Physiology and Pathology of Blood Coagulation

A review of the literature of 1957 (first part)

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Index

a) General Aspects

Intérêt du dosage de certains facteurs de coagulation dans le liquide d'ascite. Mise en évidence d'un test caractérisant l'ascite d'origine cirrhotique. Combrisson A. G., Debray, J., Housset, E., Clin. thér. méd., Hôp. Saint-Antoine, Paris, France, Presse méd. *65:* 1229 (1957).

The authors studied the biological characteristics of ascitic fluid in 39 patients with alcoholic cirrhosis or neoplastic ascites. Determination of total proteins, of fibrinogen, proaccelerin or proconvertin did not yield any diagnostic indications. On the other hand prothrombin values vary considerably in ascites according to presence or absence of cirrhosis, thus permitting an etiologic diagnosis in the laboratory.

Über die Auslösung des Gerinnungsvorganges. Koller, F., Baer, P., Geiger, M., Gerinnungsphysiol. Lab., Med. Klinik, Univ., Zürich, Switzerland, Acta haemat. (Basel) *18:* 33 (1957).

The clotting factors indispensable for the formation of blood thromboplastin are all present in active form in plasma except factor IX. Activation of the latter by contact with glass, or with the vascular wall deprived of endothelium, probably initiates the clotting process. Platelet disintegration does not represent the first step of coagulation, being possible only in the presence of thrombin already formed. Clotting with tissue thromboplastin does not require activation of clotting factors by contact with wettable surfaces.

Lisozima e coagulazione del sangue. I. Ricerche sperimentali sul meccanismo dell'azione coagulante del lisozima. Perugini, S., Gobbi, F., Ghisleri, G., Ist. Patol. Spec. Med. Univ., Modena, Italy, Haematologica *42:* 831 (1957).

The authors report the results of in vivo and in vitro experiments carried out to study the coagulating activity of lysozyme. This substance causes in vivo a marked shortening of clotting- and recalcification-time without having a thromboplastic, a prothrombin-like or a thrombin-like activity. It does not influence vascular factors or clot retraction but has in vivo and in vitro an anti-heparin effect. The mechanism of the effect seems to be enzymatic and needs further study.

II. *Ricerche clinico-terapeutiche sull'attività antiemorragica del lisozima.* The authors studied the therapeutic effect of lysozyme in 14 patients with various hemorrhagic disorders. This substance temporarily controlled hemorrhagic incidences and had a prophylactic effect primary to small injuries or minor surgery. Purpura, however, remained uninfluenced. It is concluded that lysozyme represents a new symptomatic antihemorrhagic substance worthy of further studies, especially useful in emergencies and as a prophylactic drug in pre-operative treatment.

Effect of Dietary Triglycerides on Recalcification Time of Plasma. Kingsbury, K. J., Morgan, D. M., Surg. Unit, St. Mary's Hosp. London, England, Lancet *273:* 212 (1957).

When 50 g of emulsified arachid oil were fed to normal volunteers the effects were a postprandial lipemia, endogenous production of phospholipid, and a shortening of plasma recalcification time. The feeding of a mixture of glycerides of the C 8/10 fatty acids resulted in no lipemia, but a phospholipid increase and a shorter recalcification time. The feeding of tobacco-seed oil resulted in marked lipemia, and a shorter recalcification time, but very little increase in the phospholipids. Lipemia is not necessary for the clotting effect seen when the plasma phospholipids are increased in vivo by amounts previously found effective in vitro. The small amount of phospholipid present on the chylomicron's surface during lipemia can accelerate clotting even when the plasma-total-phospholipid has fallen.

La nomenclatura dei fattori della coagulazione. Recenti riunioni e proposte. Nivola, P. de, Ist. Clinica med. Generale, Univ., Pavia, Italy, Progr. med. *13:* 118 (1857).

The author presents a detailed review of the nomenclature ob blood coagulation factors. The various synonyma are tabulated as well as the terminology proposed at the Hematology Congresses of Oxford and Boston.

A Study of Changes in Platelets, Antihemophilic Globulin, Factor V and Factor VII During Blood Collection and Storage by Different Technics. Mustard, J. F., Dept. Med., Univ., Cambridge, England, Brit. J. Haemat. *3:* 202 (1957).

Loss of factor V activity during blood collection and storage is directly related to the degree of platelet loss and to the number of platelets present in the blood at the time of collection. On the other hand factor VII activity is least in blood which has had minimal platelet loss during collection and storage and in blood deficient in platelets. Like factor V, AHG activity is most stable in stored blood when platelet loss has been minimal. The use of silicone-coating minimizes platelet loss, and improves platelet-, factor V- and AHG-stability during storage. It retards the activation of factor VII and appears to diminish platelet adhesiveness. Activation of the coagulation mechanism is probably the factor responsible for loss of platelets and factor V- and AHG-activity during blood collection and storage.

Coagulation Studies on "Reptilase", an Extract of the Venom from Bothrops jararaca. Blombäck, B., Blombäck, M., Nilsson, I. M., Chem. Dept. II, Karolinska Inst., Stockholm, Sweden, Throm. Diath. haem. *1:* 76 (1957).

Reptilase was found to have a thrombin-like activity. No effect could be demonstrated in the first phase of coagulation. Unlike bovine thrombin it was not inactivated by heparin + heparin-cofactor or by the antithrombin of normal plasma. Analysis of N-terminal aminoacids in the fibrin formed by reptilase revealed the same aminoacids as in the fibrin formed by bovine thrombin. Quantitative differences found may reflect different specifity of the 2 enzymes. It is concluded that the use of Reptilase as a hemostaticum is unwarranted.

Utilisation de la "céphaline" dans les tests de coagulation. Larrieu, M. J., Weilland, C., Inst. National d'Hygiène, Paris, France, Rev. Hémat. *12:* 199 (1957).

The preparation of a lipid chloroform extract allows the substitution of the platelet extract in various coagulation tests: the cephaline time differentiates coagulation disorders of platelet- or plasmatic origin. The thromboplastin formation test measures activity of antihemophilic factors A and B and of the 3rd plasmatic factor (PTA, Hageman).

Neue Auffassungen über Hämorrhagie, Hämostase und Thrombose. Copley, A. I., Centre Nat. Transfusion Sang., Paris, France, Ärztl. Forsch. *11:* I/114 (1957).

A review of new concepts, based mainly on studies made by the author and co-workers since 1932, is presented under several headings. They relate to: 1. The blood vessel with emphasis on the physiologic occurrence of the endo-endothelial film of fibrin, produced and deposited on the endothelial cells of all vessels and controlled by fibrinolysis continually, with disturbances leading to thrombosis or to hemorrhage. II. Mechanisms involved in hemorrhage. III. Blood clotting, thrombosis and thromboembolization, where clotting is considered a general term for cellular agglutination, plasma coagulation and for a process in which agglutination and coagulation are mixed. IV. Mechanism of coagulation with particular stress on the third or gelation phase. V. Factors in the phase of initiation and maintenance of hemostasis, and VI. The interrelationship between hemorrhage and thrombosis.

Jahreszeitliche Schwankungen der Blutgerinnung beim Hunde. Rosival, V., Selecky, F. V., Chem. Inst., Slowakische Akad. Wiss., Bratislava, Czechoslovakia, Experientia (Basel) *13:* 84 (1957).

Blood coagulation in dogs was observed from December to August. Quick values showed no significant alterations, while the recalcification time is prolonged during the warm periods in summer. In cases of increased recalcification time, an increased amount of circulating heparin was found in blood.

