Literaturzusammenfassungen — Abstracts — Résumés de la litérature

Physiology and Pathology of Blood Coagulation
A Review of the Literature of 1956 (Second Series)

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a) General Aspects (incl. Thromboelastography and Hemostasis)

Untersuchungen über die Gerinnungsfähigkeit des Blutes unter der Geburt. Niesert, H. W., Univ.-Frauenklinik, Rostock, Germany, Geburts- u. Frauenheilk. *16:* 862 (1956).

The author studied the coagulability of blood during parturition and immediately after separation of placenta by means of heparin tolerance test, prothrombin-, Ac globulin-, antithrombin-, and thrombin-inhibitor-determinations, as well as by determination of fibrinolysis and fibrinogen level. Findings: Parturition is immediately followed by marked fibrinolytic activity resulting in considerable decrease of fibrinogen. Clotting time decreased postpartum in $^2/_3$ of the cases and increased in one third. In some cases thrombin inhibitor was activated during labour. Other alterations were insignificant. These findings are explained either by occurrence in the maternal blood of thromboplastin of decidual origin, or by domination of the sympathetic over the parasympathetic nerve system during and after parturition.

Influence of Vasodilatation upon the Blood Clotting. Cermák, L., IV. Univ. Clinic, Prague, Czechoslovakia, Vnitřní lékařství *2:* 431 (1956).

Following an experimental vasodilatation in 42 patients, substantial prolongation of blood coagulation time was noted. This occurred more frequently in subjects with clinically normal blood vessels than in those suffering from a vascular disease.

L'action des antimitotiques sur les facteurs de l'hémostase. Introzzi, P., Clin. méd., Univ. Pavia, Italy, Schweiz. med. Wschr. *86,* 1441 (1956).

The hemostatic deficiency resulting from antimitotics and antimetabolites has been studied by thrombelastographic determinations. The study revealed the mainly thrombocytopenic and thrombocytopathic nature of the occurring alterations. The possible interference of circulating anticoagulants in these conditions has been excluded by comparative analysis with other thrombocytopenic conditions.

Phlegmasia caerulea dolens und Blutgerinnungsuntersuchungen vor der Entbindung und im Wochenbett. Szirmai, E., Gerinnungsphysiol. Lab., Allgem. Krankenhaus Arpad, Budapest, Hungary, Zbl. Gynäk. *78:* 1327 (1956).

The author discusses coagulation disorders connected with obstetrics. In the first part a very rare case of Phlegmasia caerulea dolens following parturition is reported. In the second part of the paper the author reports his investigations of the blood coagulation following parturition in healthy and in toxemic women. The results indicate that the severe hemorrhages occuring during delivery are caused by several factors together.

The Pharmacy of Blood its Products and Substitutes. The Blood Clotting Mechanism. Jorpes, J. E., Chem. Dept., Karolinska Inst., Stockholm, Sweden, J. Pharm. Pharmacol. *8:* 73 (1956).

The author presents a paper on the historical development of the knowledge of the coagulation mechanism. Beginning with the first mentioning of fibrin in the literature in 1666 he goes on to discuss the most recent theories on blood coagulation, concluding that the main problem, yet unsolved, is how the two mechanisms in blood which cause or prevent coagulation counter-balance each other.

Terapia antireumatica ed emostasi. Ricerche sull'influenza del piramidone nei processi di coagulazione del sangue. Crolle, G., Bianco, S., Ist. Patol. Spec., Univ. Torino, Italy, Minerva med. *47:* 38 (1956).

Based on the literature it appears that salicylate therapy decreases the prothrombin level, and that on the other hand ACTH and cortisone probably have an activating effect on hemostasis. The authors' clinical and experimental studies revealed that Pyramidon does not influence plasma coagulation time and prothrombin activity.

Influence de l'acide acétyl salicylique dans les maladies hémorragiques. Beaumont, J. L., Caen, Jos., Bernard, J., Serv. Pédiatrie, Hôp. Hérold, Paris, France, Sang *27:* 243 (1956).

Acetyl-salicylic acid markedly increases bleeding time of patients suffering from a hemorrhagic diathesis. On the other hand bleeding time of normal subjects is but faintly increased. Acetyl-salicylic acid is believed to act by decreasing platelet adhesiveness more than by lowering prothrombin level or blood coagulability. It is furthermore capable of favoring hemorrhagic incidents in patients with deficient hemostasis, such as hemorrhagic diathesis, anticoagulant therapy, vascular disorders or after even minor surgical operations.

Über Änderungen einiger Gerinnungsfaktoren bei Poliomyelitis. Koch, F., Schultze, H. E., Schwick, G., Marburg/Lahn, Germany, Mschr. Kinderheilk. *104:* 145 (1956).

The authors studied the alteration of coagulation factors in poliomyelitis, in particular polio-encephalitis, and found a marked deficiency in the first coagulation phase (factor II, V, VII, and antithrombin). These results explain the frequently encountered intestinal bleedings in such cases. The pathogenesis of this coagulation deficiency remains to be studied. The authors suggest the interference of neuro-vegative i.e. humoral factors. The injection of ACC 76 (a purified preparation of factor V/VI and VII) is proposed as a therapeutical measure.

Surgical Intervention in Patients Suffering from Hemorrhagic Diathesis. van Creveld, S., Hoorweg, P. G., Stijn, R. W., Kinderkliniek Univ., Amsterdam, Holland, Ned. T. Geneesk. *100:* 3345 (1956).

The authors discuss the measures taken before and (or) after operation in 3 patients with congenital hemorrhagic diathesis. The following operations were carried out: a) partial resection of stomach and duodenum followed by anastomosis according to Billroth I, on account of 2 bleeding ulcers in the duodenum of a patient with classic hemophilia. b) operation of a subdural hematoma in a patient suffering from hemophilia B (Christmas Disease). c) Patient with congenital essential hypoprothrombinemia with severe hemorrhage following a squint — operation without previous correction of his clotting disorder.

Symposium on the Laboratory Aspects of Blood Coagulation. Dacie, J. V., Pitney, W. R., Hardisty, R. M., Wolf, P., Dept. Path., Postgraduate Med. School, London, England, Proc. roy. Soc. Med. *49:* 185 (1956).

In this symposium the authors stress the importance of the thromboplastin generation test as a weapon in diagnosis and show the value of a modification of this test for measuring antihemophilic globulin quantitatively. Circulating anticoagulants and functional platelet deficiencies are discussed. The most sensitive method for the detection of the former is the thromboplastin generation test. This test can be used, too, to demonstrate a qualitative abnormality of platelets. The variations produced in thrombin generation and other two-stage clotting tests by different batches of fibrinogen are discussed. A formula for prothrombin conversion ratio determination is presented. This ratio retains the sensitivity of the thrombin generation test, and yet has the advantage of giving the result as a simple numerical index and minimizing certain variable factors. The largest single variable factor in clotting experiments is produced when platelet-containing plasma is stored in the refrigerator. A chloroform extract of acetone-dried human brain is a convenient substitute in most instances, but not in a heparin-containing system.

The Operative Risk in Disease of the Haemopoietic System and Defects in Coagulation. Macpherson, A. I. S., Sir James Learmonth, Dept. Surg., Univ. of Edingburgh, Scotland, Scott med. J. *1:* 32 (1956).

Über das Verhalten einiger Gerinnungsfaktoren bei unbehandelten und behandelten Keuchhusten-Patienten. Koch, F., Schultze, H. E., Schwick, G., Kinderklinik, Justus-Liebig-Hochschule, Gießen, Germany, Arch. Kinderheilk. *154:* 39 (1956).

The authors present a report on the results obtained by determination of coagulation factors in patients with whooping-cough. One group was untreated, whereas the other group received vitamin K_1 or terramycin. A lability of certain factors of the first phase was found and was more pronounced in the treated group. It is discussed whether this lability is due to mild temporary liver damage or to vegetative disfunction. Treatment of pertussis with vitamin K_1 seems to be without clinical success.

Alcuni aspetti della emocoagulazone nella malattia vascolare ipertensiva. Muccio, G., Ist. Patol. Spec. Med., Univ., Pisa, Italy, Rass. Fisiopat. clin. ter. *28:* 395 (1956).

Fehldiagnosen bei hämorrhagischen Diathesen. Holzknecht, F., Med. Univ.-Klinik, Innsbruck, Austria, Med. Klin. *51:* 1559 (1956).

Blood Coagulation and its Clinical Significance. Koller F., Dept. Med., Neumünster Hosp., Zollikerberg/Zürich, Switzerland, German med. monthly *1:* 193 (1956).
Das Verhalten der Blutgerinnungsfaktoren bei der Anwendung von Cortison und Prednison. Günther, P. G., Kiefer, E., Med. Univ.-Klinik, Mainz, Germany, Med. Klin. *51:* 1633 (1956).

Effetto de la methoxamina sul tempo di coagulazione in soggetti normali. Rubino, M., De Blasi, S., Ist. Patol. Spec. Chir., Univ., Bari, Italy, Minerva anestesiol. *22: 7* (1956).

Methoxamino-hydrochloride administered by slow intravenous infusions in doses from

8 to 20 mg causes a shortening of the coagulation time from one to 2½mins. This effect is probably due to an adrenergic response, as previous administration of regitin prevents the pressor effect as well as that on coagulation.

Su di un nuovo coagulante attivo per via orale. Maccanico, A., Tugnoli, F., Ospedali Riuniti, Roma, Italy, Policlin. *63:* 1388 (1956).

Die Beeinflussung der Serumlipide durch Roßkastanienextrakt (Venostasin). Trenkmann, H., Med. Klinik, Akademie, Magdeburg, Germany, Münch. med. Wschr. *98:* 1436 (1956).

Über die Beeinflussung der Blutgerinnung durch Polycarbonsäuren. Reinhardt, F., Riess, H., II. Med. Univ.-Klinik, Wien, Austria, Wien. klin. Wschr. *106:* 812 (1956).

Untersuchungen über die Hämostase uteriner Blutungen durch Protaminsulfat und Toluidinblau. Beller, F. K., Naegele, M., Frauenklinik, Justus-Liebig-Hochschule, Gießen, Germany, Arch. Gynäk. *188:* 123 (1956).

Beitrag zum Problem Blutgerinnung und Thrombose. Gross, R., Med. Univ.-Klinik, Marburg/L., Germany, Ärztl. Wschr. *11:* 555 (1956).

Aspects particuliers de la coagulation sanguine du nouveau-né. Masure, R., Schonne, R., Lab. d'Hématol. Clin. Méd. A., Louvain, Belgium, Brux. méd. *36:* 1434 (1956).

Variazioni emocoagulatorie da barbiturici. de Dominicos, E., Rolandi, L., Ospedale Maggiore, Milano, Italy, Minerva Anestesiol. *22:* 215 (1956).

Erfahrungen bei Blutungen in einer Lungenabteilung — mit besonderer Berücksichtigung des Hämostatikums Reptilase. Schill, R., Abtlg. für Lungenkranke, Landeskrankenhaus, Graz, Austria, Wien. klin. Wschr. *68:* 576 (1956).

Blood Coagulation With Particular Reference to the Early Stages. Macfarlane, R. G., Radcliffe Infirmary, Oxford, England, Physiol. Rev. *36:* 479 (1956).

In this extremely competent review the theories of coagulation have been synthetized according to most recent research results. The author concludes that, complex though it seems to be, the mechanism of coagulation is only part of a far more complex mechanism by which the blood reacts to injury.

Knochen- und Blutgerinnungsveränderungen bei Urticaria pigmentosa. Deutsch, E., Ellegast, H., Nosko, L., I. Med. Univ.-Klinik, Wien, Austria, Hautarzt *7:* 257 (1956).

It was found that some patients with urticaria pigmentosa do not suffer from an isolated skin disease but from an increase of mast cells occurring in tissues where mast cells are normally found. Besides skin alterations these patients also show abnormal blood coagulation and more rarely changes in the bone system, which are considered a consequence of increased mast cells. Etiology of the increase of mast cells remains totally obscure. Eight cases are reported.

Beiträge zur Gewinnung von Hirudin, der Wirksubstanz des medizinischen Blutegels (Hirudo medicinalis L.). Schremmer, F., Hromatka, O., Deutsch, E., Csoklich, C., II. Zool. Inst., Univ., Wien, Austria, Mt. h. Chemie *87:* 87 (1956).

Über den Einfluß kreislaufwirksamer Substanzen auf die Blutungszeit. Sartori, C. H., Univ.-Frauenklinik, Hamburg, Germany, Münch. med. Wschr. *98:* 1727 (1956).

Weitere Beobachtungen über das Vorkommen schwerer Blutungen post partum als Folge von Gerinnungsstörungen. Runge, H., Hartert, I., Univ.-Frauenklinik, Heidelberg, Germany, Medizinische, *37:* 1289 (1956).

Three cases of postpartal bleeding caused by coagulation disorders are reported. Differential diagnostic problems regarding hemorrhages not due to defibrination are discussed. Most recent

findings regarding therapy in these cases are mentioned. It is pointed out that in every case of clinically manifest premature separation of the placenta the uterus should be emptied immediately before plasma fibrinogen level sinks below 100 to 60 mg%. Uterus exstirpation is not recommended in any case, and least when a hemorrhagic diathesis already exists.

Reassessment of Effect of Fatty Meals on Blood Coagulability. Hall, G. H., Brit. med. J. *4986:* 207 (1956).

Phospholipids from Brain Tissue as Accelerators and Inhibitors of Blood Coagulation. Barkhan, P., Dept. Med., Univ. Cambridge, England, Lancet *271:* 234 (1956).

Two substances are isolated from acetone-dried human brain tissue by ethanol extraction and subsequent fractionation. These 2 substances were active in various coagulation tests such as thromboplastin generation test, antithromboplastin test, and Russell viper venom test. One fraction (III) containing mostly phosphatidylserin had coagulation inhibiting effect, the other (V) consisting mostly of phosphatidyl-ethanolamine accelerated coagulation.

Food Lipids and Blood Coagulation. Maclagan, N. F., Dept. chem. Path., Westminster Med. School, London S. W. 1, England, Lancet *271:* 236 (1956).

The coagulation time of normal plasma is more or less significantly shortened by various alimentary fats. The coagulation promoting action seems to be independant of the fat content of the various products. It was in fact proved that pure alimentary fat is completely inactive, and that the coagulation active principle of milk products is probably bound to protein. According to the in vitro findings the coagulation time of control persons was markedly shortened after ingestion of butter but only slightly decreased after margarine.

Große und kleine Blutungen in der inneren Medizin. Bock, H. E., Gross, R., Med. Univ.-Klinik, Marburg/Lahn, Germany, Dtsch. med. Wschr. *81:* 1377 und 1451 (1956).

Glass Surface and Blood Coagulation. Margolis, J., Dept. Path., Radcliffe Infirmary, Oxford, England, Nature (Lond.) *178:* 805 (1956).

Haemorrhage in Association with Dextran Infusion. McKenzie, J. M., Langlands, A. C., Therapeutics Unit, Maryfield Hosp., Dundee, Scotland, Scott. med J. *1:* 323 (1956).

Inversione della riposta emocoagulatoria all'ACTH dopo surrenalectomia monolaterale. Bounous, G., Ist. Clin. Chir., Univ., Pavia, Italy, Minerva cardioangiol. *4:* 563 (1956).

Coagulation Defects in Liver Diseases. Cowling, D. C., Dept. Path., Postgraduate Med. School, London, England, J. clin. Path. *9:* 347 (1956).

Ciclo ovarico e coagulazione del sangue. Paoletti, I., Ist. Provinciale Ospedaliero di Maternità, Bologna, Italy, Riv. ital. Ginec. *39:* 399 (1956).

Recherches sur les altérations hémostatiques provoquées par le dextran. Observations in vitro, in vivo et dans un cas de shock hyperfibrinolytique par dextran. De Nicola, P., Clinique méd., Univ., Pavia, Italy, Sang *72:* 708 (1956).

Erythromycin und Blutgerinnung. Sartori, C., Univ.-Augenklinik, Hamburg, Germany, Medizinische *49:* 1758 (1956).

Fréquence des hémorragies digestives hautes dans les dithèses hémorragiques. Traitement des hémorragies digestives hautes. Vandenbroucke, J., Service Méd. int. B., Univ., Louvain, Belgium, Acta gastro-ent. belg. *19:* 64 (1956).

Effect of a Meal of Eggs and Different Fats on Blood Coagulability. O'Brien, J. R.: Portsmouth and Isle of Wight Path. Serv., England, Lancet *271:* 232 (1956).

The coagulation time of platelet-poor plasma plus Russell viper venom (Stypven-time) was

considerably decreased after ingestion of 50 g of fat, as well as after intake of 2 eggs containing together about 10 g of fat and 3 g of phosphatides.

Weitere Untersuchungen und Überblick über die verschiedenen immunbiologisch bedingten Formen der hämorrhagischen Diathese. Steffen, C., Klin. Labor., Hanusch Krankenhaus, Wien, Austria, Wien. Z. inn. Med. *37:* 452 (1956).

Profilassi delle malattie emorragiche. Baserga, A., Univ., Ferrara, Italy, Minerva med. *47:* 2085 (1956).

Untersuchungen über den Mechanismus der blutgerinnungshemmenden Wirkung des Hirudins. Markwardt, F., Greifswald, Germany, Arch. exp. Path. Pharmak. *229:* 389 (1956).

Les médications hémostatiques générales. Etude Pharmacodynamique et applications thérapeutiques. Roskam, J., Inst. Clin. et Pathol. méd., Univ., Liège, Belgium, J. thér. Paris 249 (1956).

Les hématostatiques généraux. Leurs critères d'activité chez l'animal et chez l'homme. Roskam, J., Inst. Clin. et Pathol. méd., Univ., Liège, Belgium, Journées thér. Paris 127 (1956).

Über den Einfluß des Myokardinfarktes auf einige Gerinnungsfaktoren. Heinecker, R., Lösch, H. W., I. Med. Univ.-Klinik, Frankfurt a. M., Germany, Medizinische 16, 614 (1956).

The authors found that fresh myocardial infarction is followed by increased activity of fibrinogen, factor V and VI, factor VII, and thromboplastin. Highest values are found at the end of the first week following the incidence and again following the 2nd to 3rd week. These results are in favor of anticoagulant therapy in cases of myocardial infarction. As decreased coagulability occurs immediately after the incidence of infarction and often also during the 2nd to 3rd week, and above all in cases with simultaneous severe cardiac insufficiency, dosage of anticoagulants must carefully be controlled.

Beitrag zur Frage der postmortalen Blutgerinnung. Erfahrungen aus der Praxis. Prantl, K., Gerichtlich-Med. Inst. Univ., Zürich, Switzerland, Praxis *45:* 886 (1956).

Prostatic Carcinoma with Hemorrhagic Diathesis. Meuwissen, T., Zaman, C. L., Int. Afdeling R. K., Binnenziekenhuis, Eindhoven, Holland, Ned. T. Geneesk. *100:* 1697 (1956).

The authors report the case of a patient suffering from carcinoma of the prostata with metastases of the liver, spleen, and bone marrow, who had also developped a hemorrhagic diathesis. The importance of an examination of the bone marrow in cases of prostatic carcinoma is discussed.

Action anticoagulante et fibrinolytique de la trypsine par la voie parentérale. Observations expérimentales. Piomelli, S., Schettini, F., Inst. Path. méd., Univ., Naples, Italy, Rev. Hémat. *11:* 378 (1956).

The administration of small doses of trypsin has no significant effect on blood coagulation. Strong doses of trypsin have an anticoagulant effect combined with a destructive activity on proteins pertaining to the coagulation system. This activity seems to be directly proteolytic and not via intravascular coagulation. The fibrinolytic-antifibrinolytic system is not influenced by the administration of the enzyme. It is concluded that the therapeutic use of trypsin is not proved experimentally: Small doses have no effect and large doses exert a very serious toxic effect.

Indications des dérivés du sang dans les syndromes hémorragiques. Revol, L., Croizat, P., 22, quai du Général Serrail, Lyon, Rhône, France, Sang *27:* 39 (1956).

Le alterazioni della coagulazione del sangue nell'epatite virale. Crisalli, M., Cotellessa, G., Ist. Clinica ped., Univ., Genova, Italy, Minerva pediat. *8:* 235 (1956).

Elektronenmikroskopische Befunde bei der Blutgerinnung. (Untersuchungen über einen in der Nähe von Thrombozytenanhäufungen vorkommenden, von der Plasmagerinnung unabhängigen Gerinnungsvorgang im menschlichen Plasma.) Haschè, E., Seeliger, R., Neurochir. Abtlg., Univ. Freiburg i. Br., Germany, Ärztl. Forsch. *10:* 261 (1956).

An immediate spontaneous but limited coagulation can occur in human plasma in the neighbourhood of accumulated thrombocytes even in the presence of anticoagulant substances. By means of the electron-microscope this coagulation is found to be characterized by the union of basic plasma bodies of about 5 μ in diameter to elements of 10 to 15 μ in diameter. These again form fibres and bundles which are larger the closer they are to platelets.

Atherosclerosis and Blood Coagulation. Aspenström, G., Bengtsen, K. K., Med. Klin. II, Sahlgrenska Sjukhuset, Göteborg, Sweden, Nord. Med. *56:* 1319 (1956).

Hypercoagulability as a possible cause of some types of atherosclerosis is discussed. The vascular lining seems to react to most noxious agents in essentially the same way. Thrombotic material as well as other normal or pathological blood constituents precipitated intravascularly have been shown to cause intimal proliferation and narrowing of the vascular lumen with the same appearance as in human atherosclerosis. The simultaneous occurrence of hypercoagulability and factors disposing to atherosclerosis is discussed. Fat meals, hyperlipemia, infections and stress situations all seem to be both atherogenic and to produce a hypercoagulable state. Administration of 3 ml of 40% cream/kg body weight resulted in shortening of whole blood coagulation time and a simultaneous increase of phospholipids involved in thromboplastin generation. The simultaneous drop in platelets reported by others has been confirmed. It is suggested that platelet adhesiveness is increased, that they adhere to vessel walls, and that the platelet aggregates might cause an endothelial proliferation similar to that seen in atherosclerosis. The importance of thrombosis as an accelerator of atherosclerosis is stressed. The possibility of reducing the vascular damage by anticoagulants in hypercoagulable and atherogenic conditions is suggested.

The Use of Buffers in Blood Coagulation Studies. Stormorken, H., Newcomb, T. F., Coagulation Lab., Rikshosp., Oslo, Norway. Scand. J. clin. Lab. Invest. *8:* 237 (1956).

The effect of imidazol, veronal, and tris (hydroxymethyl) aminomethane (Sigma 7—9) buffers were compared in several coagulation systems. At comparable ionic strengths the 3 buffers gave similar results. Buffers used in coagulation work should be adjusted to the same ionic strength as physiological saline. Buffer capacity varied slightly within the actual range (pH 7—8), but not sufficiently to be of practical importance. From the standpoint of allround utility (solubility, cost etc.) the tris (hydroxymethyl) aminomethane buffer is preferable.

Het verband tussen het LE fenomeen en de stolling van het bloed. Vries, S. I. de, Kettenborg, H. K., van der Pool, E. T., Wilhelmina-Gasthuis, Amsterdam, Holland, Ned. T. Geneesk. *100:* 1218 (1956).

For some years it has been known that blood coagulation activates the formation of LE cells. *Lee* thought this activation to be increased by increasing number of circulating platelets. Based on this the authors studied platelet-poor, centrifuged LE plasma and white cell suspension of a patient with thrombocytopenia but found no correlation between platelet number and LE-cell frequency. It was, however, found that the formation of LE-cell is activated by the last coagulation phase, namely the conversion of fibrinogen into fibrin.

Hemorrhagic Diathesis in Poliomyelitis. Bennike, T., Grandjean, L. C., Blegdamshosp., Copenhagen, Denmark, Acta med. scand. *155:* 225 (1956).

During the epidemic of poliomyelitis in Copenhagen it was found that 15% of 349 patients with respiratory paralysis had clinically manifest hemorrhagic diathesis in the form of bleedings in the skin, from mucous membranes, and internal organs, as well as following tracheobronchial aspiration. The bleeding tendency was most pronounced in the most severely affected patients, and occurred especially in the first 2 weeks of illness. The bleeding tendency must be supposed to be attributable to an interplay between the reduced capillary resistance and one or more unknown factors, possibly resulting from the unphysiologic state of many patients during the acute stage of the disease. The etiology of the demonstrated impaired capillary resistance is discussed.

Über die Anwendung der Plasmafraktion I bei unstillbaren Blutungen. Egli, H., Kessler, K., Physiol. Inst., Univ. Bonn, Germany, Dtsch. med. Wschr. *81:* 875 (1956).

In cases of uncontrollable bleeding due to acute deficiency of fibrin, administration of Cohn's fraction I is usually successful. This fraction contains fibrinogen (60%) and factor VIII. Isolation and preparation of this fraction are described in detail. The authors successfully used this fibrinogen concentrate in 10 patients to stop severe hemorrhage of various etiology (postoperatively, oesophagal varices, aplastic anemia, melena in a newborn). Coagulation time in the newborn with melena decreased from 6 mins., to 1 mins., following administration of plasma fraction I.

Plasma déspécifié et coagulabilité sanguine. Kleeping, J., Tanche, M., Inst. Physiol. Faculté de Méd., Lyon, France, Presse méd. *64:* 1494 (1956).

Despecified bovine plasma has been used clinically as a substitute for human plasma. The effect of this plasma on blood coagulation has been studied, and it was found that it induced coagulation disorders. One of them occurs immediately following the injection and consists of a marked increase of coagulation time caused by dilution of blood volume. The other is secondary and progressive; it reaches its maximum after 24 hours and consists in partial or total incoagulability of the blood. This incoagulability decreases rapidly and is usually normalized within 48 to 60 hours. The mechanism of this secondary incoagulability remains unexplained. It is improbable that the quantities of formol and urotropine in the plasma are responsible.

Über die hämostyptische Wirkung der Plasmafraktion I nach Cohn. Imdahl, H., Egli, H., Kessler, K., Chir. Klinik, Univ., Germany, Münch. med. Wschr. *98:* 1323 (1956).

The authors report the administration of Cohn's fractions I in 11 cases of bleeding following major surgery. Plasma fraction I is is poor in inhibitory factor and in profibrinolysin, contains about 60% fibrinogen and large amounts of factor VIII. Fracton I excerted a significant hemostyptic effect in all cases described, the effect was not attributable to fibrinogen substitution only. The clinical success obtained are in favor of further clinical use of fraction I as a hemostatic agent.

Action des enzymes protéolytiques sur le sang total „in vitro" modifications de facteurs de coagulation et du complément. Alagille, D., Soulier, J. P., Centre Nat. Transfusion Sanguine, Paris 15e, France, Sem. Hôp. (Paris) *32:* 355 (1956).

The in vitro action of proteolytic enzymes was studied by mixing the enzymes concerned with oxalated blood and by testing, after a 4 hours' incubation, the following coagulation factors: factors VIII, and IX, prothrombin, factors V and VII, as well as complement. The data obtained with trypsin were equivocal, owing to the coagulant activity of this enzyme under certain conditions. The most sensitive factors were factor V and factor VIII. Complement was only destroyed at high concentrations of the enzymes.

Experimentelle Untersuchungen zur Frage der Blutungszeitveränderung durch Salizylate. Hofmann, H., Neugasse 23, Jena/Thür., Germany, Med. Mschr. *10:* 84 (1956).

Animal experiments showed that a significant prolongation of the bleeding time after administration of salicylates occurs only if toxic doses are given. The influence of sodium salicylate is more pronounced after oral than after subcutaneous administration. 2-methyl-1,4-naphtohydrochinon prevents prolongation of bleeding time after salicylate medication.

Die instrumentale Registrierung der Blutgerinnung. Szirmai, E., Gerinnungsphysiol. Labor IV Arpad-ut 126, Budapest, Hungary, Zbl. Chir. *81:* 1218 (1956).

The author discusses the variety of the more important instruments for the registration of blood coagulation.

La fonction hémostatique du foie. Place des protéines de la coagulation dans l'exploration hépatique. Alagille, D., Centre Nat. de Transfusion Sanguine, Paris, France, Rev. franç. Etudes clin. and biol. *1:* 79 (1956).

The role of the liver in the synthesis of most of the globulins which take part in coagulation is established or has been postulated. The relationship of liver function to plasma levels

of antithrombin, prolysin, antihemophilic factor A and B and factor X is not yet clear and cannot be used clinically for the diagnosis of hepatic diseases. On the other hand, levels of fibrinogen, prothrombin, proconvertin and proaccelerin are influenced by hepatic function, and may lead to recognition of disturbed liver function. However fibrinogen determination and measure of the prothrombin complex (Quick) are only very insensitive indices of hepatocellular function. The differential concentrations of prothrombin, proconvertin and proaccelerin, on the other hand, are of great diagnostic and prognostic value.

Der Einfluß der Lebertotalextrakte bei der akuten und chronischen Vergiftung mit Tetrachlorkohlenstoff, insbesondere auf den Prothrombinspiegel und die Faktoren V und VII. Fumarolo, D., Inst. Allgem. Path., Univ., Bari, Italy, Z. ges. inn. Med. *11:* 571 (1956).

Rabbits were exposed to acute and chronic poisoning with CCl_4. The behaviour of prothrombin, factor V and VII was studied in these animals, whereby one group was simulatenously treated with Ripason (liver extract). The group with untreated poisoning showed significant decrease of the coagulation factors studied, whereas no alterations of coagulation factors occurred in the liver-extract-treated group.

Die humoralen Gerinnungsfaktoren bei Anämien. Maurer, H., Kiefer, E., Med. Univ.-Klinik, Mainz, Germany, Folia haemat. (Lpz.) *74:* 36 (1936).

Ricerche sperimentali sull'influenza del testosterone sulla coagulazione del sangue. Fumarolo, D., Ist. Patol. Generale, Univ., Bari, Italy, Riv. Biol. *48:* 159 (1956).

Coagulation studies were carried out in rabbits treated with testosterone. During administration of this drug the thrombelastogram showed a marked increase of the elasticity index (m.a.) and a reduction of r and K. Coagulation spontaneously normalized 10 days after discontinuation of testosterone administration. It is concluded that testosterone treatment results in an increase of activity of tissue thromboplastin and of platelet thromboplastic component.

