./kg.) of crystalline penicillin G. It may be concluded, therefore, that the preparations of streptomycin employed have antisyphilitic action but that penicillin G is more than 3,000 times as effective.

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[2] Obtained through the courtesy of Dr. O. P. Wintersteiner and Dr. Max Adler, Division of Organic Chemistry, The Squibb Institute for Medical Research.

Scanning Science—

National University

The bill establishing a National University of the United States has been reported favorably by the Senate committee. It grants a charter to the University, provides for its government, grants it the ground in the city of Washington designated by President Washington as a site for a national university, and appropriates $15,000 for the fiscal year ending on June 30, 1897, and $25,000 for the year following.

Princeton University

At the recent meeting of the Board of Trustees of the College of New Jersey at Princeton it was voted to change the charter name of the institution to Princeton University. The fund which is being raised in commemoration of the Sesquicentennial next October is already over $900,000, a large proportion of which, it is said, will be devoted to the development of the graduate department.

—20 March 1896