Blood Coagulation Defects in Kwashiorkor and Infantile Gastroenteritis. Merskey, C., Hansen, J. D. L., Dept. Med. and Child Health, Univ., Cape Town, S. Africa, Brit. J. Haemat. *3:* 39 (1957).

An investigation into the incidence of purpura, thrombocytopenia and abnormalities of the prothrombin complex has been carried out on a series of patients with kwashiorkor or gastroenteritis. It was found that purpura occurred in 9 out of 58 cases of kwashiorkor. 3 of the 9 patients had platelet counts below 100 000/cmm 6 other patients had also counts below 100 000/cmm but without purpura. A significant decrease in the prothrombin index was found

in the majority of cases. This was due to a deficiency of factor VII and possibly factor X; some cases had in addition a prothrombin deficiency. Other coagulation factors were normal. After a suitable diet, in which vitamin K appeared to be an important element, the defects rapidly disappeared.

Zur Frage der Magnesiumwirkung auf die Blutgerinnung. Schimpf, K., Hartert, H., Med. Univ.-Klinik, Heidelberg, Germany, Klin. Wschr. *35:* 50 (1957).

The results show that in the range of possible therapeutic doses, magnesium has no significant effect on the blood coagulation mechanism.

Störungen der Blutgerinnung beim Plasmazytom. Kautzsch, E., Med. Abtg., Städt. Krankenhaus, München-Schwabing, Germany, Klin. Wschr. *35:* 77 (1957)

The rather frequent hemorrhages occurring in patients with myeloma are caused by a complex coagulopathia, which has been analyzed in a case of β_2 plasmacytoma. Not only is the activity of the known coagulation factors decreased, but also an inhibitor of the pre-phase could be demonstrated for the first time.

Elektronenmikroskopische Befunde bei der Blutgerinnung. 2. Mitteilung: Zur Natur der in Thrombozytennähe vorkommenden atypischen Plasmagerinnung im frischen menschlichen Thrombozyten-Zitratplasma. Hasché, E., Seeliger, R., Neurochir. Klinik, Univ. Freiburg/Br., Germany, Ärztl. Forsch. *11:* I/127 (1957).

The clotting material occurring in the vicinity of platelets was identified as fibrin by electronmicroscopical examination. Fibrin precipitates chiefly in an "amorphous" state and only to a small extent in "bundles". The "bundled" fibrin may temporarily show transverse striation. Fibrin in its final state shows no transverse striation. This fibrin formation as caused by thrombocytes under certain conditions, occurs also in the presence of anticoagulants. It thus explains certain cases of thrombosis affecting healthy individuals without obvious reason, which are resistant to anticoagulants. Notably thrombotic thrombocytopenic purpura is likely to belong to this type of thromboses.

Reptilase — Ein Hämostatikum? Kock, N. G., Kirurgiska Kliniken I, Sahlgrenska Sjukhuset, Göteborg, Sweden, Nord. Med. *57:* 331 (1957).

The hemostatic preparation Reptilase has been studied in vivo and in vitro. In contrast to other authors no significant effect on coagulation time and no inhibitory effect on hemorrhagic manifestations were noticed following subcutaneous injection. A certain influence on coagulation time was found in vitro, however, at concentrations much too high for practical use.

Les variations de la coagulabilité appreciées in vitro par le test à l'héparine de Marbet et Winterstein en fonction des valeurs de Quick et des différentes concentrations plaquettaires. Pettavel, J., Wuilleret, B., Serv. Univ. Chir., Lausanne, Switzerland, Helv. chir. Acta *24:* 39 (1957).

The authors present an experimental study concerning the relation in vitro between whole blood coagulation time (as measured by a heparin test), the plasmatic coagulation factors adsorbable by $Al(OH)_3$, (as measured by Quick's time), and thrombocytosis.

Experimentelle Studien zur Frage der Beeinflussung der Blutgerinnung durch Reptilase. Hohnen, H. W., Med. Univ.-Poliklinik, Bonn, Germany, Z. ges. exp. Med. *128:* 427 (1957).

It was found that fibrinogen solutions and citrated plasma coagulate after addition of Reptilase whether calcium is present or not. This suggests a thrombin-like activity of this preparation. It is, however, not identical with thrombin, as further results demonstrate. The therapeutic possibilities of Reptilase were not studied.

Studio comparativo dei raporti trombelastografici ed emocoagulativi nell' uomo e in varie specie animali. Rapporti con i problemi della fisiopatologia. Nicola, P. de, Cappelletti, G., Sartori, S., Ist. Clin. Med. Generale, Univ., Pavia, Italy, Haematologica *42:* 179 (1957).

Thrombelastogram, prothrombin time, and recalcification time were studied in humans, and comparatively in a group of mammals. For each species a characteristic behaviour was found.

In addition to a species specifity, a group specifity was also evidenced. Of particular interest were the results regarding variations related to age and sex of the animals. They suggest a certain relation between sexual hormones and coagulation factors, especially platelets. The significance of these findings is discussed regarding identification of standard values for each species, selection of the most suitable animals for research, and most suitable technic of blood withdrawal for such studies.

Blood Coagulation After the Ingestion of Saturated and Unsaturated Fats. Merskey, C., Nossel, H. L., Dept. Med. Univ. Cape Town, South Africa, Lancet *272:* 806 (1957).

An attempt was made to confirm the claim that feeding mixed animal fats shortens the coagulation time, and at the same time to determine the effect of feeding fat rich in unsaturated fatty acids. The tests included coagulation time of whole blood in silicone tubes, calcium time of plasma with varying numbers of platelets, thrombin generation test, blood thromboplastin generation test, prothrombin consumption, and accelerated one-stage prothrombin time (stypven time). With the exception of the stypven time, neither the high fat nor the low-fat meal produced any significant change in coagulation. The measurement of the stypven time is affected by the presence of fat in the plasma. This is true of both saturated and unsaturated fat. The importance of this remains to be fully evaluated.

L'action du lysozyme sur la coagulation du sang. Perugini, S., Inst. de Pathol. méd., Univ., Modena, Italy, Presse méd. *65:* 719 (1957).

The coagulant activity of lysozyme has first been reported upon in 1952 by Violle, in 1953 Dumarez and Ghiglione have found that this preparation has an antiheparin effect in dogs. Most recently this problem has been studied by various authors and their observations lead to the conclusion that lysozyme can be considered an antihemorrhagic drug of particular practical and theoretical interest. The author discusses its action in vivo and in vitro, its mechanism of action and its therapeutic administration and indication.

Bestimmung der Blutgerinnung an chininhaltigem Kaninchenblut und Kaninchenplasma. (Weitere Untersuchungen zur gerinnungsphysiologischen Wirkung von Medikamenten). Szirmai, E., Gerinnungsphysiol. Lab., Arpad-ut 124—126, Budapest IV, Hungary, Z. ges. exp. Med. *128:* 446 (1957).

The author presents results obtained in studies of quinine — containing rabbit blood and plasma. It is concluded that quinine has no effect on blood coagulation neither in vivo nor in vitro.

Der Protamintoleranztest als Abwandlung des Heparintoleranztestes und der Protamintitration. Beller, F. K., Steichele, D., Univ.-Frauenklinik, Tübingen, Germany, Z. ges. exp. Med. *128,* 458 (1957).

A method is described where coagulation time is prolonged by protamine sulfate. According to results obtained with the heparin tolerance test coagulation times were found to be prolonged in hemorrhagic diatheses. Heparin activity in the investigated blood is only detectable if protamine tolerance test and heparin tolerance test are carried out at the same time. With this method no heparin activity could be detected in cases of meno-metrorrhagia nor in umbilical cord blood.