Eritromicina e fattori della coagulazione. Modica, F., Fumarolo, D., Ist. Patol. Generale, Univ., Bari, Italy, Arch. Sci. biol. (Bologna) *40:* 457 (1956).

Rabbits were given erythromycin (isolated from Streptomyces erythraeus) in doses of 25 mg/kg every 8 hours for 8 days either orally or intravenously. In both groups a secure and constant thromboplastic effect was noted.

La thrombelastographie et ses applications cliniques. Benhamou, E., Griguer, P., Alger, Presse méd. *64:* 2157 (1956).

Based on the study of over 800 thrombelastograms the authors come to the conclusion that this technic is simple, easy and very useful for studying hemophilia, hypoconvertinemia, afibrinogenemia, arterial and venous thrombosis, spontaneous hypocoagulabilities, hypocoagulability caused by anticoagulants, cirrhosis, and many other coagulation disorders. Associated with all other coagulation tests it permits better control of therapy in thrombosis.

Rilievi trombelastografici nel bambino normale. Fumarolo, D., Li Moli, S., Ist. Patol. Generale, Univ., Bari, Italy, Haematologica. *41:* 78 (1956).

Thrombelastographic studies were carried out in the normal child. During the first year of life the thrombelastogram resembles that of a thrombophilic disease, in the following years it becomes similar to that of healthy adults. The authors assume that in the first stages of life platelets have some particular characteristic causing thrombus elasticity and maximum amplitude of thrombelastogram to increase.

Rilievi trombelastografici nelle apatopatie spermentali. Capaldo, A., Fumarolo, D., Ist. Patol. Generale, Univ., Bari, Italy, Arch. Sci. biol. (Bologna) *40:* 445 (1956).

Two groups of rabbits were treated respectively with chloroform 200 mg/kg till they died, and with phosphor 4 mg/kg till they died. Thrombelastographic studies were carried out. Alterations were noted in all characteristic thrombelastographic values, indicating the severe coagulation deficiency following experimental liver damage.

Rilievi trombelastografici nel neonato a termine e nell'immaturo. Fumarolo, D., Li Moli, S., Ist. Patol. Generale, Univ., Bari, Italy, Haematologica. *41:* 68 (1956).

The authors carried out thrombelastographic studies in full-term newborns and in immature babies, furthermore they determined recalcification time, prothrombin, factor V and VII. The full-term infant showed a moderate prolongation of reaction time r with normal other thrombelastographic values, besides a modest decrease of prothrombin and factor VII. The immature showed a marked, constant increase of r, k, and thrombus elasticity alterations besides marked deficiency of prothrombin, which is considered responsible for the thrombelastographic alterations.

Sull'interpretazione dei quadri similemofilici da anticoagulanti indiretti (cumarinici, indan- Patol. Generale, Univ., Bari, Italy, Haematologica *41:* 85 (1956).

The genetic mechanism of the hemophilia-like aspects occurring in anticoagulant therapy has been analyzed by administration of high doses of anticoagulants to animals and studying the thrombelastographic and histologic modifications. Results: constant prolongation of reaction time and of thrombus formation rate, slight decrease of maximal amplitude. Histologic patterns: liver and kidney alterations with simple vacuolar, turbid and fatty degeneration or necrosis and atrophy with disappearance of normal structure and parvicellular infiltrations. It is concluded that this thromeblastographic behaviour resembles more that of hemophilic or heparinized blood than that of thrombocytopenia, as is also indicated by the complex deficiency of plasmatic factors and the histological pattern.

Rilievi trombelastografici nei difetti di coagulazione dell'infanzia. Fumarolo, D., Li Moli, S., Ist. Patol. Generale dell'Univ. Bari, Italy, Haematologica *41:* 591 (1956).

The authors describe thrombelastographic results obtained in some hemorrhagic diseases of infancy (hemophilia, Werlhof's disease, secondary thrombocytopenia, Willebrand-Jürgens thrombopathia, peliosis rheumatica, acute hepatitis). The findings are discussed. Thrombelastographic research was found to be most valuable and demonstrative in hemophilia and in diseases with deficient number or function of platelets.

Problems in Bleeding Disorders. Stefanini, M., Dept. Med., Tufts Coll., Med. School, Boston, Mass., USA, Postgrad. Med. *19:* 420 (1956).

New Theory of Interference in Clotting Mechanism by Abnormal Plasma proteins. Henstell, H. H., Feinstein, M., Inst. Med. Research, Cedars of Lebanon Hosp., Los Angeles, Calif., USA, Science *123:* 1118 (1956).

Immediate Effects of Rapid Hemorrhage on Hemodynamics in the Dog. Waud, R. A., Waud, D. D., Dept. Pharm., Univ. Western Ontario Med. School, London, Ont., Canada, Canad. J. Biochem. Physiol. *34:* 827 (1956).

Blood Coagulation after a Fat Meal. Buzina, R., Leys, A., Lab. of Physiol. Hygiene, Univ. of Minnesota, Minneapolis, Minn., USA, Circulation *14:* 854 (1956).

Plasma Lipids and Coagulation of Blood. Sohar, E., Rosenthal, M. C., Adlersberg, D., New York, USA, Clin. Chem. *2:* 270 (1956).

The viper venom preparation „Stypven" decreases the prothrombin time of healthy individuals after a fatty meal, and of patients with hyperlipemia. Thrombocytes had a similar action. It is suggested that triglycerides accentuate the effect of thromboplastin.

The Preservation of Coagulation Factors in Human Plasma. Fantl, P., Marr, A. G., Baker Med. Research Inst., Melbourne, Australia, Aust. J. exp. Biol. med. Sci. *34:* 433 (1956).

The prolonged thrombin clotting time of sterile human oxalated or citrated plasma stored in open vessels at room temperature is not due to an increase of antithrombin, to heparin-like substances, nor to loss of thrombin-accelerating factors. It is due to a physical change of the surface structure of fibrinogen resulting from storage at an alkaline pH. Normal fibrinogen reactivity can be preserved by storage at pH 6.1 to 6.5. The losses of proaccelerin and anti-

hemophilic factor during storage are also due to hydroxyl ions. The former can be partly and the latter almost completely prevented by storage at a pH of 6.1 to 6.5. Either mineral acid or carbon dioxide can be used for the preservation of the plasma clotting factors because the process is independent of oxygen. For transfusion purposes storage of plasma in carbon dioxide is suggested.

The Hemostatic Defect of Uremia. I. Clinical Investigation of 3 Patients with Acute Post-Traumatic Renal Insufficiency. Larrain, C., Adelson, E., Dept. Hematol. Walter Reed Army Inst. of Research, Walter Reed Army Med. Center, Washington D. C., USA, Blood *11:* 1059 (1956).

The abnormalities of the hemostatic mechanism in 3 consecutive patients with acute renal insufficiency have been studied. In every case a prolonged clotting time in silicone and a prolonged bleeding time were found. In cases defective prothrombin consumption was also present. Coagulation studies revealed no significant deficiency of plasma factors, no serious deficiency of platelet number or function and no well-defined anticoagulant effect to explain the changes. All 3 cases developed significant clinical bleeding at some time during the course of the benal insufficiency.

II. Investigation of Dogs with Experimentally Produced Acute Urinary Retention. Larrain, C., Langdell, R. D., Walter Reed Army Med. Center, Washington D. C., USA, Blood *11:* 1067 (1956).

Acute urinary retention was produced in 15 dogs by ligation of the ureters. Studies of the hemostatic mechanism were made as the uremia progressed. All animals developed a coagulation defect characterized by abnormally long clotting time of whole blood in siliconized glassware. Other indices of coagulation efficiency were found to be normal or only slightly impaired. It is not clear whether the basic defect is a lack of an essential clotting factor or an excess of an inhibitor. Urea does not seem to be the cause of the defect. The data suggest that the duration of urinary retention is important as the degree of azotemia.

Bleeding Tendency in Uremia. Lewis, J. H., Zucker, M., Ferguson, J. H., Dept. Physiol., Univ. N. Carolina, Chapel Hill, N. C., USA, Blood *11:* 1073 (1956).

Hemostatic function studies were carried out in 12 patients with elevations in blood of non-protein nitrogen (or urea). 11 were found to suffer from one form of platelet abnormality. Mild thrombocytopenia was present in 3 and thrombocytopathia in 8. Four patients showed deficiency of 2 or more of the plasma factors: prothrombin, proconvertin, proaccelerin or PTC.

Blood Disorders Caused by Drug Sensitivity. Wintrobe, M. M., Cartwright, G. E., Arch. int. Med. *98:* 559 (1956).

The authors present a review of the literature on agents occasionally associated with the development ob blood dyscrasias. There appear to be several mechanisms whereby such dyscrasias may develop. As yet no means has been devised whereby the potential toxicity of an agent or the sensitivity of an occasional person may be detected.

The Diagnosis of Hemorrhagic States in Childhood. Colebatch, J. H., Wilson, B. M., Royal Children's Hosp., Melbourne, Australia, Med. J. Aust. *43:* 226 (1956).

Does a Hemorrhagic Tendency exist in Patients Under Isoniazid-Streptomycin Treatment? Vysniauskas, C., Molly Stark Hosp., Canton, Ohio, USA, Dis. Chest *29:* 533 (1956).

287 patients with pulmonary tuberculosis were studied in order to determine whether isoniazid-streptomycin increases the hemorrhagic tendency. Apparently the drug definitely decreased the incidence of hemoptysis in tuberculous patients. No other bleeding attributable to chemotherapy was noted during the study. There was a normal incidence of operative and postoperative bleeding. Laboratory study of clotting, bleeding, and prothrombin time and of platelet counts showed variations within physiological limits. In 12.5% of the patients with increased capillary fragility chemotherapy could be considered as one of the possible factors. Further studies are suggested.

Problems in the Coagulation of Plasma by Staphylocoagulase. Tager, M., Dept. Bacteriol. and Immunol., Emory Univ., Emory Ga., USA, Ann. N. Y. Acad. Sci. *65:* 109 (1956).

The properties of higly purified staphylocoagulase are presented. The evidence for the identification of the coagulase-reacting factor of plasma is discussed. On the basis of studies with highly purified preparations it is concluded that CRF activity is linked with the prothrombin molecule, but that smaller molecules, devoid of prothrombin activity but presumably derived from prothrombin, are also effective in reacting with coagulase.

Some Effects of Ultrasonic Energy Upon Blood Coagulation. Axelrod, S. L., Throndike Memorial Lab., Boston City Hosp., Boston, Mass., USA, J. Labor. and clin. Med. *48:* 690 (1956).

High-frequency sound waves provided an effective means of lysing platelets without altering the accelerator, antiheparin, or vasoconstrictor properties of the platelet constituents which were released. Suspension of platelets lysed by sonic energy, exhibited the same altered properties as did platelet suspensions lysed by other technics. No differences between normal and hemophilic platelets were observed. The activity of commercial rabbit brain thromboplastin was diminished by sonic energy. Sonic energy induced a coagulation defect in plasma, which seemed, primarily, to be due to partial destruction of labile factor and AHG, and possibly to the formation of an anticoagulant. Accelerator activity was diminished in sonically treated serum but SPCA generation was unaffected, as were prothrombin and thrombin. The effect on fibrinogen was variable.

Studies on the Clot-Promoting Activity of Glass. Shafrir, E., de Vries, A., Dept. clin. Research, Hebrew Univ.-Hadassah Med. School, Jerusalem, Israel, J. clin. Invest. *35:* 1183 (1956).

The effect of glass on the evolution of clot-promoting activity in „platelet-free" plasma was examined. Data are presented on the influence of the amount of glass, of the duration of contact, of the temperature, and of the method of decalcification of the plasma on this process. Contact of glass with isolated platelets or with platelet factors liberated by freezing and thawing, did not result in increase of their clotting activity. Contact with glass induced a clot-promoting activity in oxalated hemophilia A plasma, free of platelets, prothrombin, PTC, proconvertin, proaccelerin and fibrinogen. Attempts to demonstrate the adsorption of a plasma clotting inhibitor onto glass were unsuccessful. Contact with large area of glass was shown to remove some prothrombin from oxalated plasma.

A Simplified Technic for Performing Blood Coagulation Tests. Peeters, H., Lab., St. Jans Hospitaal, Brugge, Belgium, Amer. J. clin. Path. *26:* 823 (1956).

Blood coagulation tests may be performed conveniently in series of cupules that are pressed into a sheet of inexpensive, impermeable, nonwettable polyvinyl plastic that will float on the surface of the water-bath. Statistical analysis of the results from tests on normal persons indicates that the method is reliable.

The Effect of Trypsin on Blood Coagulation and the Mechanism of its Action. Stormorken, H., Med. Dept. A, Univ. Med. School, Oslo, Norway, J. Lab. clin. Med. *48:* 519 (1956).

Trypsin is able to clot decalcified plasma and to convert „purified" prothrombin to thrombin. Calcium and cephalin accelerate this activity of trypsin. Cephalin requires calcium for its effect. The activity of a trypsin-cephalin-calcium mixture depends on proaccelerin, but not on the antihemophilic factors A and B, nor on factor VII. The action of trypsin on blood coagulation is similar to that of Russell's viper venom, but less specific. Like the latter, trypsin together with calcium, cephalin and proaccelerin constitutes a prothrombin-converting principle similar in effect to plasma prothrombinase (plasma thromboplastin) and to tissue prothrombinase (the product of tissue thromboplastin, calcium, and factor VII and V), though less active.

The Effects of Various EDTA Complexes on Coagulation. Leikin, S., Bessman, S. P., Dept. Pediatrics, D. C. General Hosp., Washington, D. C., USA, Blood *11:* 916 (1956).

Disodium Ethylenediamine Tetraacetate (EDTA) incubated with oxalated plasma results in a prolongation of the one-stage prothrombin time. This is due to a destruction of Ac-globulin or the inhibition of its production from a precursor stage. A marked prolongation of the prothrombin time occurred on incubation with cu nie, ferrous, stannous, cobaltous, and

magnesium EDTA, but manganous, zinc and nickel EDTA produced no prolongation. This would support the concept that a metal ion may be concerned with the maintenance of Ac-globulin or its conversion into an active form.

Studies of Hemostasis in the Ehlers-Danlos Syndrome. Frick, P. G., Krafchuck, J. D., Univ. Minnesota Hosp., Dept. Med. and Div. Dermat., Minneapolis 14, Minn., USA, J. invest. Derm. *26:* 453 (1956).

Tests of hemostasis have been performed on 3 patients with Ehlers-Danlos syndrome, who showed easy of the skin, and on members of the families of 2 of them. A positive Rumpel-Leede test was consistently found as the only hemostatic abnormality. All known plasma clotting factors were present in normal amounts and there were no qualitative or quantitative deficiency of platelets. The increased capillary fragility is discussed in relation to the histopathological collagen abnormality found in this disease.

Hemorrhagic Diathesis in Patients with Carcinoma of the Prostate. Prout, G. R., 444 E. 68th Street, New York, N. Y., USA, J. amer. med. Ass. *160:* 840 (1956).

b) Fibrinogen (Factor I), Fibrin, Fibrinolysis

Die Beziehung des fermentativen Fibrinabbaues zur Fibrinreifung. Bierstedt, P., Chir. Klinik, Städt. Krankenhaus, Friedrichshain, Berlin, Germany, Hoppe-Seyl. Z. physiol. Chem. *305:* 158 (1956).

The optimum substrate for fibrinolysin is a qualitatively and quantitatively fully mature fibrin. As a result of coagulation the immature substrate fibrinogen attains an optimal enzyme specificity after acquiring a certain degree of elasticity following the conversion into fibrin network. Between the two clotting points the substrate goes through a non-receptive phase which in vitro prevents lysis of fibrin in statu nascendi. Attention is drawn to the possible physiologic significance of this fact. Acceleration of fibrin degradation and progressive increase of the enzymatic attack on fibrin are the 2 possibilities whereby the total fibrinolytic process can be accelerated by increasing enzyme activity. Fibrinolysin influences fibrin structure which results in reduced elasticity of clot by way of change of fibrin structure and not by reduction of fibrin formation.

Die Störung der Blutgerinnung bei vorzeitiger Plazentalösung. Roemer, H., Beller, F. K., Frauenklinik, Akad. Med. Forschg., Justus-Liebig-Hochschule, Gießen, Germany, Geburts- u. Frauenheilk. *16:* 8 (1956).

The authors describe 2 cases of abruptio placentae with acute afibrinogenemia. Different theories exist on the origin of this afibrinogenemia: 1. circulating thromboplastin originating from the site of lesion, 2. fibrinogenolysis, and 3. deficient fibrinogen formation due to liver damage. Determination of coagulation factors is very important in these cases, and the authors consider thrombelastography the most reliable method. The therapy of these conditions is discussed: 3 possibilities exist for the normalization of afibrinogenemic state: 1. interruption of the thromboplastin flow from the site of lesion, 2. blocking of thromboplastin and the tryptic ferment, and 3. administration of lacking fibrinogen. The various aspects of these therapeutic means are evaluated.

The Inhibition of Clot Lysis by Corticotrophin. Kwaan, H. C., McFadzean, A. J. S., Dept. Med. Univ. Hongkong, Lancet *270:* 136 (1956).

The authors investigated the influence of stimulation of the suprarenal cortex on the lysis of clots produced experimentally in rabbits. Before the production of thrombosis and throughout the period of observation one group of rabbits were given corticotrophin the other served as controls. In each of the controls the clot disappeared in an average of 20 hours. In the treated rabbits the thrombus persisted until the experiment was terminated by the removal of thrombosed segments for histological examination. It is suggested that the clots in the veins of the control rabbits stimulated the production of fibrinolysin, and that corticothrophin inhibited this production. It is considered that the disappearance of fibrinolytic activity is a possible

factor in the development of portal vein thrombosis in cirrhosis of the liver after splenectomy or during corticotrophin therapy. The inhibition of fibrinolysis by suprarenal cortex activity may be a factor in determining the persistence of mural thrombi, and these observations may have a value in the investigation of atherosclerosis.

L'application thérapeutique du fibrinogène humain. Les fibrinoses aigues obstétricales. Lewin, J., Centre Nat. Transfusion Sanguine, Paris 15, France, Rev. mens. Médicin Prat. *6:* 1663 (1956).

The Fibrinolytic Activity of the Human Endometrium. Albrechtsen, O. K., Biol. Inst., Carlsberg Found., Copenhagen, Denmark, Acta endocrin. *23:* 207 (1956).

Human endometrium contains an activator of plasminogen. The stability of the activator at different temperatures and pH values shows it to be a normal tissue activator. Normal endometrium in the secretory stage and endometrium from women suffering from proliferative bleeding and endometrial hyperplasia contain large amounts of the tissue activator. Decidual tissue from normal pregnancies gives negative results. Placenta is completely inactive. Decidual tissue from spontaneous abortions is apparently active. No inhibitory compounds similar to the inhibitor from ox lung tissue were found in any of the samples. A correlation between the presence of large amounts of the tissue activator and the occurrence of uterine hemorrhage is demonstrated.

The Fibrinolytic Activity of Menstrual Blood. Albrechtsen, O. K., Biol. Inst., Carlsberg Found., Copenhagen, Denmark, Acta endocr. (Kbh.) *23:* 219 (1956).

Human menstrual discharge contains an activator of plasminogen, a fibrinolytic enzyme, large amounts of a precursor of plasminogen activator, and no plasminogen. The activator of plasminogen is similar to the one present in the human endometrium and in other tissues. It differs in stability from the plasminogen activator formed in blood by addition of streptokinase. The presence of this activator explains the absence of fibrin in normal menstrual discharge and is the cause of the fluidity of menstrual blood.

Untersuchungen zur Verwertbarkeit der Plasmaelektrophorese auf Filterpapier mit vergleichender Kjeldahlometrischer Fibrinogenbestimmung. Scheiffarth, F., Berg, G., König, E., Med. Univ.-Klinik, Erlangen, Germany, Klin. Wschr. *34:* 1282 (1956).

The accuracy of fibrinogen determination by means of plasma electrophoresis on filter paper has been tested. In 133 cases fibrinogen was determined by the difference of parallel serum and plasma electrophoresis. The conformity of all other fractions was statistically secured. In 55 cases the comparison of electrophoretic and kjeldahlometric method of fibrinogen determination showed a strictly linear relation. The usefulness of plasma electrophoresis on filter paper is thus confirmed.

Serum Proteins and Fibrinolysis in Polycythemia vera. Bjørkman, S. E., Laurell, C. B., Nilsson, I. M., Dept. int. Med., Malmö General Hosp., Malmö, Sweden, Scand. J. clin. Lab. Invest. *8:* 304 (1956).

The fibrinogen content is normal in polycythemia vera and secondary polycythemia. Plasma from 19 patients with polycythemia vera contained an active fibrinolytic factor. In contrast, plasma from 3 patients with secondary polycythemia showed no fibrinolytic activity.

Modifications „in vivo" des facteurs de coagulation dans les fibrinolyses. Valeur du déficit en proaccélérine pour le diagnostic des protéolyses frustes ou latentes. Soulier, J. P., Alagille, D., Larrieu, M. J., Centre Nat. Transfusion Sanguine, Paris, France, Sem. Hôp. (Paris) *7:* 359 (1956).

The authors studied the behaviour of coagulation during acute and latent fibrinolysis in order to determine the responsable factor of proteolysis in vivo. During acute postoperative fibrinolysis in addition to lysis of fibrinogen a decrease of complement and coagulation factors, in particular proaccelerine is observed. During fibrinolysis Quick coagulation time is increased, proaccelerine decreased, whereas total fibrinogen remains normal. Fibrinolysis occurs during surgical interventions of the thorax, during abortus, sepsis, purpura fulminans, and prostatic cancer. Polyglobulia and thrombocythemia belong to the group of latent proteolysis with

discrete increase in Quick's time and in proaccelerine time. It is concluded that decrease of proaccelerine is the most sensitive and stable indication of proteolysis, although it may have another reason such as liver disorder or circulation of a spontaneous anticoagulant of the heparin type.

Fibrinogenbestimmung mittels Papierelektrophorese. Berkes, I., Berkes-Tomasevic, P., Kalpakdzijan, M., Biochem. Inst., Med. Fakultät, Skopje, Jugoslavia, Schweiz. med. Wschr. *86:* 909 (1956).

It is possible to determine fibrinogen levels by means of paper electrophoresis. Compared to other precipitation methods the differences in 91% of the analyses is below 0.1%. Statistical analyses show that the determination is at least as accurate with fibrinogen than with other serum proteins determined by means of paper electrophoresis.

Hypofibrinogenaemia in Pregnancy: Report of a Case. Johnstone, J. M., McCallum, H. M., Dept. Path., Univ. and Western Infirmary, Glasgow, Scotland, Scott. med. J. *1:* 360 (1956).

A case of hypofibrinogenemia is reported developing in abruptio placentae: many fibrin deposits were found in the renal glomerular capillaries as well as in the pulmonary vessels, and this unusual distribution of the deposits was reproduced in rabbits by intravenous thromboplastin injections. The fibrin deposits in the vessels are thought to be the results of intravascular blood coagulation rather than local thrombosis.

Eine neue Fibrinogenbestimmung durch Invertseifentitration. Gräf, W., Kimbel, K. H., Med. Univ.-Klinik, Erlangen, Germany, Hoppe-Seyl. Z. physiol. Chem. *304:* 273 (1956).

Two new methods for the determination of fibrinogen in plasma by invert soap titration are described. In one method, for clinical purposes in particular, the fibrin clot obtained by recalcification is dissolved in 2n NaOH and the protein content titrated with a 0.1% invert soap solution. The second method includes a photometric determination but allows exact fibrinogen determination in 0.1 cc of plasma or serum.

Titolazione del potere antifibrinolitico del siero umano: descrizione di una nuova metodica. Bozzo, A., Piomelli, S., Schettini, F., Ist. Patol. Spec., Napoli, Italy, Riv. Ist. sieroter. ital. *31:* 362 (1956).

Sur quelques propriétés du fibrinogène oxydé. Structure du caillot. Pouvoir anticoagulant. Burstein, M., Lewi, S., Guinand, A., Centre Nat. Transfusion Sanguine, Paris, France, Rev. Hémat. *11:* 503 (1956).

Fibrinogen partially oxidated by a peroxide solution after coagulation forms a clot which differs from the control clot in so far as it is much more sensitive regarding alterations of pH. At higher concentrations peroxide makes fibrinogen incoagulable and this fibrinogen has the property of prolonging thrombin time of normal fibrinogen.

Acute Fibrinogen Deficiency in Pregnancy: Diagnosis and Treatment. Hjort, P., Dept. Med., Rikshosp., Oslo, Norway, T. norske Laegeforen *76:* 756 (1956).

Acute fibrinogen deficiency in pregnancy is a rare complication that is dangerous to life. The patient's fate depends on early diagnosis and prompt treatment. Fibrinogen deficiency can be established immediately by determining the thrombin coagulation time. The degree of fibrin deficiency can be measured by the modified Schneider dilution test. Treatment of grave cases requires administration of fibrinogen, which should be available in all major hospitals.

Das Verhalten der Fibrinolyse unter der Geburt und post partum. Niesert, H. W., Univ.-Frauenklinik, Rostock, Arch. Gynäk. *187:* 144 (1956).

Pathogenese und Therapie der akuten Defibrinierung unter der Geburt. Niesert, H. W., Univ.-Frauenklinik, Rostock, Germany, Ärztl. Wschr. *11:* 805 (1956).

The author presents a review of the recent theories on pathogenesis and therapy of acute defibrination during parturition.

Slow Hypofibrinogenaemic Action of Adrenaline and Related Substances. Henriques, S. B., Inst. Butantan, Sao Paolo, Brazil, J. Pharm. a Chemother. *11:* 99 (1956).

Untersuchungen über Fibrinolyse und mögliche Schädlichkeit des Serothorax nach Pneumonektomie. Löhr, B., Laqua, H., Chir. Univ.-Klinik, Heidelberg, Germany, Chirurg *27:* 49 (1956).

Sur le pouvoir antithrombinique du fibrinogène de poule. Burstein, M., Guinand, A., Centre Nat. Transfusion Sanguine, Paris, France Sang *27:* 940 (1956).

Isolated chicken fibrinogen was found to delay the coagulation of human plasma with added thrombin.

Experimentelle Untersuchungen über die Identität freier und gebundener Koagulase. Jacherts, D., Hygiene Inst., Univ., Tübingen, Germany, Z. Hyg. Infektk. *142:* 502 (1956).

Comparative Hyperfibrinogenemic Action of D- and L-Adrenaline. Mandelbaum, F., Lab. of Biochem., Inst. Butantan, C. P. 65, Sao Paolo, Brazil, Nature (London) *178:* 363 (1956).

Foetal Death in Utero with Hypofibrinogenemia. Jennison, R. F., Walker, A. H. C., St. Mary's Hosp. Manchester, England, Lancet *271:* 607 (1956).

Studien über Fibrinstruktur im Tropfentest. Dihlmann, W., Inn. Abtlg., Kreiskrankenhaus Wanzleben, Bahrensdorf, Germany, Dtsch. GesundhWes. *11:* 1316 (1956).

Action remarquable du fibrinogène intraveineux dans une afibrinogénémie aigue obstétricale. Battle, R., 8, place Gambetta, Perpignan, France, Sang *27:* 80 (1956).

The author describes a typical case of acute afibrinogenemia caused by delivery following prolonged retention of a dead fetus. Severe hemorrhage occurred with total incoagulability of blood containing a fibrinolysin. The injection of 6 g of human fibrinogen immediately and definitely interrupted the bleeding.

Fibrinolisi e vascolopatie trombotiche. Crolle, G., Ciancaglini, L., Ist. Patol. Med., Univ., Torino, Italy, Minerva med. *47:* 714 (1956).

After a short review of current methods of determination of fibrinolysis the authors report their results concerning fibrinolysis in 25 patients with peripheral thrombosis and in 13 with myocardial infarction. Almost none of the patients revealed fibrinolysis not even during anticoagulant therapy. Only in some cases of coronary thrombosis a slight increase of fibrinolysis was found. The data presented confirm the necessity of increasing the fibrinolytic capacity of blood for an efficient treatment of thrombosis.

L'influenza dell'adrenalina sulla fibrinolisi. Giacomazzi, G., Ist. Patol. Spec. Med., Univ., Milano, Italy Policlin. *63:* 855 (1956).

If epinephrine or norepinephrine are added to oxalated plasma before recalcification, fibrinolysis is inhibited in cases with spontaneously high fibrinolytic activity, whereas in cases with little fibrinolytic activity it is increased. Whenever epinephrine or norepinephrine are added to plasma after coagulation the result is an inhibition of fibrinolysis.

Untersuchungen zur Frage eines fibrinolytischen Fermentes in der Plazenta. Niesert, H., Bachmann, F., Univ.-Frauenklinik, Rostock, Germany, Zbl. Gynäk. *78:* 649 (1956).

Vergleichende Untersuchungen der modernen quantitativen Plasma-Fibrinogen-Bestimmungsmethoden. Hirsch, A., Cattaneo, C., Lab. Chimica biol., Inst. C. Forlanini, Univ. Roma, Italy, Hoppe-Seyl. Z. physiol. Chem. *304:* 53 (1956).

Fibrinolytic and Coagulant Activities of Certain Snake Venoms and Proteases. Didisheim, P., Lewis, J. H., Dept. Med., Univ. Pittsburgh Med. School, Pittsburgh., O., USA, Proc. Soc. exper. Biol. (N. Y.) *93:* 10 (1956).

Of the 16 snake venoms studied, 11 actively lysed human blood clots. However, only one of these, C. basiliscus, was devoid of thrombic, hemolytic, and hemagglutinating properties. This venom was fibrinolytic as well as fibrinogenolytic. The possible therapeutic use of certain venoms as dissolving agents for intravascular clots presents a theoretical advantage over most other fibrinolytic agents in that their fibrinolytic activity is not readily inhibited by human serum. Fractionation of a pure fibrinolytic principle may be possible.

Coagulase Activity in vivo. Smith, D. D., Johnstone, J. M., Dept. Bacteriol., Univ., Glasgow, Scotland, Nature (London) *178:* 982 (1956).

The Biological Significance of Fibrinolysis. Astrup, T., Biol. Inst., Carlsberg Found., Copenhagen, Denmark, Lancet *271,* 565 (1956).

The author presents a survey of the fibrinolytical system and the physiology of fibrinolysis with 46 references.

Heat Changes During the Clotting of Fibrinogen. Laki, K., Kitzinger, C., Nat. Inst. of Arthritis and Metabolic Dis., Nat. Inst. of Health, Bethesda, Md., USA, Nature *178:* 985 (1956).

Hypofibrinogenemia in Pregnancy and the Puerperium. Kinch, R. A. H., Dept. Obst. and Gynecol., Univ., Toronto, Ontario, Canada, Amer. J. Obstet. Gynec. *71:* 746 (1956).

Les syndromes hémorragiques obstétricaux avec défaut de coagulation du sang par défibrination. Leroux, M., Nantes, France, Gynéc. et Obstét *55:* 357 (1956).

Fibrinolisi e anticoagulanti. Giacomazzi, G., Massari, N., Ist. Patol. Spec. Med., Univ., Milano, Italy, Policlin. *63:* 241 (1956).

When heparin is injected in medium doses to patients with thrombosis, it causes an increase of fibrinolysis. This increase is not directly proportional to the anticoagulant power developed by heparin. A direct relation between the speed of thrombolysis and the fibrinolytic activity has been noticed in thrombosis of the central retinal vein. In the same subjects, treated with phenylindanedione the initial lysis increased proportionally to the degree of hypoprothrombinemia, but when prothrombin sank below 10%, the time of the total lysis of the clot was significantly lengthened.

Action des enzymes protéolytiques sur le sang total "in vitro". Modifications des facteurs de coagulation et du complément. Alagille, D., Soulier, J. P., Centre Nat. Transfusion Sanguine, Paris 15e, France, Sem. Hôp. Paris *32:* 7 (1956).

Modifications of antihemophilic globulin A and B, of proaccelerin, of proconvertin, of prothrombin and of the complement were studied in the presence of various dilutions of trypsin, of fibrinolysin, and of streptokinase, and then compared to those of fibrinogen. The antihemophilic factor A and proaccelerin are by far the most sensitive regarding proteolysis. The observations made in vitro indicates explanations of abnormal observations in vivo in cases of fibrinolysis, for which the authors propose the name of proteolysis. The sensitivity of proaccelerin towards lysis makes this factor a valuable indicator of latent lysis.

Afibrinogenemia. Murphy, C. J., Picot, H., Thompson, H. G., Amer. J. Obstet. Gynec. *72:* 1197 (1956).

Fibrinogen Concentration in Various Clinical Conditions. Losner, S., Volk, B. W., Isaac. Albert Research Inst., Jewish Chron. Disease Hosp., Brooklyn, N. Y., USA, Amer. J. med. Sci. *232:* 276 (1956).

In acute myocardial infarction the maximum fibrinogen concentration is an indicator of the extent of myocardial damage and of the severity of the affection. Coronary insufficiency can rapidly be differentiated from myocardial infarction as it shows normal fibrinogen values. Rheumatic affections also are indicated regarding their activity by the fibrinogen level. In bacteriemia due to acute or subacute bacterial endocarditis the fibrinogen content remains normal. Parenchymatous hepatitis is accompanied by low fibrinogen values, where as one finds high values in obstructive jaundice.

Hypofibrinogenemia in Surgical Patients. Pillips, L., Dept. Obst. Gynecol. Coll. Physicians and Surgeons, Columbia Univ., New York, N. Y., USA, Surg. Gynec. Obstet. *103:* 443 (1956).

Presentation of 9 cases. Discussion of diagnosis and therapy.

Plasma Fibrinogen and Serum Aldolase in Acute Myocardial Infarction. Losner, S., Volk, B. W., Isaac Albert: Research Inst., Jewish Chron. Disease Hosp., Brooklyn, N. Y., USA, Angiology 7: 454 (1956).

Experience with Fibrinogenopenia. Taylor, E. S., Dept. Obst. and Gynecol., Univ. of Colorado Med. School, Denver, Col., USA.

Plasma Fibrinogen Determination. A Rapid Titration Method. Rosenberg, A. A., Albany, N. Y., USA, Clin. Chem. *2:* 331 (1956).

Methylen-blue and thrombin are added to a geometrical dilution series of oxalated plasma. Methylen-blue allows exact identification of the appearance of a compact clot.

Effect of Fibrinolytic Activation on Survival and Cerebral Damage Following Periods of Circulatory Arrest. Crowell, J. W., Smith, E. E., Jackson, Miss., USA, Amer. J. Physiol. *186:* 283 (1956).

12 out of 14 dogs survived circulatory arrest lasting 10 to 15 mins. when they were given varidase (streptodornase), whereas only 1 out of 15 animals survived without this preparation. It is demonstrated that a blood coagulation disorder appears during cardiac arrest.

Fibrinolysis in the Organism. Astrup, T., Biol. Inst., Carlsberg Foundation, Copenhagen, Denmark, Blood *11:* 781 (1956).

Analytical review with 169 references.

Hemorrhage from Fibrinolysis in Pulmonary Surgery. Walker, W., Laforet, E. G., Dept. Med. and Surg., Boston, Univ. Med. School, Boston, Mass., USA, thorac. Surg. *32:* 548 (1956).

The coagulation mechanism was studied in a patient dying of hemorrhage following pulmonary surgery and the findings are discussed with reference to the literature. There was no fibrinogenopenia, but rapid lysis by the patient's serum of his own and of standard fibrin clots was demonstrated. The plasma was deficient in antihemophilic globulin and SPCA precursor.

Radiation-Induced Alteration of Fibrinogen Clotting Rate and Clot Lability. Rieser, P., Dept. General Physiol., Zool. Lab. Univ. of Pennsylvania, Philadelphia, Pa., Proc. Soc. exp. Biol. (N. Y.) *91:* 654 (1956) and Nature (Lond.) *178:* 257 (1956).

Hemostatic Defects in Pregnancy. Pritchard, J. A., Dept. Obst. and Gynecol, The Univ. of Texas Southwestern Med. School, Dallas, Texas, USA, Amer. J. Obstet Gynec. *72:* 946 (1956).

Hypofibrinogenemia frequently develops in pregnant women associated with death of the fetus followed by intrauterine retention of the fetus. Clinically significant hypofibrinogenemia was detected in 6 of 22 such women who were studied initially only because of intrauterine death and not because of any abnormal bleeding. Normal clotting time or normal plasma prothrombin activity does not rule out the possibility of clinically significant hypofibrinogenemia. In the cases described the concentration of fibrinogen increased fairly rapidly following delivery. A case of infected abortion with serious disorders of the hemostatic mechanism and massive hemolysis due to Clostridium perfringens septicemia is presented.

Enzymatic Properties of Bovine Plasmin Preparations. Evidence for Similarity to but Non-Identity with Trypsin. Ronwin, E., Dept. Biochem., Purdue Univ., Lafayette, Ind., USA, Canad. J. Biochem. and Physiol. *34:* 1169 (1956).

The enzymatic properties of both chloroform-only activated and trypsin-chloroform activated bovine fibrinolysin (plasmin) have been studied and compared with trypsin. These studies accentuate the remarkable similarity between plasmin and trypsin but definitely establish their distinct individuality and the validity of the procedure using trypsin to activate plasminogen to plasmin.

A Study of Fibrin Deposition in the Placenta. Its Clinical Significance. Ashworth, C. T., Stouffer, J. G., Dept. Path., Harris Hosp., Fort Worth, Texas, USA, Amer. J. clin. Path. *26:* 1031 (1956).

Six cases are described that represent various forms of deposition of fibrin in the placenta. These cases are demonstrative of the type and amount of deposits that occurs in patients with a dead fetus in utero, or an abruptio placentae, or a premature separation of the placenta. In these patients, most of whom had the clinical and laboratory findings of fibrinogenopenia,

the postulated cause of the depletion of fibrinogen is the local deposition of fibrin (1) in the placenta of women with a dead fetus in utero, or (2) at the site of premature separation of the placenta in women with abruptio placentae. The discussion deals with the significance of local intervillous thrombosis and other forms of coagulation in the placenta.

The Conversion of Fibrinogen to Fibrin. XVIII. Light Scattering Studies of the Effect of Hexamethylene Glycol on Thermodynamic Interactions in Fibrinogen Solutions. XIX. The Structure of the Intermediate Polymer of Fibrinogen Formed in Alkaline Solutions. Casassa, E. F., Dept. Chem., Univ. of Wisconsin, Madison, Wisc., USA, XVIII. J. physiol. Chem. *60:* 926 (1956); XIX. J. Amer. chem. Soc. *78:* 3980 (1956).

Stability of the Activator of Bovine Plasminogen. Ablondi, F. B., Hagan, J. J., Biochem. Research Section, Amer. Cynamid, Lederle Lab., Peael River, N. Y., USA, Proc. Soc. exper. Biol. (N. Y.) *93:* 414 (1956).

The ability of a mixture of streptokinase and human plasminogen to activate bovine plasminogen was shown to be dependent upon the concentrations of both components. The "activator" which was formed, may deteriorate on incubation even though streptokinase and human plasminogen when incubated separately were stable. The decrease was partially or completely restored by addition of streptokinase. The rate of disappearance of the activator was affected by the plasminogen preparation and by the initial streptokinase concentration. The inactivation occurred at physiological pH as well as at pH 6.4. The significance of the data are discussed.

Antifibrinolytic Activity of Derivatives of Fibrinolysin. Djerassi, I., Klein, E., Children's Cancer Res. Found., Children's Med. Center, Boston, Mass., USA, Proc. Soc. exp. Biol. (N. Y.) *93:* 440 (1956).

Derivatives of bovine fibrinolysin have been prepared which inhibited the enzyme from which they are derived, but did not inhibit human fibrinolytic activity.

Dynamic Concept of Fibrin Formation and Lysis in Relation to Hemorrhage (Capillary Permeability) and to Thrombosis. Jensen, H., Biochem. Dept., Army Med. Research Lab., Fort Knox, Ky., USA, Exp. Med. Surg. *14:* 189 (1956).

A review of the literature as it relates to a possible role of the fibrin formation system in the pathogenesis of hemorrhage and thrombosis is presented. One stage of biochemical hemostasis appears to be related to a balance between the rate of fibrin formation and fibrin dissolution. The controlling mechanism of fibrin formation and lysis are apparently very closely interrelated. There appears to exist an intimate relationship between fibrin formation, fibrinolysis and the integrity of the vessel wall. Alterations in the physical character of the vessel lining may play a role in hemorrhagic or thrombotic syndromes. The fibrinolytic system seems to be partly under the control of the pituitary-adrenal cortex axis. It is, therefore, likely that certain adrenocortical hormones play a role in the maintenance of capillary permeability and also in the pathogenesis of either hemorrhagic or thrombotic syndromes.

c) Prothrombin (Factor II), Thrombin

Prothrombinverbrauch und Bromsulfaleintest bei Blutkrankheiten. Brichta, G., Kühböck, J., Reimer, E. E., II. Med. Univ.-Klinik, Wien, Austria, Dtsch. Arch. klin. Med. *203,* 312 (1956).

In cases of untreated chronic leukemia, lymphogranuloma, and lymphosarcoma a regular correlation was found between decreased prothrombin consumption and pathologic bromsulfalein retention.

Le Complexe Prothrombinique et son importance clinique. Koller, F., Bounameaux, Y., Clin. méd., Univ., Zurich, Suisse, Journées thér. Paris, p. 159 (1956).

The prothrombin complex represents an entity of factors measured by Quick's method namely fibrinogen, prothrombin, factors V and VII, antithromboplastin, and antithrombin. After explaining their concept of blood coagulation, of mechanism, of hemostasis, and of structure of thrombus, the authors discuss the importance of each element of the prothrombin

complex. It is pointed out that the coagulation time obtained in the presence of an optimum of tissue thromboplastin has only little physiopathologic significance in so far as this same tissue thromboplastin plays only a limited part in the accumulation of agglutinated platelets, in the formation of the white thrombus, or the hemostatic clot. Finally the control of anticoagulant therapy is discussed and it is mentioned that Quick's time does not measure the physiologically most important factors.

A Familial Form of Idiopathic Hypoprothrombinemia. Post, C. R., Den Ottolander, G. J. H., Hoorweg, P. G., Central Lab., Bloedtransfusiedienst, Roode Kruis, Amsterdam, Holland, Ned. T. Geneesk. *100:* 1981 (1956).

Quick distinguishes 3 forms of idiopathic hypoprothrombinemia. In the first form free and inactive prothrombin are diminished (= panhypoprothrombinemia). In the second form only free, and in the third only inactive prothrombin are reduced. The authors report 4 cases of the first form of idiopathic hypoprothrombinemia in a mother and her 3 children. Two of the children suffered from recidivating hemorrhages, which were stopped by blood transfusions.

The Prothrombin Conversion Ratio. Wolf, P., The Lister Inst., London, England, Brit. J. Haemat. *2,* 367 (1956).

The determination of the prothrombin conversion ratio is described. The ratio is given by the maximum quantity of thrombin produced per ml of undiluted plasma within 5 mins. of recalcification, divided by the maximum-quantity of thrombin found per ml of undiluted plasma on the addition of brain thromboplastin after a further 5.5 mins. incubation. It is proportional to the rate of prothrombin conversion in a recalcified plasma. The estimation is carried out on a platelet-free plasma, in the presence of *Bell and Alton's* platelet substitute. The prothrombin conversion ratio of platelet-free plasma increases with increasing volumes of platelet suspension or substitute until a maximum value is reached, after which there is a progressive fall. The conversion rate of platelet-containing plasma increases at storage of 4° C and reaches a maximum after 18 hours. The increase does not occur when platelets are first removed by centrifuging.

Le temps de Quick et ses facteurs au cours des leucoses. Samama, M., Colombani, J., Clin. des Malagies du Sang, Hôp. Broussais, Paris, France, Sang *27:* 304 (1956).

Sensibilidad de diversos plasmas frente a la trombina. Estudio del "tiempo de trombina" en los hépaticos. Soulier, J. P., Alagille, D., Centre Nat. Transfusion Sanguine, Paris, France, Sangre *1:* 193 (1956).

Plasma Prothrombin Time in Skin Diseases. I. Whole and 12.5% Plasma Prothrombin Time in Skin Diseases. Yoshiro, Hamada, Dept. Derm., Tohoku Univ., Sendai, Japan, Tohoku J. exp. Med. *63:* 297 (1956).

Plasma prothrombin time was determined on whole and 12.5% saline diluted plasma in 665 cases of skin diseases including 316 allergic diseases. Both, whole and 12.5% plasma prothrombin time were increased in allergic diseases, no definite increase was found in congenital endocrine and pigmentary diseases except for Addison's disease and Riehl's melanosis.

II. Clinical Investigation on Plasma Prothrombin Time. p. 305.

Plasma prothrombin time was determined on whole and 12.5% saline diluted plasma during treatment of patients with skin diseases. Prothrombin time determination in 12.5% saline diluted plasma was found to be a more sensitive indicator of prothrombin activity than in whole plasma. Plasma prothrombin time determination is considered the best method of examining liver functions.

Die Therapie von Prothrombinmangelblutungen im Neugeborenenalter. Haupt, H., Krebs, H., Kinderklinik, Bonn, Germany, Z. Kinderheilk. *78:* 665 (1956).

The therapy of hemorrhage caused by prothrombin deficiency in the newborn is thus outlined: The site of origin of the deficient coagulation factors must be stimulated by administration of vitamin K_1 (Konakion); deficient coagulation factors must be substituted by ACC 76 (factor V plus VII). Best results are obtained by combination of the 2 preparations.

Note technique sur la consommation de la prothrombine. Samama, M., Fac. de Méd., Paris, France, Sang *27:* 603 (1956).

Zur Frage des diagnostischen Wertes täglicher Prothrombinbestimmungen hinsichtlich postoperativer Emboliegefährdung in der Thoraxchirurgie. Maassen, W., Opderbecke, H. W., „Ruhrlandklinik" der LVA Rheinprovinz, Essen-Heidhausen, Ruhr, Thoraxchir. *4:* 312 (1956).

Un nouveau test de consommation de la prothrombine sensibilisée par l'héparine. Ducos, J., Centre de Transfusion Sanguine, Toulouse, France, Sang *72:* 947 (1956).

The author describes a new method for the measurement of prothrombin consumption, whereby serum sensitized by heparin is used.

Erfahrungsbericht über das blutstillende Thrombinpräparat Topostasin. Schmidt, K. E. A., Fuhlsbüttelerstr. 125, Hamburg 33, Germany, Medizinische 1956 :322.

Een modificatie van der "thrombin generation test". Van der Pol, E. T., Labor. Bloedtransfusiedienst, Wilhelmina Gasthuis, Amsterdam, Holland, Ned. T. Geneeskd. *100:* 1900 (1956).

A Preliminary Communication on the Degeneration of Thrombin in Serum of Normal Controls and of Patients Before and After Surgery. Berry, C. G., St. James' Hosp., Balham, England, J. clin. Path. *9:* 363 (1956).

Quantitative Concepts Related to Prothrombin and Autoprothrombin I Activity. Seegers, W. H., Dept. Physiol., Wayne Univ., Coll. Med., Detroit, Mich., USA, Canad. J. Biochem. and Physiol. *34:* 887 (1956).

The Activation of Prothrombin. Seegers, W. H., Wayne State Univ., Coll. of Med., Detroit, Mich., USA, Angiology *7:* 436 (1956).

Activation of Prothrombin. Penner, J. A., Seegers, W. H., Wayne State Univ. Med. Coll., Detroit, Mich., USA, Amer. J. Physiol, *186:* 343 (1956).

Prothrombin can be converted to thrombin either "directly" or via 2 of its derivatives autoprothrombin I and II. Factor V, platelet factor 3, platelet co-factor I and ionic calcium are necessary for direct conversion. When thrombin and factor V are added to a prothrombin solution autoprothrombin II generates and converts into thrombin in the presence of ionic calcium, factor V and platelet factor 3. The addition of ionic calcium, factor V and platelet factor 3, or of ionic calcium and thromboplastin to prothrombin yields autoprothrombin I which is activated to thrombin by ionic calcium, factor V and thromboplastin.

Concentration of a Prothrombin Conversion Accelerator and Thrombin Precursor from Serum. McClaughry, R. I., Detroit, Mich., USA, Amer. J. Physiol. *186:* 335 (1956).

The authors from bovine serum obtained a protein fraction which converted prothrombin to thrombin. From this preparation, containing only very little prothrombin, thrombin was obtained by activation with citrate.

Electrophoresis of Autoprothrombin and Biothrombin. Seegers, W. H., Dept. Physiol., Wayne Univ. Med. Coll., Detroit, Mich., USA, Canad, J. Biochem. and Physiol. *34:* 270 (1956).

A Study of the Relationship of Concentrations of Prothrombin, Proconvertin, and Proaccelerin to Three Methods for Measuring "Prothrombin Time". Gonyea, M. L., Hjort, P., Owren, P. A., Dept. Med., Rikshop., Oslo, Norway, J. Labor clin. Invest. *48:* 624 (1956).

Three one-stage methods for measuring "prothrombin-time" (Quick's method, prothrombin-proconvertin method, and Russell viper venom-cephalin method) were investigated with the use of serial dilutions of prothrombin, proaccelerin, and proconvertin. The Quick method was similarly sensitive to variations in each of the 3 factors. At concentrations above 40% no significant difference could be detected. Owren's prothrombin-proconvertin method was insensitive to variations in proaccelerin. A marked effect resulted when both prothrombin and proconvertin were deficient and a definite but less strong effect was seen when either of them was deficient. The Russel viper venom-cephalin method was insensitive to variations in pro-

accelerin and proconvertin. The partial thromboplastin time with cephaline was prolonged when the concentration of proaccelerin was lower than 30%, but the results were not influenced by a deficiency of proconvertin. This finding suggests that proconvertin may not be involved in the formation of the final prothrombin conversion principle from blood, whereas it is essential for the formation of this principle from tissue thromboplastin.

Determinants of the So-called "Prothrombin Time". Ferguson, J. H., Patch, M. J., Dept. Physiol., Univ. N. Carolina, Chapel Hill, N. C., USA, Proc. Soc. exper. Biol. (N. Y.) *93:* 193 (1956).

In analyzed systems representing artificially reconstituted plasmas of known composition with respect to prothrombin, proconvertin, and AcG, one-stage clotting times with Ca-thromboplastin, essentially in the manner of Quick's prothrombin time, show: 1) prothrombin concentration is a major variable. 2) proconvertin concentration is a minor variable, which, except at very low levels, affects the clotting time significantly only at very low prothrombin levels, 3) high proconvertin levels, short of an unexplained inhibitory phenomenon, do not compensate significantly for low prothrombin or AcG levels, 4) AcG levels are a major variable, 5) excessively high (200—300%) AcG levels can compensate for moderately low prothrombin and proconvertin, 6) It seems valid to apply this last result to explain the normal „prothrombin time" in normal healthy newborn infants.

Conversion of Prothrombin to Autoprothrombin II. Penner, J. A., Duckert, F., Johnson, S. A., Seegers, W. H., Dept. Physiol. Pharm., Wayne Univ. Med. Coll., Detroit, Mich., USA, Canad. J. Biochem. Phys. *34:* 1199 (1956).

With thromboplastin, Ac-globulin, and calcium ions, purified prothrombin converts to biothrombin. This prothrombin derivative is also obtained with purified platelet factor 3, Ac-globulin, calcium ions, and autoprothrombin II. Need for the latter substance by platelet factor 3 is one marked distinction between thromboplastin and platelet factor 3. Ether extracts of dried brain or of purified platelet factor 3, or of whole platelets yield lipid material. The lipids obtained are active in the thromboplastin generation test but in contrast to the material they are obtained from they do not activate prothrombin to thrombin. Extraction of purified platelet factor 3 leaves a protein residue and it is believed that platelet factor 3 is a lipoprotein. From the absorption pattern it is concluded that the lipid is not a heterogeneous mixture, but most likely a single substance or consists of several that are nearly alike. Platelet factor 3 lipid(s) is most likely a cephalin-like compound.

Postoperative Thrombin Production. Reich, T., Sternberger, L. A., New York, N. Y., USA. Surg. Gynec. Obstet. *102:* 463 (1956).

The Proteolytic Action of Thrombin on Fibrinogen. Laskowski, M., Donnelly, T. H., Van Tijn, B. A., Scheraga, H. A., Dept. Chem., Cornell Univ., Ithaca, N. Y., USA, J. biol. Chem. *222:* 814 (1956).

By using an analytic procedure designed to permit ultramicro-Kjeldahl determinations of nitrogen to be carried out in solvents containing NaBr, it has been demonstrated that Lorand's fibrinopeptide is liberated by the action of thrombin on fibrinogen under conditions in which the subsequent polymerization of the fibrin monomer is inhibited. The inhibitor used for this purpose is 1 M NaBr at pH 5.3. The function of the proteolytic step in the fibrinogen-fibrin conversion appears to be to liberate groups on the fibrin monomer which are required for the subsequent polymerization, via hydrogen bonding, to intermediate polymers which ultimately form the fibrin clot.

Coagulation-Promoting and Inhibitory Properties of Modified Thrombin Preparations. Klein, E., Djerassi, I., Farber, S., Children's Cancer Research Found., Children's Med. Center, Boston, Mass., USA, Proc. Soc. exp. Biol. (N. Y.) *93:* 436 (1956).

An alcohol precipitate, obtained from heated bovine thrombin preparations, promoted the early phases of the coagulation mechanism, but did not clot fibrinogen in the manner of the unheated preparation. These materials inhibited bovine thrombin at lower concentrations than human thrombin in the clotting of fibrinogen.

d) Thromboplastin (Factor III)

Etude comparative des facteurs nécessaires à la thromboplastinoformation dans le sang de l'homme et du lapin. Wartelle, O., Centre Nat. de la Transfusion Sanguine, Paris, France, Rev. Hémat. *11:* 414 (1956).

Thromboplastin formation was compared in man and rabbit and was found to be almost identical. Some factors, however, are different regarding their content. Rabbit plasma contains more antihemophilic factor A and less antihemophilic factor C. Rabbit platelets seem to contain an inhibitor of thromboplastin formation. Quick's time varied according to the thromboplastic substance used. In rabbit plasma factor V was higher, prothrombin slightly lower, and factor VII nearly equal to human plasma. Finally it was demonstrated that a marked quantity of so-called "active thromboplastin" exists in the plasma of the rabbit.

The Separation of Human and Bovine Plasma Thromboplastin with Ether and a Study of its Properties. Nour-Eldin, F., Wilkinson, J. F., Dept. Hemat. Royal Infirmary, Manchester, England, J. Physiol. (Lond.) *132:* 164 (1956).

Many unsuccessful attempts have been made to isolate plasma thromboplastin, a very labile substance. The present paper deals with its precipitation from a solution where all factors necessary for its formation are allowed to react. After attaining full activity the plasma Thromboplastin is precipitated, under controlled conditions, with ether. Details of the method are given and the physico-chemical and biological properties of the isolated thromboplastin are described. The action of plasma thromboplastin on prothrombin was weak in the absence of calcium which seemed to be the only activator of plasma thromboplastin. Plasma thromboplastin seems to be a protein with attached lipid, but the exact nature of the latter is uncertain.

Uso delle „frazioni plasmatiche liofilizzate" nella correzione „in vitro" dei deficit di tromboplastinoformazione. Vecchio, F., Ist Clin. Paed., Univ. Napoli, Italy, Pediatria (Napoli) *64:* 365 (1956).

The Coagulant Action of Russell Viper Venom Investigated by the Thromboplastin Generation Test. Hall, G. H., R. A. F. Inst. Pathol., Aylesbury, England, J. clin. Path. *9:* 237 (1956).

Two Stages in the Formation of Active Plasma Thromboplastin. Nour-Eldin, F., Wilkinson, J. F., Dept. Haemat., Royal Infirmary, Manchester, England, Nature (London) *178:* 856 (1956).

$CaCl_2$ is more active in the activation of plasma thromboplastin than Ca-gluconate, Ca-lactate, $SrCl_2$ and $MgCl_2$. The activation occurs in 2 stages.

Extraction and Concentration of Thromboplastic Material from Human Urine. von Kaulla, K., Dept. Med. Univ. Colorado Med. School, Denver, USA, Proc. Soc. exp. Biol. (N. Y.) *91:* 543 (1956).

A method is described whereby thromboplastic material is extracted from normal male human urine by adsorption on $BaSO_4$ and subsequent elution. The thromboplastic material is relatively resistant to heat; its activity is enhanced by incubation with serum and prothrombin-free plasma. As little as 6 μg/cc of the thromboplastic material per cc of hemophilic plasma was found to restore the clotting properties of this plasma to normal.

Methods for Preparation of Purified Human Thromboplastin and Fibrinolysokinase from Urine. von Kaulla, K. N., Dept. Med. Univ. Colorado Med. School, Denver, Col., USA, Acta haemat. (Basel) *16:* 315 (1956).

II. Basic Mechanisms and Theoretical Aspects.

Data are presented which indicate that the reactions involved in the thromboplastin generation test are complex and poorly understood. These studies confirm the concept that thrombin plays an important role in all phases of blood coagulation. Thrombin generated during the test may affect the apparent generation of a thromboplastic substance by influencing related reactions.

Studies on the Thromboplastin Generation Test. I. Method and Clinical Applications. Miale, J. B., Wilson, M. P., Dept. Path., Univ. Miami Med. School, Miami, Florida, USA, Amer. J. clin. Path. *62:* 969 (1956).

The method of the thromboplastin generation test is outlined in detail. Its application to the diagnosis of hemorrhagic states is illustrated and discussed.

Activation of Phospholipid Thromboplastin by Lecithin. Rapport, M., Div. Lav. and Research, N.Y., State Dept. of Health, New York, USA, Nature (London) *178:* 592 (1956).

Lecithin of various origin activates the cephalin fraction of bovine brain (thromboplastin). Large amounts of lecithin have, however, an inhibitory effect.

e) Calcium (Factor IV)

Note on Calcium Ion Requirements for Threone Activity. Johnson, S. A., Seegers, W. H., Dept. Physiol. and Pharm., Wayne Univ. Med. Coll., Detroit, Mich., USA, Proc. Soc. exp. Biol. (N. Y.) *92:* 597 (1956).

When threone is involved in the conversion of purified prothrombin to thrombin, the optimum calcium concentration ranges from 0.009 M to 0.04 M. This is a much broader range than found when thromboplastin is used for the activation of prothrombin.

f) Factor V (and VI)

Hypoaccéléríné congénitale (parahémophilie d'Owren). Larrieu, M. J., Hôp. Hérold, Paris, France, Sang. *27:* 117 (1956).

The authors have observed an isolated factor V deficiency in a 6-year old child suffering from a minor hemorrhagic syndrome, namely hemorrhage following dental extraction. Quick's time was persistently prolonged, factor V level varied from 0 to 3% whereas prothrombin and factor VII values were normal. The thromboplastin generation test carried out on adsorbed plasma of the patient showed a moderate disturbance. No anti-proaccelerine could be demonstrated. The platelet factor, the activity of which is analogous to that of factor V, was found to be markedly decreased in the patient. It seems, however, that it was no platelet factor, but plasmatic proaccelerin adsorbed on platelet surface.

Prothrombin Accelerator Deficiency Associated with Tuberculosis. Fantl, P., Sawers, R. J., Baker Med. Res. Inst., Melbourne, Australia, Med. J. Australia p. 536 (1956).

A fatal hemorrhagic disease in an elderly female patient suffering from tuberculosis has been investigated. The clotting defect was due to a 90% deficiency of prothrombin accelerator (factor V). In contrast to normal serum the patient's serum showed limited stability of serum factors which accelerate prothrombin conversion. Although there are some indications of an inherited bleeding tendency, none of the relatives of the patient who were examined have shown a clotting deficiency, and it is believed that the patient's hemorrhagic disease was acquired.

