The Effect of Terramycin and Aureomycin on Blood Coagulation[1]

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Within recent years, with the rapid development of new antibiotics and the widespread practice of their almost routine administration, there has been an increased interest in their effect upon the coagulability of blood and thromboembolic phenomena (*1*). Published data, experimental and clinical, both support (*2–4*) and deny (*5–7*) the role of antibiotics as a causative agent in increasing the coagulability of the blood in patients receiving these drugs.

Large doses of the streptomyces-derived antibiotics (aureomycin used) could also affect the normal heparin content of the blood (*8*). This would have an effect that would not always be in the anticipated direction of increased coagulability, for heparin may normally function to regulate the elaboration of plasma thromboplastin, and, in the absence of the latter, decreased coagulability might ensue (*9*).

Macht and Farkas (*4*), working with rabbits and observing them over a 3-hr period, reported that aureomycin caused an increase in the coagulability of the blood. Shapse and Wright (*7*) in this clinic noted no alterations of clinical importance in the blood coagulation time of 30 patients after the administration of aureomycin.

The question of embolism is of such great surgical importance that we checked the experimental work of Macht and Farkas on the effect of aureomycin on the blood coagulation time in rabbits, and in the same study we included the effect of terramycin on the blood coagulation time in rabbits and on the bleeding, clotting, and prothrombin times in patients.

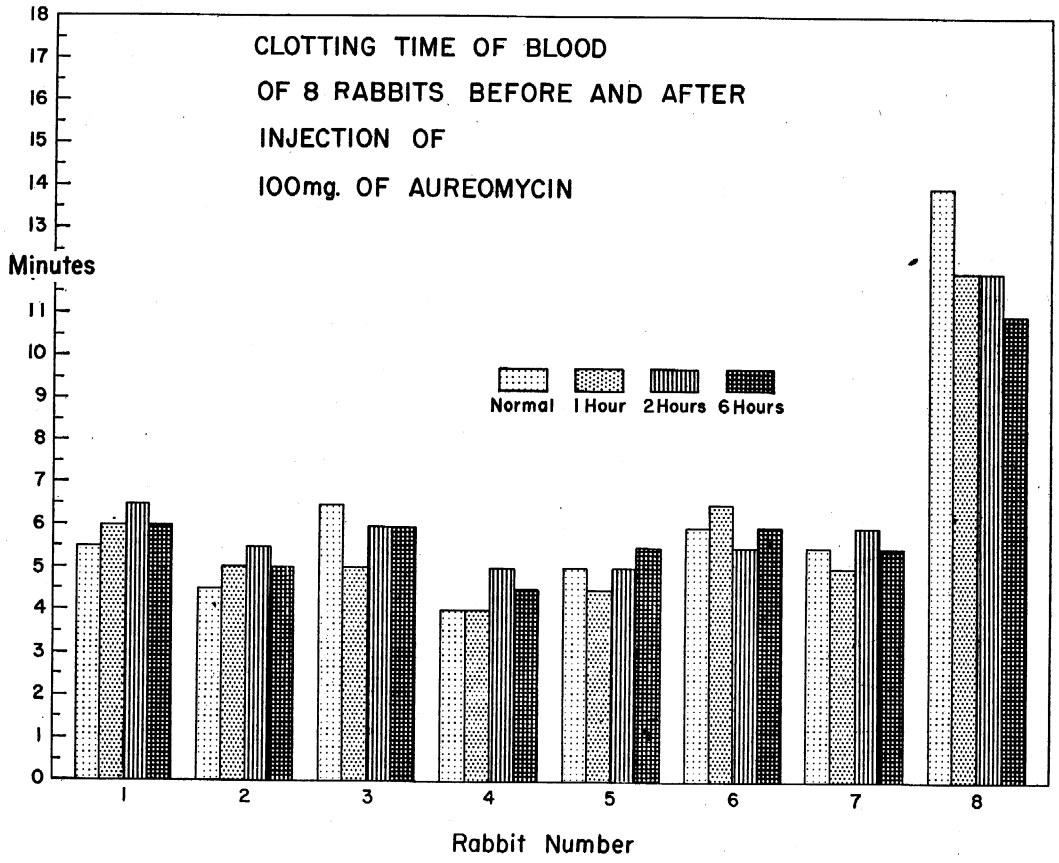

FIG. 1.