Studies on the Effect of Dextran on the Coagulation of Blood. Jacobaeus, U., Dept. Int. Med., Karolinska Sjukhuset, Stockholm, Sweden, Acta med. scand. *157:* suppl. 322 (1957).

Since 1953 impairment of hemostasis has been observed after in vivo infusion or in vitro admixture of dextran. The author presents a detailed study of this phenomenon. The methods and reagents used in the study are described. Clinical studies are presented. Infusion of dextran resulted in the following changes: Decrease of prothrombin, proaccelerin and proconvertin, corresponding approximately to the hemodilution. Reduced prothrombin consumption. Delayed clot retraction. The laboratory studies are reviewed. Dextran had both inactivating and activating effects on the process of coagulation. The total action of dextran is discussed. It is concluded that the decrease in prothrombin consumption was sufficient in some cases to pro-

duce defective hemostasis. Finally it is stated that the ideal dextran preparation should be narrowly fractionated, having molecules weighing from 60 000 to 80 000.

Therapeutische Möglichkeiten bei hämorrhagischer Diathese. Hörder, M. H., Med. Univ.-Klinik, Freiburg/Br., Germany, Münch. med. Wschr. *99:* 666 (1957).

The author gives a general survey on the therapeutic possibilities in hemorrhagic diatheses. General therapeutic measures as well as advancements in therapy are discussed. Differential diagnosis is pointed out.

Changes in Plasma Prothrombin, Ac-Globulin, and Antithrombin Concentration Following Intravenous Administration of Estrogens. Johnson, F., Dept. Physiol. and Pharm., Wayne State Univ. Med. Coll., Detroit, Mich., USA, Proc. Soc. exp. Biol. (N. Y.) *94:* 92 (1957).

Solutions of estrogenic steroids were administered intravenously to dogs. There was a sharp rise in plasma Ac-globulin and prothrombin concentration. These changes began within the first 15 mins., reached a peak in about 1½ hours. In about 3 or 4 hours normal concentrations were again found. A small decrease in antithrombin activity of plasma was found. Theoretically all these alterations tend to enhance coagulability of blood.

Estimation of Clotting Accelerator Activity in Plasma After Ingestion of Fat. Tilden, J. H., Shipley, R. E., Lilly Lab. for Clin. Research, General Hosp., Indianapolis, Ind., USA, Circulation Res. *5:* 298 (1957).

A relatively simple method is presented which permits a quantitative estimation of a "coagulation accelerator activity" which appears in plasma of human and dog blood after oral ingestion of various fats. Accelerator activity and increased plasma turbidity were observed after ingestion of cream, peanut oil, cocoanut oil, linseed oil, or sodium oleate. Peak responses were seen between 3 and 5 hours after fat intake with gradual return towards control levels in 7 hours.

Methylcellulose as a Wetting Agent in Blood Clot: In Vivo Studies. Rosenfeld, M., Dept. Pharm. and exp. Ther., The Johns Hopkins Univ. Med. School, Baltimore, Md., USA, Blood *12:* 373 (1957).

Primary Hemorrhagic Diseases. Lewis, J. H., Dept. Physiol., Univ. N. Carolina, Chapel Hill, N. C., USA, J. Lab. clin. Med. *49:* 211 (1957).

Effects of Meals of Different Fats on Blood Coagulation. Keys, A., Lab. Physiol. Hygiene, Univ. Minn., School of Public Health, Minneapolis., Minn., USA, Circulation (N. Y.) *15:* 274 (1957).

Blood Coagulation During Normal Pregnancy, Labor and the Puerperium. Kennan, A. L., Bell, W. N., Amer. J. Obstet. Gynec. *73:* 57 (1957).

20 normal pregnant patients were followed from their 34th week of gestation through delivery and the early part of puerperium. The changes that occurred during the puerperium seemed to result from a reparative stimulus consisting of the increased ability of the blood to clot. There is an apparent sudden decrease in the plasma volume which approaches the predelivery value. With the beginning of postpartum diuresis the plasma volume gradually returns to the prepregnancy level. The hematocrit determinations carried out support the thesis that the changes during puerperium contributed to the increase of the clotting factors. There was a definite increase in the coagulation factors associated with the loss of plasma volume.

Effect of Intravenous Soy Bean Phosphatides on Blood Coagulation in Rabbits. Spaet, T. H., Kropatkin, M., Div. Labor., Montefiore Hosp., New York City, N. Y., USA, Proc. Soc. exp. Biol. (N. Y.) *95:* 493 (1957).

Emulsions of soy bean phosphatides with platelet-like coagulant activity were given intravenously to rabbits. Small doses were followed by little change in blood coagulation, but larger doses produced depression of prothrombin, Ac-globulin, and AHF. Fibrinogen and the "serum

factors" were unaffected. The observed changes resulted from direct anticoagulant activity, and probably also from partial conversion of prothrombin.

Standard Clotting Time. Mayer, G. A., Dept. Med., Queen's Univ. and Kingston General Hosp., Kingston, Canada, J. Lab. clin. Med. *49:* 938 (1957).

A standardized test for determination of clotting time is described. After a short period of training, it is easily performed with inexpensive material and gives reproducible results. The standard error of the technic is ± 0.13 min. The normal value is 11.9 mins., standard deviation being about ± 0.9 min. Since subjective error is minimal, control blood for reference value is superfluous and the comparison of results of different workers is possible.

b) Fibrinogen (Factor I), Fibrin, Fibrinolysis

Vorzeitige Plazentalösung und Afibrinogenämie. Hartl, H., Univ.-Frauenklinik, Göttingen, Germany, Landarzt *33:* 35 (1957).

Die Bedeutung der Lungen für einige Gerinnungsfaktoren. I. Mitteilung: Lungen und Fibrinogen. Michel, D., Schulz, F. H., Hartleb, O., Med. Univ.-Klinik, Leipzig, Germany, Klin. Wschr. *35:* 401 (1957).

The authors report upon studies on the fibrinogen content of mixed venous blood and of arterialized blood. It was found that with the increase of pulmonar capillary pressure in arterialized blood the fibrinogen content increases to values above those of mixed venous blood. Opposed results are found with normal or only slightly increased pressure. The cause of these findings is discussed regarding a possible role of the lungs in metabolic processes.

II. Mitteilung: Fibrinolyse und Lungen. Schulz, F. H., Michel, D., Hartleb, O., Klin. Wschr. *35:* 404 (1957).

The authors report upon the fibrinolytic activity of mixed venous blood and of arterialized blood in the pulmonar blood flow. Frequency and degree of fibrinolysis did not reveal an ascertained connection with the pressure in the pulmonary blood flow. Fibrinolysis is more frequently found with decreasing oxygen saturation.

Studio sulla protidogenesi. — Nota I: concentrazioni plasmatiche di fibrinogeno nel sangue venoso, arterioso e midollare nei soggetti normali e patologici. Bugaro, L., De Castro, B., Ist. Clin. med. Generale e Ter. med., Univ., Padova, Italy, Haematologica *42:* 358 (1957).

Plasma fibrinogen was studied in venous, arterial, and medullary blood of 35 patients with various diseases and of 5 controls. In the majority fibrinogen concentration differences were found with a decrease from the vein to the artery and to the marrow. These results and the high fibrinogen level in 3 splenectomized subjects and in some cases with severe liver damage plus some other findings suggest a possible systemic fibrinogenopoietic activity of the reticuloendothelial system, as is admitted by most researchers.