Further Data on the Evaluation of Platelet Ac-Globulin and its Plasmatic Origin. Turpini, R., Dept. Int. Med., Univ. Pavia, Italy, Experientia (Basel) *12:* 220 (1956).

g) Factor VII

Recherches sur la Proconvertine. Haanen, C. A. M., Clin. Méd. Hôp. St. Canisius, Nimêgue, Holland, Acta haemat. (Basel) *16:* 363 (1956).

The activity of proconvertin increases in stored plasma. No such increase occurs in siliconed vessels at low temperature, nor does it occur with purified proconvertin. A relation between this phenomenon and the influence of other coagulation factors in plasma must therefore be presumed. The spontaneous increase of proconvertin in stored plasma can be explained by the hypothesis that proconvertin is set free during the conversion of prothrombin into thrombin.

Based on the literature and own observations arguments are presented in favor of the identity of proconvertin and Christmas factor. In 20 patients with various hepatic disorders the proconvertin level was reduced. In 20 patients with right-sided heart insufficiency relationship between venous pressure and proconvertin content was noted. The importance of proconvertin determination as a test of liver function is stressed.

The Function of Factor VII. Ackroyd, J. F., Med. Unit., St. Mary's Hosp. Med. School, London, England, Brit. J. Haemat. *2:* 397 (1956).

A case of uncomplicated factor VII-deficiency is described. The deficiency was probably congenital. All his life the patient has suffered from bleeding closely resembling that seen in hemophilia, although he has also chronic purpura on his leg. The clotting mechanism is essentially normal except for the prolonged clotting time of the plasma when tissue extract is used as a source of thromboplastin. Based on the study of this case it is concluded that there is apparently no incontrovertible evidence at present available to show that factor VII is important in the coagulation when this occurrs normally, i.e. without the addition of tissue extracts. The function of this factor needs further investigation.

Some Observations on the Blood of Patients with „Factor VII" Deficiency. Biggs, R., Dept. Path., Radcliffe Infirmary, Oxford, England, Brit. J. Haemat. *2:* 412 (1956).

A mild clotting defect in twins was investigated. As judged by one-stage prothrombin time tests the patient would have been said to have factor VII deficiency. A study was made of thromboplastin formation using the thromboplastin generation test and substituting for the normal serum various pathological sera and mixtures of pathological sera. The results are difficult to interpret without postulating deficiencies of 3 serum factors in addition to factor VII.

Congenital Factor VII Deficiency. Greig, H. B. W., Dept. Hematol., S. African Inst. Med. Research, Johannesburg, S. Africa, Arch. Dis. Childh. *31:* 293 (1956).

Il fattore labile ed il fattore stabile dell'emocoagulazione nel lattante. Nicolini, R., Rottini, G., Ospedali Riuniti, Centro Trasfusionale, Trieste, Italy, Minerva ped. *8:* 41 (1956).

Factor V and VII were determined in 79 infants aged from 2 days to 12 months. The values of factor V were slightly lower than those found by other authors. A gradual increase in factor VII was observed from birth to the second month, an abrupt increase from the second to the third month, constant values from the 3rd to the 9th month with values of about 60%, and later again a gradual up to normal values attained in the 12th month.

Congenital Hypoproconvertinemia. Van Creveld, S., Veder, H. A., Blans, M. M., Dept. Pediatrics, Univ. Hosp., Amsterdam, Holland, Ann. pediatr. *187:* 373 (1956).

The author reports the cases of 3 sisters with congenital factor VII deficiency. 2 of the patients died at the age of one and two months of severe cerebral hemorrhage. The third child is still alive but showed frequent symptoms of cerebral hemorrhage. Vitamin K_1 intravenously and vitamin K_3 intramuscularly had only a small transient effect on content of factor VII and prothrombin.

Activité thromboplastique du sang et du plasma conservés. Soulier, J. P., Wartelle, O., Centre Nat. Transfusion Sang., Paris, France, Vox Sang. *1:* 110 (1956).

Stored, platelet-rich plasma or whole blood was studied regarding its capacity of normalizing prothrombin consumption of a platelet-poor or hemophilic plasma. In opposition to the former theory: the fresher the plasma the higher its hemostatic activity, the authors found that stored plasma acquires hemostatic properties of thromboplastic nature to be used in the treatment of certain hemorrhagic syndromes, in particular thrombocytopenias and thrombocytopathias.

Untersuchungen über das Vorkommen einer aktiven Thrombokinase im Fruchtwasser. Wille, P., Geburtsh.-Gynäk. Abtlg., Städt. Krankenhaus Berlin-Kaulsdorf, Germany, Zbl. Gynäk. *78:* 1514 (1956). (Ein Beitrag zur Ätiologie der Afibrinogenämie unter der Geburt.)

Amniotic fluid of 22 women has been tested for its coagulation activity and compared to the activity of brain thromboplastin solutions. The coagulation time was as an average twice

as long as that obtained with brain thromboplastin. In a dilution of 1: 1000 amniotic fluid lost only half its original activity. The results are discussed and it is concluded that even very small amounts of amniotic fluid reaching circulating blood can cause afibrinogenemia.

Die klinische Bedeutung des „Thromboplastin-Generation-Test" bei den Gerinnungsstörungen. de Nicola, P., Med. Univ.-Klinik, Pavia, Italy, Z. ges. inn. Med. *11:* 644 (1956).

Het verband tussen het proconvertinegehalte van het plasma en de functie van de lever. Haanen, C. A., Inter afdeling, St. Canisius Ziekenhuis, Nijmegen, Holland, Ned. T. Geneesk. *100:* 1085 (1956).

Un cas d'hypoconvértinémie congénitale chez le nourrisson. Gillot, F., Alger, Pédiatrie *11:* 439 (1956).

The author presents a new case of congenital hypoproconvertinemia. Hemorrhagic manifestations started at the age of 2 months, and consisted in fugitive but repeated bleeding of the digestive tract. Hematologic findings: Slightly prolonged Quick's time, prolonged proconvertine time not affected by administration of vitamin K. Prothrombin time and proaccelerin level normal. Review of the literature on similar cases.

Sindrome emorragica di tipo emofilico da diffetto congenito di fattore VII. Presentazione di due casi. Serafini, E. M., Pericoli, F., Ist. Clin. Med. Generale, Univ. Roma, Italy, Boll. Soc. ital. Ematol. *4:* 70 (1956).

Two case reports of congenital factor VII deficiency.

Kongenitaler Faktor VII (SPCA)-Mangel als Ursache einer hämophilieartigen hämorrhagischen Diathese. Jürgens, J., II. Med. Univ.-Klinik, Frankfurt a. M., Germany, Acta haemat. (Basel) *16:* 181 (1956).

In a case of congenital factor VII deficiency with 1.2% factor VII, the hemorrhagic tendency was only moderate. There were no antibodies. Platelet number, bleeding time, whole blood clotting time, prothrombin time, factor V, prothrombin consumption, antithrombin were normal. Thromboplastin time was prolonged and could be normalized by addition of normal or Christmas disease-serum. Thromboplastin generation test and thrombelastogramm were normal. It is concluded that factor VII and Christmas factor are not identical, and that factor VII is not essential for thromboplastin formation in the early stages of clotting.

Interaction of Convertin with Platelets and with Platelet-Free and Hemophilic Plasma. Shafrir, E., De Vries, A., Krejnis, E., Dept. Clin. Res., Hebrew Univ. Hadassah Med. School, Jerusalem, Israel, Acta haemat. (Basel) *16:* 204 (1956).

A serum convertin preparation obtained from normal blood clotted in glass in the presence of brain extract, it accelerates the clotting of platelet-containing as well as platelet-free normal and hemophilia A plasma, and decreases their serum prothrombin content. Incubation of the convertin preparation with normal or hemophilia A platelet-free plasma, with whole platelets or platelet extract, but not with platelet fragments, markedly enhances its clot accelerating activity. Platelet fragments in high concentration inhibit the clotting of platelet-free normal plasma.

A propos d'un cas d'hypoproconvertinémie congenitale. Choremis, C., Padiatellis, C., Tsevrenis, I., Hadjidimitriou, E., Clin. Pédiatr., Univ., Athens Greece Helv. paediat. Acta *3:* 301 (1956).

The authors describe a case of congenital hypoproconvertinemia in which the blood coagulation factors were studied and in which the action of an eluate of the electrophoretic band of normal serum on the plasma of the patient was determined.

h) Factor VIII (Antihemophilic Globulin)

Mangel an antihämophilem Globulin bei einer Frau mit hämorrhagischer Diathese. Beller, K., Koch, E., Akad. f. Med. Forschg., Justus-Liebig-Hochschule, Gießen, Germany, Folia haemat. *1:* 132 (1956).

The authors report the case of a woman of 31 who has been suffering from hemorrhages into the skin, mucuous membranes, and joints, since childhood. During a 5-year observation

period the antihemophilic globulin was constantly 30—40% below normal. Examination of the patient's family gave no clue to the existence of familial hemorrhagic diathesis. With reference to similar observations by Fantl et al the question is raised whether or not this deficiency of AHG which occurs in women and also sporadically in men should be associated with recessive sex-linked hereditary hemophilia A.

Un cas d'hémophilie par manque du facteur A de Koller. Niemegeers, L., van de Vyver, W., Policlinique méd., Zwijnaarde-Gand, Belgium, Brux.-méd. *36:* 1757 (1956).

La globulina antiemofilica caratteristiche e possibilità attuali di isolamento e di impiego terapeutico. Serafini, U. M., Centurelli, G., Ist. Clin. med. Generale, Univ., Roma, Italy, Clin. terap. *2:* 236 (1956).

After outlining the physical, chemical and biological characteristics of the antihemophilic globulin and discussing its role in the physiology of coagulation and its various methods of determination the authors review today's possibilities of isolating plasmatic fractions containing antihemophilic activity and their clinical use. They come to the conclusion that the preparations commercially available do not represent any advantage as compared to adequate amounts of fresh plasma transfusions.

Hémophilie A chez une fille agée de deux ans. Choremis, K. B., Zevros, N., Tsevrenis, H., Apostolopoulou, E., Manaliki, T., Clin. Pédiatr., Univ., Athens, Greece, Helv. paediat. Acta *3:* 305 (1956).

The authors describe a case of hemophilia A in a 2-year-old girl.

AHG — Deficiency in a Girl Treated with Antihemophilic Globulin. Nilsson, I. M., Blombäck, B., Blombäck, M., Svennerud, S., Allmänna Sjukhuset, Malmö, Sweden, Nord. Med. *56:* 1654 (1956).

The authors describe a probably hereditary hemophilia in a 17 year-old girl. The AHG deficiency in her blood was aggravated with menstruation. In contrast to classical hemophilia A, the bleeding time was also prolonged. After a large amount of blood transfusions she became sensitized to blood. Hysterectomy was required. Good normalization of the coagulation findings was obtained with a purified fraction of fibrinogen containing AHG, and the operation was performed without complications. The fact that the AHG preparation corrected even the prolonged bleeding time and the capillary bleeding tendency is worth being noted.

Assay of Antihemophilic Factor Using the Prothrombin Conversion Ratio. Wolf, P., The Lister Inst., London, England, Brit. J. Haemat. *2:* 386 (1956).

A method for assaying antihemophilic factor is described, based on the prothrombin conversion ratio. The method requires only a small number of reagents which can all be stored. No blood from a hemophilic patient is required. The assay can be modified to provide a simple method of estimating the effect of specific therapy on a hemophilia.

The Isolation of Antihemophilic Globulin from Brain Tissue. Nour-Eldin, F., Wilkinson, J. F., Dept. Med., Western Reserve Univ. Med. School, Cleveland, O., USA, J. clin. Invest. *35:*

Antihemophilic Globulin, free from fibrinogen, has been isolated from human and bovine brains. Heparin is used to inhibit the reaction between antihemophilic globulin, Christmas factor and phospholipid which are believed to exist as separate components in the fresh brain tissue. Certain steps necessary before the subsequent precipitation of antihemophilic globulin with phosphate and citrate are described.

A Laboratory Study of the Carrier State in Classic Hemophilia. Margolius, A., Ratnoff, O. D., Dept. Med., Western Reserve Univ. Med. School, Cleveland, O., USA, J. clin. Invest. *35:* 1316 (1956).

The medical literature relating to the detection of hemophilic conductors by laboratory technics is conflicting. Routine clotting studies and assays for anti-hemophilic factor were performed in 27 carriers of classic hemophilia. A definitely reduced concentration of anti-hemo-

philic factor was demonstrated only in one carrier, although minor abnormalities of the clotting mechanism were found in several others. In the families of hemophiliacs, it is possible to detect only a small number of carriers of the trait with currently available technics.

Relative Stability of Plasma Antihemophilic Factor (AHF) under Different Condition of Storage. Penick, G. D., Brinkhous, K. M., Dept. Path., Univ. of N. Carolina, Chapel Hill, N. C., USA, Amer. J. med. Sci. *232:* 434 (1956).

AHF activity in bank blood and plasma shows variable stability. Deterioration of AHF on storage tends to be slow but progressive, with about 30—60% of AHF remaining after 3 weeks of storage. Several factors appear to determine the amount of remaining AHF. The lower the temperature of storage, the better the preservation of AHF. In fresh frozen plasma variable stability of AHF was observed; about half is lost in one month, after which time the remaining AHF tends to be stable. At 56° C AHF is rapidly inactivated. AHF in lyophilized plasma is remarkably stable for years. Its potency is about half that of fresh plasma following reconstitution. Nearly normal AHF levels were maintained in frozen plasmas with citrate or cation exchange resin as an anticoagulant. AHF is unstable in oxalated plasma. Possible mechanism of inactivation of AHF are discussed.

Immunization of Rabbits against Human Antihemophilic Factor. Richards, M. D., Spaet, T. H., Blood *11:* 473 (1956).

i) Factor IX (Christmas Factor, PTC)

The Stability of Christmas Factor. A Guide to the Management of Christmas Disease. Brafield, A. J., Case, J., Area Lab., Whipps Cross Hosp., London, England, Lancet *271,* 867 (1956).

The content of Christmas factor in plasma and serum and its stability under different conditions of storage were studied by the thromboplastin generation test. On the basis of these findings a guide to the management of Christmas disease is offered.

The Effect of Cobra Venom and Bee Venom on Plasma: Some Evidence on the Possible Chemical Composition of the Christmas Factor. O'Brien, J. R., Central Lab., Milton Road, Portsmouth, Hants., England, Brit. J. Haemat. *2:* 430 (1956).

Cobra and bee venoms, at critical concentrations, diminish the formation of thrombin in thrombin generation tests carried out on platelet-rich plasma. The venoms may inactivate the Christmas factor. Evidence has been presented which may indicate that the Christmas factor contains phospholipoid.

Lack of Christmas Factor in Horse Plasma. Sjølin, K. E., Biol. Inst., Carlsberg Found., Copenhagen, Denmark, Nature (London) *178:* 153 (1956).

Die Hämophilie B und ihre Behandlung. Heni, F., Krauss, I., Med. Univ.-Klinik, Tübingen, Germany, Dtsch. med. Wschr. *81:* 1603 (1956).

Among 14 patients of different families with hemophilia studied by the authors, there were 3 men with hemophilia B. In one of these it was possible despite a severe course of the disease, to extract 4 teeth under the protection of serum transfusions. However, after the 9th transfusion it was no longer possible to achieve normal blood coagulation. This indicates that in hemophilia B, as in hemophilia A, antibodies against plasma thromboplastin may develop.

Investigation of a Hemorrhagic Disease Due to Betaprothromboplastin Deficiency Complicated by a Specific Inhibitor of Thromboplastin Formation. Fantl, P., Sawers, R. J., Marr, A. G., Baker Med. Research Inst., Melbourne, Australia, Austr. Ann. Med. *5:* 163 (1956).

The authors present a case of complete absence of β-prothromboplastin. The patients blood contained an inhibitor of coagulation. The characteristics of this inhibitor are described. Although serological proof could not be obtained, it is believed that the inhibitor has appeared as a result of an immune reaction due to blood transfusions. A new adsorbate technic was developed. It indicated that the inhibitor combined specifically with β-prothromboplastin of human origin. Studies with this technic indicate that β-prothromboplastin deficiencies can be

divided into 2 groups. In the one the patients develop a defective β-prothromboplastin, which is inactive in clotting but is still antigenic. The other group cannot produce even deficient β-prothromboplastin with antigenic properties. It is thought that the latter group is most likely to develop anticoagulants after blood transfusions.

k) Other Factors

Mitteilung über eine bisher noch nicht beschriebene hämorrhagische Diathese bei einem Neugeborenen. Schultze, H. E., Schwick, G., Sachs, F., Ihringer, G., Behringwerke, Marburg/Lahn, Germany, Medizinische *1956:* 578.

Umbilical cord bleeding in a 2-days old girl was diagnosed as morbus hemorrhagicus neonatorum and successfully treated with transfusions, vitamin K, Birutan, and ACC 76. 5 days later bleeding started again: coagulation time and prothrombin time markedly increased, platelet level normal. Administration of vitamin K without effect. Suspected hemophilia B. Therapy with fresh blood and ACC 76 cannot prevent formation of hematoma. Coagulation tests revealed the following unusual findings: Quick's test markedly prolonged, prothrombin, factor V and factor VII levels, however, normal. Impaired plasma thromboplastin formation not caused by factor VIII or IX deficiency. No coagulation deficiency to be found in other family members. In spite of fresh blood transfusions and ACC 76 the child died with 5 months from cerebral bleeding due to a coagulation defect characterized by total absence of fibrin formation at the site of bleeding.

Syndrome hémorrhagique due au défaut du facteur prothromboplastique de Rosenthal (PTA). Caen, J., Bernard, J., Hôp. Hérold, Paris, France, Sang *27:* 249 (1956).

En marge de l'hémophilie: la déficience en facteur Hageman. Chevallier, P., Clinique des Maladies du Sang, Hôp. Broussais, 96, rue Didot, Paris, France, Sang *27:* 950 (1956).

Observations on the Hereditary Nature of Hageman Trait. Margolius, A., Ratnoff, O. D., Dept. Med., Western Reserve Univ., Med. School, Cleveland, O., USA, Blood *11:* 565 (1956).

A study was made of the family tree of 2 sisters with Hageman trait, an asymptomatic disorder of blood coagulation. In this family the defect behaves genetically as if it is due to the transmission of an autosomal recessive gene.

Hageman Factor (HF) Deficiency. Ramot, B., Singer, K., Heller, P., Zimmerman, H. J., Dept. Hematol. Res., Michael Reese Hosp., Dept. Med. West Side, V. A. Hosp., Chicago, Ill., USA, Blood *11:* 745 (1956).

A patient with HF deficiency is described. This syndrome is characterized by complete absence of any hemorrhagic tendency in the presence of laboratory findings which, as a rule are associated with severe disturbances in the hemostatic mechanism. The clotting time was markedly prolonged, the plasma prothrombin time was normal, but prothrombin consumption was decreased. The thromboplastin generation test revealed that HF is essential for blood thromboplastin formation at least in vitro. Procedures for the differentiation of HF deficiency from AHF, PTC and PTA deficiency are outlined. Transfusions of as little as 50 cc of 20 day old blood normalized the abnormal clotting tests immediately for a period of about 36 hours. The basis for the apparent lack of need for preoperative preparation with blood transfusions in HF deficiency is discussed.

Evidence for the Existence of a Third Serum Clotting Factor. Greig, H. B. W., Tattersall, J. C., S. African Inst. Med. Research, Johannesburg, S. Africa, Brit. J. Haematol. *2:* 421 (1956).

As a result of carrying out thromboplastin generation tests with mixtures of sera from a variety of conditions, phenomena were observed which suggest the possibility of the existence of a third serum factor. This third serum factor is deficient in patients treated with coumarin drugs, in patients suffering from hepatitis, and apparently occurred as a congenital defect in 2 cases. The implications of the findings are discussed.

Spontaneous Hemorrhages Caused by Plasma-Thromboplastin-Antecedent Deficiency. Henry, E. I., Rosenthal, R. L., Hoffmann, I., Dept. med. Long Island Jevish Hosp., New York, USA, J. Amer. med. Ass. *162:* 727 (1956).

In a case of PTA deficiency with unusual features of brain-stem bleeding, cutaneous ecchymoses, and recurrent menorrhagia, successful therapy of the acute bleeding and prevention of further episodes were accomplished with administration of stored plasma and bank blood.

Effect of Russell's Viper Venom (Stypven) on Stuart Clotting Defect. Hougie, C., Dept. clin. Path., Univ. of Virginia, Charlottesville, Virg., USA, Proc. Soc. exp. Biol. (N. Y.) *93:* 570 (1956).

It is shown that Stypven does not correct the prolonged one-stage prothrombin time of a patient with a congenital hemorrhagic diathesis previously thought to be deficient in factor VII. The factor deficient in this patient which is referred to as the Stuart factor, is readily distinguishable from both the Prower factor and factor VII since the prolonged prothrombin times of plasma deficient in either of these two factors are completely corrected by Stypven. The finding that Stypven does not correct the clotting defect of Stuart factor deficiency implies that certain modified one-stage „specific" assay methods for prothrombin using Stypven as a source of factor VII are not, in fact, specific, and measure both prothrombin and Stuart factor.

l) Combined Deficiencies of Coagulation Factors

Severe Coagulation Anomalies in a Family of Haemophiliacs. Scardigli, G., Guidi, G., Clinic of General Med., Univ., Florence, Italy, Acta haemat. (Basel) *16:* 338 (1956).

The authors describe a family where in 2 generations they found one pure AHG deficiency, one sister of this patient with a deficiency of CFA (= activation cofactor, a factor described by the authors as cofactor of PTA), the other sister with a deficiency of PTA and AHG, and a nephew lacking PTA. The data obtained in this family became understandable only by admitting that PTA and AHG are not completely independant substances, as classically accepted, but directly linked to one another, and that PTA is merely an activator of AHG. This activator in turn requires the presence of a cofactor (probably of enzymatic nature) called activation cofactor CFA.

Su un caso di emofilia da difetto associato di AHG e di PTA. Grasso, E., Quintè, V., Ist. Clin. Pediatrica, Univ., Milano, Italy, Minerva pediat. *8:* 1153 (1956).

Combined Mild PTC (Plasma Thromboplastin Component) and Factor VII Deficiencies. Stein, H. B., Abrahams, O. L., Dept. clin. Path., Univ. of the Witwatersrand, Johannesburg, S. Africa, S. Afr. J. med. Sci. *21:* 13 (1956).

A case of mild hemorrhagic tendency due to PTC deficiency combined with mild factor VII deficiency is described. The whole blood coagulation time was normal, but the prothrombin consumption relatively poor. The one-stage prothrombin time was slightly prolonged and found to be due to factor VII deficiency, while thromboplastin generation studies revealed a deficiency in PTC.

Coagulation Defects in a Sprue Case. Cetingil, A. I., Ulutin, O. N., Karaca, M., IInd Int. Clinic, Univ. Istanbul, Turkey, N. Istanbul Contr. clin. Sci. *4:* 95 (1956).

This paper presents a case of sprue combined with factor VII and IX deficiency and lack of platelet factor 3 and 4. Thrombocytopenia of a moderate degree and factor VII deficiency were found to be secondary. It could not definitively be decided, it is, however, assumed that the thrombopathy and the deficiency of factor IX also were acquired and not primary.

Vascular Hemophilia. A Familial Hemorrhagic Disease in Males and Females Characterized by Combined Antihemophilic Globulin Deficiency and Vascular Abnormality. Schulman, I., Smith, C. H., Erlandson, M., Fort, E., Lee, R. E., Dept. Pediatrics, N. Y., Hosp.-Cornell Med. Center, New York, N. Y., USA, J. Pediat. *18:* 347 (1956).

The coagulation and vascular aspects of the von Willebrand syndrome have been studied in 7 children, 6 of them demonstrated a severe defect in the coagulation mechanism resulting

from a marked deficiency of AHG. It was found in boys and girls, was familial, and apparently occurred in a manner distinct from the sex-linked recessive inheritance of classical hemophilia. Morphologic capillary abnormalities were noted with or without associated AHG deficiency. Administration of fresh plasma resulted in correction of both bleeding time and coagulation defects in patients with the combined vascular-coagulation abnormality. The vascular abnormality was found to be independent of deficiency of AHG or any of the known platelet factors. Classification of the von Willebrand syndrome into at least 2 groups was recommended: patients with vascular defect plus AHG deficiency (vascular hemophilia), and patients with only vascular defect (pseudohemophilia).

Su un nuova sindrome emorragica in una neonata (deficit assiciato di PTC, fattore VII e protrombina). Vecchio, F., Ist. Clinica Pediatr., Univ., Napoli, Italy, Pediatria (Napoli) *64:* 188 (1956).

Vascular Hemophilia: The Association of a Vascular Defect with a Deficiency of Antihemophilic Globulin. Matter, M., Newconmb, T. F., Melly, A., Finch, C. A., Dept. Med. Univ. Washington Med. School, Seattle, Wash., USA, Amer. J. med. Sci. *232:* 421 (1956).

The pedigrees of 5 families with a hemorrhagic diathesis are presented. The clinical and routine laboratory findings are compatible with the diagnosis of pseudohemophilia or v. Willebrand's syndrome. A detailed study of the hemostatic mechanism revealed vascular abnormalities as demonstrated by prolonged bleeding time, increased capillary fragility and changes in capillary morphology. In addition a deficiency of antihemophilic globulin was present (3 to 75%; controls 60 to 190%). This disorder is designated vascular hemophilia. The possible etiology of the defect and its role in the pathogenesis of bleeding are discussed. Since the inheritance pattern in 4 of 5 families is that of an autosomal dominant with high penetrance and variable expressivity, it is apparent that AHG deficiency can occur in a disorder genetically different from classical hemophilia (A).

A Case of Hemophilia AB in a Girl. Fukutake, M., Oya, T., Fujiwaki, M., Dept. of Blood, Tokyo Med. Coll., Shinjiku-ku, Tokyo, Japan, Saishin Igaku *11:* 189 (1956).

Among 12 cases of hemophilia who have been treated by the authors, a 10-year-old girl was diagnosed as hemophilia AB. No inheritance was proved. Her hemorrhagic symptoma started at the age of 3. Main sign was general hemorrhage with prolonged clotting time (15 ') but with normal bleeding time, normal platelet count, and normal prothrombin time. The results of-cross-matching tests of her serum with that of hemophilia A and B were both negative, but the clotting time was shortened by he addition of serum treated with barium sulphate.

Sulle diatese emorragiche miste: coesistenza di trombopeno-patia e di angiomatosi emorragica nello stesso complesso familiare. Avogaro, P., Caturelli, G., Ist. Patol. Spec. Med. Univ., Padova, Italy, G. Clin. med. *37:* 589 (1956).

m) Hemophilia, General Aspects

Neurological Complications of Hemophilia and Christmas Disease. Douglas, A. S., McAlpine, S. G., Univ. Dept. Med. Royal Infirmary, Glasgow, Scotland, Scott. med. J. *1:* 270 (1956).

Neurological complications occurred in 5 patients with hemophilia and 4 patients with Christmas disease, an incidence of 10% in a series of 90 patients with these disorders. 6 of the 9 patients had peripheral nerve lesions, the remaining 3 had central nervous system involvement. The importance of immediate and adequate replacement therapy is stressed.

Traitement de l'hémophilie. Alagille, D., Centre Nat. Transfusion Sanguine, Paris, France, Rev. Practicien *6:* 2329 (1956).

Transfusion of whole blood or plasma is thought to be still the essential means in the treatment of hemophilia. This presents, however, only a substituting therapy, the indication of which has to be thoroughly discussed, as one has the choice of the hemostatic effect obtainable and the risk of inducing a refractory state.

Etude biologique de l'hémophilie, tests de l'hémostase — dosage des facteurs anti-hémophilique. Larrieu, M. J., Inst. Nat. d'Hygiène, Paris, France, Rev. Practicien *6:* 2307 (1956).

The author presents a review of the classical and of the more recently described tests used in the diagnosis of hemophilia, such as coagulation time, heparin tolerance test, prothrombin consumption, bleeding time, various mixture tests, and thromboplastin generation test.

Formes cliniques de l'hémophilie. Soulier, J. P., Centre Nat. Transfusion Sang., Paris, France, Rev. Practicien *6:* 2295 (1956).

The author describes the various clinical forms of hemophilia. They all have the following characteristics in common: it is a sex-linked, congenital affliction, characterized by hemorrhages due to the deficiency of a plasmatic factor necessary for the formation of thromboplastin. In about 85% of the cases it is the antihemophilic factor A and in 15% the antihemophilic factor B. As far as hemophilia C and D are concerned, they remain exceptional and can only be traced by highly specialized laboratories.

Rarer Cases of Hemorrhagic States from the Group of So-Called Hypothromboplastinemias. Hermansky, F., Pudlak, P., Ist Med. Clinic, Charles Univ. Praha, Czechoslovakia, Čas. lék čes. *95:* 182 (1956).

2 cases of hemophilia B in the same family and one sporadic case are described. The latter was diagnosed mainly with the thromboplastin generation test, which showed the defect even when prothrombin consumption was normal. One case of hemorrhagic disease in a woman is discussed. The coagulation time was slightly prolonged and prothrombin consumption lowered. Some of the laboratory results indicated hemophilia C, there was, however, a poor mutual correction ability with blood of hemophilia A and B. 3 cases of sporadic thrombocytoasthenia are then discussed. The occurrence of the various hemorrhagic states belonging to the group of hypothromboplastinemias is discussed together with difficulty of diagnosis.

Etude clinique de l'hémophilie classique. Revol, L., Brizard, C. P., Fac. de Méd., Lyon, France, Rev. Practicien *6:* 2287 (1956).

Diagnostic différential de l'hémophilie. Bernard, J., Beaumont, J. L., Hôp. Hérold, Paris, France, Rev. Practicien *6:* 2323 (1956).

Haemophilia Involving Pharynx and Larynx. Colman, B. H., Edinburgh, England, J. Laryng. *70:* 540 (1956).

Beitrag zur Differenzierung und Therapie der hämophilen Gerinnungsstörung. Landbeck, G., Univ.-Kinderklinik, Hamburg-Eppendorf, Germany, Z. Kinderheilk. *78:* 480 (1956).