Experiments were conducted on 16 rabbits in which 8 were given 100 mg aureomycin glycinate intravenously, and 8 were given 100 mg terramycin glycinate intravenously. The drugs were dissolved in 2 ml distilled water and injected into the marginal veins. Blood specimens were obtained by both marginal vein and intracardiac punctures in various animals. Clotting times were done before the first injection and again at 1-, 2-, and 6-hr intervals after administration of the antibiotics. The clotting times were done by the

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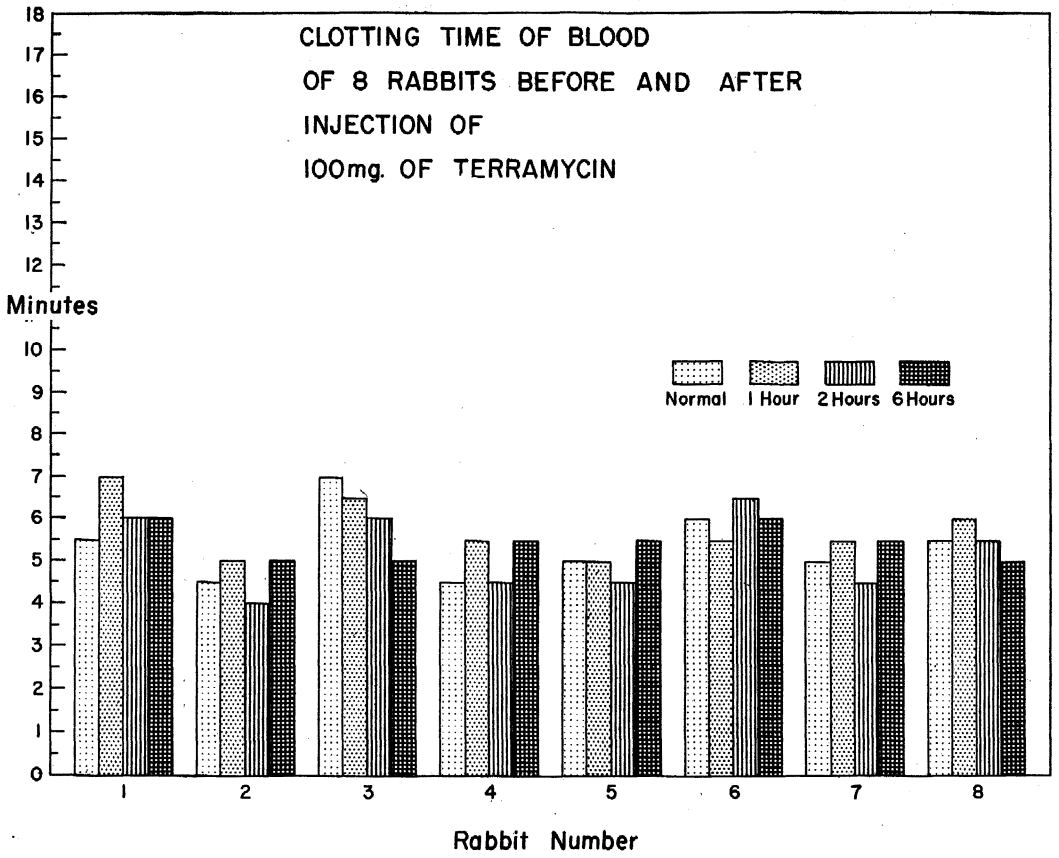

FIG. 2.

method of Lee and White. One ml of blood was placed in each of three tubes (10 mm in diam), which had been rinsed with normal saline. The tubes were inverted at 30-sec intervals until the clot could not be displaced.

The results in each rabbit are expressed graphically in Figs. 1 and 2. Fig. 3 presents the average alteration in clotting time according to the time interval after administration of each drug.

Bleeding and clotting times were done on 30 patients before and at 1-, 24-, and 48-hr intervals after the initiation of terramycin therapy. Eleven patients received 500 mg terramycin intravenously every 12 hr, and the remainder received 250 mg of terramycin orally every 6 hr. The bleeding times were determined by puncturing the ear lobes of the patients with a #20-gauge needle and blotting the area with filter paper every 30 sec until bleeding ceased. The clotting times were determined by the method of Lee and White. In 16 patients concurrent prothrombin times by the method of Quick were done before and at 24- and 48-hr intervals after institution of terramycin therapy.

The cases used were all adults and consisted of the following diagnoses: Cellulitis of extremities, 5; breast abscesses, 3; infected lacerations, 3; appendicitis, 3; human bites, 2; infected 2° and 3° burns, 2; ruptured peptic ulcers, 2; penetrating stab wounds of the abdomen, 2; and one each of the following: compound fracture of tibia, thrombophlebitis of leg, cervical cellulitis and adenitis, periurethral abscess with urinary extravasation, cystitis and pyelonephritis, ischiorectal abscess, incarcerated inguinal hernia, and acute orchitis. Table 1 shows the average bleeding, clotting, and prothrombin times and their variations at the indicated times.