A Stable Standard for the Colorimetric Determination of Total Protein, Albumin, Globulin and Fibrinogen. Rappaport, F., Loew, M., Biochem. Lab., Beilinson Hosp., Petah Tikva, Israel, Clin. chim. Acta *2:* 126 (1957).

A method is described for the preparation of inexpensive and stable standards for colorimetric determinations of total proteins, albumin, and fibrinogen in serum and plasma. The standard is a 10% solution of commercial peptone.

Enzymatische Karzinomdiagnostik und Fibrinolyse. Schuler, R., Med.-Diagnostisches Inst., Berg/Starnbergersee, Austria, Ärztl. Forsch. *11:* II/53 (1957).

The author attempted the identification of the enzyme known as "Nitsche-Ferment" in the literature and found it to be identical with plasmin. Nitsche's method of early detection of malignous tumors is based on the determination of this enzyme in urin. The high value of this method is emphasized.

Plasma Fibrinogen in Rheumatic Fever. Reid, J., Sproull, D. H., Clin. Chemotherapeutic Research Unit, Med. Research Council, Western Infirmary, Glasgow, Scotland, Brit. med. J. no. 5027, 1089 (1957).

The abnormally high plasma fibrinogen concentrations found on admission to hospital in 33 patients with acute rheumatic fever fell rapidly and uniformly during a continuous intensive course of aspirin, controlled by serum salicylate estimations. This clearly demonstrates the advantage of proper aspirin therapy.

Über das Vorkommen eines fibrinolytischen Systems in der Plazenta. Wille, P., Geburtshilfl.-Gynäkol. Abtg., Städt. Krankenhaus, Berlin-Kaulsdorf, Germany, Folia haemat. *1:* 230 (1957).

Human placenta contains measurable amounts of profibrinolysin (plasminogen) and considerable amounts of antifibrinolysin. No cytofibrinokinase and no fibrinolytic activity could be found. Based on these results it cannot be concluded that fibrinolytic enzymes of the placenta cause afibrinogenemia during parturition.

Autoaktivierung und Autofibrinolyse. Eine einfache Schnellmethode zur Gewinnung hochaktiven menschlichen fibrinolytischen Materials. Kaulla, K. N. von, Dept. Med., Univ. of Colorado Med. School, Denver, Col., USA, Klin. Wschr. *35:* 667 (1957).

The author describes a method to obtain fibrinolytic preparations using urine-treated plasma. All components of the fibrinolytic system may be taken from the same patient.

Das Verhalten des Fibrinogens in pleuralen Ergüssen und die Nutzbarmachung neuerer Erkenntnisse für die Differentialdiagnose. Balogh, A., Abtlg. f. Tbc., Krankenhaus, Wien-Lainz, Austria, Wien. klin. Wschr. *69:* 82 (1957).

Vergleichende Untersuchungen über den Nachweis der Fibrinolyse nach Injektion eines bakteriellen Lipopolysaccharids (Pyrexal). Hörder, M. H., Kickhöfen, B., Med. Univ.-Klinik, Freiburg/Br., Germany, Acta haemat. (Basel) *17:* 321 (1957).

Lipopolysaccharide was obtained from salmonella abortus equi and injected intravenously into healthy volunteers. Fibrinolysis was produced regularly in whole blood samples. Measurements of the fibrinolytic activity were carried out with various methods and corresponding results were obtained. Fibrinolysis developed at the same time as rise in temperature and fall in number of neutrophile granulocytes. When temperature reached its maximum, fibrinolysis was no longer demonstrable.

Analysis of the Streptokinase Activated Fibrinolysis by Means of Thrombelastography. Nicola, P. de, Mazzetti, G. M., Dept. Int. Med., Univ. Pavia, Italy, Blut *3:* 20 (1957).

The streptokinase activated fibrinolysis was studied after operations and deliveries by means of thrombelastography. A shortening of the lysis time was observed during the first hours following operation or delivery. This was followed by an increase with maximum values on the 2nd and 3rd day. Normal values are reached after 6 to 8 days. A linear proportion on a logarithmic basis was found between the various components of the thrombelastogram. The analogies between the variations of streptokinase activated fibrinolysis after operation and delivery and other coagulation factors are discussed.

Defibrinierungsblutungen unter der Geburt. Puder, H.: Landesfrauenklinik, Bochum, Germany, Münch. med. Wschr. *99:* 293 (1957).

The cause of hemorrhage by defibrination occurring during pregnancy and parturition and its relation to the normal mechanism of separation of the placenta is discussed. One case of afibrinogenemia, as observed among 3000 deliveries, is reported on. The problems of diagnosis and therapy of such a case are mentioned.

Gerinnungsphysiologische Schnellmethode zur Bestimmung des Fibrinogens. Clauss, A., Gerinnungsphysiol. Lab. Med. Univ.-Klinik, Zürich, Switzerland, Acta haemat. (Basel) *17:* 237 (1957).

A clotting system containing a weak fibrinogen concentration (5—50 mg%) and a high thrombin concentration (25 NIH units/ml) is very sensitive to alterations in fibrinogen con-

centration. This fact can be used for a method of fibrinogen estimation. The details of the method are described and its accuracy evaluated at ± 10%.

Dangerous Bleeding Associated with Carcinoma of Prostate. Swan, H. T., Wood, K. F., Owen, D., Dept. Hematol., Royal Infirmary, Sheffield, England, Brit. med. J. no. 5017, 496 (1957).

Two cases are described in which the patients suffered from metastatic carcinoma of the prostate and developed a generalized hemorrhagic state. During these episodes the blood of both patients was incoagulable owing to a deficiency of plasma fibrinogen. In the first patient, who died, this loss was probably associated with fibrinolysis. The second patient recovered on receiving 4 g of human fibrinogen. Simple methods are described for the emergency laboratory diagnosis of hypofibrinogenemia. The therapy of hypofibrinogenemia and of fibrinolysis is discussed.

Der kjeldahlometrisch bestimmte Normalwert der Fibrinogenfraktion des Blutes in seiner Abhängigkeit vom Lebensalter und Geschlecht. Richter, W. C., Med. Univ.-Poliklinik, Bonn, Germany, Z. ges. exp. Med. *128:* 408 (1957).

Average fibrinogen values were determined in 451 subjects of all ages and of both sexes by means of a kjeldahlometric method. The results are compared with values obtained by means of gravimetric methods and show satisfactory conformity.

Evaluation of Synthetic Substrate Methods for Clinical Determination of Fibrinolysis. Schultz, R. L., Moorman, J. A., Matoush, L. O., Lincoln, A. F., Chem. Unit, Fitzsimons Army Hosp., Denver, Col., USA, Proc. Soc. exp. Biol (N. Y.) *94:* 198 (1957).

An attempt was made to determine a normal level of enzyme activity in human plasma as measured by the lysine-ethyl-ester and tosyl-arginine-methyl-ester assays. There was not only a variation in activity from one individual to the other, but also variations in one individual from day to day and within one day. When normal blood and blood with marked fibrinolytic activity were compared, no difference in enzyme activity was noted. Therefore, these methods are not suitable clinically for the demonstration of fibrinolytic activity.

Amniotic Fluid Embolism, Afibrinogenemia, and Disseminated Fibrin Thrombosis. Tuller, M. A., Dept. Path., Mount Sinai Hosp., New York, N. Y., USA, Amer. J. Obstet Gynec. *73:* 273 (1957).

Studies on the Fibrinogen Polymerization Test. Losner, S., Volk, B. W., Fremont, R. E., Isaac Albert Research Inst., Jewish Chronic Disease Hosp., Brooklyn, N. Y., USA, Amer. J. clin. Path. *27:* 609 (1957).

