THE PASSOVOY DEFECT: FURTHER CASE REPORTS AND PRELIMINARY CHARACTERIZATION.
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Since the first report of a patient with a deficiency of the Passovoy factor
(Lancet II:220, 1975) we have encountered 10 other cases from six kinds. The
pattern have a small and significant partial thromboplastin time which is corrected by normal plasma. They have normal
levels of all the hitherto reported clotting factors, including Fletcher and
Fitzgerald. No evidence of an inhibitor, and no further correlation. The
condition is transmitted as an autosomal dominant. Most of the patients have
had a moderate to mild bleeding diathesis, though the proband in the original
kindred recently bled profusely into the mouth three days following the removal
of a small cervical node and was given 6 units of blood to control the bleeding.
Attempts to characterize the factor have been hampered, the factor has been
insensitive to the assay method; however a fraction has been found which
shortens the clotting time of Passovoy deficient plasma, but not plasmas
deficient in other clotting factors; the biochemical properties of this factor
are currently under investigation.

This work was supported by USPHS research grant HL 19272.

PHARMACOKINETICS OF HUMAN FACTOR IX IN A DOG WITH SEVERE HEMOPHILIA B.
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In preparing a factor IX concentrate with a high yield and low heparin and chromo-4mobic
risks, we have tested this material for survival in an in vivo system, the hemophilic dog. By
following the disappearance of radiolabeled, isolated factor IX in addition to the classic clotting
assays, data on protein survival and more accurate kinetic parameters were obtained.

Guinea factor IX concentrate was prepared by batchwise adsorption-elution with DEAE-Sephadex
using cryoprecipitate-poor human plasma. Isolated human factor IX was radiolabeled with 125I by
chloramine-T without in vitro loss of clotting activity (Thompson, J Clin Invest, 64, press,
1977). A preparation containing less residual radioactivity (0.2 μm) and lyophilization; clotting and radioactivity were not altered by these steps.

Following infusion of the combined preparation into a dog with severe hemophilia B (IX base-
line factor IX) 10 post infusion samples were taken every 6 hours. The labeled factor IX clotting activity. These data were then analyzed by fitting to a two exponential expression using a Marquard non-linear least squares numerical procedure for a two compartment open model. The central volume was 14.5% of the animal's body weight; the total volume of distribution was 28% with a t 1/2 distribution of 11.4 min. The t 1/2 elimination was 20 h; the slower phase of elimination (b, c: that affected by redistribution) had a t 1/2 of 40 h. Factor IX clotting activity from the isolated factor IX throughout the 96 h; t 1/2 was slightly longer from the clotting activity data.

IN VITRO THROMBOGENICITY TEST FOR CLINICAL FACTOR IX CONCENTRATES USING SYNTHETIC SUBSTRATES
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Venous thromboses have been reported following the clinical use of some factor IX preparations.
This may be due to several causes as for instance traces of PFA or thrombin formed during
processing or presence of surface activation products involved in the early stages of the
coagulation pathway. There is an urgent need for simple and reliable thrombogenicity tests.
Activation by Ca2+ should preferentially be avoided, as Ca2+ by itself is capable of activating
the prothrombin complex. All clotting methods are affected by the heparin content (4-5 μM)
and excess amount of sodium citrate present in the IX concentrates. We have therefore de-veloped a colourimetric method using synthetic substrates. The assay is performed in the absence
of presence of known proteolytic inhibitors in order to improve the specificity of the test
system and identify the nature of the thrombogenicity. Using this method, various concentrations
of this group can be classified in three groups according to the rate of cleavage of the substrates. The
materials have been titrated with several inhibitors. The contaminating enzymes have also been
isolated and characterized. The results clearly indicate the presence of two entirely different
types of hot material. One group contains mainly PFA and thrombin and can be neutralized by
AT III. The other group probably contains large amounts of surface products. The "thrombogen-
icity" of this group can be mimicked by kaolin activation of plasma and inhibited by Trasylol.