a strongly inhibitory influence upon the formation of granulation tissue of turpentine abscesses in white rats. It resembles the blocking effect of cortisone and hydricortisone upon such tissues. The appearance of the fibroblasts, the vascular pattern and the intercellular substance of the inhibited granulation tissue is the same, regardless of which one of the suppressing agents were administered. Some of the possible mechanisms of action of these drugs were studied.

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Congenital Hypoproconvertinemia.* (20741)

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Congenital hemorrhagic diathesis associated with a prolonged one-stage "prothrombin time" (Quick test) is uncommon. Quick(1) recognized that his test was also dependent upon factor(s) other than the component usually regarded as prothrombin and substantial experimental evidence from many laboratories(2) indicates these non-prothrombin factors to be (A) proaccelerin (labile factor, factor V, AcG, etc.), (B) proconvertin (stable factor, SPCA, factor VII, co-thromboplastin, etc.), (C) fibrinogen, (D) certain inhibitors of coagulation. Additional confirmation comes from study of clinical bleeding disorders and the present communication deals with 2 new cases of congenital proconvertin (SPCA) deficiency, a condition first clearly identified by Alexander *et al.*(3) and further studied by Owren(4).

Case histories. I. A 14-year white school girl (M.T.), who had a bleeding tendency since birth, was seen in 1950. The mother had shown easy bruising and some menorrhagia. A son of one of the mother's sisters was said to be a bleeder. No defect was found in another sister and her children. No information concerning the father could be elicited. M.T. bled from the umbilical cord on the 7th day after birth and during childhood had gum bleeding, easy bruising, hematuria, and attacks of abdominal pain with pallor and jaundice. No epistaxis, hemarthrosis, hematemesis or melena were reported. Menstrual periods, starting at age 14, were frequently excessive, requiring hospitalization and transfusions. Vit. K, including synthetic K_1 (obtained through courtesy of Dr. A. Gibson, Merck & Co.) did not change the

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prothrombin time. She died in another hospital in 1952 after admission in hemorrhagic shock from which she failed to rally despite transfusions, etc. No autopsy was performed. Our physical examination (1950) revealed marked pallor, gingivitis, and ecchymoses of cutaneous area. Liver and spleen were barely palpable. Laboratory tests were carried out in 1950 and restudy of frozen (—20°C) specimens 3 years later afforded additional significant results. II. A 32-year white farmer (R.S.) with an obscure hemorrhagic diathesis was seen in 1950 and again in 1953. His father had frequent epistaxis and a distant paternal relative had "bled to death." Of the patient's 4 sons, one bruises easily, while another had frequent epistaxis. R.S.'s hemorrhagic history started with umbilical cord bleeding and easy bruising as an infant. Epistaxis was common in childhood. Since puberty he has had hematuria, melena, hematomata, and hemarthroses, but no hemoptysis or hematemesis. Vit. K, including 2 weeks on 250 mg daily of synthetic K_1 (Merck's), failed to alter his clotting defect. He has never had a blood transfusion. The residual findings are minor, chiefly impairment of right elbow and both knee joints.

Methods. Standard laboratory routines and tests previously described(5) need no review. *AHG and PTC assays.* Compare reductions in recalcification clotting-time (at 37°C) of 0.2 ml test standards (hemophilic or plasma-thromboplastin-component deficient plasmas, stored at −20°C) mixed with 0.05 ml patient's plasma or normal plasma dilutions. *Prothrombin* assays: include use of Soluplastin (courtesy Dr. E. W. Blanchard, Schieffelin Co.) as thromboplastin and our own tested preparations of other reagents, in methods: (A) usual AcG-modified 2-stage(6), also adding bovine proconvertin (ProC); (B) a new one-stage: 0.1 ml plasma (1:10), 0.1 ml substrate ($BaSO_4$ adsorbed beef plasma + ProC), 0.2 ml Ca-thromboplastin; (C) a new 2-stage: citrate (0.2 M) eluate of $BaSO_4$ plasma, first tested after one minute activation with optimal Ca, thromboplastin and AcG; then ProC added and activation continued to a stable clotting time. Using a standard dilution curve, unitage at one minute divided by final unitage gives *"proconvertin index"* (percentage). Owren's *proconvertin* assay (7) was also used. In the data of Tables I and II, values are expressed as percentages of the mean for a large series of normal controls.