TABLE 1

AVERAGE BLEEDING AND CLOTTING TIMES OF 30 PATIENTS AND AVERAGE PROTHROMBIN TIMES OF 16 PATIENTS ON TERRAMYCIN THERAPY

	Av bleeding time (min)	Av clotting time (min)	Av prothrombin time (sec)
Pretreatment	3.40	8.37	17.10
1 hr	3.63	8.63	
24 "	3.60	8.48	16.90
48 "	3.51	8.68	17.10

Although there were some individual variations in the clotting times in the rabbits, and in the bleeding, clotting, and prothrombin times in the patients, there were no significant changes in any of these tests. Re-

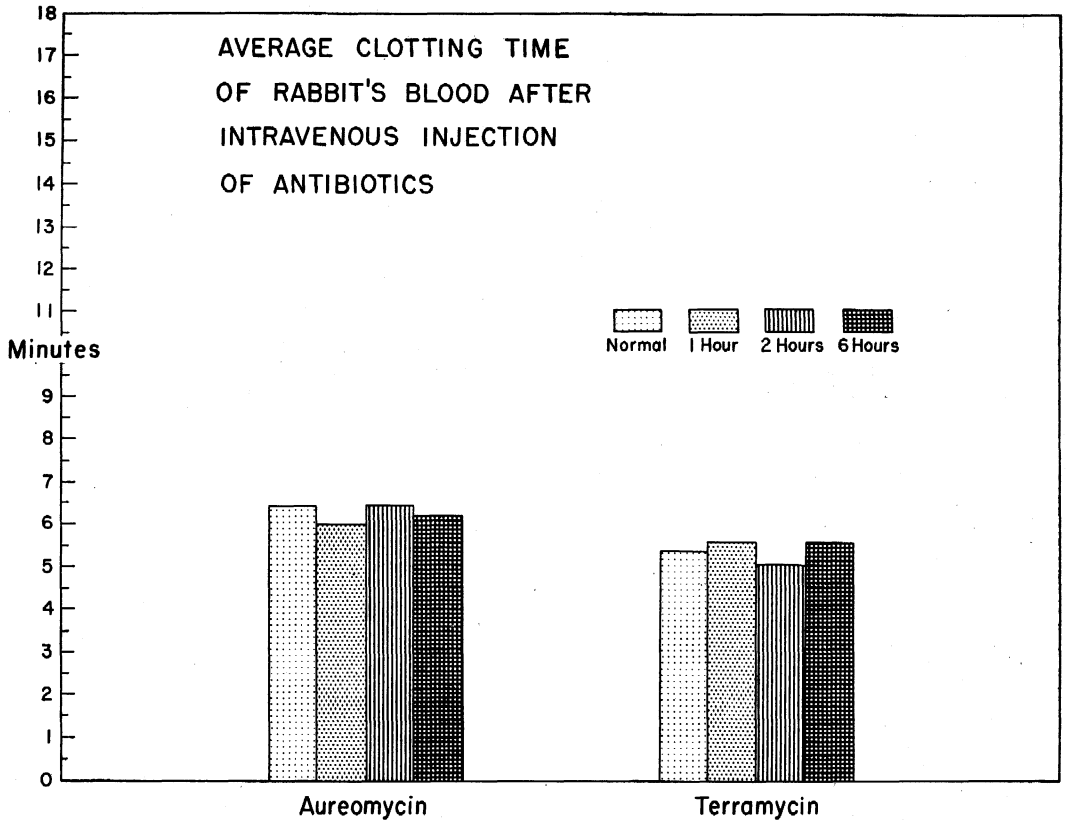

FIG. 3.

cent articles (*9, 10*) have shown terramycin to have no appreciable effect on the prothrombin time of human blood.

We have treated several hundred patients with both aureomycin and terramycin and have noted no increased frequency of embolism. Thus we feel that neither aureomycin nor terramycin in the recommended dosages produces any alteration in the blood coagulation mechanism that is of any clinical significance, and that neither drug should be withheld from any patient because of the fear of producing an intravascular clot.

References

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Comments and Communications

The Scientist as Citizen

I WAS gratified to read in Comments and Communications (May 16, 1952) "A Citizen's Duty," by Paul D. Foote, of Gulf Research and Development Company, urging that national meetings of scientific, technical, and trade associations be arranged so that they do not fall on election day. Mr. Foote wisely says, "The votes of the readers of this journal, who represent a group of the highest intelligence, are especially desirable;" and again, "Why not recognize our obligations as citizens and, throughout the country, arrange all association meetings on dates that will not conflict with voting?"