Contribution to the differentiation and therapy of hemophilic coagulation disorders. Report of 34 own cases from 25 families. 17 families with 21 cases of hemophilia A., 5 families with 9 cases of hemophilia B and one family with 4 cases of PTA deficiency. Among the hemophilia A cases 2 brothers were studied with a simultaneous platelet factor deficiency. In 8 cases out of 9 with hemophilia B also factor VII deficiency was noted. PTA cases were found in both sexes, the term hemophilia C, therefore, does not seem to be indicated.

n) Platelets

A propos des thrombopathies familiales sans thrombopénie. Neimann, N., Sem. Hôp. Paris *32:* 3849 (1956).

Cerebrospinal Fluid Thrombocyte-Agglutinating Substance in Multiple Sclerosis. Persson, I., Copenhagen, Denmark, Arch. Neurol. *76:* 343 (1956).

Hépatite épidémique et purpura thrombocytopénique. Huguenin, A., Alger, Sem. Hôp. Paris *32:* 4158.

Indications actuelles de l'hormonthérapie et de la splénectomie dans le traitement des purpuras thrombopéniques idiopathiques. Bernard, J., Beaumont, J. L., Caen, J., Centre de Recherches de L'Association Claude Bernard, Hôp. Hérold, Paris, France, Sang *27:* 882 (1956).

In cases of thrombocytopenic purpura (TPP) hormones may frequently influence haemorrhage, and capillary fragility more than the increased bleeding time. Thrombocytopenia,

deficient clot retraction and prothrombin consumption are much more rarely influenced. Cortison (or similars) represents best initial therapy of TPP. Permanent thrombocytopenia should not be treated with hormones but with splenectomy. Intermittent thrombocytopenia should according to its severity be treated either one way or the other. After failure of splenectomy to improve the condition (30 to 40%) hormones should be administered, which in general exert a moderate effect.

Contributo clinico allo studio delle porpore trombopeniche acute. Re A., Poretti, F., Osp. di Circolo "Luvini" Cittiglio/Varese, Italy, Minerva med. *47:* 1827 (1956).

Plaquettes et parois vasculaires dans la pathogénie du purpura thrombopénique chronique. Roskam, J., Clin. méd., Univ. Liège, Belgium, Sang *27:* 856 (1956).

In chronic thrombocytopenique purpura and most probably also in all other types of purpura with quantitative or qualitative platelet deficiency, the pathogenesis is characterized by the following points: 1. the type of hemorrhage points to a mixed pathogenesis where as well the decrease in number or in adhesiveness of platelets takes part, as a peripheric vascular factor. 2. The spontaneity and the general ubiquity of the hemorrhages seem to be above all caused by an, as yet unexplained, vascular factor.

Thrombopenie bei Serpasilbehandlung. Schmidt, K., Wien. klin. Wschr. 28: 579 (1956) und Wien. med. Wschr. *38/39:* 820 (1956).

Report of a case.

Encephalitis and Thrombocytopenic Purpura after Rubella. Steen, E., Torp, K. H., Pediatric and Epidemiolgy Dept., Ulleval Hosp., Oslo, Norway, Arch. Dis. Childh. *31:* 470 (1956).

Kongenitale hypoplastische Thrombopenie mit Radiusaplasie. Ein Syndrom multipler Abarten. Gross, H., Univ.-Kinderklinik, Wien, Austria, N.-Österr. Z. Kinderheilk. *1:* 583 (1956).

Lipid Extracts of Platelets and Brain as Substitutes for Platelets in Coagulation. Tests. Wolf, P., The Lister Inst., London, England, Brit. J. Haematol. *2:* 375 (1956).

A comparison has been made of coagulation properties of fresh and aged platelet suspensions, an ether extract of platelets, and a chloroform extract of brain. All these preparations were active prothrombin conversion; the prothrombin conversion ratio was increased by increasing the amount of platelets or of lipid extracts to a maximum, after which further increases were inhibitory. Undiluted lipid extracts inhibit prothrombin conversion by inhibiting factor VII, and not by antithrombin activity. The extracts had neither factor V — nor VII — activity, and the slight factor V-activity of washed platelets seems to be due to adsorbed plasma proteins. Platelet suspensions differ from lipid extracts in having anti-heparin activity; this is evident only in the presence of plasma. It is concluded that ether extracts of platelets or chloroform extracts of brain can replace platelet suspensions in clotting test systems not containing heparin. The prothrombin conversion factor of platelets and of the lipid extracts may be the same; they may also be identical with the clotting factor in the cephalin-like material studied by Howel (1912).

Die thrombotische Thrombopenie, eine noch wenig bekannte Erkrankung. Simon, K., Inst. G. Rousky, Centre clin. et thérap., Villejuif/Seine, France, Med. Mschr. *10:* 502 (1956).

Aglutinnias plaquetares. I. Aglutination inespecifica por un factor de la coagulation contenido en el suero normal (factor VII). Maspes, V., Verrastro, T., Coelho, E., Jamra, M., Hosp. de las Clin. de la Faculdad de Med., Univ., Sao Paolo, Brasil, Sangre *1:* 156 (1956).

The authors demonstrate the existence of a serum factor able to agglutinate platelets in vitro. Serum looses this property after adsorption on tricalcium phosphate gel. Based on serial experiments the authors come to the conclusion that the factor involved is factor VII.

Purpura thrombopénique et ictère transfusionnel. Junet, R., Cruchaud, A., Clin. Méd. int., Genève, Switzerland, Rev. méd. Suisse rom. *76:* 939 (1956).

Case report.

Anemia emolitica acuta felbrile con piastrinopenia trombotica in ustionato. Saita, G., Arrigoni, E., Galli, P., Clin. del Lavoro "L. Devoto", Univ., Milano, Italy, Minerva med. *47:* 94 (1956).

The authors report a case of acute hemolytic anemia with thrombotic thrombocytopenia and fever (Moschowitz's syndrome) in a patient of 38 following 2nd and 3rd degree burns on one hand and fore-arm.

La reazione di consumo di siero antiglobuline umane nella diagnosi di porpora piastrinopenica autoimmune. Ruggieri, P., Bolognesi, G., Ravetta, M., Ist. Clin. Med. Generale, Univ. Roma, Italy, Boll. Soc. ital. Ematol. *4:* 66 (1956).

The authors used the Steffen test (human serum antiglobulin consumption) for the diagnosis of immuno-thrombocytopenic purpura. This test offers the possibility to demonstrate the existence of antiplatelet antibodies in the serum of patients with thrombocytopenic purpura.

Recherches sur le mécanisme de la rétraction du caillot et de la métamorphose visqueuse des plaquettes. Bounameaux, Y., Clin. méd. Labor de Coagulation, Univ., Zurich, Switzerland, Experientia (Basel) *12:* 355 (1956).

The theory that viscous metamorphosis of platelets and clot retraction are initiated by thrombin and a dialyzable factor has been confirmed. Under certain circumstances glucose acts as dialyzable factor. Clot retraction seems to depend upon the catabolism of glucose.

Study of Transfused Platelets in a Case of Congenital Hypoplastic Thrombocytopenia. Doyne Bell, A., Mold, J. W., Oliver, R. A. M., Shaw, S., Dept. Pediatrics and clin. Path., Charing Cross Hosp., London, England, Brit. med. J.,1956: 692.

A case of congenital hypoplastic thrombocytopenia associated with other congenital defects is described with post-mortem findings. Similar cases are briefly reviewed and the differential diagnosis considered. The progress and treatment with platelet transfusions, cortisone and splenectomy are described and discussed. Repeated platelet transfusions have been found to be of value and a simple technic is outlined. Information regarding the survival of platelets in vivo and in vitro following transfusion has been obtained. The value and limitations of platelet transfusion are discussed.

Die Fermente der menschlichen Thrombozyten und ihre wahrscheinliche Bedeutung im Mechanismus der Hämostase. Pedrazzini, A., Salvidio, E., Med. Abtlg., Kantonsspital, Winterthur, Switzerland, Schweiz. med. Wschr. *86:* 1097 (1956).

Investigation of the proteinic and the fermental system of human thrombocytes in normal individuals as well as in physiologic or functional disorders of blood coagulation lead to the assumption that the fermental systems play an important role in hemostasis. Thrombocytes, with descreased activity due to various fermental disorders, may favor the appearance of hemorrhagic manifestations.

Hämorrhagische Diathese nach Splenektomie. (Thrombocythaemia haemorrhagica). Koller, F., Bounameaux, Y., Gerinnungsphysiol. Lab. Med. Klinik, Univ., Zurich, Switzerland, Bull. schweiz. Akad. med. Wiss. *12:* 248 (1956).

An excessive increase of platelets (several millions) which sometimes occurs after splenectomy or for other reasons, may lead to severe hemorrhagic diathesis. The authors were able to show that thromboplastin generation is inadequate in these cases. The reason for it consists probably in the disproportion between the concentration of platelet factor 3 and the other clotting factors essential in blood thromboplastin formation. Clinically the patients present characteristics of coagulopathy (no petechiae).

Über die Morphologie und den Gestaltwandel der hämophilen Thrombozyten. Fonio, A., Poststraße 19, Chur, Switzerland, Schweiz. med. Wschr. *86:* 1439 (1956).

A sample of hemophilic blood shows a greater number of small, round, distinct forms of platelets than a normal sample. The disintegration of these platelets also occurs later than in normal blood. This indicates increased resistance of hemophilic platelets and thus delayed liberation of certain factors necessary for normal coagulation.

Hemopatia trombopénica y embarazo. Rosenvasser, E., Ramazzi, P., Clin. Ost. Med., Hosp. Alyear, Buenos Aires, Argentina, Rev. esp. Obstet. Ginec. *15:* 17 (1956).

Zur Behandlung der thrombozytopenischen hämorrhagischen Diathese mit 5-Oxytryptamin (Serotonin). Siegenthaler, W., Med. Klinik, Kantonsspital, St. Gallen, Switzerland, Schweiz. med. Wschr. *86:* 1443 (1956).

In 25 cases of essential or symptomatic thrombocytopenia the author investigated the effect of serotonin therapy, studying platelet levels and bleeding time. An increased serotonin level in serum results in an increase of platelets if thrombocyte depots are not exhausted or damaged. Serotonin is therefore useful as a therapy of temporary thrombocytopenia and control of critical stages. All patients reacted with shorter bleeding times to serotonin administration.

Der Einfluß von Thrombozytenprotein auf die Permeabilität der Blutkapillare. Wilbrandt, W., Lüscher, E., Asper, H., Pharmakol. Inst., Univ., Bern, Switzerland, Helv. physiol. pharmacol Acta *14:* 81 (1956).

The authors studied the influence of protein "S" (an albumin fraction contained in thrombocytes) on capillary walls. This protein has great affinity to calcium. It is suggested that this protein "S", originating from platelets, coats capillary walls as a calcium salt. Protein "S" together with calcium is able to normalize decreased capillary permeability. Calcium alone does not have this property.

Cytochemical Assessment of Megakaryocytic Activity. Chatterjea, J. B., Chowdhury, A. B., DasGupta, C. R., Ray, H. N., Dept. Hematol. School of Tropical Med., Calcutta, India, Bull. Calcutta School Trop. Med. *4:* 64 (1956).

The concentration of alkaline phosphatase was found to be high in the cytoplasm of "active" megakaryocytes and low in the "inactive" megakaryocytes. The intracytoplasmic alkaline phosphatase reaction of megakaryocytes appears to be an index of its physiological activity.

Effects of Splenectomy on the Polysaccharidic Content of the Bone Marrow Megakaryocytes in Werlhof's Disease. Scavo, D., Andrea, G., Clinica Med. Generale, Univ., Pisa, Italy, Boll. Soc. med. chir. Pisa *24:* 45 (1956).

Five cases of hemorrhagic thrombocytopenic purpura were studied immediately before splenectomy, and after 2, 24 and 48 hours. It was observed that before splenectomy, the glycidic and particularly, glycogenic content is markedly reduced in the bone marrow megakaryocytes. After splenectomy there is a rapid increase of the polysaccharidic content.

Das Thrombozytenbild bei akuten Leukosen im Kindesalter und seine Beeinflussung durch moderne Therapeutika. Quaiser, K., Univ.-Kinderklinik, Graz, Austria, Neue Österr. Z. Kinderheilkunde *1:* 255 (1956).

The Similarity of the Action of Phosphatidyl-ethanol-amine and platelets in Blood Coagulation O'brien, J. R., Central Lab., Pathol. Serv., Milton Road, Portsmouth, England, J. clin. Path. *9:* 47 (1956).

Microméthode pour l'isolement des plaquettes sanguines chez l'homme et chez les petits mammifères. Copley, A. L., Baléa, T., Vo-Vinh-Hoa, Centre Nat. de Transfusion Sanguine, Paris, France, Rev. Hémat. *11:* 324 (1956).

The authors describe a micromethod for the isolation of platelets from human blood and from blood of small mammals. This method permits the use of blood from cutaneous vessels in small mammals where veins are hardly accessible; on the other hand in humans, in particular children, blood samples can be taken repeatedly. This method is of interest for the study of hemorrhagic disorders and for the investigation of the role and various properties of platelets.

Das Syndrom Hämangiom, thrombopenische Purpura und Anämie im Säuglingsalter. Stuber, H. W., Kant. Bern, Säuglings- und Mütterheim Elfenau, Bern, Switzerland, Helv. paediat. Acta *11:* 194 (1956).

Purpura thrombopénique aigu mortel avec thrombo-agglutinines hétérophiles. D'Eshougues, J. R., Griguer, P., Alger, Sang *27:* 138 (1956).

Su di un nuovo metodo per il conteggio diretto delle piastrine. Palumbo, E., Dini, E., Ist. Semeiotica Med., Univ. Napoli, Italy, Haematologica *41:* 373 (1956).

The authors describe a method of direct platelet count using a solution containing quinine lactate and nicotin-acid dethylamide. The counts are made by means of a normal microscope.

Die Ausreifungszeit der Thrombozyten. Hess, D., Moeschlin, S., Med. Klinik, Bürgerspital, Solothurn, Switzerland, Schweiz. med. Wschr. *86:* 1435 (1956).

The ripening time of human thrombocytes has been calculated to 6 to 8 days.

Cytochemical Studies of the Megakaryocytes and Platelets in Pathological Conditions. Perugini, S., Soldati, M., Inst. Med. Path., Univ. Modena, Italy, Schweiz. med. Wschr. *86:* 1437 (1956).

The identification of polysaccharides in megakaryocytes permits conclusions concerning their platelet-forming activity. The observations confirm the physiopathologic and pathogenetic difference between thrombocytopenic and thrombocytotic syndromes, although the clinical findings are frequently similar. Cytochemical studies permit a more precise means of characterizing and differentiating these syndromes.

Die klinische Bedeutung des Nachweises von Antikörpern gegen Thrombozyten bei thrombopenischer Purpura. Pfeiffer, E. F., Spielmann, W., Ditschuneit, H., I. Med. Univ.-Klinik, Frankfurt a. M., Germany, Dtsch. med. Wschr. *81:* 735 (1956).

One part of the cases of so-called idiopathic chronic thrombocytopenias are probably caused by immunologic processes, as proved by the demonstration of an antibody against thrombocytes. 2 cases of the so-called idiopathic form of this condition were found to have complete and incomplete pan- and autoantibodies against platelets, and their sera caused severe thrombocytopenia when injected into rabbits. Serological findings and clinical condition were closely related, in that highest antibody titer was recorded during periods of lowest platelet levels. The results of therapeutic measures (splenectomy, ACTH, cortisone) also showed correlation with antibody titers. It is concluded that the determination of antibodies against platelets is of great clinical importance.

Plaquettes et réaction antigène-anticorps in vitro. Bounameaux, Y., Lecomte, J., Int. Clin. and Pathol. Méd. A, Univ., Liège, Belgium, Acta allerg. (Kbh.) *9:* 288 (1956).

La milza nelle porpore trombopeniche idiopatiche. Caltabioano, S., Clinica Med. Generale, Univ., Pisa, Italy, Pass. Fisiopatol. *28:* 137 (1956).

Histologic studies were carried out on spleens removed from 10 patients suffering from idiopathic thrombocytopenic purpura. Marked hyperplasia of the splenic pulp was found in all cases. Follicular hyperplasia, however, was less frequent. Significant eosinophilia could always be found. It is concluded that the spleen in idiopathic thrombocytopenic purpura is constantly irritated by hyperplasia of the reticuloendothelium, caused by constant allergic sensitization. The physio-pathologic significance of these findings is discussed with regard to most recent knowledge of the pathogenesis of ITP.

Rilievi sulla diagnostica delle teleangio-trombopatie. Camera, A., Romagnoli, A., Ist. Semeiotica Med. Univ., Napoli, Italy, Pediatria (Napoli) *64:* 263 (1956).

Thrombocytopenic Purpura Following Quinine Medication. Kissmeyer-Nielsen, F., Inst. General Path. Univ., Aarhus, Denmark, Acta med. scand. *154:* 287 (1956).

A case of quinine-induced thrombocytopenia is reported. Serological studies show that the patient's serum contained a factor which in the presence of quinine was able to agglutinate platelets, fix complement, and reduce clot retraction. Various studies seemed to show that quinine acts as a link between platelets and the serum factor. Quinine could be replaced by optochin, but not by quinidine. It is emphasized that serological studies should as much as possible replace in vivo experiments in the clarification of the etiology of drug-induced thrombocytopenias.

Indications des dérivés du sang dans les affections de la série plaquettaire. Maupin, B., 101 ave. Henri-Barbusse, Clamart, Seine, France, Sang *27:* 29 (1956).

Vorkommen leukozytenagglutinierender und thrombozytärer Antikörper bei einem akuten Fall von Lupus erythematosus disseminatus. Müller W., Radojicic, B., Med. Univ.-Klinik, Freiburg/Br., Germany, Klin. Wschr. *34:* 577 (1956).

Über die Brauchbarkeit des Kollidons zur Herstellung von Thrombozytenanreicherungen für Transfusionszwecke. Matthes, M., Sickinger, K., Med. Univ.-Klinik, Freiburg/Br., Germany, Klin. Wschr. *34:* 586 (1956).

Essential Thrombocythemia, Chronic Myeloid Leukemia or Polycythemia Vera? Gouldsmith, R., Univ. Med. Clinic, Binnengasthuis, Amsterdam, Holland, Ned. T. Geneesk. *100:* 1236 (1956).

Report of a 76-year-old woman who was admitted to the hospital on several occasions with anemia caused by unexplained intestinal hemorrhages. At first the only finding consisted of increased thrombocytes and leukocytes in the patient's blood. After 3 years the whole syndrome of polycythemia vera developed.

Le trombocitopenie. Cardinali, G., Ospedale Riuniti, Roma, Italy, Policlin. *63:* 461 (1956).

Steigerung der Thrombozytenzahl unter akuter Erregung, sowie auf Adrenalin und Noradrenalin. Parchwitz, E., Wacholder, K., Physiol. Inst., Univ., Bonn, Germany, Klin. Wschr. *34:* 1212 (1956).

Die direkte phasenoptische Thrombozyten- und Retikulozytenzählung. Derlath, S., I. Med. Univ.-Klinik, München, Germany, Ärztl. Forsch. *10:* 552 (1956).

Two methods for counting thrombocytes and reticulocytes in a counting chamber are described. The platelet method described is a modification of the one published by Feissly and Lüdin and allows the enumeration of leukocytes, platelets and reticulocytes in one counting chamber within 15 mins.

Thrombocytopenic Purpura in Tuberculosis. Kalinowski, S. Z., Walker, J. M., St. Wulstan's Hosp., Malvern, Worcs., England, Brit. J. Tuberc *1956:* 239.

Two cases of thrombocytopenic purpura in tuberculosis are reported. One patient died and post-mortem revealed acid-fast bacilli in the spleen and liver. A second case recovered after splenectomy.

Einfluß der Thrombozyten auf die durch das gerinnungsfördernde Schlangengiftenzym bedingte Blutgerinnung. Klobusitzky, D. v., Sao Paolo, Brasil, Klin. Wschr. *34:* 1262 (1956).

La cholinestérase dans le mégakaryocyte et la plaquette sanguine. Rogister, G., Lab. Anatomie, Serv. F. Vandervael, Univ., Liège, Belgium, Rev. franç. Etudes clin. and biol. *1:* 1078 (1956).

Megakaryocytes of various mammalien species show a high, but variable acetyl-cholinesterase activity. The enzyme is contained in the cytoplasm of the megakaryocytes. In the mouse platelets show marked acetyl-cholinesterase activity as was to be expected from the finding of the enzyme in megakaryocytes. Human platelets apparently never show this activity. The possible role of acetyl-cholinesterase derived from platelets in vasoconstriction can, therefore, only be considered in certain species.

Hémorragies thrombocytopénique arrêtées par injections intraveineuses de fibrinogène humain. Cazal, P., Graafland, R., Izarn, P., Faculté de Méd., Monpellier, France, Sang *27:* 84 (1956).

Cohn's unpurified fraction I contains about 60% of fibrinogen, and only very small amounts of active plasmin and antihémophilic factor. The authors have used this fraction in the treatment of hemorrhages of 4 thrombocytopenic subjects. 9 times out of 10 rapid arrest of hemorrhage was obtained. The authors suggest that platelet insufficiency is compensated for by excess of fibrinogen.

Glukose als Cofaktor bei der Retraktion des Blutgerinnsels. Lüscher, E. F., Theod. Kocher Inst., Univ. Bern, Switzerland, Experientia (Basel) *12:* 294 (1956).

The dialysable factor, besides thrombin, necessary for the retraction of a platelet-containing fibrin clot was identified as glucose. During retraction lactic acid was liberated, indicating a relationship between the retraction mechanism and the enzymatic activity of platelets.

A propos d'un cas de thrombocytopénie avec hémorragie dû à la quinidinothérapie. Perrin, M., Nantes, France, Arch. Mal. Coeur *49:* 551 (1956).

Über einen Fall von hyporektraktiler, granulopenischer Thrombozytopathie. Fonio, A., Poststraße 19, Chur, Switzerland, Schweiz. med. Wschr. *86:* 1150 (1956).

La valeur clinique de l'agglutinabilité et de l'adhésivité des thrombocytes. Inceman, S., 3e Clinique méd. Univ., Istanbul, Turkey, Sang *27:* 565 (1956).

Phasenoptische Thrombozytenzählung. Siering, H., Med. Univ.-Klinik, Jena, Germany, Yokohama med. Bull. *7:* 79 (1956).

A Case of Hemorrhagic Thrombocythemia. Browne, M. K., Ballochmyle Hosp., Mauchline, Ayrshire, Scotland, Scott. med. J. *1:* 365 (1956).

Thrombocytopénie, hyperagglutinabilité et adhésivité plaquettaire provoquées par le BCG chez le lapin. Copley, A. L., Lab. de Physiol., Centre Internat. de l'Enfance, Paris, France, Ann. Inst. Pasteur Lille *91:* 736 (1956).

Einfluß der Thrombozyten auf die durch das gerinnungsfördernde Schlangengiftenzym bedingte Blutgerinnung. Klobusitzky, D., Forschungslabor Dr. Klobusitzky, Sao Paolo, Brazil, Klin. Wschr. *34:* 1262 (1956).

Die Bedeutung thrombozytärer Antikörper für die Klinik der Thrombocytopenien. Weinreich, J., Univ.-Klinik, Freiburg/Br., Germany, Folia haemat. *1:* 1 (1956).

Die essentielle Thrombopenie nach 40 Jahren. Frank, E., IInd Int. Clinic, Univ., Istanbul, Turkey, N. Istanbul Contr. clin. Sci. *4:* 43 (1956).

Essential thrombopenia reconsidered after 40 years. Review.

Die isolierten und assoziierten Athrombien. Frank, E., Ulutin, O. N., Karaca, M., IInd. Int. Clinic, Univ. Istanbul, Turley, N. Istanbul Contr. clin. Sci.*4:* 62 (1956).

The phenomenon of prolonged bleeding time in consequence to the insufficiency of the platelet thrombus despite numerically sufficient platelets has been termed "Athrombia" by Frank. This paper describes 5 cases of thrombopathia (Willebrand-Jürgens), and 2 cases of thrombasthenia (Glanzmann-Nägeli-Braunsteiner), and discusses their defect hemostatic mechanism. The authors then discuss the problem whether thrombin or a combination of factor VIII, IX and calcium are responsible for the agglutination of platelets and their viscous metamorphosis.

Untersuchungen über die Physiopathologie der Blutplättchen. Introzzi, P., De Nicola, P., Ist. Clin. Med. Generale, Univ., Pavia, Italy, Sci. med. ital. *4:* 697 (1956).

The following problems were studied and are discussed in this paper: Alterations of thromboplastin activity of isolated platelets in hypo- and hypercoagulability. Relationship between thromboplastic and adhesive function of platelets, and between lysis and agglutination of platelets with special regard to morphologic characteristics and to the liberation of thromboplastin. Description of platelet antigens. Comparative study of adhesive and retractive function of platelets in cases of platelet deficiency and other coagulation studies. Clinical importance of these problems is mentioned.

Conditions étiologiques et évolution des thrombopénies idiopathiques. Bernard, J., Mathé, G., Toulouse, J., Sang *27:* 907 (1956).

Identification of 5-Hydroxytryptamine in Thrombocytes of Birds. Bracco, M., Curti, P. C., Ist. Patol. Med., Univ., Genova, Italy, Experientia (Basel) *12:* 32 (1956).

5-Hydroxytryptamine was isolated from extracts of purified bird thrombocytes. Chemical, spectrophotometric and biological properties were identical to those of 5-hydroxytryptamine contained in mammalien platelets.

Vue actuelle sur le rôle des plaquettes dans la coagulation sanguine. Seegers, W. H., Serv. Prof. J. Bernard, Hôp. Hérold, Paris, France, Sang *27:* 866 (1956).

Thrombocytopenic Purpura Due to Drugs. Divekar, M. V., K.E.M. Hospital, Bombay, India, Indian J. med. Sci. *10:* 41 (1956).

Five cases thrombocytopenic purpura, presumably due to drugs, are described. The alleged offending drugs were para-amino-salicylic acid, isonicotinic-acid-hydrazide, sulphothiazole, streptomycin, a tonic preparation containing vitamin B_{12} and crude liver ectract, and a homeopathic pill. In all the cases spontaneous remission followed withdrawal of the suspected drug.

Reserpine and Human 5-Hydroxytryptamine. Hardisty, R. M., Ingram, G. I. C., Stacey, R. S., Dept. Path. and Ther., St. Thoma's Hosp., Med. School, London, England, Experientia (Basel) *12:* 424 (1956).

One single intramuscular injection of 1 mg of Reserpine in the man results in a decrease of the 5-hydroxytryptamine content of blood platelets which continues for 2 days and which remains then at undeterminable values until the 9th day.

Osservazioni sulla piastrinopenia da trattamento estrogenico. Tusini, G., Dall'Orso, G., Ist. Patol. Spec. Chir., Univ. Genova, Italy, Biol. lat. (Milano) *9:* 88 (1956).

Zur Verteidigung meiner Methoden der Trennung der Strukturelemente der Thrombozyten. Fonio, A., Poststr. 19, Chur, Switzerland, Wien. Z. inn. Med. *37:* 255 (1956).

Zur Methode der Trennung von Hyalomer und Granulomer. Braunsteiner, H., Med. Univ.-Klinik, Wien IV, Austria, Wien. Z. inn. Med. *37:* 256 (1956).

Viscous Metamorphosis of Blood Platelets and Clot Retraction. Lüscher, E. F., Physiol. Inst., Univ. Bern, Switzer land, Vox sang. *1:* 133 (1956).

Sur la spécificité des anticorps antiplaquettaires. Rapports avec le phénomène de Forssman. De Nicola, P., Clinique méd., Univ. Pavia, Italy, Sang *27:* 708 (1956).

Thrombotic Thrombocytopenic Purpura Diagnosed by Random Lymph Node Biopsy. Morey, D. A. J., White, J. B., Daily, W. M., Dept. int. Med., Southwestern Med. School, Univ. of Texas, Dallas, Texas, USA, Arch. intern Med. *98:* 821 (1956).

A case of thrombotic thrombocytopenic purpura is reported in which the ante-mortem diagnosis was confirmed by lymph node biopsy. It is suggested that in the precense of the triad of hemolytic anemia, thrombocytopenia, and cerebral disfunction, the use of lymph node biopsy may prove valuable in establishing a diagnosis of thrombotic thrombocytopenic purpura.

Exacerbation of Lupus Erythematosus Following Splenectomy in "Idiopathic" Thrombocytopenic Purpura and Autoimmune Hemolytic Anemia. Dameshek, W., Reeves, W. H., Dept. Med. Tufts Univ. Med. School, Boston, Mass., USA, Amer. J. Med. *21:* 555 (1956).

Cerebrospinal Fluid Thrombocyte-Agglutinating Substance in Multiple Sclerosis. Persson, I., Nørre Hosp., Copenhagen, Denmark, Arch. Neurol. Psychiat. (Chicago) *76:* 343 (1956).

Elevation of Platelets in Mid-Cycle: an Indication of Ovulation. Pepper, H., Lindsay, S., Sequoia Hosp., Red Wood City, Calif., USA, Science *124:* 180 (1956).

Release of Blood Platelet Serotonin by Reserpine and Lack of Effect on Bleeding Time. Shore, P. A., Pletscher, A., Tomich, E. G., Kuntzman, R., Brodie, B. B., Bethesda, Md., USA, J. Pharmacol. *117:* 232 (1956).

The administration of reserpine to rabbits, rats, and guinea-pigs resulted in a release of serotonin from platelets without destroying them. A release of 90% of serotonin has no influence on blood coagulation, it is, therefore, assumed that serotonin does not take part in blood coagulation.

Thrombocytopenic Purpura Related to the Induction of Labor. Hofmeister, F. J., Dept. Obst. Gynecol., Milwaukee Hosp., Wis., USA, Amer. J. Obstet. Gynec. *72:* 594 (1956).

Platelet Decrease and Disappearance in Obstetric Conditions. Ferguson, J. H., Dept. Obst. and Gynec., Tulane Univ. Med. School, New Orleans, USA, Amer. J. Obstet. Gynec. *72:* 1315 (1956).

