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The Rectal Administration of Dicumarol.*

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It has been demonstrated that Dicumarol, 3,3′-methylenebis (4-hydroxycoumarin), synthesized by Link and his associates,[1] can be successfully administered to human beings orally, and intravenously as the disodium salt in an alkaline solution of pH 10 or slightly higher. Upon administration of the drug in proper dosage—5 mg/kg—by either route there is, in 80% or more of individuals, a significant prolongation of the prothrombin time following a latent period of 24 hours or more. Both methods, however, have their limitations: it is often undesirable to apply oral therapy, as after certain operations, and the intravenous solution is not very stable. Hence the rectal administration of the drug would be advantageous if good absorption and a satisfactory decrease in the prothrombin time and coagulability of the blood could be achieved by this method.

The feasibility of the rectal administration of Dicumarol was first tested in a 46-year-old male suffering from thrombosis of the right postero-inferior cerebellar artery and resultant inability to swallow. In this patient the effect was very satisfactory: the rectal administration of 3 mg/kg (258 mg) in a water suspension increased the prothrombin time within 2 days from a pre-administration level of 15.5 seconds to 25.5 seconds. A second dose of the same size 4 days later maintained the elevated prothrombin time for 6 days more. This was fully as satisfactory an effect as would be expected from a similar dose given orally.

Later 2 doses of the drug, incorporated in cocoa butter suppositories, 5.0 mg/kg, were administered, 5 days apart, to an 86-kg man of 65 afflicted with posterior inferior cerebellar artery thrombosis. In this patient the prothrombin time was increased from a control level of 11 seconds to a maximum of 42 seconds the second day after the second dose. The coagulation time was increased from 8 minutes to a maximum of 19 minutes on the seventh day after the second dose.

These two cases demonstrate that Dicumarol may be effective when administered rectally in aqueous suspension or in a suppository. However, in only 2 of 34 other patients with a variety of diseases to whom the drug was administered rectally in doses of 5, 7.5, and 10 mg/kg in aqueous suspension or suppositories (11 of the 34 received the largest dose) was there a significant decrease in the coagulability of the blood, and prothrombin.

Discussion. It is of interest that Dicumarol can, on occasion, be absorbed when administered rectally and produce effects similar to those resulting from oral or intravenous exhibition of the drug. When it is effective, the latent period is no longer than when the Dicumarol is given orally.

Conclusion. The administration of Dicumarol rectally in aqueous suspension or in cocoa butter suppositories is only occasionally effective; hence its routine employment cannot be relied upon.

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1 Stahmann, M. A., Huebner, C. F., and Link, K. P., *J. Biol. Chem.*, 1941, **138**, 513.