centrating the hypothetical pressor substance in blood by similar chemical procedures. The present report is concerned with the vasomotor properties of extracts of human and of dog's blood containing protein fractions prepared in the following way.

Approximately 100 cc of freshly drawn blood was defibrinated and centrifuged. The serum was drawn off and half saturated with ammonium sulfate, and the resulting precipitate dialyzed against tap water until free of sulphate. The dialysate was then dried in a Florsdorf-Mudd apparatus[6] and taken up in a small volume of saline. The final solution was tested by intravenous injection into small unanesthetized dogs with Van Leersum (carotid) loops, and the effect on the blood pressure noted.

Observations were made on the blood of 5 patients with persistent hypertension, and 3 dogs with hypertension due to renal ischemia.[7] In no instance was a well-defined pressor response noted.

The failure to find the renal pressor material in the blood stream may be due to a number of possible causes, such as inefficient extraction, insufficient amount of the pressor substance in the blood stream, or differences between the chemical properties of renal pressor substance in man and rabbits. It is also possible that ultimately the pressor substance may prove to have no relation to hypertension.

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Measurement of the Inhibitory Action of Anticoagulants.

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A method for measuring the inhibitory activity of heparin on the clotting of blood has been worked out by Fischer and Schmitz.[1] Instead of using as Howell[2] does an arbitrary effect as a unit for the inhibitory activity, this method gives a curve of the action of varying concentrations of the anticoagulant, and from the equation for this curve the activity of the substance is defined. From the activity (k) obtained in this way a unit for inhibitory substance has been

6 Florsdorf, E. W., and Mudd, S. J., *J. Immunology*, 1935, **29**, 389.

7 Goldblatt, H., Lynch, J., Hanzal, R. F., and Summerville, W. W., *J. Exp. Med.*, 1934, **59**, 346.

1 Fischer, A., and Schmitz, A., *Z. Physiol. Chem.*, 1932, **210**, 129.

2 Howell, H., *Bull. Johns Hopkins Hosp.*, 1928, **42**, 199.

defined by Astrup and Behrnts Jensen[3] as the quantity of active substance contained in one gram of a material which gives the value 1 for k under the given experimental conditions.

This method has been modified by Chargaff, Bancroft and Stanley-Brown[4] and used in their recent work on blood coagulation. By this modification, curves for the inhibitory action of various concentrations cannot be determined as by the original method of Fischer and Schmitz (l.c.) and the necessity of determining such curves is here pointed out.

As the measurement of the clotting time of a blood plasma is far from being an ideal method, it is obvious that the accuracy is greatly increased with the estimation of an inhibition curve. For 5 different concentrations of an inhibitory dye, Chlorazol fast pink (Boot's Pure Drug), the activity was determined only from the differences between the clotting time of these solutions and the solutions containing one-half the original concentrations (Fischer and Schmitz[1]). The following values for k were obtained: 0.184, 0.247, 0.232, 0.140, 0.304. The average value was 0.221 in good agreement with the value 0.215 obtained from the slope of the straight line established when the logarithm of the clotting time was plotted against the concentration of the inhibitory substance.

It has been shown by Astrup[5] that the inhibitory action of various anticoagulants (not including the calcium-binding substances) differ not only quantitatively but qualitatively. When, for instance, solutions of different inhibitory substances, showing the same inhibitory effect on the same plasma system, are diluted to one-half the original concentrations, the inhibitory effects of these diluted solutions are not always equal. To show this, in Fig. 1, the logarithm of the clotting time has been plotted against the concentration of heparin in curve 1 and of Germanin in curve 2.

The anticoagulant action shows a qualitative difference which makes direct comparison of the activity of two such substances impossible. A comparison can only be made between known concentrations of the two substances.

It is then necessary, for comparative determination of the anticoagulating activities of various substances, to know the qualitative nature of the action of the different substances, and in this respect the determination of inhibitory curves is a valuable help.

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[3] Astrup, T., and Behrnts Jensen, H., to be published.

[4] Chargaff, E., Bancroft, F. W., and Stanley-Brown, M., *J. Biol. Chem.*, 1936, **115**, 149.

[5] Astrup, T., to be published.

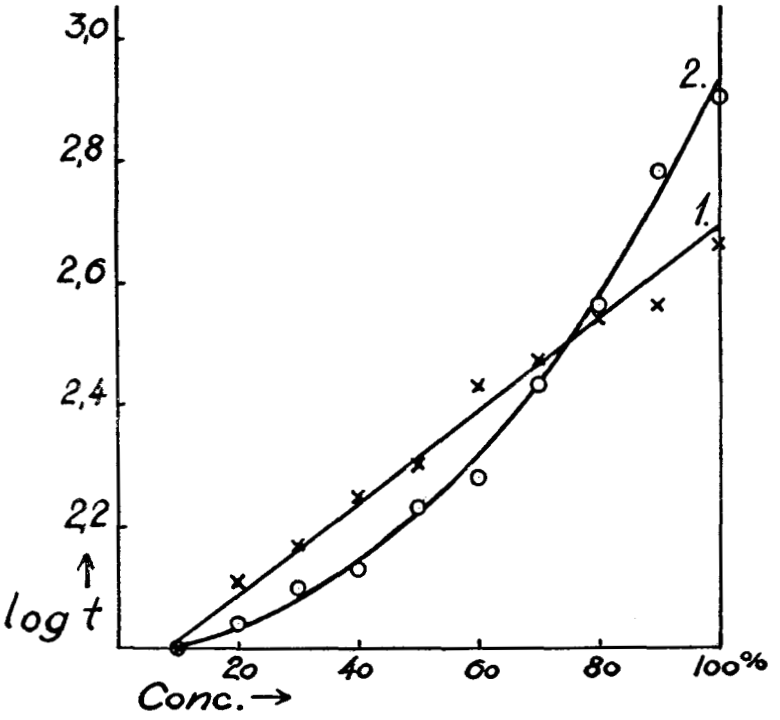

FIG. 1.
Heparin (1) and Germanin (2) in % of the original solutions.

For estimation of the activity of heparin it should be of great value in the comparison of the various methods to establish a standard for inhibitory activity. The difficulties encountered here are discussed by Astrup.[5] As the method of Fischer and Schmitz[1] yields an inhibition curve this method seems the most suitable. Furthermore, it is inexpensive and convenient to use and has proved serviceable during the past 6 years. It has been used by Dam and Schønheyder in their work on vitamin K (Schønheyder[6]).

[6] Schønheyder, F., *Biochem. J.*, 1936, **30**, 890.