TABLE I. Clotting Tests.

Procedure	M. T.	R. S.
Bleeding time	2′ 15″	1′ 15″
Tourniquet test	Negative	Negative
Platelet count	240000	240000
" "thromboplastin"	——	Normal
Coagulation time		
Glass	13′-28′	30′-88′
Silicone	45′-120′+	120′+
Clot retraction	4+	4+
" lysis	0	0
Fibrinogen, mg %	310	330
AHG assay, %	100	100
PTC " , %	90*	100
Anticoagulant titer	Negative	Negative
Antithrombin		
Plasma	Normal	Normal
Serum	"	"

* Frozen plasma tested in 1953.

TABLE II. Plasma "Prothrombin" Tests.

Test	M. T.	R. S.
Quick test, %	1-2 (73"-110")	2-3 (48"-55")
Proaccelerin assay, %	90	100+
Prothrombin assay		
(A) 2-stage, %	85*	103
(B) New one-stage, %	84*	108
(C) $BaSO_4$ eluate 2-stage, %	82*	105
Proconvertin		
(A) Index	3.0*	2.5
(B) Owren's assay, %	0*	0

* Frozen plasma tested in 1953.

TABLE III. Prothrombin Consumption.*

Method	M. T.	R. S.
Quick test	0	0
2-stage	79†	60
$BaSO_4$ eluate	N.D.	58

* Prothrombin consumption $=$

$$\frac{(\text{plasma prothrombin}) - (\text{serum prothrombin}) \times 100}{\text{plasma prothrombin}}$$

† Frozen serum tested in 1953.

Results. Essentially normal results (Table I) were obtained in tests of bleeding time, capillary resistance (tourniquet test), platelet count and thromboplastic function, clot re-

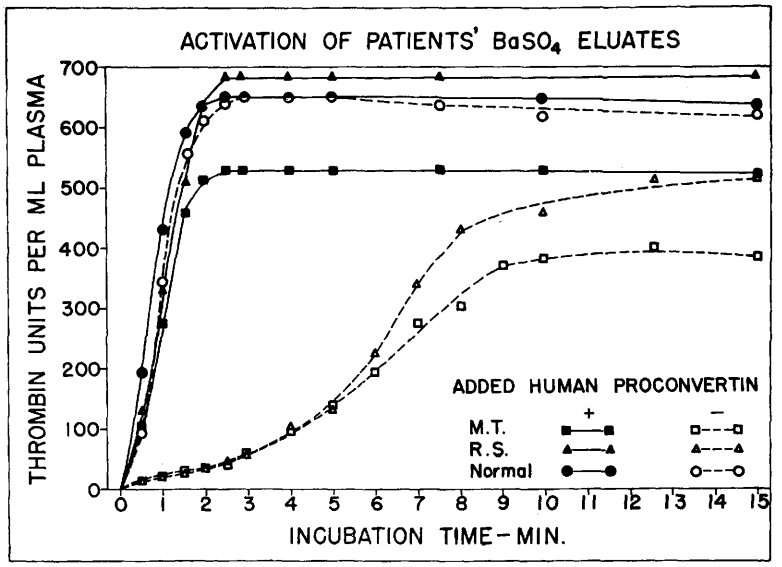

FIG. 1. Thrombin evolution from patients' $BaSO_4$ eluates in presence of optimal calcium, thromboplastin and accelerin with (+) and without (—) added human proconvertin.

traction, clot lysis, fibrinogen, AHG, PTC, and antithrombin. No circulating anticoagulant was detected. The Quick test (Table II) was extremely prolonged in both cases, corresponding to 1-3% of normal "prothrombic" activity. Proaccelerin was normal in both. The usual(6) 2-stage (A) gave prothrombin values of 63% in 6 minutes (M.T.) and 70% in 10 minutes (R.S.), compared with the normal 100 % in about 2 minutes. Activation times were shortened to normal and the prothrombin unitage significantly increased (Table II) when ProC was also added. Methods (B) and (C) gave prothrombin values which were normal and corresponded well with the proconvertin-modified (A). The proconvertin indices, 2.5-3.0, were both very low, compared with the normal 30-60. No proconvertin was detected with the Owren technic.