Bovine Platelets, Serotonin and the Retraction of Human Plasma Clots. Fenichel, R. L., Detroit, Mich., USA, Clin. Chem. *2:* 281 (1956).

Factors inducing clot retraction were removed from human citrated plasma by $BaCO_3$ adsorption and by dialysis. After addition of serotonin $BaCO_3$ eluate or of eluate from bovine platelet dialysate, normal retraction is restored.

Thrombocytopenic Purpura Due to Quinidine. I. Clinical Studies. Bolton, F. G., Dameshek, W., Blood Res. Lab., Ziskind Lab., N. England Center Hosp., Boston, Mass., USA, Blood *11:* 527 (1956).

Five cases of thrombocytopenic purpura due to quinidine are described and the relevant literature is reviewed. Quinidine purpura is an acute self-limiting disease occurring most commonly in women over 50 years of age. The prognosis is excellent providing quinidine therapy is stopped early in the disease. Purpura occurs after varying periods of administration of quinidine in variable quantities; purpura usually follows quickly upon the causative dose. Intraoral hemorrhagic bullous lesions should suggest the possibility of drug thrombocytopenic purpura. In vitro serologic tests are an efficient method of establishing a diagnosis.

Thrombocytopenic Purpura Due to Quinidine. II. Serologic Mechanism. Bolton, F. G., Blood Res. Lab., Ziskind Lab. N. England Center Hosp., Boston, Mass., USA, Blood *11:* 547 (1956).

Investigations of serologic reactions in a case of quinidine purpura showing a strong concentration of platelet antibody are described. In the presence of quinidine, but not of quinine, the antibody of the patient was able to cause platelet agglutination, and, in the presence of complement, lysis of both normal platelets and platelets from the patient. The platelet-quinidine antibody complex fixed complement. Platelets in the presence of quinidine were able to absorb antibodies, this complex could be separated by centrifugation and it was then capable of fixing complement. By serologic testing no union was demonstrable between normal platelets and quinidine and between plasma from the patient and quinidine. Dialysis of the platelet-quinidine-antibody complex against saline readily split the complex in its 3 constituents. The antibody lay in the gamma globulin fraction; it was destroyed by heating at 65—70 ° C. for 30 mins. The antibody was found to be inactive against blood vessels. The mechanism by which quinidine confers antigenicity, presumably upon platelets, was not elucidated in these experiments.

Hemostasis in Thrombocytopenic Bleeding Following Infusion of Stored, Frozen Platelets. Klein, E., Toch, R., Farber, S., Freeman, G., Fiorentino, R., Children's Cancer Res. Found., Children's Med. School, Boston, Mass., USA, Blood *11:* 693 (1956).

Platelets concentrated and stored in their own plasma at — 15 C. up to 6 weeks were administered to severely ill, thrombocytopenic bleeding children in whom hemostasis had not been attained by other measures. 18 of 29 infusions in 15 children appeared to result in transitory hemostasis. Transient elevation of the blood pressure and local vasoconstriction accompanied the administration of platelet material. No evidence of serius toxicity or thrombosis have been encountered.

Specifity of Lytic Factors for Erythrocytes, Leukocytes and Platelets in a Case of Pancytopenia. Matoth, Y., Elian, E., Nelken, D., Nevo, A. C., Dept. Pediatrics, Rothschild Hadassah Univ. Hosp., Jerusalem, Israel, Blood *11:* 735 (1956).

A case of chronic idiopathic pancytopenia in a young girl is presented in which the pancytopenia was shown to be due to increased destruction of all 3 blood cell types. Antileukocyte and antiplatelet antibodies were demonstrated by transfusion methods as well as by in vitro agglutination, while differential agglutination provided evidence of a plasma factor causing increased red cell destruction. Cross adsorption experiments demonstrated the presence in the patient's serum of at least 2 separate and distinct antibodies, specific for leukocytes and platelets respectively. Observations on the phagocytic behaviour of leukocytes and on the electrophoretic mobility of leukocytes and platelets exposed in the patient's serum are reported.

A Practical Method for the Aseptic Preparation of Human Platelet Concentrates Without Loss of Other Blood Elements. Klein, E., Arnold, P., Earl, R. T., Wake, E., Children's Med. Center, Harvard Univ., Boston, Mass., USA, N. England J. Med. *254:* 1132 (1956).

The following procedures can be carried out simultaneously, successively, or alternatively in the closed system described: preparation of platelet concentrates; preparation of packed red blood cells; separation of the buffy coat; preparation of cell-free plasma; reconstitution of one or more blood elements without risk of mismatching; removal of aliquots of whole blood or of blood elements. The closed system eliminates the risks of contamination usually inherent in procedures that require multiple entries into the primary blood container.

Determination of the Life Span of Human Blood Platelets Using Labelled Diisopropyl Fluorophosphonate. Leeksma, C. H. W., Cohen, J. A., Dept. Metabolic Dis., Univ., Leyden, Holland, J. clin. Invest. *35:* 964 (1956).

The uptake of DFP^{32} by the platelets was determined in 5 subjects without hematologic abnormalities, in 6 patients with hematologic abnormalities and in 2 postoperative patients. Results of the determination of plateletbound radioactivity during several days after the injection of DFP^{32} are presented. The results obtained suggest that the life span amounts to about 8 to 9 days. In 2 patients with chronic myeloid leukemia and polycythemia vera, respectively, both with thrombocytosis abnormal survival time of platelets was found. The data obtained on 2 patients with polycythemia vera with low platelet counts strongly suggested a considerable decrease of the life span of the platelets. Estimations carried out on 2 patients during the second week following operation are not inconsistent with a normal life span of the platelets under these conditions.

Platelets XVIII. Relationship of Platelets to Activity of 5-Hydroxytryptamine Creatinine Sulfate (5-HT). Magalini, S. I., Stefanini, M., Dept. Med., Tufts Univ. Med. School, Boston, Mass., USA, Proc. Soc. exp. Biol. (N. Y.) *92:* 788 (1956).

5-HT administered intravenously causes significant elevation of the local venous pressure at doses as small as 0.3 gamma/min. This effect is not affected by short time incubation with fresh serum, platelet-rich and platelet-poor plasma. Incubation for 16 hours causes destruction of 5-HT activity. Activity also disappears after 16 hours incubation with suspensions of washed platelets. Some of the activity, however, can be recovered after total disruption of thrombocytes. Also a protein solution from human platelets exhibits significant venopressor activity, while intact platelets are inactive. These findings suggest: a) presence of natural 5-HT or of substances with venopressor activity in human platelets; b) absorption of 5-HT by platelets upon incubation; c) strong bondage between 5-HT and platelet constituents.

Histidine Decarboxylase and Histamine Binding in Rabbit Platelets. Schayer, T. W., Kobayashi, Y., Rheumatic Fever Research Inst., Chicago, Ill., USA, Proc. Soc. exp. Biol. (N. Y.) *92:* 653 (1956).

Rabbit platelets decarboxylate C^{14} L-histidine and bind the resulting C^{14} histamine in stable condition. Soluble histidine decarboxylase has been prepared from rabbit platelets and a study of its properties is reported.

Thrombocytoasthenia and Thrombocytopathia — Old Names and New Diseases. Braunsteiner, H., Pakesch, F., Med. Univ.-Klinik, Wien IX, Austria.

Thrombocyto asthenia is a well defined disease due to defective pseudopode formation and lack of spreading of platelets, i.e., defective adhesiveness in contact with wettable surfaces. There is a manifest or latent defect of clot retraction revealed by thrombelastography. Clot retraction cannot be normalized by addition of serotonin. Coagulation factors are normal. Thrombocytopathia is a disease where decreased thromboplastic activity of platelets is ascertained. The platelets may also show marked morphologic anomalies. In the majority of patients deficient thromboplastic activity of platelets is found only temporarily or the results are only moderately pathologic. This group is designated as "probable thrombocytopathia". The third group includes patients with normal thromboplastic activity of platelets, it is designated as "possible thrombocytopathia". Capillary microscopy gave normal results in patients of all 3 groups. The relation to "vascular pseudohemophilia" is briefly discussed.

Studies on Platelets: XVII. An Experimental Study of the Development of Platelet Antibodies. Kistner, S. A., Stefanini, M., Dept. Med., Tufts Univ. Med. School, Boston, Mass., USA, J. Lab. clin. Med. *48:* 846 (1956).

An attempt was made to induce platelet antibody production in rabbits by injection of antigenically modified platelets. Modification of platelets was attempted by various methods. Treated platelets were injected into 3 groups of rabbits; one received human platelets, one received platelets from normal rabbits, and the third group received their own platelets. Development and specifity of platelet agglutinins were evaluated by standard immunologic methods in vivo and in vitro. Experimental results are discussed. They were not constant and reproducible in all animals of any given group. This is quite in agreement with the observations in humans, where only a few individuals, among many, develop thrombocytopenia after exposure to drugs, bacteria, and viruses. Some of the findings obtained in the course of these studies could be applied to the interpretation of the pathogenesis of some thrombocytopenic states in man.

Massive Steroid Therapy in Resistent Thrombocytopenic Purpura. Weisberger, A. S., Suhrland, L. G., Arquilla, E. R., Cleveland, Ohio, USA, J. Lab. clin. Med. *48:* 957 (1956).

This report deals with results obtained in treating patients exhibiting persistent thrombocytopenic despite therapy with usual doses of steroids or splenectomy. They were given large amounts of Δ_1-hydrocortisone (prednisolone) (250—300 mg/day). 6 of the 10 patients responded within 3—7 days with an increase in platelets ranging from 300 000 to 1 500 000 platelets/cmm. Bleeding manifestations subsided promptly. No severe toxic manifestations were encountered. The 4 patients who failed to respond were those who had severe marrow depletion. In summary, massive steroid therapy may raise the platelet count in patients with adequate marrow cellularity when ordinary amounts of steroid are ineffective. Such therapy appears to be applicable for emergencies rather than for prolonged maintenance.

Thrombotic Thrombocytopenic Purpura with a Positive Coombs' Reaction, Ritz, N. D., Groisser, V. W., Banowitch, M. M., Med. Serv., Maimonides Hosp., Brooklyn, N. Y., USA, Amer. J. Med. *21:* 468 (1956).

A case of thrombotic thrombocytopenic purpura is described in which the reaction to the Coombs' test, both direct and indirect, was positive in high titer. This is the third such instance in a total of 55 reported cases.

Newer Concepts of the Pathogenesis of Idiopathic Thrombocytopenic Purpura. Moore, C. V., Cincinn. J. Med. *37:* 295 (1956).

The results of studies carried out in patients with idiopathic thrombocytopenic purpura suggest that this is a syndrome rather than a specific disease entity. In many patients an immunologic mechanism seems to be of pathogenetic importance, causing both accelerated destruction of platelets and damage to megakaryocytes. The thrombocytopenic immunologic factor appears to be a platelet agglutinin. The spleen apparently participates in the removal of sensitized platelets from the circulation and probably produces some of the platelet agglutinin. Failure of splenectomy to correct the thrombocytopenia in some patients may be caused by the persistence of a high titer of platelet agglutinins after the operation. Another possibility is that the spleen is of lesser importance in the production of thrombocytopenia in those patients who do not have platelet antibodies. Neonatal thrombocytopenia may develop from placental transmission of autoagglutinins or isoagglutinins.

Morphologic Changes in Splenic Sinusoids in Idiopathic Thrombocytopenic Purpura. Bird, R. M., Joel, W., Clemens, T., Oklahoma City, Okla., USA, J. Lab. clin. Med. *48:* 784 (1956).

Hemorrhagic Thrombocythemia. A Blood Coagulation Disorder. Spaet, T. H., Bauer, S., Melamed, S., Dept. Hemat., Montefiore Hosp., New York, N. Y., USA, Arch. intern. Med. *98:* 377 (1956).

A case of hemorrhagic thrombocythemia is reported. The patients platelet counts reached 10 000 000/cmm and she presented a variety of hemorrhagic manifestations. Her platelets displayed anticoagulant activity in the thromboplastin generation test when used at circulating

levels but behaved normally when diluted to normal levels. Normal platelets were similarly anticoagulant when concentrated to thrombocythemic numbers. It is suggested that the fundamental defect in hemorrhagic thrombocythemia is a coagulation disorder resulting from the anticoagulant effect of excess platelets.

Thrombotic Thrombocytopenic Purpura: Report of a Case with a Review of the Pathogenesis of the Disease. Soumerai, S., Mac Gillivray, W. F., Dept. Path., City Hosp., Worcester, Mass., USA, N. Engl. J. Med. *255:* 585 (1956).

The basic pathologic changes in thrombotic thrombocytopenic purpura are reviewed. The lesions in thrombotic thrombocytopenic purpura and its pathogenesis are compared to the necrotizing angiitides. The resemblance to immunologic disorders is discussed. The Shwartzman phenomenon cannot be disregarded as a mechanism operative in the production of thrombotic thrombocytopenic purpura. The localization of lesions appears to be related to vascular permeability. The material found in the arteriolar walls is resistant to trypsin digestion, whereas the material found in Shwartzman phenomenon is not resistant.

Thrombocytopenia and Hemorrhage in Hemolytic Blood Transfusion Reactions. Pifer, P. W., Block, M. A., Hodgekinson, C. P., Chicago, Ill., USA, Surg. Gynec. Obstet. *103:* 129 (1956).

The Effects of Varying Concentrations of Human Platelets and Their Stored Derivatives on the Recalcification Time of Plasma. Farber, S., Freeman, G., Klein, E., Fiorentino, R., Children's Med. Center, Harvard Med. School, Boston, Mass., USA, Blood *11:* 910 (1956).

Human platelets and their stored, frozen and lyophilized derivatives do not excessively promote coagulation, as indicated by the calcium clotting time. High concentrations of platelet material inhibit coagulation, while dilutions to physiological levels return the recalcification time to normal values.

Osmotic Fragility of Human Blood Platelets. Gurevitch, A., Nelken, D., Dept. Clin. Microbiol., Hebrew Univ.-Hadassah Med. School, Jerusalem, Israel, Blood *11:* 924 (1956).

The osmotic fragility of 50 samples of platelets from normal donors has been studied. It has been found that the fragility of platelets starts at a concentration of about 0.44% NaCl and is complete at concentration of 0.34%. The serotonine released from the platelets increased with the gradual disintegration as the saline concentration fell.

Pseudohemophilia: Report of 13 New Cases and Statistical Review of Previously Reported Cases. Buchanan, J. C., Leavell, B. S., Dept. Int. Med., Univ. of Virginia Med. School, Charlottesville. Va., USA, Ann. intern. Med. *44:* 241 (1956).

The cases of 199 patients with "pseudohemophilia" (von Willebrand's disease) are reviewed. Pseudohemophilia occurs in both sexes and is often familial. The principal clinical manifestations are repeated episodes of abnormal bleeding. The only consistently abnormal laboratory finding is a prolonged bleeding time. The mechanism of the defect in hemostasis is uncertain and may not be the same in all cases. There is some evidence for both a platelet defect and a vascular defect. There is no satisfactory specific therapy.

Clot-Retraction Promoting Factor (Retractin) in Platelets and Tissue. Magalini, S. I., Stefanini, M., Joseph Stanton Memorial Lab., St. Elizabeth's Hosp., Boston, Mass., USA, Science *123:* 796 (1956).

Thrombocytopenic Purpura in Infections Mononucleosis. Pader, E., Grossman, H., New York, USA, N. Y., N. Y. J. Med. *56:* 1905 (1956).

Identification and Significance of Platelet Antibodies. Tullis, J. L., Blood Characterization Lab., Harvard Univ., Boston, Mass., USA, N. Engl. J. Med. *255:* 541 (1956).

A simple method for the clinical demonstration of anti-platelet antibodies is described. Use of this test as a screening procedure in diverse thrombopenic and hemorrhagic disorders has shown it to be of significant value in diagnosis and clinical management. 57% of all cases of ITP, 66% of all cases of hypersplenism, and 60% of all cases of neonatal purpura tested were due to circulating antiplatelet antibodies. Secondary thrombopenic purpura does not give

rise to a positive antibody test except in rare cases. The finding of a positive antiplatelet-antibody test in an undiagnosed case of thrombopenic purpura is strong evidence against the presence of an obscure leukemia or metastatic cancer. The serum factor that gives rise to antiplatelet-antibody tests can be shown to be an antibody by immunologic and chemical tests.

o) Spontaneous Anticoagulants

Inhibition de la thrombinoformation par l'héparine. Le cofacteur plasmatique de l'héparine est-il l'antithrombine? Burstein, M., Loeb, J., Centre Nat. Transfusion Sanguine, Paris, France. Rev. franç. Etudes clin. et biol. *1:* 752 (1956).

The authors present results suggesting the identity of the plasma co-factor of heparin, and antithrombin. Both are thermolabile, adsorbed on aluminium hydroxide and tricalcium phosphate and, destroyed by chloroform. Both are consumed during thrombin inactivation, the rate of disappearance increasing with heparin addition. Both are alpha-2 globulins and cannot be separated by fractionation methods. In attempts at purification both the co-factor and antithrombin are found in the same fraction in the same concentration. It is tought that heparin inhibits thrombin formation by increasing the affinity of antithrombin for thrombin, and thus suppressing the autocatalytic effect of the latter.

Sur la consommation de l'antithrombine (ou cofacteur plasmatique de l'héparine) au cours de la coagulation. Burstein, M., Guinand, A., Centre Nat. Transfusion Sanguine, Paris, France, Sem. Hôp. Paris *32:* 1 (1956).

Antithrombin activity of plasma and serum are determined by a new technic based on the fact that heparin considerably increases the rate of inactivation of thrombin by antithrombin. Antithrombin is consumed during coagulation, consumption depending on the quantity of thrombin formed. The comparative study of total antithrombin in plasma and serum yields indications concerning the total amount of prothrombin in plasma or of an eventual defect of prothrombin consumption as occurring in hemophilia and thrombocytopenia.

Die Bedeutung der Antithrombinbestimmung für die Beurteilung von Erkrankungen der Gallenwege, der Leber und des Pankreas. Zuern, H., Med. Univ.-Klinik, Dresden, Germany, Z. ärztl. Fortbild. *50:* 727 (1956).

Antithrombin determinations were carried out in cases of liver disorder gall-bladder and pancreas disturbances. Serum antithrombin was found to be markedly increased in cases of acute pancreatitis and slightly but still significantly increased in chronic recidivating cases. In severe liver damage, especially in cirrhosis, serum antithrombin level is lowered and heparin antithrombin increased. In cases of hepatitis the findings varied and no characteristic values were found.

Classification of Hemophiliacs with Development of an Anticoagulant. Bergna, L. J., Pavlovsky, A., Centro de Invest. Hematologicas, Junin 1284, Buenos Aires, Brazil, Acta haemat. (Basel) *16:* 247 (1956).

4 hemophilic patients with a circulating antithromboplastinogen are presented. In order to demonstrate such inhibitors of blood coagulation in their first stage it is advisable to determine the prothrombin consumption in the mixture of the patient's plasma (4 volumes) and normal plasma (1 volume) incubated 3 hours at 37° C before the addition of calcium chloride in order to make the test more sensitive. A method is described which makes it possible to classify the different kinds of hemophilia when the patients have developed an anticoagulant. The presence of an anticoagulant was demonstrated in 4 of 41 patients observing that this complication is more frequent in hemophilia B (in 2 patients of 7) than in hemophilia A (in 2 patients of 34)

Anticoagulant Specifity and Physiologically Inactive Beta-Prothromboplastin. Fantl, P., Sawers, R. J., Baker Med. Research Inst., Melbourne, Australia, Nature (Lond.) *177:* 1233 (1956).

A small number of hemophiliacs at first benefit by transfusions but later develop an anticoagulant which renders further transfusions ineffective. A 7 year-old baby with Christmas

disease, after 9 blood transfusions, developed an anticoagulant that inhibited thromboplastin formation. By various tests it was shown that the anticoagulant reacted specifically with beta-prothromboplastin of human origin but showed little activity with that of rabbits' plasma. Further studies suggest that a proportion of patients with Christmas disease can produce substances that are closely related to the prothromboplastin in their antigenic properties but are inactive in the formation of blood thromboplastin. Other patients are unable even to produce a prothromboplastin with antigen properties or physiological activity. These are the ones likely to develop antibodies following the transfusion of the particular prothromboplastin they lack.

A Case of Hemorrhagic Diathesis Due to a Circulating Anticoagulant. Post, C. R., Den Ottolander, G. J. H., Hoorweg, P. G., Central Lab., Blood Transfusion Serv., Red Cross, Amsterdam, Holland, Ned. T. Geneesk. *100:* 1703 (1956).

The authors report the case of a femal patient, age 37, whose hemorrhagic diathesis was explained by the presence of an acquired circulating anticoagulant, which prevented the formation of sufficient amounts of thromboplastin for a normal coagulation process. It was not possible to determine the exact role of the anticoagulant, however a possible inhibition regarding brain thromboplastin is considered. Various types of anticoagulants and the therapeutic measures in these cases are discussed.

Le cofacteur plasmatique de l'héparine et ses rapports avec l'antithrombine. Loeb, J., Centre Nat. de Transfusion Sang., Paris, France, Arch. Sci. physiol. *10:* 129 (1956).

The antithrombin-like cofactor of heparin has been isolated from Cohn's fraction IV_1 by means of adsorption on aluminium gel. A product with 100-fold activity of plasma was obtained from bovine plasma. The cofactor is most probable an α-lipoprotein. It was found that the antithrombin-like cofactor of heparin is identical with antithrombin and that heparin acts by activating natural antithrombin.

Species Differences in Heparin. Bell, H. J., Jaques, L. B., Dept. Physiol., Univ. Saskatchewan, Saskatoon, Sask., Canada, Bull. Soc. Chim. Belges *65:* 36 (1956).

Dog, beef, sheep alpha-heparin, β-heparin, and a crude sample of human heparin were assayed for metachromatic, antithrombin- and anticoagulant-activity, for carbohydrate (anthrone reagent) and glucuronic acid (naphthoresorcinol reagent). Metachromatic activity was about the same for the purified samples. Great differences were found in anticoagulant and antithrombin activity. Dog heparin had the highest, while beta-heparin and the crude human heparin had very low activity. All contained anthrone-reacting carbohydrate. Two new methods of extraction of heparin from tissue are shortly described. Pork heparin has been separated by paper chromatography.

Seudohemofilia producida por un anticogulante. Pavlovsky, A., Quintana 39, Buenos Aires, Argentine, Pren. méd. argent. *43:* 166 (1956).

Temps de thrombine et pouvoir antithrombinique du plasma au cours du choc peptonique. Burstein, M., Guinand, A., Centre Nat. Transfusion Sanguine, Paris, France. Sang *27,* 941 (1956).

Thrombin inactivation by plasma is accelerated following heparin secretion of the liver during peptonic shock in dogs. Heparin cofactor level remains unaltered during shock. Dextran sulfate markedly reduces thrombin time of animals in shock. Plasma antithrombin activity does not increase during peptonic shock of the rabbit. Peptone was found to increase the thrombin time to a certain degree in vitro. No antagonism was found between heparin and histamin.

Zur Heparinbehandlung der Angina pectoris. Gubser, J., Basel, Switzerland, Medizinische 1190 (1956).

Die Bedeutung der Gewebemastzellen für die Histaminfreisetzung. Keller, R., Burkard, W., Inst. Hygiene und Arbeitsphysiol., ETH, Zürich, Switzerland, Helv. physiol. pharmacol. Acta *14:* 289 (1956).

Il comportamento dell'antitrombina plasmatica nelle epatopatie. Facchini, G., Garagnani, A., Ist. Clinica Med. a Terap., Univ., Bologna, Italy, Blut *2:* 4 (1956).

Influenza della bile e dei sali biliari sull'emocoagulazione "in vitro" con particolare riguardo all'attività antitrombinica. Garagnani, A., Facchini, G., Ist. Clinica Med. e Terap., Univ., Bologna, Italy, Arch. Patol. Clin. med. *33:* 203 (1956).

The authors confirm the in vitro anticoagulant action of bile. The substances responsible for this action are discussed. Studies of antithrombin time revealed the mechanism of the anticoagulant action which is characterized by an inhibition of the thrombin-fibrinogen reaction.

Les anticoagulines du plasma sanguin. Chevallier, P., Fiehrer, A., Clinique des Maladies du Sang, Faculté de Méd., Paris, France, Sang *27:* 735 (1956).

Aparicion de un Anticoagulante Circulante en un Caso de Lupus Eritematoso diseminado. I. Estudio Clinico. Newhall, A. R., Lopez, G. G., Spies, T. D., Tellecha, C. M. D., Toca, R. L., Ser. de Investigaciones, Catedra de Patol., Univ., La Habana, Cuba, Arch. Soc. Estud. clin. Habana *49:* 75 (1956).

II. Estudio Hematologico. Piedra, J. H., Vegas, F., Dept. Investigaciones Especiales, Catedra de Patol., Hosp. Univ., Habana, Cuba, Arch. Soc. Estud. clin. Habana *49:* 1 (1956).

Production of Anti-Human PTC and Anti-Human Proconvertin in Rabbits. Lewis, J. H., Didisheim, P., Dept. Med., Univ. of Pittsburgh, Pa., USA, Proc. Soc. exp. Biol. (N.Y.) *93:* 429 (1956).

Rabbits injected with human serum PTC (factor IX) developed inhibitors to human PTC and also to human proconvertin (factor VII). These two activities could be separated by differential adsorption.

Quantitative Aspects of Antithrombin and Heparin in Plasma. Waugh, D. F., Fitzgerald, M. A., Cambridge, Mass., USA, Amer. J. Physiol. *184:* 627 (1956).

Plasma antithrombin inactivates thrombin. Heparin increases this property of antithrombin. It is assumed that the heparin cofactor(s) is connected with normal antithrombin.

The Extractable Heparin in Different Animal Tissue. Monkhouse, F. C., Dept. Physiol., Univ., Toronto, Ont., Canada, Canad. J. Biochem. and Physiol. *34:* 757 (1956).

A Serum Anticoagulant Factor in Systemic Lupus Erythematosus. Swift, S., Div. Dermatol., Univ. Oregon Med. School, Portland, Oregon, USA, Arch. Derm. Syph. (Chicago) *74:* 296 (1956).

Investigation of a Hemorrhagic Disease Due to Beta-Prothromboplastin Deficiency Complicated by a Specific Inhibitor of Thromboplastin Formation. Fantl, P., Baker Med. Research Inst., Melbourne, Australia, Austral. Ann. Med. *5:* 163 (1956).

Hemorrhagic Disease with Circulating Inhibitors of Blood Clotting: Anti-AHG and Anti-PTC in Eight Cases. Lewis, J. H., Ferguson, J. H., Arends, T., Dept. Physiol., Univ. N. Carolina, Chapel Hill, N. C., USA, Blood *11:* 846 (1956).

In 8 patients suffering from severe hemorrhagic disease it was possible to demonstrate the presence of circulating inhibitors, not heparin-like in nature. Anti-PTC was identified in 2 PTC deficients, anti-AHF in 5 hemophiliacs and both, primarily anti-AHF, in one idiopathic case. Possible etiologic factors inducing the appearance of such inhibitors included repeated transfusions of whole blood and plasma in all, and a previous pregnancy in the idiopathic case. Two patients showed increases of gammaglobulin and presence of inhibitor in 25—33% ammonium sulfate plasma fractions. Cortisone therapy was ineffective in 2 cases.

Occurrence and Mode of Action of Endogenous Circulating Anticoagulants. Verstraete, M., Vandenbroucke, J., Physiopath. Lab., Dept. Med. Univ., Louvain, Belgium, J. Lab. clin. Med. *48:* 673 (1956).

The occurrence of different types of circulating anticoagulants in hemorrhagic diatheses is described. The most frequent is the anticoagulant acting on thromboplastin formation. The mode of action and some physicochemical properties of the circulating anticoagulant complicating a hemophilia A case and occurring in a nonhemophilic man are compared. Both first phase inhibitors are present in the serum. Their activity is not neutralized by protamine sul-

fate, but by Cohn's fraction I, in the presence of calcium ions only. They are not adsorbed on $BaSO_4$, or $Al(OH)_3$. They both prevent plasma thromboplastin formation but are inactive on plasma thromboplastin already formed. They do not inactivate tissue thromboplastin. Some arguments suggesting an immunologic mechanism of development of the anticoagulant are presented.

Hyperheparinemia — Clinical Picture and Treatment. Quick, A. J., Hussey, C. V., Dept. Biochem. Maruette Univ. Med. School, Milwaukee, Wisc., USA, J. Lab. clin. Med. *48:* 932 (1956).

The authors report a case of hyperheparinemia in a woman of 23 who has had a history of a bleeding condition since the age of 3 years. This chronic heparinemia was sufficiently severe to keep the clotting time in the range of 30 to 60 mins. Yet the patient has bled severely only on a few occasions. She has had no internal bleeding, has always had normal menstruation, and only rarely abnormal bruises. Emergent tooth extraction necessitated correction of hyperheparinemia. Protamine sulfate and toluidine blue worsened the condition. Following an oral dose of 100 mg of cortisone, both the clotting time and thrombin time decreased. Further reduction was obtained by additional cortisone and three times 250 ml units of fresh-frozen plasma.

p) Vitamin K

Innenkörperbildung durch wasserlösliche Vitamin-K-Präparate. Willi, H., Kant. Säuglingsheim, Univ.-Frauenklinik, Zürich, Switzerland, Schweiz. med. Wschr. *86:* 1453 (1956).

Synkavit-Schädigung bei Frühgeborenen. Willi, H., Säuglingsheim, Frauenklinik, Univ., Zürich, Switzerland, Helv. paediat. Acta *11:* 325 (1956).

Synkavit is a toxic substance inducing formation of inclusion bodies (Heinz). When administered to premature infants with immature splenic function in current dosage it can lead to high degree, even lethal hemolytic anemia with formation of Heinz's corpuscules.

L'effetto antagonista delle vitamine K_1 e K_4 nell'avvelenamento da ratticidi ad effetto dicumarolico (ricerche sperimentali). Gagliardi, L., Abelli, G., Scuola Ost. Vercelli, Italy, Igiene mod. *49:* 449 (1956).

Die Verminderung der Blutungsgefahr bei der Antikoagulantienbehandlung mit Cumarinderivaten durch Vitamin K_1. Thedering, F., Böwing, G., Med. Univ.-Klinik, Tübingen, Germany, Münch. med. Wschr. *98:* 340 (1956).

Therapeutic examples are given for the effect of vitamin K_1 in various doses and ways of administration in order to diminish the danger of hemorrhages during anticoagulant therapy. All doses indicated refer to the long-acting dicumarol derivative Marcoumar.

Avitaminosi K sperimentale ed esofago. Borasi, G., Clin. Otorinolaringol., Univ., Genova, Italy, Minerva otorino *6:* 27 (1956).

The Effectiveness of an Oral Vitamin K_1 in Controlling Excessive Hypoprothrombinemia during Anticoagulant Therapy. Cosgriff, S. W., Dept. Med., Columbia Univ., New York, N. Y., USA, Ann. intern. Med. *45:* 14 (1956).

Vitamin K_1 tablets in doses of 2.5 to 20 mg were administered to 75 patients in whom excessively elevated prothrombin time values were produced by anticoagulant therapy. In 85% of the patients the prothrombin time returned to a safe range within 12 hours after the oral administration of vitamin K_1 and in 98% within 24 hours. The prothrombin time fell below the therapeutic level of adequate anticoagulation in 15% of the patients 12 hours following Vitamin K_1. Under such circumstances the administration of heparin ensured a continuing antithrombotic effect, until subsequent doses of coumarin or indanedione agent again achieved an adequate hypoprothrombinemia. Since most hemorrhages during anticoagulation occur in association with prothrombin time values above 35 secs, Vitamin K_1 tablets provide an additional safeguard in anticoagulant therapy.

The Effect of Oral and Intravenous Administration of Vitamins K on the Prothrombin and Proconvertin Levels of Cholecystnephrostomized Dogs. Fisher, L. M., Dept. Physiol. and Pharm., Univ. Saskatchewan, Saskatoon, Sask., Canada, Canad. J. Biochem. Physiol. *34:* 1039 (1956).

q) Heparin and Heparin-like Substances

Duration of Anticoagulant Effect in Relation to Urinary Excretion Dextran Sulphate. Jeavons, S. M., Walton, K. W., Ricketts, C. R., Dept. exper. Path., Univ. Birmingham, England, Brit. med. J. 5000, 1016 (1956).

Dextran sulphate, administered intravenously to 5 patients with thromboembolic disease, was found to have a marked cumulative effect when treatment was prolonged over 3 to 5 days. As a result reduction of dose and/or increased spacing of injections could be effected without materially affecting the clinical efficacy of the anticoagulant. The cumulative effect could not be accounted for on the basis of the urinary excretion of a smaller percentage of the injected dose than that of heparin. It is suggested that in man dextran sulphate differs from heparin in duration of effect because of a slower rate of metabolic breakdown in the body and consequent accumulation, probably in extravascular fluid. In addition to its direct effect on coagulation mechanism, dextran sulphate relieved oedema in cases of thrombophlebitis and produced effects similar to those of heparin on the plasma lipoproteins and plasma cholesterol.

Dextran Sulphate: Use as an Anticoagulant, and Action in Lowering Serum Cholesterol. Cohen, H., Tudhope, G. R., Dept. Pharm. Univ., Sheffield, England, Brit. med. J. 5000, 1023 (1956).

A single intravenous injection of dextran sulphate (7500 units) produced an increase in clotting time to more than twice for 4 to 6 hours. With repeated injections cumulation occurred so that the clotting time could be maintained at more than twice normal by a dosage of 15 000 units in the first 24 hours, 10 000 units daily the next 4 to 10 days, and thereafter 5000 daily. During treatment there was at first a marked fall in serum cholesterol. This reduction persisted while the dosage was 10 000 to 15 000 units daily. It is suggested that dextran sulphate is an effective anticoagulant and provides a possible alternative to the usual combination of heparin and oral anticoagulant. However, toxic effects may occur.

Heparinoid and Heparin. An Investigation into the Anticoagulant Effect of the Dextran Sulphate Dexulate. Arge, E., Med. Dept. E., Frederiksberg Hosp., Copenhagen, Denmark, Acta med. scand. *155:* 469 (1956).

Clinical comparison is made between the dextran sulphate dexulate, and heparin Leo. Dexulate has an anticoagulant effect resembling that of heparin, but the prolongation of the clotting time response is somewhat greater with heparin, while the duration of the anticoagulant effect is nearly the same. No cumulative effect, nor serious side-effects were observed.

The Assay of Heparin. Pritchard, J., Evans Biol. Inst., Runcorn, England, J. Pharm. Pharmacol *8:* 523 (1956).

A method is described for the assay of heparin consisting essentially in the comparison by eye of the clots produced in approximately 16 hours when sheep plasma is recalcified in the presence of varying amounts of Standard Heparin and the heparin under test. The results obtained are believed to be accurate and reliable and the technic of the assay reasonably simple.

Sur l'isolement d'une fraction des lipoprotéines sériques après précipitation par l'héparine ou par des héparinoides de synthèse. Burstein, M., Centre Nat. Transfusion Sanguine, Paris, France, C. r. Séances Acad. Sci. *243:* 1 (1956).

Beta-lipoproteins are precipitated from human serum by heparin and heparinoids in the presence of $CaCl_2$. The preparation of practically pure beta-lipoproteins is thus possible. The obtained product is highly soluble, electrophoretically homogenous, and includes about four times as many lipids as the protides.

Sur l'action anti-héparinique de quelques héparinoides de synthèse. Burstein, M., Guinand, A., Centre Nat. Transfusion Sanguine, Paris, France, Sang *27:* 558 (1956).

The coagulation time of heparinized human plasma with added thrombin is normalized by dextrane sulphate. At the same time dextran sulphate decreases the rate of thrombin inactivation by defibrinated heparinized plasma. Treburon reduces considerably the thrombin time of heparinized human plasma, without, however, interfering with the inactivation of thrombin. An even considerable increase of antithrombin activity of plasma does not necessarily include prolonged thrombin time.

Héparine et consommation de l'antithrombine. Burstein, M., Guinand, A., Centre Nat. Transfusion Sanguine, Paris, France. Arch. int. Pharmacodyn. *104:* 435 (1956).

When thrombin is added to defibrinated plasma, antithrombin is partially consumed. The amount of destroyed antithrombin is a function of the neutralized thrombin units and is independent of the rate of thrombin inactivation. Antithrombin consumption during the inactivation of a given amount of thrombin is increased by heparin. Antithrombin is partially consumed during clotting and the rate of consumption is increased by heparin. Heparin has 2 effects: It increases the affinity of antithrombin for thrombin and it increases antithrombin consumption.

Possibilities of Heparin Therapy Control. Hladovec, O., Cermák, L., IV. Med. Clinic, Univ., Prague, Czechoslovakia, Vnitrni lekarstvi *2:* 407 (1956).

Influenza dell'eparina sui lipidi epatici in ratti trattati con tetracloruro di carbonio. Angeli, G., Cavazzuti, F., Ist. Clin. Med. Generale e Terapia, Univ., Modena, Italy, G. Biochim. *5:* 293 (1956).

The behavior of lipidic liver fractions with or without temporary heparin administration has been studied in CCl_4-poisoning of rats. Heparin induces increased steatosis in the intoxicated liver, and increased stanching of phospholipids and neutral fats, but inhibits accumulation of cholesterol.

Heparin in Thrombosis and Pulmonary Embolism. Brennhovd, Dept. Surg., Sykehus, Drammen, Norway, Nord. Med. *56:* 1325 (1956).

Heparin was used in a total of 197 patients with deep venous thrombosis and pulmonary embolism. The mortality rate was 1.5%. The patients stayed in bed an average of 8 days, were febrile an average of 7.2 days. 50% had no sequelae of thrombosis. 38% an significant swelling of the calf, and 10% severe sequelae of thrombosis. Heparin is considered fully effective in the treatment of thrombosis and pulmonary embolism.

L'inhibition de la thrombinoformation par l'héparine. Burstein, M., Loeb, J., Centre Nat. Transfusion Sang., Paris, France, Rev. franç. Etudes clin. and biol. *1:* 752 (1956).

Heparin inhibits the transformation of fibrinogen into fibrin and the formation of thrombin. This double action takes place only in the presence of 2 cofactors contained in normal human plasma. The authors' experiments are based upon the study of the influence of various plasma fractions on the coagulation time of a heparinized euglobulin solution which does not contain the albuminic cofactor. The results obtained suggest the identity of the two heparin cofactors.

Untersuchungen über die Heparinwirkung am histaminkontrahierten Meerschweinchen-Ileum. Keller, R., Burkard, W., Inst. f. Hygiene E. T. H., Zurich, Switzerland. Experientia (Basel) *12:* 394 (1956).

Freshly dissolved heparin substance, in contrast to commercially available heparin, causes no decontraction of the isolated, atropinized guinea-pig ileum contracted in response to histamin. Phenol and Cresol, in amounts usually contained in commercially available heparin preparations, have the same effect as commercial heparin.

Hochdruckbehandlung mit Heparin. Achenbach, W., Med. Univ.-Poliklinik, Köln, Germany, Medizinische 919 (1956).

Beitrag zur Heparinbehandlung des Pemphigus vulgaris. Meyhöfer, W., Beller, F. K., Hautklinik, Med. Akademie, Justus-Liebig-Hochschule, Gießen, Germany, Hautarzt *7:* 78 (1956).

The authors report a case of severe pemphigus vulgaris treated with heparin after failure with all other drugs. Vesicles disappeared with heparin but returned immediately after discontinuation of the drug. The patient was treated over a period of 5 months without any side-effects. Intensive shock therapy was preferred to the use of depot preparations.

Zur Physiologie der Mastzellen als Träger des Heparins und Histamins. Werle, E., Amann, R., Wiss. Labor, Chir. Klinik, Univ., München, Germany, Klin. Wschr. *34:* 624 (1956).

Selection for Anticoagulant Therapy in Cardiac Infarction Using the Heparin Retarded Coagulation Time. Peel, A. A. F., Victoria Infirmary, Glasgow, Scotland, Brit. Heart. J. *18:* 378 (1956).

Über die Thromboembolie-verhütende Wirkung des „Liquemin-Depot". Tierexperimentelle Prüfung mit dem Myotoxin-Thrombokinase-Test. Goossens, N., Gastpar, H., Med. Poliklinik, Univ., München, Germany, Schweiz. med. Wschr. *86:* 104 (1956).

L'héparine en thérapeutique cardio-vasculaire. Raynaud, R., Alger, Sem Hôp. Paris *32:* 656 (1956).

Ein Beitrag zur klinischen Bedeutung des Heparin-Toleranztestes und zur Verbesserung seiner Methodik. Zürn, H., Med. Akademie, Dresden, Germany, Z. ges. inn. Med. *11:* 183 (1956).

The Anticoagulant Action of Chlorazol Fast Pink. Merskey, C., Sapeika, N., Dept. Med., Univ., Cape Town, S. Africa, Brit. J. Haemat. *2:* 276 (1956).

Chlorazol fast pink BKS has an anticoagulant action when given parenterally. Subcutaneous administration produces a more prolonged effect than intravenous injection. Its action resembles that of heparin and it is neutralized by protamine sulphate. The dye appears to produce its effect by inhibiting the thrombin-fibrinogen reaction. It also causes some inhibition of the formation and action of plasma thromboplastin. The possible value of this type of compound in human medicine is discussed.

Indications et limites du test de tolérance à l'héparine in vitro. Masure, R., Acta clin. belg. *11:* 93 (1956).

Kochsalztoleranztest zur Aufdeckung latenter Gerinnungsstörungen. Heparintoleranztest ohne Heparin. Jürgens, J., II. Med. Univ.-Klinik, Frankfurt a. M., Germany, Blut *2:* 301 (1956).

The author describes a simple method for carrying out the tolerance test, using a 2.5% saline solution, platelet-rich- plasma and the usual recalcification technic. It is found that the principle of the heparin tolerance test, namely the unspecific increase of coagulation time influencing all phases of blood coagulation together, can also exert its effect by increasing the ionic strength by way of a suitable saline solution. A series of examples shows that this modification allows the detection of latent hypocoagulation and hypercoagulation. The significance of this test for diagnosis of platelet disorders is discussed.

The Anticoagulant Activity of Dextran Sulphate. 1. An in vitro Comparison between the Actions of Dextran Sulphate and Heparin on the Various Stages of Blood Coagulation. Forwell, G. D., Ingram, G. I. C., Dept. Surg., Univ., Edinburgh, Scotland, J. Pharm. Pharmacol. *8:* 530 (1956).

Compared to heparin dextran sulphate did not greatly affect the thrombinfibrinogen reaction, and reacted only slightly with progressive antithrombin and the heparin co-factor over the concentrations tested in this investigation. No effect upon prothrombin conversion was noted. The relative effect of dextran sulphate upon thromboplastin generation was similar to the potency ratio derived from-whole-blood clotting time measurements.

Influenza esplicata dalla vitamin E sull'attività eparinica del plasma in vivo: studio clinico. Bottiglioni, E., Facchini, G., Ist. Clinica Med. Generale, Univ. Bologna, Italy, Clin. terap. *10:* 571 (1956).

II. The Effect of Dextran Sulphate on the One-Stage Prothrombin Time. Ingram, G. I. C., Forwell, G. D., p. 589.

Dextran sulphate in concentrations which do not inhibit coagulation anymore, still decreases the time of Quick's test, even in the precense of heparin. Partially hydrolysed heparin exerts the same effect. The latter is ascribed to the absence of N-sulphate groups in these preparations.

Die papierchromatographische Charakterisierung von Heparin, Heparinoiden und heparinartigen Stoffen. Awe, W., Stüdemann, K. D., Inst. angew. Pharm., Techn. Hochschule, Braunschweig, Germany, Arzneimittelforschung *6:* 349 (1956).

Attività e tolleranza eparinica del plasma in condizioni normali e patologiche. Meneglini, P., Ist. Clin. Med. Generale, Univ., Genova, Italy, Minerva med. *47:* 2013 (1956).

L'influenza della eparina sulla conglomerabilità eritrocitica. Cantoni, L., Giacomazzi, G., Ist. Patol. Spec. Med., Univ., Milano, Italy, Minerva med. *47:* 387 (1956).

Ein neues Anticoagulans und Antithrombotikum vom Typ der Heparinkörper. Marx, R., I. Med. Univ.-Klinik, München, Germany, Arzneimittel-Forschung *6:* 667 (1956).

Unterstützung der Chemotherapie bei Tuberkulose mit Heparin. Albert-Weil, J., Hôp. Central des Prisons de France, Paris-Fresnes, France, Med. Mschr. *10:* 529 (1956).

Über Wirkungsweise und Anwendung eines neuen Heparinkörpers. Kautzsch, E., Med. Abtlg., Städt. Krankenhaus, München-Schwabing, Germany, Dtsch. med. Wschr. *81:* 1846 (1956).

(Elheparin, Luitpoldwerk, München).

Sull'intolleranza all'eparina. de Matteis, F., Turbiglio, P. C., Osp. Maria Vittorio, Torino, Italy, Minerva med. *47:* 882 (1956).

The Neutralization of Heparin by Protamine in Extracorporeal Circulation. Hurt, R., Dept. Surg., Stanford Univ. Med. School, San Francisco, Calif., USA, J. thorac. Surg. *32:* 612 (1956).

Blood Globulins Reducing the Anticoagulant Activity of Heparin. Triantaphyllopoulos, C. D., Dept. Med., Univ., Alberta, Canada. Canad. J. Biochem. and Physiol. *34:* 939 (1956).

Sur une nouvelle méthode de dosage des β-lipoprotéines sériques par l'héparine. Burstein, M., Samaille, J., Centre Nat. Transfusion Sanguine, Paris XV, France, C. r. Séances Acad. Sci. *243:* 2185 (1956).

The precipitation of β-lipoproteins from serum by heparin, in the presence of $CaCl_2$ allows an opacimetric measurement of this fraction. The total of lipoproteins is much higher in the human than in other mammals. It is low in cord blood, and frequently considerably high in various pathologic conditions.

Mechanism of Heparin Protection Against a Histamine Releasor (48/80). Higginbotham, R. D., Dougherty, T. F., Dept. Anatomy, Univ. Med. Coll., Utah, USA, Proc. Soc. exp. Biol. (N. Y.) *92:* 493 (1956).

Mice pretreated with various amounts of heparin exhibit resistance, relative to heparin dose, to the toxic effects of subsequent injections of otherwise lethal doses of 48/80. There is a straight-line relationship between the 50% protective heparin pretreatment doses and the various 48/80 challenge doses. Fibroblasts exposed to the heparin-48/80 complex rapidly sequester and deposit this material as metachromatic granules in their cytoplasm. The possible significance of these results is discussed.

The Effect of Heparin on Fibrinolysis. Kaulla, K. N. von, McDonald, S. T., Taylor, G. H., Denver, Colo., USA, J. Lab. clin. Med. *48:* 952 (1956).

The results obtained suggest that repeated injection of small doses of heparin might enhance rather than inhibit fibrinolysis.

Studies on the Heparin-Like Effect of Dextran-Sulfate. Griffith, D. R., Landaburu, R. H., Ann. Arbor, Mich., USA, J. Lab. clin. Med. *48:* 812 (1956).

The Degradation of Heparin by Bacterical Enzymes. I. Adaptation and Lyophilized Cells. Payza, N. A., Korn, E. D., Labor. Cellular Physiol. and Metabolism., Nat. Heart Inst., Bethesda, Md., USA, J. biol. Chem. *223:* 853 (1956).

Flavobacterium heparinum, a bacterium which is able to utilize heparin as its sole source of carbon, nitrogen, and sulfur, has been isolated from soil by enrichment culturing. A procedure has been described whereby bacteria grown on a non-heparin medium can be adapted to heparin. The degradation of heparin by lyophilized, adapted cells has been studied.

II. Acetone Powder Extracts. Korn, E. D., Payza, A. N.

The degradation of heparin by extracts of acetone powders of flavobacterium heparinum has been studied. It has been found that the extract contains a sulfamidase, a sulfesterase, and at least one glycosidase which, together, catalyze an extensive cleavage of heparin.

Studies in Regional Heparinization. I. The Use of Simultaneous Neutralization with Protamine Preliminary Studies. Gordon, L. A., Richards, V., Perkins, H. A., Dept. Med. and Surg., Stanford Univ. Med. School, San Francisco, Calif., USA, N. Engl. J. Med. *255:* 1025 (1956).

A high level of heparin effect was achieved in one extremity of a dog by infusion of heparin into the femoral artery. General heparinization was prevented by the simultaneous infusion of protamin into the femoral vein of the same extremity. Further work will be necessary before it can be determined whether the procedure can be safely carried out for the period of days necessary to prevent thrombosis after endarterectomy.

r) Other Anticoagulants

Beitrag zur intravenösen Anwendung von Marcoumar. Deutsch, E., I. Med. Univ.-Klinik, Wien, Austria, Wien. klin. Wschr. *68:* 553 (1956).

Intravenous administration of marcoumar is reported upon. A single dose of 30 mg reduces prothrombin to therapeutic levels within 24 to 48 hours. Prothrombin, factor VII and a serum factor necessary for thromboplastin formation are influenced by marcoumar. Vitamin K_1 is an effective antidote. Indication for intravenous administration exists during the first postoperative days when oral medication is excluded, or in rare cases of incompatibility towards oral application.

Behandlung der Zentralvenenthrombose mit Antikoagulantien. Hummelt, K., Augenabtlg., Allgem. Krankenhaus Heidberg, Hamburg, Germany, Klin. Mbl. Augenheilk. *129:* 799 (1956).

18 thromboses of the central retinal vein and 17 thromboses of the tributaries of this vein have been treated with anticoagulants. There was no significant improvement of the prognosis compared to the course previously observed. Anticoagulants may only be effective in young patients with an unimpaired circulatory system.

Wird die postoperative Emboliesterblichkeit durch Behandlung mit Antikoagulantien gesenkt? Purschke, H., Chir. Klinik, Städt. Krankenhaus Ost, Lübeck, Germany, Zbl. Chir. *81:* 1213 (1956).

Based on the study covering a period of 9 years the author comes to the conclusion that the mortality of embolism in operated patients decreased by 40% since prophylaxis of thrombosis with anticoagulants has been introduced at this hospital.

Beitrag zur Frage einer kombinierten Thrombosebehandlung mit Panthesin und Marcoumar. Deutsch, E., Leeb, H., I. Med. Univ.-Klinik, Wien, Austria, Klin. Med. (Wien) *11:* 293 (1956).

The infusion of 500 mg of panthesin did not result in a marked alteration of any of the coagulation factors. A moderate increase of spontaneous fibrinolysis was noted. The results were identical in normals and in patients with thrombosis. The effect of marcoumar was not influenced by panthesin treatment and neither were its maintenance dose nor the clinical

course of thrombosis. No danger exists in continuing therapy with marcoumar following panthesin treatment. A combination of the two seems practicable and might be advantageous considering the pain relieving and fibrinolysis activating effect of one and the coagulation inhibitory effect of the other of the two drugs.

Thromboseverhütung in der Herzchirurgie. Neugebauer, J., Neurochir. Univ.-Klinik, Freiburg/Br., Germany, Chirurg *27,* 496 (1956).

Zur Frage der Wirtschaftlichkeit der modernen Antikoagulantientherapie (I und II). Sartori, C. H., Chir. Abtlg., Städt. Krankenhaus r. d. Isar, München, Germany, Medizinische 921, 951 (1956).

The following 3 questions are discussed and, based on the literature and own calculation, answered: How high is, statistically speaking, the danger of thrombo-embolism for each patient, i.e. is thromboembolism also a social problem and an important factor for medical insurance? Answer: Thromboembolic disease are very serious medical and social problems. How satisfactory are therapy and prophylaxis with anticoagulants? Therapy and prophylaxis with anticoagulants are considered the only possible causal means to reduce to a minimum morbidity and mortality of embolism, to improve prognosis of infarction, and to decrease frequency of postthrombotic disorders. In what proportion stands anticoagulant therapy and prophylaxis to the success obtainable? The financial profitableness of this treatment is undoubted by the author.

Anticoagulant Therapy. Ferriman, D., North Middlesex Hosp., England, Med. illustr. *10:* 379 (1956).

Thrombose-Gefährdung und -Prophylaxe in der allgemeinen Praxis. Wagner, W., Evang. Krankenhaus, Wanne-Eickel, Germany, Med. Klin. *51:* 1093 (1956).

Il trattamento anticoagulante nelle sindromi da occlusione coronarica. De Nicola, P., Tartara, A., Ist. Clin. Med. Gen., Univ., Pavia, Italy, Minerva cardioangiol. *4:* 275 (1956).

Anticoagulans "Sintrom". Jürgens, J., I. Med. Univ.-Klinik, Charité, Berlin, Germany, Arch. int. Pharmacodyn. *105:* 1 (1956).

Sintrom belongs to the 4-hydroxycoumarin series of anticoagulants with a transient effect on coagulation. The duration of its action and the specific effect have been studied in 162 patients with thromboembolic disorders. The particular advantage of Sintrom for routine use lies above all, in the high degree of security which it offers against overdosage and thus against accumulation, while the therapeutic level may easily be held at a constant value. In this respect Sintrom surpasses the so-called superdicumarols with their prolonged action. This specific property is of particular value where anticoagulant therapy is indicated in a patient with cardiac defect accompanied by decompensation. Such cases show a primary defect of coagulation as a consequence of the cardiac hepatic stasis, and on the other hand a particularly strong tendency to retention of any vitamin K antagonists which may be administered. Sintrom therefore considerably reduces the dangers of anticoagulant therapy in these difficult cases.

Thrombosing Arteriosclerosis. Result of Long-Term Anticoagulant Therapy. Dedichen, J., Oslo, Norway, Brit. med. J. 5000, 1038 (1956).

The mortality rate in a series of 149 out-patients with thrombosing arteriosclerosis on long-term treatment with anticoagulants has been shown to be 5% a year. It makes no difference whether the process is localized to the heart or to the arteries of the limbs.

Selection for Anticoagulant Therapy in Cardiac Infarction Using the Heparin Retarded Coagulation Time. Peel, A. A. F., Brit. Heart J. *18:* 378 (1956).

Treatment of Thrombosis and Embolism with Indirect Anticoagulants. Kettenborg, H. K., Lab. Bloedtransfusiedienst, Wilhelmina Gasthuis, Amsterdam, Holland, Ned. T. Geneeskd. *100:* 2186 (1956).

Description of the principles of indirect anticoagulant therapy. Requirements for control determinations are mentioned and the interpretation of results in relation to anticoagulant dosage is indicated. Directions to be followed in case of overdosage are given.

Les accidents hémorragiques des traitements anticoagulants. (A propos de 32 observations). Favre-Gilly, J., Thouverez, J. P., Hôp. E. Herriot, Lyon, France, Rev. Lyonnaise Méd. *5:* 181 (1956).

32 cases of hemorrhagies complicating anticoagulant therapy are reported. The complications appeared in 8% of the 400 patients treated. They were more frequent during therapeutic than during prophylactic administration; more frequent with dicumarin than with heparin, and more frequent with dicumarin than with tromexan or pindione. The most frequent types of hemorrhagies were hematoma, hematuria, and melaena. 2 fatal cases occurred one due to cerebral, the other to peritoneal hemorrhage. Very often hemorrhage is due to overdosage, but locally organic causes are frequent: gastrointestinal ulcers, hemorrhoides, diaphragmatic hernia, renal lithiasis etc. Therefore, in order to prevent these hemorrhages frequent coagulation tests as well as complete clinical examinations are necessary for the determination of local possibilities of hemorrhages.

Anticoagulant action of isonicotinate-sulpho-3 of neodyme. Hunter, R. B., Walker, W., Dept. Pharm. and Ther., Queen's Coll., Dundee, Scotland, Nature (Lond.) *178:* 47 (1956).

Die heutigen Anschauungen über den Vorgang der Blutgerinnung und die Möglichkeit seiner Beeinflussung durch Antikoagulantien. Wille, P., Geburtsh.-Gynäkol. Abtlg. Städt. Krankenhaus, Berlin-Kaulsdorf, Germany, Dtsch. GesundhWes. *11:* 1724 (1956).

Retardwirkung von Butazolidin auf die Antikoagulantien vom Dicumaroltyp. Pestalozzi, H., Clauss, A., Sigg, A., Med. Abtlg., Krankenanstalt Neumünster, Zollikerberg/Zürich, Switzerland, Helv. med. Acta *23:* 589 (1956).

Butazolidin has not only an antiphlogistic effect on thrombosis, it also increases the anticoagulant effect of dicumarol-like drugs. This must be considered in order to prevent bleeding episodes during combined treatment with the 2 drugs.

Livedo Reticularis with Summet Ulcerations. Report of a Case Treated with Long Term Anticoagulant Therapy. Gjessing, H. C., Dedichen, J., Oslo Public Health Center, Oslo, Norway, Acta med. scand. *156:* suppl. 319, 74 (1956).

A case of livedo reticularis with summer ulcerations is described. The patient, a woman of 59, has been successfully treated with long-term anticoagulant therapy.

Long-Term Prognosis of Myocardial Infarction. Analysis in Relation to Russek's Classification of „Good" and "Poor" Risk Cases. Olsen, O. C., Kahrs, T., Romcke, O., Lngjaerde, P., Drammen Hosp., Med. Dept., Drammen, Norway, Acta med. scand. *156:* suppl. 319, 17 (1956).

The paper deals with the long term prognosis of untreated cases of myocardial infarction. The cases are divided into 2 groups according to Russek's criteria of "good" and "poor", risk. It is shown that the "good" risk cases live longer than the "poor" risk cases, but that they die as frequently of a new infarction. It is stressed that the "good" as well as the "poor" risk cases need long-term anticoagulant therapy.

Klinische Erfaringen met het Anticoagulans Sintrom. Nanninga, H. S., Int. Afdeling, Ziekenhuis a. d. Coolsingel, Rotterdam, Holland, Ned. T. Geneesk. *100:* 3343 (1956).

The author has used Sintrom (Geigy) in approximately 70 cases during a period of 5 months. Clinical results were satisfactory.

Un cas de tentative d'empoisonnement par le tromexan. Catalano, V., Progr. med. (Napoli) *12:* 274 (1956).

Thrombusforming in het linker hartoor en arteriele embolie bij de chirurgische behandeling van mitralis-stenose. Schlesinger, F. G., Verhey, J. B., Wagenvoort, C. A., Geneeskundige Universiteitskliniek, Utrecht, Holland, Ned. T. Geneesk. *100:* 3698 (1956).

The authors tried to reduce the risk of arterial embolism from the left atrium in mitral surgery by administering anticoagulants for 6 weeks prior to operation. It was assumed that thrombi already present would become organized during this period, and no new thrombus

would be formed during treatment. 12 cases of atrial fibrillation were thus treated. In a total of 69 commissurotomies, thrombi were found in the left atrial appendage in 17 cases, 8 of which had been treated with anticoagulants. In 6 of the pretreated cases only old well-organized thrombi were found; and in 2 cases old as well as recently formed thrombi. In the remaining 9 untreated cases only old thrombi were found in 4 atrial appendages, and a combination of old and recent thrombi in 5 cases.

The Value of a Chemical Test for the Detection of Blood in the Urine During Anticoagulant Therapy. Peyman, M. A., Charing Cross Hosp., London, England, Lancet *271:* 496 (1956).

Although regular one-stage prothrombin time estimations remain essential in the control of anticoagulant therapy, daily examination of the urine for blood by the orthotolidine test is a useful additional safety measure, particularly for out-patients. A detailed report of this work is in course of preparation; also some of the etiological factors associated with hemorrhage in these cases, and in particular the possible part played by capillary damage are being studied.

Verstärkung der Antikoagulantienwirkung durch Butazolidin. Sigg, A., Pestalozzi, H., Claus, A., Koller, F., Med. Abtlg., Krankenhaus Neumünster, Zollikerberg-Zürich, Switzerland, Schweiz. med. Wschr. *86:* 1194 (1956).

Butazolidine exerts an antiphlogistic and analgetic effect in cases of thrombosis; furthermore it was found to increase the effect of dicumarol-like anticoagulants. If combined therapy with butazolidine and dicumarin is instituted, dosage of the anticoagulant must be decreased in order to prevent hemorrhagic accidents.

Sul controllo della terapia dicumarolica. Confronto fra il metodo di Quick e il metodo "P and P" di Owren e Aas. Bianco, S., Crolle, G., Ist. Patol. Spec. Med., Univ. Torino, Italy, Minerva med. *47:* 39 (1956).

A comparison was made of Quick's method and of the P and P technic of Owren and Aas for the control of dicumarol therapy. The laboratory data obtained showed that there exists a close relationship between the results of the 2 methods for values below 50%. The determinations with the Owren and Aas method are more reliable and the authors did not observe variations due to storage of the plasma.

Neodymium 3-Sulpho-Isonicotinate and Blood Coagulation. Hunter, R. B., Walker, W., Dept. Pharm. and Ther. Queen's College, Dundee, Scotland, Brit. med. J. 5003, 1214 (1956).

In intravenous doses of the order of 5 mg/kg in man and rabbits, neodymium 3-sulphoisonicodinate leads to impairment of intrinsic blood thromboplastin generation by inhibiting two factors normally present in serum — Christmas factor and factor X — and also to variable reduction of factor VII. There is no detectable effect on prothrombin. The effect is demonstrable in 4 hours and lasts for 24 hours. With much larger doses in animals, in addition to the above effects, the clotting time of whole blood is prolonged and the activity of antihemophilic globulin is reduced.

Untersuchungen über den Angriffspunkt von gerinnungshemmenden Stoffen am Komplement. Klein, P., Inst. f. Hygiene and Mikrobiol., Med. Akademie, Düsseldorf, Germany, Z. Hyg. u. Infektk.*142:* 457 (1956).

Der Angriffspunkt der seltenen Erden Neodym im Gerinnungssystem. Beller, F. K., Mammen, E., Frauenklinik, Akad. Med. Forschung, Justus-Liebig-Hochschule, Gießen, Germany, Arch. Gynäk. *187:* 319 (1956).

It was found that neodym-salts can only slightly decrease prothrombin, whereas they reduce factor VII activity markedly and, in high doses, also factor V. Thromboplastin time is prolonged as well as heparin tolerance time. Accelerated coagulation is always found as a reaction 3 hours after the injection. No real fibrinolysis was found, but very often so-called pseudofibrinolysis. The decreased prothrombin complex could not be neutralized by vitamin K_1. To carry out studies in neodym-blood the ion exchanger "Permutit" was used as anticoagulant because oxalat and citrate were found to falsify results.

Un nuovo derivato cumarinico nel trattamento dell'infarto miocardico. Roncallo, E., Boggero, C., Ospedali Civili S. Martino, Div. Med., Genova. Italy, Minerva med. *47:* 1 (1956).

The importance of anticoagulant therapy in myocardial infarction is reviewed. A new cumarin compound G 23 350 was administered to 10 patients with infarction. It is concluded that this drug completes the range of hydroxycoumarine derivatives as it holds an intermediate position between fast and slow acting compounds. The preparation is well tolerated and easy to handle.

Herzglykoside und Antikoagulantien in der Therapie des frischen Myokardinfarktes. Aschenbrenner, R., Foth, K., Allgem. Krankenhaus, Hamburg-Altona, Germany, Med. Klin. *51:* 716 (1956).

Zur Antikoagulantientherapie mit Marcoumar. Hoffmann, K., Med. Univ.-Klinik, Mainz, Germany, Medizinische 830 (1956).

A New Coumarin Derivative (G 23350): A Preliminary Study. Lander, H., Hunter, G. A., Dept. Med. Univ., Adelaide, Australia, Med. J. Aust. *43:* 680 (1956).

Anticoagulant Therapy with Tromexan and Marcoumar and Determination of the Prothrombin-Proconvertin Activity by a Micro-Method. Iversen, T., Dept. Med. Amtssygehus, Aarhus, Denmark, Acta med. scand. *155:* 161 (1956).

Anticoagulant therapy was initiated with a combined dose of 900 mg of Tromexan and 9 mg of Marcoumar in 84 patients. The therapy was maintained with Marcoumar. 24 hours after the initial dose the prothrombin-proconvertin (P-P) activity had fallen to an average of 26%. The P-P activity was determined at intervals of 1—3 days during the first few weeks and later at intervals of 1—3 weeks. The average daily dose of Marcoumar was about 2.5 mg. No hemorrhagic complications were observed. The determinations of the P-P activity were carried out on capillary blood (plasma) by a micro-method which is described, and proved to be reliable and useful in control of anticoagulant therapy.

A Clinical Trial of a New Anticoagulant for Oral Use. McRose, I., Forster, G., Royal Melbourne, Australia, Med. J. Aust. *II/43:* 519 (1956).

Sull'azione anticoagulante dell'alpha-tocoferolo. Mazzetti, G. M., Ist. Clin. med. Generale, Univ., Pavia, Italy, Acta vitamin. (Milano) *10:* 213 (1956).

Thromboembolieprophylaxe nach gynäkologischen Operationen mit dem Cumarinderivat Marcoumar. Hansen, A., Frauenklinik, Stadtkrankenhaus Rendsburg (Schleswig-Holstein), Germany, Zbl. Gynäk. *78:* 1321 (1956).

The hospital mentioned has used Marcoumar for the last 2 years for general prophylaxis of thrombosis. The frequency of postoperative thrombosis has decreased significantly, whereas fatal embolism could not always be prevented.

Est-il légitime de laisser un malade durant des mois à un traitement anticoagulant et, dans l'affirmative, comment faut-il conduire ces traitements au long tours. Facquet, M. J., Presse méd. *67:* 1536 (1956).

The author indicates some directions for long-term anticoagulant therapy, which is considered uncomplicated but rather dangerous. Indications: recidivation of myocardial infarction, severe cases of infarction with secondary left-sided insufficiency, permanently decreased plasma coagulation time in cases of angina pectoris. Antidote: Vitamin K1 (Roche).

Vergleichende Untersuchungen und neuere Ergebnisse über die Wirkung der Cumarin- und Indandionpräparate. Nicola, P. de, Gori, E., Clin. Medica Generale, Univ., Pavia, Italy, Medizinische 1675 (1956).

Cumarin- and indanedione-like anticoagulants were compared in a physiopathologic-pharmacologic study. No significant difference was found regarding the alterations they induce. The duration of action of the anticoagulants was found to be the best way of differentiation. It was found that Sintrom belongs to the long-acting group. The recently described neutralizing

effect of certain Hg-diuretics (thiomerin) regarding anticoagulants (marcoumar) could not be confirmed.

Sulle possibilità terapeutiche di un anticoagulante assorbibile per via cutanea nella cura e profilassi della flebotrombosi in ostetrica e ginecologia. Malagoli, F., Clin. Ostetrica e Ginecol. "L. Mangiagalli", Univ., Milano, Italy, Ann. Ostet. Ginec. *78:* 431 (1956).

Effect of Phenylindanedione on Capillary Resistance. Tawast, M., Mäkitalo, R., Central Communal Hosp., Pohjois-Kymi, Finland, Ann. Med. intern. Fenn. *45:* 45 (1956).

Prime ricerche cliniche su di un nuovo anticoagulante prothrombinopenico: La 3.3'-metiltiopropiliden-bis-(4-idrossicumarina). Fiore, G., Gori, E., Ist. Farmacol., Univ. Milano, Italy, Clin. terap. *11:* 593 (1956).

Experiencia con marcumar, un nuevo agente protrombopenico del tipo cumarinico. Roeschmann, W., Hosp. del Salvador, Santiago, Chile, Rev. méd. Chile *84:* 291 (1956).

Zur Anwendung von Cumarinderivaten. Thies, H. A., Chir. Univ.-Klinik, Hamburg-Eppendorf, Germany, Medizinische 1650 (1956).

Infarctus mésenterique total par thrombose de la veine mésentérique. (Guérison par traitement anticoagulant). de Thomasson, Mém. Acad. Chir. (Paris) *82:* 843 (1956).

Therapie des Myokardinfarktes. Wollheim, E., Med. Univ.-Klinik, Würzburg, Germany, Dtsch. med. Wschr. *81:* 2080 (1956).

Four problems concerning the treatment of acute myocardial infarction are discussed. (1) the use of purine derivatives and vasodilator drugs. (2) the use of anticoagulants, which — with few exceptions — is recommended for all acute cases. (3) the indication for sympathicomimetic substances and cardiac glycosides. (4) barbiturates and other analgetics should wherever possible replace morphine in the relief of pain. A combination of the listed therapeutic mesures has effected a significant decrease in the mortality of myocardial infarction.

Blutungen unter Cumarin-Derivaten. Imdahl, H., Chir. Klinik, Univ. Bonn, Germany, Ärztl. Wschr. *11:* 1077 (1956).

Based on 8 hemorrhagic incidences under marcoumar therapy and one under tromexan, the author discusses genesis, therapy, and prophylaxis of bleeding emphasizing the central role of the liver cell in the biology of coagulation. Therapy consisted of oral and partly intramuscular konakion, which was more effective than synkavit. In addition also rutin was administered.

Beitrag zur Frage der Antikoagulantientherapie während der Gravidität auf Grund von tierexperimentellen Untersuchungen mit ^{147}Nd markiertem Thrombodym. Seitz, R., Med. Abtlg., Allgem. Krankenhaus, Heidberg-Hamburg, Germany, Zbl. Gynäk. *78:* 1923 (1956).

Coumadin (Warfarin) Sodium: A New Anticoagulant. Nicholson, J. H., Leavitt jr., T., Dept. Med., General Hosp., Lawrence, Mass., USA, New Engl. J. Med. *255:* 491 (1956).

Coumadin Sodium (Link's warfarin sodium) was used intravenously and orally in 100 cases requiring anticoagulant therapy. The induction of therapeutic hypoprothrombinemia was relatively prompt. The use of heparin was limited to patients with pulmonary embolism. Initial dose: average 60 mg, daily maintenance dose about 10 mg. Fewer periods of "escape" from the therapeutic range occurred than with the other anticoagulants used by the authors. Hemorrhagic phenomena attributable to the drug occurred in 5 cases. The bleeding occurred only in patients who had undergone surgery, and cleared promptly after administration of phytonadione. No deaths ascribable to the drug occurred.

Anticoagulant Therapy in Coronary Artery Disease. Cosgriff, S. W., Dept. Med., Columbia Univ. Coll. of Physicians and Surgeons, New York, N. Y., USA, J. chron. Dis. *4:* 402 (1956).

The author treats all cases of coronary infarction with anticoagulants, as long as no contraindication exists. Better prognosis regarding second infarction is obtained with long-term anticoagulant therapy in cases of acute infarction. It seems most probable that in cases of

early onset or significant increase of anginal pain the prophylactic administration of anticoagulants can delay or prevent the final occlusion of the vessel. Patients with arteriosclerotic heart affection and intracardial embolism are protected from recurrent embolism by anticoagulant therapy. The therapy must not necessarily be life-long as in rheumatic heart diseases, about 6 months are sufficient. Among the various anticoagulants available every physician should choose one to become acquainted with.

Clinical Experience with Syntrome, a New 4-Hydroxycoumarin. Schilling F. J., Kruesi, O. R., St. Luke's Hosp., Amer. J. med. Sci. *231:* 558 (1956).

65 patients were treated with Sintrome for an average of 27 days. Most effective dosage: 20 mg on the first day, 8 to 16 mg on the second, and an average of 4 to 6 mg for maintenance. Vitamin K_1 again is considered the efficient antidote. Advantageous characteristics of Syntrome: Efficiency of a small single daily dose, absence of side-effects, easy management.

Rectal Administration of Warfarin (Coumadin) Sodium. Freeman, D. J., Meyer, O. O., Dept. Med., Univ. of Wisconsin Med. School, Madison, Wisc., Proc. Soc. exp. Biol. (N. Y.) *92:* 52 (1956).

Warfarin was administered to 23 patients in 100 mg rectal suppositories with a polythylene glycol base. The rectal administration of warfarin sodium was consistently effective and appeared to be as reliable as the oral or intravenous; and is therefore available when the latter are not possible or desirable.

A New 4-Oxycoumarin Derivative G-23350 (Sintrom). Long, L. A., Univ. Montreal, Canada, Canad. med. Ass. J. *75:* 261 (1956).

Sintrom (Geigy) has been tested in 92 patients mostly suffering from coronary thrombosis or thrombophlebitis. The author comes to the conclusion that sintrom has all the characteristics required of a rapidly effective, easily compatible anticoagulant preparation.

Retroperitoneal Hemorrhage Simulating an Acute Abdominal Lesion During Dicumarol Therapy. Reiter, M. D., Charleston, W. Virg., USA, W. Va. med. J. *52:* 205 (1956).

The author reports on 3 patients in whom acute abdominal symptoms developed during dicumarol therapy. The recognition of retroperitoneal hemorrhage during dicumarol therapy is important, especially when the primary disease is a recent myocardial infarction and unnecessary surgery must be avoided. Some disturbing factors in these patients were the absence of cutaneous or urinary bleeding and a prothrombin time that was not strikingly abnormal. The author empasized that, as long as dicumarol remains popular in the therapy of myocardial infarction, retroperitoneal hemorrhage may develop in other patients, the more so since hemorrhage from hypoprothrombinemia has no predilection for a special portion of the body, and since dicumarol intoxication is admittedly common.

Extradural Spinal-Cord Hematoma: Report of a Case Due to Dicumarol and Review of the Literature, Alderman, D. B., Vet. Adm. Hosp., Newington, Conn., USA, New Engl. J. Med. *255:* 839 (1956).

A case of spinal cord extradural hematoma in a patient receiving dicumarol is presented. This syndrome masqueraded a lumbosacral strain until neurologic signs and subcutaneous ecchymoses appeared. 14 well documented cases of extradural hematoma of the spinal cord previously reported in the literature are reviewed. This is the third reported case ascribed to dicumarol toxicity. This diagnosis should be entertained in any patient receiving anticoagulants in whom low-back or sciatic pain develops. The need for frequent prothrombin time determinations is stressed. Repeated examination of the urinary sediment for red cells in patients receiving dicumarol seem indicated.

Experience with a New Anticoagulant Coumadin (Warfarin) Sodium. Goodman, D. H., Phoenix, Ariz., USA, Arizona Med. *13:* 389 (1956).

The Effect of Dicumarolization on the Erythrocyte Sedimentation Rate in Dogs. Trimmer, R. W., Olwin, J. H., Presbytarian Hosp., Chicago, Ill., USA, Angiology *7:* 537 (1956).

Anticoagulant Therapy of Acute Myocardial Infarction. An Evaluation from Autopsy Data with Special Reference to Myocardial Rupture and Thrombo-Embolic Complications. Lee, K. T., O'Neal, R. M., Dept. Pathol., Washington Univ. Med. School, St. Louis, Miss., USA, Amer. J. Med. *21:* 555 (1956).

The use of necropsy findings to estimate the effectiveness of anticoagulants in patients with myocardial infarction admittedly involves selection of fatal cases but nevertheless yields relevant information, as this report attests. Perhaps the most pertinent inference drawn is that anticoagulant therapy does not accomplish such protection against thromboembolism as is attributed to it if treatment is intiated after the third day of clinical onset of infarction. Myocardial rupture occurred five times more frequently in patients treated with anticoagulants as in patients not so treated; selection of cases may have had some part in this difference.

s) Thrombosis

Thromboangiitis Obliterans in Women. Hiertonn, T., Karolinska Inst., Stockholm, Sweden, Angiology *7:* 233 (1956).

The Alteration and Regeneration of the Endothelium in Venous Thrombosis. Impallomeni, G., Div. Chir., Centro di Flebogia, Osp. Maggiore di San Giovanni Battista, Torino, Italy, Angiology *7:* 268 (1956).

Zur Ätiologie und Pathogenese der Thrombo-Embolischen Krankheit und der Praxis ihrer Bekämpfung. Eysholdt, K. G., Chir. Univ.-Klinik, Göttingen, Germany, Med. Klin. *51:* 1281 (1956).

Clinical Aspects of Renal Vein Thrombosis. Harrison, C. V., Dept. Pathol., Postgraduate Med. School, London, England, Quart. J. Med. *25:* 285 (1956).

Thrombosis arteriae pulmonalis. Iversen, K., Kommunehosp. II. Afdeling, Copenhagen, Denmark, Nord. Med. *56:* 1286 (1956).

Postoperative Venous Thrombosis. Wilson, W. C., Univ. Aberdeen, Scotland, Med. illustr. *10:* 545 (1956).

Roentgen Diagnosis of Thrombosis of the Inferior Vena Cava. Laitinen, H., Meurman, K., Roentgen Dept., Kivelä Hosp., Helsinki, Finland, Ann. Med. intern. Fenn. *45:* 107 (1956).

Phenylbutazone (Butazolidin) in the Treatment of Thrombophlebitis. Kos, R., 2nd Dept. Surg., Univ. Med. School, Budapest, Hungary, Acta med. Acad. scient. hung. *9:* 273 (1956).

Über einige praktische Fragen der Venenthrombose. Horn, Z., Lazarits, E., Labor. d. Hauptstädt. "Karoly" Krankenhaus, Budapest, Hungary, Wien. med. Wschr. *106:* 873 (1956).

Lungenembolie und Lungeninfarkt. Wick, A., Med. Klinik, Kantonsspital, Winterthur, Switzerland, Helv. med. Acta *23:* 663 (1956).

Hämodynamische Thrombose-Embolieprophylaxe bei gynäkologischen Operationen. Holtdorff, J., Bergander, U., Med. Akademie, Dresden, Germany, Zbl. Gynäk. *78:* 1910 (1956).

Déformations et thromboses de la veine splénique. de Scoville, A., Leroux, G., Univ. Liège, Belgium, Acta gastro-ent. belg. *19:* 629 (1956).

Experimenteller und klinischer Beitrag zur Charakterisierung der thrombophilen Zustände. de Nicola, P., Mazzetti, G. M., Med. Univ.-Klinik, Pavia, Italy, Dtsch. Arch. klin. Med. *203:* 300 (1956).

Thrombelastographic studies were carried out in order to characterize thrombophilic conditions. Thromboelastographic alterations following addition of excess of coagulation factors to recalcified plasma were studied, and found that addition of high platelet concentrations in particular lead to TEG pattern of the thrombophilic type. A similar pattern resulted from

ligation of vena femoralis in the dog. A clinical study revealed that the majority of thrombophilic pattern is found in the following disorders: hypertonia, arteriosclerosis, thrombophlebitis, thrombosis, myocardial and pulmonary infarction, and in some cases of hyperglobulia, malignoma and malignous hemoblastosis. In all these cases a significant correlation was found between decrease of k-values and increase of ma-values. Similar thrombophilic pattern was also found following cortisone administration in the human. The results are discussed.

Stato attuale della terapia della tromboflebite del seno cavernoso. Latteri, N., Ist. Clin. chir. Univ., Palermo, Italy, Minerva chir. *11:* 339 (1956).

Thrombosis of the Sigmoid Sinus. Past and Present. Reading, P. V., Schurr, P. H., Guy's Hosp., Ear and Throat Dept., London, England, Lancet *271:* 474 (1956).

Renal Vein Thrombosis with Nephrotic Syndrome and Renal Failure. Brumfitt, W., O'Brien, W., Military Hosp., Cambrigde, England, Brit. med. J. 4995, 751 (1956).

A case of intrarenal branch vein thrombosis associated with nephrotic syndrome is described. The possibility that the nephrotic syndrome was secondary to the multiple thrombosis is discussed.

Kontrolle des Behandlungseffektes bei Ulcus cruris und Thrombophlebitis mittels Infrarotphotographie. Schuster, A., Maistr. 11, München 15, Germany, Med. Klin. *51:* 982 (1956).

Der Herzinfarkt, seine Diagnose und Behandlung. Hittmair, Med. Univ.-Klinik, Innsbruck, Austria, Wien. klin. Wschr. *68:* 385 (1956).

Prophylaxe der postoperativen Thromboembolie und Schilddrüse. Kazda, F., Wiedner Hauptstraße 36, Wien IV, Austria, Wien. med. Wschr. *106:* 590 (1956).

Acute Mesenteric Arterial Occlusion. Successful Treatment by Embelectomy and Limited Intestinal Resection. van Weel, M. W., Surg. Dept., Bergweg Municipal Hosp., Rotterdam, Holland, Arch. chir. neerl. *8:* 147 (1956).

Ricerche cliniche e sperimentali sull'azione trombofilica del cortisone. De Nicola, P., Clin. Dermosifilopatica, Univ., Pavia, Italy, Minerva dermat. *31:* 173 (1956).

Zur Bedeutung der Hämodynamik für die Thromboseprophylaxe. Lungmuss, F., Chir. Klinik, Städt. Krankenhaus, Hamm/Westf., Germany, Med. Mschr. *10:* 381 (1956).

During the last 5 years the author used Venostasin (vitamin B_1 containing horse chestnut extract) for the early prophylaxis of thrombosis. A decrease of the number of postoperative thrombosis from 1.86% to 1.01% has thus been obtained.

La trombofilia del puerperio. Ciulla, U., Clin. Ost. and Ginecol. "L. Mangiagalli", Univ., Milano, Italy, Ann. Ostet. Ginec. *78:* 383 (1956).

La trombosi venesa nel vecchio. Serrano, S., Mazza, E., Ist. Clin. chir. gener., Univ., Parma, Italy, Minerva med. *47:* 1535 (1956).

The Familial Tendency in Thrombo-Embolic Disease. Jordan, F. L. J., Nandorff, A., Med. Dept., Univ., Utrecht, Holland, Acta med. scand. *156:* 267 (1956); Ned. T. Geneesk. *100:* 2574 (1956).

After presenting a survey of the literature on familial and constitutional occurrence of thrombosis, the authors describe the cases of 22 patients mentioned in the literature and add the description of 21 own observations. The authors advocate a more liberal prophylactic use of anticoagulants in patients with a positive family history.

Über die Thrombose der Venen der Kubitalgegend. Sinapius, D., Path. Inst. Univ., Heidelberg, Germany, Arch. KreislForsch. *24:* 26 (1956).

Trombose van de arteria pulmonalis. Schmidt, W. J., Chir. Univ. Kliniek, Wilhelmina Gasthuis, Amsterdam, Holland, Ned. T. Geneesk. *100:* 1968 (1956).

Über die Ursachen thromboembolischer Komplikationen bei dekompensierten Herzkranken. Remde, W., Felsch, G., Med. Univ.-Klinik, Jena, Germany, Dtsch. GesundhWes. *11:* 845 (1956).

Über die Terramycinbehandlung der Thrombo-Embolien. Horanyi, M., Ferko, S., I. Univ. Klin. Inn. Med., Budapest, Hungary, Wien. med. Wschr. *106:* 152 (1956).

A patient with pyelonephritis has been treated with terramycin whereby he surprisingly recovered from previously therapy-resistant thrombophlebitis and recurrent pulmonary embolism. Further cases of thromboses or thrombophlebitis resisting to therapy with antibiotics and anticoagulants were then successfully treated with terramycin. As other similar antibiotics did not produce the same effect this phenomenon cannot be ascribed to a mere antibacterial action of terramycin. Terramycin must have some kind of influence on the coagulation system which, however, could not be demonstrated by in vivo or in vitro examinations.

Massive Pulmonary Embolism in a Boy Aged 9. Cashman, M., Royal Bershire Hosp., Reading, England, Arch. Dis. Childh. *31:* 474 (1956).

The Use of Alpha Tocopherol in Acute and Subacute Thrombophlebitis. Suffel, P., Shute Inst., London, Ont., Canada, Canad. med. Ass. J. *74:* 715 (1956).

Unfall und Thrombose. Hasse, G., Chir. Univ.-Klinik, Jena, Germany, Münch. med. Wschr. *99:* 14 (1956).

Behandlung der Venenthrombose mit Pyrabutol. Bobek, K., Cepelak, V., Med. Univ. Klinik, Pilsen, Czechoslovakia, Z. ges. inn. Med. *11:* 1035 (1956).

Zum Problem postthrombotischer Spätschäden. Rässler, R., Univ.-Frauenklinik, Charité, Berlin, Germany, Zbl. Gynäk. *78:* 1416 (1956).

On the Probable Mechanism of Intravascular Clotting. Quick, A. J., Dept. Biochem., Marquette Univ. Med. School, Milwaukee, Wisc., USA, Angiology *7:* 419 (1956).

Observations on Venous Thrombosis. McLachlin, J., Paterson, J. C., Westminster Hosp., London, Ont., Canada, Arch. Surg. (Chicago) *73:* 606 (1956).

Thromboembolism, Pulmonary Arteriosclerosis, and Fatty Meals. Thomas, W. A., Dept. Pathol., Washington, Univ. Med. School, St. Louis, Mi., USA, Arch. Path. (Chicago) *61:* 380 (1956).

The Angiocardiographic Diagnosis of Left Atrial Thrombosis. Soloff, L. A., Zatucchni, J., Circulation *14:* 25 (1956).

The Management of Hemorrhoidal Thrombosis. Jackman, R. J., Mayo Clinic Staff Member, Rochester, Minn., USA, Gen. Pract. Clin. *14:* 82 (1956).

Massive Thrombotic Occlusion of the Large Pulmonary Arteries. Ball, K. P., Goodwin, J. F., Harrison, C. V., Circulation *14:* 766 (1956).

The authors report on 23 cases of thrombotic occlusion of the large pulmonary arteries, not caused by acute massive embolism. Prolonged anticoagulant therapy offers the only hope of preventing extension of the thrombus. Ligation of the inferior vena cava might have to be considered if the thrombosis is secondary to repeated pulmonary emboli from thrombosis of the leg veins that cannot be controlled by anticoagulants.

Renal Vein Thrombosis and the Nephrotic Syndrome. Pollak, V. E., Karl, R. M., Pirani, C. L., Shafter, H. A., Muehrcke, C., Dept. Med. Presbytarian Hosp., Chicago, Ill., USA, Amer. J. Med. *21:* 496 (1956).

The authors give what is perhaps the fullest available account of the clinical, laboratory and pathologic findings in that rare but intriguing cause of the nephrotic syndrome, renal vein thrombosis. They describe an illustrative case (with survival) from their own experience, giving in considerable detail the development of the course, including serial renal biopsies.

A Clinical Study of Pulmonary Embolism. De Laughter, G. D., Anlyan, W. G., Surg. Gynec. Obstet. *103:* 695 (1956).

Mesenteric Vascular Occlusion. Wilson, G. S. M., Crumpsall Hosp., Manchester Mass., USA, Arch. Surg. (Chicago) *73:* 330 (1956).

The Reaction of the Wall of a Vein to the Presence of Experimental Thrombus. Robertson, R. H., Dept. Surg and Pathol., Shoughnessy Hosp., Vancouver Brit. Columbia, Canada, Surg. Gynec. Obstet. *103:* 323 (1956).

Coagulation thrombus, when it lies dormant in a vein, such as the inferior vena cava of a dog, becomes organized and covered by endothelium. It does not incite an inflammatory reaction in the wall of the vein. When such a thrombus is injected into the portal vein of a dog, it partially disappears with the remainder becoming organized and endothelialized. In no instance was there any evidence that a thrombus introduced into the lumen of a normal vein would excite any but the mildest inflammatory reaction in the wall of the host vein and never was there any evidence that an injected thrombus excited any additional clotting or thrombosis.

The Temporary Thrombotic State. Application of this Concept to the Therapy of Recurrent Thromboembolism, with Bacteriologic and Roentgenologic Considerations in the Differential Diagnosis of Pulmonary Infarction and Pneumonia. Wessler, S., Cohen, S., Fleischner, F. G., Dept. Med. and Radiol. Harvard Med. School, Boston, Mass., USA, New Engl. J. Med. *254:* 413 (1956).

Various experimental and clinical observations have led to a concept that the authors have named the temporary thrombotic state. This state and its treatment are discussed and a case is reported to illustrate the usefulness of the concept of the temporary thrombotic state.

Treatment of Thrombosis Occurring in Individuals with Hereditary Hemorrhagic Telangiectasis. Blaustein, A., N. Y. City Hosp., Welfare Island, New York 17, N. Y., USA, Angiology *7:* 55 (1956).

Sequelae of Venous Thrombosis of the Lower Limbs Following Various Methods of Treatment. Höjensgard, I. C., Dept. Surg., County Hosp., Aarhus, Denmark, Angiology *7:* 517 (1956).

Intrahepatic and Extrahepatic Portal Venous Thrombosis. Da Silva Prado, W., Carmargo Barbosa, J. L., Santa Casa de Misericoria, Sao Paolo, Brazil, J. int. Coll. Surg. *25:* 306 (1956).

Thrombosis of Internal Carotid Artery. Shapiro, B. J., Simor, E. S., Toronto, Ontario, Canada, J. Canad. Ass. Radiol. *7:* 5 (1956).

Treatment of Phlebothrombosis and its Sequale with Intraarterial Trypsin. Villamil, M. F., Ayacucho 1165, Buenos Aires, Argentine, Angiology *7:* 179 (1956).

The Syndrome of Chronic Thrombosis of the Major Pulmonary Arteries. Hollister, L. E., Cull, V. L., Vet. Admin. Hosp., Palo Alto, Calif., USA, Amer. J. Med. *21:* 312 (1956).

Bilateral renal Vein Thrombosis and the Nephrotic Syndrome. Kaplan, B. M., Kaplan, E., Baker, L. A., Lee, J. M., Vet. Adm. Hosp., Hines Ill., USA, Ann. intern. Med. *45:* 505 (1956).

The seventh case of bilateral renal vein thrombosis associated with the nephrotic syndrome is reported. The literature of this entity is reviewed in detail.

Organized Thrombus Occluding a Main Pulmonary Artery. Laufer, S. T., Gray, J. D., Halifax Infirmary, Halifax, Nova Scotia, Canada, New Engl J. Med. *245:* 893 (1956).