mechanism(5).

Summary. Cortisone acetate depressed adrenal weight and reduced adrenal cholesterol concentration in male and female rats. Methylandrostenediol (MAD) depleted adrenal cholesterol in both sexes while not influencing adrenal weight. When cortisone acetate and MAD were injected concomitantly, normal adrenal weights were observed in male and female rats. However, adrenal cholesterol content was protected by MAD only in cortisone-treated males. MAD did not prevent adrenal weight loss due to thiouracil, but did deplete cholesterol by 67%.

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Plasma Thromboplastin Antecedent Levels in Patients Receiving Coumarin Anticoagulants and in Patients with Laennec's Cirrhosis.* (26863)

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Naeye reported(1) that plasma thromboplastin antecedent (PTA) levels were depressed by Dicumarol (bishydroxycoumarin). However, Waaler later found(2) a normal formation of activation product (which requires PTA) in plasma from 10 patients receiving long term therapy with Dicumarol or phenylindanedione. In addition, a recent preliminary report by Rodermund, Schneider and Egli(3) describes a normal formation of activation product in subjects given Marcoumar for 10 days.

Naeye also reported(1) that PTA levels fell in liver disease. Other reports of the quantitative measurement of PTA activity in liver disease have not been found.

A specific one-stage assay for PTA has been reported from this laboratory recently(4). This test has been used to measure PTA levels in a group of patients receiving coumarin anticoagulants and in another group of patients with advanced Laennec's cirrhosis.

Methods. Blood for testing was drawn with Monocote (Armour and Co.) coated needles and silicone (Dri-film, G.E. SC-87) coated syringes. Nine parts of blood were added to 1 part of anticoagulant (made by mixing 2 parts of 0.1 M citric acid and 3 parts of 0.1 M sodium citrate) in a polyethylene tube. Platelet-poor plasma was prepared by centrifuging for 20 minutes at 14,500 g at 4°C and was tested within about 3 hours after the blood was drawn.

The technic and standardization of the quantitative assay for PTA have been reported elsewhere(4). The clotting system consists of: 0.1 ml of a "cephalin" reagent diluted in a suspension of kaolin powder, 0.1 ml of hereditary PTA deficiency substrate plasma, 0.1 ml of a 1/5 or a 1/10 dilution of the test plasma, and 0.1 ml of 35 mM calcium chloride solution. Neither the substrate plasma nor the test plasma contacts an activating surface prior to its addition to the clotting mixture.

The assay measures PTA activity accurately at levels above about 15% of a standard reference plasma. For example, the 90% confidence limits for a single observed value of 50% PTA vary between 42 and 60% of the reference plasma.

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TABLE I. PTA Levels in Patients Receiving Coumarin Anticoagulants.

Subject	PTA level, %	Prothrombin time (P & P), %
Dicumarol pts.		
A.H.	80	10
R.R.	88	7
M.L.	140	15
J.F.	160	10
L.A.	128	18
Coumadin pts.		
T.	100	29
B.	108	22
H.	84	9
W.	120	30
U.	100	17
L.	92	22
Mc.	120	22
O.	88	22
39 normal subjects: Mean 97%, range 63-136%		

Prothrombin times were measured by the P&P technic of Owren and Aas(5).

Results. PTA levels and prothrombin times of 5 patients receiving Dicumarol and 8 patients receiving Coumadin (sodium warfarin) are listed in Table I. All of the patients had received anticoagulants for at least 2 weeks; several had received anticoagulant therapy for many weeks. As can be seen from the prothrombin times, all of the patients were receiving therapeutic amounts of anticoagulant. PTA levels were normal in every patient.

PTA levels were measured on 3 occasions in an additional patient who had received phenylindanedione for many months. His prothrombin time was consistently below 30%; his PTA levels were 68, 88, and 88%, respectively. Thus, no evidence was found that coumarin or coumarin-like anticoagulants interfere with synthesis of PTA.

TABLE II. PTA Levels in Advanced Laennec's Cirrhosis.

Patient	PTA level, %	Prothrombin time (P & P), %
Roz.	87	94
M.	52	63
So.	59	56
Rod.	52	45
Ra.	49	44
Sm.	48	50
W.	47	55
MaG.	35	33
E	27	35

PTA levels and prothrombin times of 9 patients with advanced Laennec's cirrhosis are summarized in Table II. These patients had decompensated disease with jaundice or ascites or both. Their PTA levels were depressed; the degree of depression closely paralleled the value for prothrombin time. Two of the patients, MaG. and E., had PTA levels of about 30%, which is thought to be the minimum PTA level for effective hemostasis (6).

Discussion. These data, obtained with a specific assay for PTA, confirm the findings of Waaler(2) and of Rodermund and coworkers(3), obtained with less specific technics. They do not agree with the observations of Naeye(1). It appears that the coumarin and coumarin-like anticoagulants do not affect PTA. Therefore, one may conclude that PTA synthesis does not require Vit. K.

The low PTA levels found in patients with chronic parenchymal liver disease confirm the findings of Naeye(1). One may strongly suspect that the liver cell is the site of synthesis of PTA. It would appear that the PTA level of the patient with Laennec's cirrhosis is predictable from his prothrombin time value.

Summary. 1. Plasma thromboplastin antecedent (PTA) levels are normal in patients receiving Dicumarol, Coumadin, or phenylindanedione. 2. PTA levels are depressed in patients with Laennec's cirrhosis. Degree of depression parallels prothrombin time value.

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