Prothrombin consumption tests (Table III) on the one hour (37°C) sera of M.T. and R.S. showed significant elevation of residual prothrombin. One-stage (Quick) tests could not be interpreted because plasma "prothrombin times" were prolonged also. In the 2-stage tests (C) and (A) with ProC, R.S. consumed only 60% of the initial plasma prothrombin. M.T.'s serum sample had been preserved (1950-53) at —20°C and a residual prothrombin of over 20% may be accepted as significant, since normal sera seldom contain as much as 5-10%.

As some doubt might be raised concerning the validity of the tests on M.T.'s plasma, which had been stored frozen for some 3 years, a sample of normal plasma frozen on the same date, was also tested. The concentrations of prothrombin and proconvertin were normal, but only traces of proaccelerin could be detected. This old normal plasma was employed as the control in the following experiment.

Three ml samples of oxalated plasma from the 2 patients and the "normal" were adsorbed with 300 mg $BaSO_4$; the $BaSO_4$ sedimented, washed with distilled water, and eluted with one ml 0.2 M sodium citrate. The eluates were activated with (+) and without (—) added proconvertin (human (8)) in addition to the usual calcium, thromboplastin and accelerin (Fig. 1). Without added proconvertin, thrombin formation was rapid and complete from the normal eluate, but very slow and incomplete in eluates from both patients. When proconvertin was added. little effect was noted in the normal, whereas, in the patients, both activation rates and final

thrombin yields were increased essentially to normal.

Discussion. Owren's(4) nomenclature impresses us with the advantages of clarity and adaptability to differentiation of precursor (pro) and active forms. Thus, we have designated these 2 cases as hypoproconvertinemia, probably familial in type as suggested by their histories. In severity, frequency and types of bleeding episodes, these cases are indistinguishable from other kinds of congenital hemorrhagic disorders. Hence, the laboratory tests are essential for the differential diagnosis. Quick tests on both patients were markedly prolonged. Our initial examination(9) showed that this was not due to abnormality of fibrinogen, antithrombin or proaccelerin and, therefore, a diagnosis of hypoprothrombinemia, unresponsive to Vit. K, seemed justified. Re-examination of R.S. and restudy of M.T.'s frozen specimens refutes this diagnosis and establishes hypoproconvertinemia. Normal plasma prothrombin levels in both patients are clearly demonstrated by the 3 test methods, but it should be noted that the addition of proconvertin, either bovine (Table II) or human (Fig. 1) was required. The very low proconvertin index denotes a severe deficiency and its small positive value, rather than the completely negative Owren's test, is in keeping with the facts that clotting did occur, albeit slowly, in whole blood and the Quick tests. The finding of a moderate deficiency in prothrombin consumption in our cases is new. This may depend upon the severity of the proconvertin deficiency.

Summary. Two unrelated patients had a congenital, probably familial, hemorrhagic disorder associated with a prolonged "prothrombin time." Laboratory examination showed that this prolongation was not due to deficiency of prothrombin, proaccelerin, or fibrinogen, nor to excess of inhibitors. The diagnosis of hypoproconvertinemia was established by the findings of a low "proconvertin index," by Owren's test, and by the ability of added proconvertin to restore normal prothrombin conversion *in vitro*. Prothrombin consumption tests in both cases showed a moderate but significant decrease.

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Metabolic Patterns in Experimentally Induced Muscular Dystrophy.* (20742)

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Lesions in striated and cardiac muscle have been described in animals receiving large amounts of desoxycorticosterone(1), and in animals maintained on diets deficient in vit. E, or in potassium(2). Recently Ellis noted degenerative changes in the striated muscles of rabbits treated with cortisone(3) and main-

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