The fibrinogen polymerization test is described. It was performed on blood from patients with a variety of diseases, and the results were compared with those of acute-phase reactants such as the corrected erythrocyte sedimentation rate, C-reactive protein, plasma fibrinogen, and the titer of antistreptolysin O. The fibrinogen polymerization test, in contrast to acute-phase reactants, is not suppressed by the therapeutic administration of steroid hormones. It remains positive for long periods in some instances, after all of the other laboratory tests reveal normal results. It is suggested that it may reflect more accurately the activity of the rheumatic state. It may be of significance, therefore, in deciding when to discontinue therapy with steroids.

Comparison of Certain Properties of Human Plasminogen and "Proactivator". Ablondi, F. B., Hagan, J. J., Biochem. Research Section, Amer. Cyanamid Co., Pearl River, N. Y., USA, Proc. Soc. exp. Biol. (N. Y.) *95:* 195 (1957)

Human plasma and highly purified soluble human plasminogen contain the same "proactivator : plasminogen ratio". The difference in apparent stability of plasminogen and proactivator was traced to the difference in solubility as effected by the pH of the respective assays. During the autocatalytic conversion of plasminogen to plasmin, proactivator content diminishes as plasmin is formed. A discussion of these observations is presented, wherein it is proposed that human plasminogen and the proactivator of bovine plasminogen in human plasminogen are the same factor.

A Heparin-Precipitable Fraction of Human Plasma. I. Isolation and Characterization of the Fraction. Smith, R. T., von Korff, R. E., Pediatric Clinic, Variety Club Heart Hosp., Minneapolis, Minn., USA, J. clin. Invest. *36:* 596 (1957).

Some of the physical and chemical properties of a fraction of human plasma which is characterized by cold-insolubility in the presence of heparin are described. The data indicate that the fraction is a fibrinogen-like protein loosely combined with heparin, the resultant complex having altered solubility properties. The amount of this fraction obtained from a given plasma is a function of the heparin concentration. Evidence was obtained that the fraction is closely related to or associated with fibrinogen in that it is partially clottable, has similar mobility on electrophoresis, and is absent from serum. The possible relationship between heparin-precipitable fraction and previously reported fibrinogen-like proteins are discussed.

II. Occurrence and Significance of the Fraction in Normal Individuals and in Various Disease States. Smith, R. T., J. clin. Invest. 36: 605 (1957).

The occurrence in health and disease and the clinical significance of the protein fraction described above have been studied by means of an empirical technic of measurement. The data allow the conclusions that normal individuals have low levels of the fraction, and that these become greatly increased as a result of most acute inflammatory or necrotizing diseases. The appearance of increased amounts of the fraction represents another reaction in the category of "acute phase" phenomena. The data support the other items of evidence indicating that the fraction may fulfill a different physiological role from clottable protein. The nature of this function is as yet unrevealed.

Effect of Estradiol on Fibrinolytic Activity of Rat Uterus. Albrechtsen, O. K., Biol. Inst., Carlsberg Found., Copenhagen, Denmark, Proc. Soc. exp. Biol. (N. Y.) *94:* 700 (1957).

Concentration of tissue activator of plasminogen in the rat uterus has been estimated in different stages of the estrous cycle. An increase in concentration was recorded during late estrous, whereas castration had no influence upon the concentration. These results are in accordance with those found for human endometrium and myometrium.

A Case of Congenital Afibrinogenemia. Fernando, P. B., Dharmasena, B. D., Dept. Med., Univ. Ceylon, India, Blood *12:* 474 (1957).

A case of congenital afibrinogenemia in a boy of 22 is reported. The main features of the other reported cases are reviewed. The principal features of this case are total absence of fibrinogen and coagulability, history of several episodes of hemorrhage dating from infancy, low erythrocyte sedimentation rate, consanguinity of the parents, and the occurrence of spontaneous hemiperitoneum from which the patient recovered after operation. Treatment consisted of blood or fibrinogen transfusions.

On Plasma Fibrinolytic Activity in Cryptogenetic Splenomegaly. Kwaan, H. C., Univ. Dept. Med., Hong-kong, Scott. med. J. *2:* 137 (1957).

Zum färberischen Fibrinnachweis. Haschè, E., Neurochir. Klinik, Univ., Freiburg/Br., Germany, Acta haemat (Basel) *18:* 175 (1957).

By suitable methods the demonstration of fibrin using the light-microscope can be much improved upon. Fibrin can be demonstrated even when platelets agglutinate spontaneously. It was found that he so-called hyaline mass of certain thrombi consists mainly of irregularly bundled fibrin.

The Fibrinolytic Activity of Human Tissues. Albrechtsen, O. K., Biol. Inst., Carlsberg Found., Copenhagen, Denmark, Brit. J. Haemat. *3:* 284 (1957).

The activator of plasminogen has been estimated in extracts of various human tissues. Large amounts are present in the uterus, adrenal lymph nodes, prostate, thyroid, lungs and ovary. Moderate or small amounts are present in the pituitary, kidney, muscles, heart, testis and spleen. Extracts from the liver were almost inactive. No correlation could be established between the activator concentration and age, sex or tissue structure, and the activator concentra-

tion in the same organ from different persons varied considerably. No inhibitors similar to the inhibitor from ox lung were demonstrated in any of the extracts.

Plasma Fibrinogen and Erythrocyte Sedimentation Rate in Myocardial Infarction. Holger-Madsen, T., Med. Dept. F., County Hosp., Copenhagen, Denmark, Acta med. scand. *156:* 351 (1957).

Plasma fibrinogen and SR were examined in 28 patients with myocardial infarction. Fairly good accord was found in most cases between plasma fibrinogen and SR levels, and between these and the clinical severity; the highest values being found in the most exhausted patients. However, deviations from this were also found; and in these cases plasma fibrinogen was not definitely more reliable than SR determinations as an indicator of the clinical severity of the individual case.

Congenital Afibrinogenemia. (The First Case From Japan). Morita, H., Kagami, M., Dept. int. Med., Med. School, Toho Univ., Tokyo, Japan, Acta haemat. (Basel) *17:* 315 (1957).

A case of congenital afibrinogenemia is described. A girl of 7 years showed a hemorrhagic tendency from birth, easy bruising, absolute afibrinogenemia, absence of blood coagulation, and very slow erythrocyte sedimentation rate.

Bleeding Diathesis Associated with a Circulating Fibrinolysin: Report of Three Cases. Firkin, B. G., Reed, C. S. H., Blackburn, C. R. B., Clin. Research Unit, Royal Prince Alfred Hosp., Sydney, Australia, Brit. J. Haemat. *3:* 193 (1957).

Three patients with bleeding diathesis associated with a circulating fibrinolysin are described. The syndrome can be suspected clinically because of the delayed onset of bleeding. The diagnosis can be confirmed with very simple technics. Whole blood transfusions, and intravenous infusions of fibrinogen and albumin are effective methods of treatment.

Fibrinolysis and Atherosclerosis. Copley, A. L., Lancet *272:* 6959 (1957).

Inhibition of Fibrinolysis in vivo by Alimentary Cholesterol. Kwaan, H. C., McFadzean, A. J. S., Univ. Dept. Med., Queen Mary Hosp., Hongkong, Nature (London) *179:* 260 (1957).

The Value of Estimating Fibrinogen and C-reactive-protein Levels in Myocardial Ischemia. Phear, D., Stirland, R., Central Middlesex Hosp., London N. W. 10, England, Lancet *273:* 270 (1957).

The Role of the Fibrinolytic Enzyme System in Obstetrical Afibrinogenemia. Phillips, L. L., Montgomery jr., G., Taylor jr., H. C., Amer. J. Obstet Gynec. *73:* 43 (1957).

The authors report on 10 patients with obstetric afibrinogenemia. The serially collected blood samples were studied for fibrinogen levels and for the various factors of the fibrinolytic enzyme system. Small but significant levels of fibrinolytic and or fibrinogenolytic activity were found. The presence of an active proteolytic enzyme in the blood may be partially responsible for the low levels of fibrinogen in patients with obstetric afibrinogenemia.

Relation Between Degree of Fibrinogen Proteolysis by Plasmin and Fibrinolytic Paracoagulation. Szuchet, S., Derechin, M., Lab. of Chem., Dental School, Univ., Santiago de Chile, South America, Proc. Soc. exp. Biol. (N. Y.) *94:* 267 (1957).

Fibrinogen proteolysis by plasmin and the clotting of lysed fibrinogen were studied. Close relationship was found between increase in non-protein nitrogen and behaviour of lysed fibrinogen.

c) Prothrombin (Factor II), Thrombin

Further Studies on Prothrombin Derivatives. Landaburu, R. H., Seegers, W. H., Dept. Physiol. and Pharm., Wayne State Univ. Med. Coll., Detroit, Mich., USA, Proc. Soc. exp. Biol. (N. Y.) *94:* 708 (1957).

Purified bovine prothrombin preparations may lose the property of clotting fibrinogen but retain esterase activity. It is likely that a single molecule possesses the 2 activities. When

biothrombin has lost clotting activity and only esterase activity remains, it is called 'esterase thrombin'.

Modification of the Heparin Clotting Time (Heparin Prothrombin Time). Losner, S., Volk, B. W., Isaac Albert Research Inst., Jewish Chronic Disease Hosp., New York City, N. Y., USA, Amer. J. clin. Path. *27:* 353 (1957).

This paper includes the description of a method for determining prothrombin time, using minimal amounts of heparin as an anticoagulant solution. The proposed method is designated as the heparin prothrombin time. Its mechanism is thought to be based on the antagonism between thromboplastin and heparin. The characteristics of the method are discussed.

Dosages différentiels de proconvertine, de prothrombine et de proaccélerine. Alagille, D., Centre Nat. Transfusion Sanguine, Paris, France, Rev. franç. clin. et biol. *2:* 517 (1957).

Proconvertin and proaccelerin participate in the activation of endogenous thromboplastin, and a deficiency of these factors will prolong Quick's test just as will a deficiency of prothrombin itself. Alterations of the Quick test can further be studied by isolated estimation of proconvertin, proaccelerin, or prothrombin. The methods are given in detail and the interpretation of the results is discussed, in particular regarding hepato-cellular function.

Acquired Hypoprothrombinemia. Lewis, J. H., Ferguson, J. H., Spaugh, E., Fresh, J. W., Zucker, M. B., Dept. Physiol. Univ. of North Carolina Med. School, Chapel Hill, N. C., USA, Blood *12:* 84 (1957).

Hypoprothrombinemia was encountered in 105 patients including cases of vitamin K deficiency, liver disease, newborns, Dicumarol-type drug therapy and a few miscellaneous disorders. The findings stress the association of acquired hypoprothrombinemia with deficiencies of proconvertin and PTC and suggest that these 3 proteins are formed in the liver and that vitamin K is essential to their production.

The Utilization of a Synthetic Substrate (TaMe) to Measure the Plasma Prothrombin in Coagulation Disorders. Glueck, I., May Inst. Med. Research, Jewish Hosp. Ass., Cincinnati, Ohio, USA, J. Lab. clin. Med. *49:* 41 (1957).

The author employs a synthetic substrate, p-Toluensulfonyl-l-arginine methyl ester (TAMe) to measure plasma prothrombin. It has been observed that the TAMe assay is almost unaffected by a deficiency of factor V, or VII. When gross deficiency of either factor are present, the addition of a fixed amount of the factor to the plasma will completely correct the deficiencies. The present study illustrates the close similarity of the TAMe and two-stage assays in response to dicumarol and vitamin K therapy, and residual serum prothrombin. Because of the reproducibility and simplicity of the method, the TAMe assay serves as a useful tool in the study of complex coagulation disorders.

The Effect of Psychological Stress Procedures on the Prothrombin Time of Rats. Mogenson, G. J., Jaques, L. B., Dept. Physiol., Univ. of Saskatchewan, Saskatoon, Sask., Canada, Blood *12:* 649 (1957).

The authors studied the effect of physiological stress on the prothrombin time of the albino rat. An increased prothrombin time occurred at certain times following forced jumping, sound-induced seizures, and electroshock. The changes in the prothrombin time following stress were more pronounced when dicumarol was administered. This was evident from two indices, prothrombin time and mortality.

Etude du "temps de thrombine" chez les hépatiques. Alagille, D., Soulier, J. P., Centre Nat. Transfusion Sanguine, Paris, France. Rev. inter. Hépatol. *7:* 1 (1957).

The authors studied the thrombin time in patients with liver disorders. Various theories explaining the prolongation of thrombin time are discussed, e.g. qualitative fibrinogen deficiency, presence of an inhibitor, deficiency of a co-thrombic factor of plasma or platelets, or unspecific physicochemical disorder. None of these theories is entirely satisfactory, and it

seems probable that in liver disorders several factors together are responsible for prolongation of thrombin time.

Prostatektomien unter Verwendung von Thrombin. Zizlavsky, M. U., Padang, Sumatra, Indonesia, Med. Klin. *52:* 462 (1957).

III. Der Einfluß des Thrombins auf die Fibrinbildung. Die Wirkung der Thrombozyten, des Thrombins und des Calciums auf das 2. und 3. Stadium der Blutgerinnung. Tsamboulas, N., Lazanas, G., Premetis, E., Med. Propädeut. Klinik, Univ., Athen, Greece, Dtsch. Arch. klin. Med. *204:* 89 (1957).

Ca-ions actively participate in the second stage of coagulation by forming thrombocalcin together with thrombin. Thrombocalcin then induces the transformation of fibrinogen into fibrin. Thrombocalcin accelerates the coagulation of fibrinogen, it has, however, no effect on the retraction of fibrin. The reaction of thrombin plus calcium regulates the normality of the 2nd and 3rd coagulation phase by primarily inducing the gel-forming of fibrinogen, than occurs the effect of thrombin on platelets resulting in retraction of the clot.

A Study of the Plasma Thrombin Time. Jim, R. T. S., Dept. int. Med., Washington Univ. Med. School, St. Louis, Mo., USA, J. Lab. clin. Med. *50:* 45 (1957).

Prolongation of the plasma thrombin time was found in a wide variety of diseases and in late pregnancy and the newborn. Further study revealed this increase to be a complex phenomenon due to a multiplicity of factors usually occurring in combination. The most constant abnormality appeared to be a deficiency of a plasma substance aiding the conversion of fibrinogen to fibrin. An increase in fibrinogen appeared to be a contributing factor. The deficient substance in plasma did not appear to be platelets or any of the known coagulation factors. The data presented suggest that it is albumin or a related substance. Clinically, prolongation of the plasma thrombin time did not appear to result in significant hemorrhagic manifestations.

Influence of Thrombin on Rate of Prothrombin Conversion. Therriault, D. G., Gray, J. L., Jensen, H., Biochem. Dept., US Army Med. Research Lab., Fort Knox Ky., USA, Proc. Soc. exp. Biol. (N. Y.) *95:* 207 (1957).

Both antihemophilic factor and Ac-globulin are necessary to obtain complete conversion of prothrombin in the presence of $BaSO_4$-eluate preparation from serum, phospholipoid-thromboplastin and $CaCl_2$. In the presence of traces of thrombin conversion of prothrombin becomes greatly accelerated. Results indicate that thrombin greatly accelerates formation of a prothrombin-conversion factor. This influence of thrombin appears to be mediated through its activating effect on plasma accelerator globulin and, perhaps, also on the antihemophilic factor.

d) Thromboplastin (Factor III)

La thromboplastino-formation. Larrieu, M. J., Centre Nat. Transfusion Sanguine, Paris, France. Rev. franç. Etudes clin. et biol. *2:* 595 (1957).

The various factors participating in active thromboplastin formation are considered: platelets, antihemophilic factors A and B, PTA, the fourth factor of Spaet, Kollers factor X, proaccelerin and proconvertin. Calcium and contact are essential. Little is known about physiological inhibitors of the first stage. The Biggs and Douglas test of thromboplastin formation has been studied in detail. The 3rd part deals with the mechanism of thromboplastin formation. Finally hemorrhagic syndromes resulting from a disturbance of the first stage have been studied.

Intermediate Reactions in the Coagulation of Blood with Tissue Thromboplastin. (Convertin, Accelerin, Prothrombinase). Hjort, P. R., Inst. f. Thrombosis Research, Rikshosp., Oslo, Norway, Scand. J. clin. Lab. Invest. *9:* suppl. 27 (1957).

In the body thrombin may be produced by 2 different but overlapping mechanisms, the intrinsic and the extrinsic mechanism. The present work is a systematic investigation of the

interactions among the 4 prothrombin conversion factors belonging to the extrinsic mechanism: thromboplastin, calcium, proconvertin and proaccelerin. The author comes to the following conclusions: Convertin is formed by a union of thromboplastin, calcium and proconvertin. Proaccelerin is activated by thrombin. The initial lag period in thrombin generation is eliminated by a preliminary formation of accelerin or by the addition of thrombin. A mixture of convertin and accelerin (= prothrombinase) converts prothrombin within a few seconds.

Effect of Ultrasonics on Thromboplastinase-Labile Component and Toxicity of Injected Thromboplastin. Feldman, D., Kirman, D., Med. Research Lab., Veterans Administration Hosp., East Orange, N. J., USA, Proc. Soc. exp. Biol. (N. Y.) *94:* 695 (1957).

The effects of ultrasonic treatment on human brain thromboplastic suspensions have been studied. Although causing a loss in clotting potency, ultrasonic treatment does not affect the toxicity of intravenous tissue thromboplastin nor does it destroy the thromboplastinase-labile component. The results are discussed and possible implications presented.

Comparison of Tissue and Plasma Thromboplastic Activities. Lewis, J. H., Didisheim, P., Dept. Med., Univ., Pittsburgh, Penn., USA, Proc. Soc. exp. Biol. (N. Y.) *94:* 686 (1957).

A lengthening of saline-recalcification time beyond normal occurred in plasma deficient in any one of the following: platelets, AHF, PTC, PTA, Hageman factor, proaccelerin or proconvertin. It also occurred in certain acquired multiple factor deficiencies, and in heparinized plasma. Brain thromboplastin recalcification times were normal in platelet, AHF-, PTC-, PTA- and Hageman-factor-deficiencies, but prolonged in proconvertin-or proaccelerin-deficiency or heparinized plasma. Plasma thromboplastin recalcification times were normal in these same deficiencies and, in addition in proconvertin-or proaccelerin-deficiency. This latter activity seemed due to incorporation of (pro)convertin and (pro)accelerin into the plasma thromboplastin complex, rather than to any free proconvertin or proaccelerin in solution. Formed plasma thromboplastin is inactive in absence of optimal calcium concentration.

Studies on the Thromboplastin Generation Test. III. The Effects of Dilution, Storage, and Concentration of Platelets. Miale, J. B., Garrett, V. R., Dept. Path., Univ. of Miami Med. School, Miami, Fla., USA, Amer. J. clin. Path. *27,* 701 (1957).

A dilute system, consisting of alumina plasma diluted 1 : 20 and serum diluted 1 : 40, results in reduced generation of thromboplastin after the reagents are stored for various periods of time at 4° C. The defect is apparent only when both of the stored reagents are used in the same incubation mixture. High concentrations of platelets are inhibitory to the generation of thromboplastic activity in a dilute system, but not in the standard test.

Recherches sur le mécanisme de la formation de la thromboplastine sanguine. Bounameaux, Y., Gerinnungslabor., Med. Univ.-Klinik, Zürich, Switzerland, Acta haemat. (Basel) *17:* 65 (1957).

The formation of blood thromboplastin does not depend on the desintegration of platelets. The initiation of clotting depends on plasmatic activities. Excess of platelet factor 3 or its equivalent inhibit thromboplastin generation. This phenomenon may explain the clinical picture of hemorrhagic thrombocythemia and provides a basis for the discussion of the mechanism of blood thromboplastin formation.

Über die Inaktivierung von Blutthrombokinase. (Zugleich ein Beitrag zur Unterscheidung von Blut- und Gewebsthrombokinase). Egli, H., Kesseler, K., Klesper, R., Physiol. Inst., Univ., Bonn, Germany, Acta haemat. (Basel) *17:* 338 (1957).

A method is described for the quantitative determination of blood thromboplastin inactivation. The inhibitory action of serum is increased after $BaSO_4$-adsorption and decreased after contact with glass. Heating up to 56° C. reduces the inactivation capacity and higher than 65° C. it is abolished. In the absence of calcium the extent of inactivation is reduced, however, still recognisable. Comparative studies of inactivation of blood- and tissue thromboplastin revealed an entirely different behaviour regarding both their reaction to $BaSO_4$ and to contact with glass.

A Modification of the "Thrombin Generation Test". Van der Pool, E. T., Kettenborg, H. K., De Vries, S. I., Lab. Blood Transfusion Serv., Wilhelmina Gasthuis, Amsterdam, Holland, Acta haemat. (Basel) *17:* 116 (1957).

Fibrinogen used in the thrombin generation test has been replaced by different substrates, and furthermore several plasma samples which were deficient in different coagulation factors were also examined. The best results were obtained with proaccelerin-free $BaSO_4$ plasma. The authors think that this modification not only simplifies the technic of the thrombin generation test, but also increases its reliability.

e) Calcium (Factor IV)

Die Wirkung der Thrombozyten, des Thrombins und des Kalziums auf das 2. und 3. Stadium der Blutgerinnung. II. Die Wirkung der Kalziumionen auf die Retraktion des Fibrins. Tsamboulas, N., Lazanas, G., Premetis, E., Med. Propädeut. Klinik, Athen, Greece, Dtsch. Arch. klin. Med. *204:* 89 (1957).

Thrombin by influencing platelets, enhances fibrin retraction. Ca-ions inhibit retraction. The mixture of thrombin and Ca has the same effect as pure $CaCl_2$. This is caused by the formation of inactive thrombocalcin which has no effect on fibrin retraction. The formation of thrombocalcin is quantitative and only after using up all Ca-ions can thrombin act on the still active platelets and thus promote retraction.

f) Factor V (and VI)

The Role of Factor V in the Formation of Blood Thromboplastin. Hougie, C., Dept. clin. Path., Univ. of Virginia, Charlottesville, Va., USA, J. Lab. clin. Med. *50:* 61 (1957).

Experimental evidence is presented indicating that factor V is not required in the formation of Product I (AHF + serum + calcium), thereby differing in this respect from PTC, Stuart factor, and AHF. Product I appears to react with the thromboplastin factor of platelets and this in turn reacts with factor V.

g) Factor VII

Über das Verhalten des Gerinnungsfaktors VII im Kreislauf der Katze. Lasch, H. G., Pfisterer, I., Schimpf, K., Med. Univ.-Klinik, Heidelberg, Germany, Acta haemat. (Basel) *17:* 280 (1957).

The various factors of the prothrombin complex were examined in sections of several vessels of the cat and comparisons were made. In 8 cats portal vein blood contained more factor VII than hepatic vein blood. Regarding prothrombin the position was reversed. These findings do not agree with the theory that the liver cells deliver factor VII produced by them into blood. In order to explain this phenomenon, the authors assume the hypothesis of the prothrombin cycle which was established by previous examinations of the mode and mechanism of prothrombin production.

Die angeborene familiäre Hypoprokonvertinämie. Serafini, M., Pericoli, F., Ist. Clinica Med. Generale e Terapia Med., Univ., Roma, Italy, Blut *3:* 135 (1957).

The authors discuss two cases of congenital hypoproconvertinemia and the blood coagulation studies carried out on other family members of the patients. A review of all cases published up to now is presented and the clinical and investigatory characteristics of the disease as well as the therapeutic possibilities are mentioned. Some hypotheses on the genesis of the disorder are pointed out.

Hypoproconvertinémie congénitale. (Avec discussion sur l'importance de la présence de proconvertine pour les résultats du dosage de la proaccélérine par la méthode en deux temps). Creveld, S. van, Veder, H. A., Blans, M. M., Clin. Pédiatrique, Univ., Amsterdam, Holland. Sang *28:* 23 (1957).

The authors studied 3 sisters showing signs of hemorrhagic diathesis from the first days of live. The eldest died of intraventricular hemorrhage at the age of 2 months. The youngest

died, 5-weeks-old, of cerebral hemorrhage. Extreme congenital hypoproconvertinemia was found to have been the cause of bleeding in the 2 girls. The parents and other family members show no hemorrhagic symptoms at all. The various therapeutic measures taken in the 2 girls had only mild temporary effect. In connection with these 2 cases the authors studied more closely the factor V determination by one and two-stage methods. It was found that the two-stage method, as a rule, yielded results too low if stored oxalated bovine plasma was used. The reason for this was found to be the too low proconvertin content of this reagent.

Hemorrhagic Diathesis Due to Factor VII Deficiency. Barnett, C. P., Pathol. Lab., Mary Washington Hosp., Fredericksburg, Va., USA, Arch. intern. Med. *99:* 280 (1957).

A patient with factor VII deficiency is reported. The patient had a life-long bleeding tendency. Proof of a familial disease was lacking, although suggestive in a decreased sibling. The one-stage prothrombin time was markedly prolonged, and bleeding and coagulation times moderately so. The defect was corrected by factor V-deficient plasma, fresh plasma and stored serum. Adsorbed and bishydroxycoumarin plasmas were without effect. Plasma prothrombin level was normal. Factor VII was all but absent in the plasma and stored serum. An unsusual feature was the very low prothrombin consumption. Serum prothrombin levels remained high for weeks. Vitamin K therapy was without effect.

h) Factor VIII (Antihemophilic Globulin)

A Concentrate of Human Antihemophilic Factor. Kerwick, R. A., Wolf, P., Dept. Chem. Biophysics, Univ., London, England, Lancet *272:* 647 (1957).

A preliminary clinical trial in 6 cases of hemophilia indicates that the intravenous injection of a concentrate of human AHF arrests internal and external bleeding, and permits surgical intervention. The concentrate of human AHF which contains not less than 85% of the initial activity, is separated aseptically from fresh citrated normal human plasma. Solutions of the concentrate may be dried from the frozen state without significant loss in activity, and the activity of the freeze-dried material is retained for several months. The dangers of circulatory overloading during treatment are largely avoided with this preparation since 100 ml is equivalent in antihemophilic activity to 1000 ml of fresh normal citrate plasma.

A Study of the Separation of Fibrinogen and Antihemophilic Factor (AHF) in Canine, Porcine, and Human Plasmas. Wagner, R. H., Richardson, B. A., Brinkhous, K. M., Dept. Path., Univ. N. Carolina, Chapel Hill, N. C., USA, Thromb. Diath. haem. *1:* 1 (1957).

Studies are reported on attempts to separate AHF from fibrinogen in plasma by selective adsorption with Fuller's earth, aluminium hydroxide gel, and Seitz filtration. Fuller's earth adsorption of canine plasma resulted in almost complete removal of fibrinogen without loss of AHF. $Al(OH)_3$ adsorption of fibrinogen from bovine, canine, and human plasma is greater than the adsorption of AHF. Seitz filtration of plasma causes loss of AHF with little or no loss of fibrinogen.

The Thromboplastinogen Activity Time (TAT) Test. Quick, A., Dept. Biochem., Marquette Univ. Med. School, Milwaukee, Wisc., USA, Thromb. Diath. haem. *1:* 9 (1957).

Thromboplastinogen = Factor VIII and IX. The thromboplastinogen activity time (TAT) test is described. The method is based on the finding that rabbit brain extract heated to 60° C loses its thromboplastin activity but retains the properties of platelet extract and can, therefore, be used as a substitute for platelet extract in the prothrombin consumption test. The application of the test to differentiate hemophilia from thrombocytopenia and thrombasthenia is illustrated by case reports. The use of the test for the differential diagnosis of hemophilia and PTC deficiency is outlined and examples of this application are given.

Dosage du facteur VIII en un temps. Bounameaux, Y., Lab. Etude de la Coagulation Sanguine, Clin. méd., Univ., Zürich, Switzerland, Acta haemat. (Basel) *17:* 355 (1957).

A one-stage method for the determination of factor VIII is described. It is quantitative and specific. The method has the advantage that no hemophilic plasma is necessary.

A Mildly Affected Female Hemophiliac. Taylor, K., Biggs, R., Nuffield Dept. Med., Radcliffe Infirmary, Oxford, England, Brit. med. J. no. 5034, 1494 (1957).

A female patient, apparently suffering from mild hemophilia (AHG 18 bis 25%), was admitted to hospital with severe postoperative bleeding. Her progress and treatment in hospital are described. A study of her near relatives was made.

Spontaneous Hemothorax in Hemophilia: Case Report and Discussion of the Hemophilia Syndromes with Remarks on the Management of Hemothorax. Kay, W. R., Kupfer, H. G., Dept. Med. and clin. Path., Med. Coll. Virginia Hosp., Richmond, Va., USA, Ann. intern. Med. *47:* 152 (1957).

A case of hemophilia with the rare manifestation of massive spontaneous hemothorax is presented. The clinical features and the special laboratory studies indicated that this patient was deficient in AHG (VIII), rather than PTC (IX) or PTA. Deficiency of any of these factors may produce the clinical picture of hemophilia. The importance of identifying the specific clotting deficiency, the methods of doing so, and the treatment of the specific deficiency are discussed. The hemothorax responded satisfactorily to repeated aspiration and intrapleural injection of streptokinase and streptodornase.

Clotting of Hemophilic Blood with Purified Platelet Cofactor I, Platelet Factor 3 and Threone. Seegers, W. H., Landaburu, R. H., Holburn, R. R., Tocantins, L. M., Dept. Physiol. Pharm., Wayne Univ. Med. Coll., Detroit, Mich., USA, