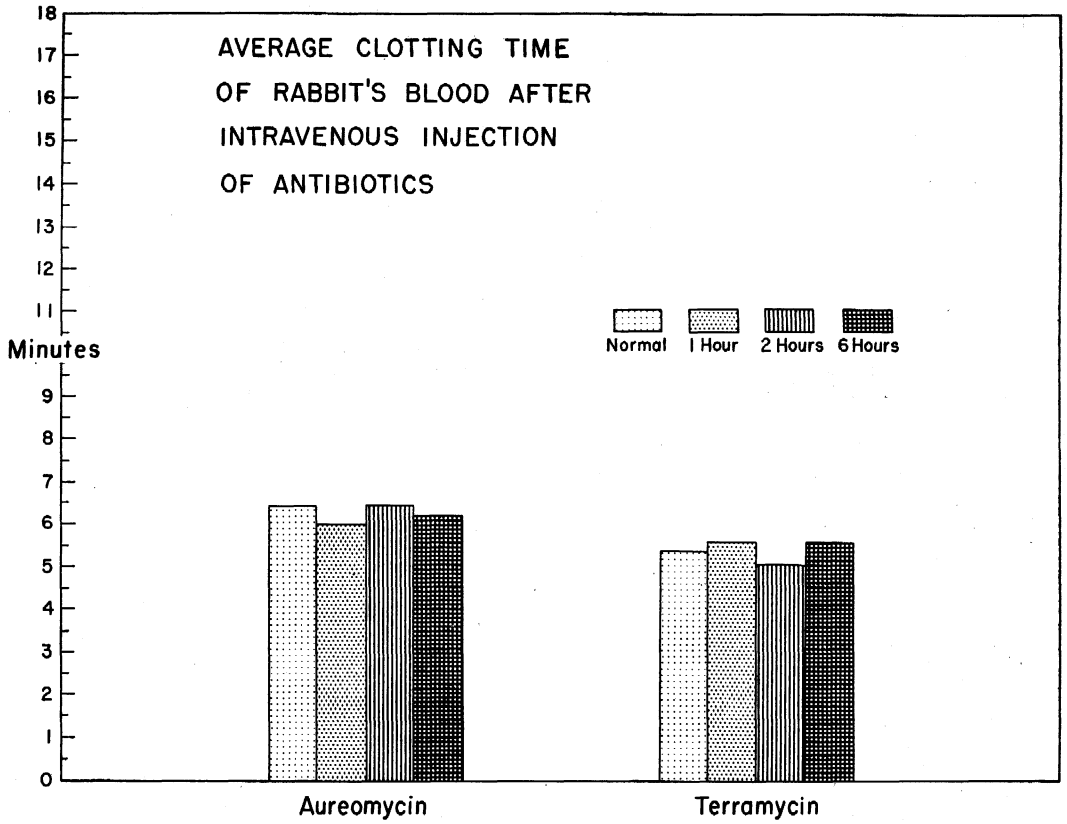

FIG. 3.

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.

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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?"

In the same issue of SCIENCE, Kirtley F. Mather, who discusses "The Problem of Antiscientific Trends Today," says,

> Scientists, by the very nature of their mental habits, are internationalistic rather than chauvinistic in their outlook. [He adds that] Scientists, moreover, are naturally devoted to the principles of democratic freedom that shine so clearly in our constitutional Bill of Rights, based as they are upon the one most important freedom of all, the freedom to think one's own thoughts and to express them so that they may be appraised in the court of public opinion.

Assuming that one's own country is worth while, one cannot be soundly "internationalistic" without being truly patriotic in the effort to protect and preserve our own country. The international situation has so deteriorated that the first thing on the agenda is to do one's best to appraise it correctly and act wisely. The danger is a real and present one.

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β-Glucuronidase and Glucuronide Synthesis

IN a recent review of the relationship between estrogens and enzymes, Fishman (*1*) discusses his hypothesis that the enzyme β-glucuronidase acts synthetically in the animal body. It therefore seems appropriate at the present time to recount briefly the principal evidence for the existence in the animal body of a glucuronide-synthesizing system, distinct from β-glucuronidase.

Fishman's hypothesis was originally put forward to explain his discovery (*2–4*) that the β-glucuronidase activity in nonsex organs, such as liver, rises in response to the administration of menthol or borneol, whereas the activity of the enzyme in uterus and vagina is increased by administration of esteriol or other estrogens. The complete explanation rests on three distinct postulates: (*a*) that the enzyme acts synthetically *in vivo*, (*b*) that the tissue activity responds adaptively to the presence of excess substrate, and (*c*) that the enzyme differs in specificity or function according to its location in the body. Without accepting the others, we shall limit ourselves here to considering the first and key postulate.

β-Glucuronidase is present in nearly all animal tissues that have been studied (*5*), and its activity is measured *in vitro* by following the hydrolysis of biosynthetic glucuronides (*6–8*); its activity in certain organs can be made to rise or fall *in vivo* by administering a variety of both glucuronidogenic and nonglucuronidogenic agents (*2–4, 9–11*); certain glucuronides cause a rise in activity (*4, 9*); *in vitro* this enzyme is powerfully inhibited by saccharate (*12–15*), an effect that has recently been shown to be due to saccharo-1:4-lactone present as impurity in the saccharate solution (*16, 17*); it is not inhibited by fluoride, iodoacetate, dinitrophenol, or sulfate (*12, 18*).

The activity of the glucuronide-synthesizing system can be measured in tissue slices and appears to require oxidation and phosphorylation; this enzyme system has been found only in liver and, to a minor extent, in the kidney (*19–21*); its activity in liver is unaltered by treating animals with agents that cause changes in liver β-glucuronidase activity (*20*); *in vitro*, glucuronide synthesis is not inhibited by saccharo-1:4-lactone (*14, 17*), but it is inhibited by anaerobiosis, cyanide, iodoacetate, fluoride, azide, dinitrophenol, and sulfate (*19, 21*); glucuronic acid in low concentration does not stimulate glucuronide synthesis by liver slices, nor does it overcome depression due to various causes (*19, 21*); in high concentration, glucuronic acid itself inhibits glucuronide synthesis *in vitro* (*21*), as it does β-glucuronidase (*12, 15*).

From their study of phenol conjugation by tissue slices (*22*), De Meio and Arnolt arrived at certain conclusions regarding glucuronide synthesis that are contrary to some of the points mentioned above. It was later shown, however, that their method did not measure conjugation of phenol with glucuronic acid (*23*), a finding that has been accepted by De Meio (*24*).

Florkin, Crismer, Duchateau, and Houet (*25*) obtained evidence for every slight condensation of glucuronic acid with borneol after prolonged incubation of the two compounds together in high concentration in presence of β-glucuronidase, but they considered that it did not follow that glucuronides are synthesized by this mechanism *in vivo*. Using a very sensitive color reaction for *o*-aminophenylglucuronide (*23*), Karunairatnam and Levvy (*12*) could find no condensation of *o*-aminophenol with glucuronic acid in presence of β-glucuronidase or crude liver homogenates. Under suitable conditions, any hydrolytic enzyme should theoretically be able to catalyze the reverse reaction, but several instances are known where resynthesis in the body proceeds by quite a different mechanism.

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