Summary

The coagulation curve obtained by the technique previously reported by the authors has been recently interpreted by J. B. Graham and E. M. Barrow as explainable to a large extent by a variation of the ionic force of the medium during dilution. In order to overcome the influence of this physico-chemical factor and to reveal the action of the biological coagulation factors, the authors have performed dilution experiments at a constant ionic force, and at a constant citric ion content. Furthermore, the coagulation-dilution test makes it possible to display, both in normal and hemophilic blood, a certain number of factors whose action is discussed.

Bibliographie


Treatment of Haemophilia with Dried Human Fibrinogen

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As mentioned, the use of fibrinogen in Danish hospitals is on the increase. Fibrinogen: It is well known that fibrinogen is extremely sensitive and must thus be handled with great care if products with satisfactory stability are to be achieved. Citrate blood from which plasma is to be made is centrifuged in a slowly rotating refrigerated separator. When the plasma is cooled down to 0 C, alcohol is carefully added to a content of 8 percent and the temperature is at the same time reduced to -3 C. The precipitated fibrinogen is centrifuged in a refrigerated separator. The sediment is dissolved by stirring with ice-cold citrate saline, and the solution is then freeze-dried. The dried product contains about 60 percent protein which is able to coagulate with thrombin, and the remaining protein is a mixture of the various other plasma proteins. The further treatment includes dissolving the dried fraction I in ice-cold saline. This solution has a more or less turbid appearance. It is then filtered, first through Seitz clearing filter and
afterwards through a Seitz EK filter. The filtrate is distributed into 500-cc flasks in quantities corresponding to 6 g dry protein per flask. Freeze-drying is then carried out.

AHF protein: Until about a year ago we also produced AHF protein. This was made from the fibrinogen solution by removing the fibrinogen by means of heat coagulation, as described by Shirwwara and Spaet. The solution was heated up to 54°C for 5 minutes, after which it was cooled down rapidly to 0°C and centrifuged. The precipitate from this coagulated fibrinogen was filtered through Seitz EK filter. The filtrate was freeze-dried in ampoule flasks, each flask containing an amount of protein corresponding to 1/2 litre plasma. The dried preparation shows a satisfactory, stable AHF titre when kept in deep freeze. However, if it is kept at ordinary refrigerator temperature, the AHF titre drops by one half in the course of eight days, and if kept at room temperature, it is halved in the course of one day.

The results obtained with treatment were consequently very variable. Professor Owren drew our attention to the fact that our fibrinogen product contained a considerable amount of AHF, the factor apparently being more stable in fibrinogen. We have therefore begun to treat haemophiles with fibrinogen, with good results. The treatment is carried out in the Childrens Department of the Rigshospital, Copenhagen, under the leadership of Professor Plum.

Here we see a curve showing treatment of a patient. An 8-year-old, boy with haemophilia A came to the hospital in a poor condition, with haematuria and joint bleeding. His plasma had a content of antihaemophilic factor of practically 0. When treated with fibrinogen, the antihaemophilic factor rose to above the critical level of 20% and the bleedings stopped. Some days later the bleedings started again and the plasma showed a AHF content below 20 percent. Further fibrinogen was given and the bleedings stopped, and the AHF rose to normal values.

The blood used in our product consists of fresh blood from volunteers bled at Statens Seruminsttitut, and of surplus blood. We have an arrangement with the majority of the hospitals and blood banks that their excess blood be sent to us. Naturally, fibrinogen manufactured from old blood contains only a little AHF, while the amount of AHF in the preparation made from fresh blood is large and varying.
Examination of each batch is made according to the method of Biggs and MacFarlane, and the lots with AHF content of more than 100 percent are used for treatment of haemophiles, and the rest in cases of afibrinogenaemia.

Rationale for a Plasma Fractionation Programme for the Preparation of Clinically Adequate Products

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Abstract

Three years experience with the manufacture of PPL (a pasteurized plasma protein solution) and over one years experience of plasma fractioning by the Nitschmann modification of the method of Cohn have led us to develop a number of own ideas concerning the approach to the whole fractionation programme as regards products, methods and clinical use and which are described in detail.