and subsequent development of thrombi deserves further investigation.

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Hypo or Hyper Coagulability of Blood with High Levels of Clotting Factors ?

ORAL contraceptive drugs have recently been reported to produce an increase in blood factors VII and VIII[1] and fibrinogen[2]. Vascular thrombosis has been suspected during the administration of these drugs, and this raises for consideration the effect of high levels of clotting factors on the coagulability of blood. Experiments were carried out before and after the blood was in contact with wettable surfaces.

The results are summarized in Table 1, and the following points emerge.

Table 1

Reagent	Final concentration ml. blood	Blood clotting time	Prothrombin consumption	Factor IX in serum	Clot retraction
Fibrinogen					
human	10 mg	*N*	*N*	*N*	*N*
bovine	10 mg	*N*	*N*	*N*	*N*
Factor V					
human	50 mg	*N*	*N*	*N*	*N*
bovine	50 mg	*N*	*N*	*N*	*N*
Factor VIII					
human	2 U.*	*N*	*N*	*N*	reduced
porcine	8 U.*	*N*	*N*	*N*	reduced
bovine	6 U.*	*N*	*N*	*N*	reduced
Platelets†	940×10^6	prolonged	abnormal	greatly reduced	*N*
Inosithin phospholipid	5 mg	*N*	*N*	*N*	*N*
Brain phospholipid	2 mg	prolonged	abnormal	*N*	*N*
Dextran	30 mg	*N*	*N*	*N*	increased
Rheomacrodex	50 mg	*N*	*N*	*N*	*N*

N, No appreciable effect when compared with appropriate controls.
* Factor VIII unit = activity in 4 ml. pooled fresh citrated normal human plasma.
† Effect apparent only when high levels are attained before the blood was in contact with wettable surfaces.

(1) High levels of platelets hinder blood coagulation. Since this occurs in intact blood, however, we cannot dismiss completely the possibility that a similar effect is produced by other clotting factors which are, at present, available only from blood which has been in contact with glass. It is therefore concluded that high levels of certain clotting factors are liable to retard rather than accelerate blood coagulation.

(2) The results of high platelet counts differ from those of high concentrations of phospholipids, which are widely used as platelet substitutes. This indicates either that the inhibitory action of excess platelets is due to a factor other than platelet factor 3 or that the thromboplastin component of platelets is different from phospholipids; this would be in conformity with previous work[3], which showed differences between blood and tissue clotting factors.

(3) A high level of factor VIII reduces the speed and extent of clot retraction, a condition which could well aggravate the consequences of a coincidental thrombosis. This is a possible explanation of the thrombosis seen in women taking oral contraceptive drugs[4].

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IMMUNOLOGY

Demonstration of Antibodies to Thyroxine and Monoiodothyronine by Mixed Haemadsorption

A TECHNICAL procedure for the application of the mixed haemadsorption technique[1] to soluble antigens has recently been described[2]. This technique, which is essentially a mixed antiglobulin reaction, is being investigated because it is potentially a means of titrating antibodies to thyroglobulin in the sera of patients suffering from thyroiditis and other thyroid diseases. In the course of this work, it became of interest to find out whether the reaction with thyroglobulin may depend to some extent on the thyroxine determinants present on the thyroglobulin molecules. Pure thyroxine coated over a glass slide should have its antigenic determinants exposed much in the same way as when thyroglobulin is similarly exposed. Glass slides were therefore coated with a layer of thyroxine applied either as a suspension of microcrystals in phosphate buffered saline (PBS), *p*H 7·4, containing 1 per cent of normal rabbit serum (NRS) or as a solution in ethanol. Monoiodothyronine was applied as a solution in PBS, *p*H 7·4, containing 1 per cent of NRS. Human thyroglobulin was applied as a solution in PBS, *p*H 7·4. The various antigen films were dried at room temperature and all slides except those coated with thyroxine in ethanol were fixed for 5 min in acetone. The antigen films were covered with layers of agar and 'Perspex' disks provided with holes, which served as serum reservoirs. Two-fold serial dilutions of the sera containing antibody were added to the holes and the antibodies were allowed to diffuse through the agar layer. The antibody zones produced when the diffusing antibody attached itself to the antigen film on the slide were marked out by red cells provided with an exterior coating of antiglobulin so that they were able to adsorb specifically on to antibodies from the animal species concerned[2,3].

Sera from fifteen cases of thyroid disease and from five healthy 20 year old male blood donors were tested against thyroglobulin, thyroxine and monoiodothyronine with the technique described. Reactions obtained with the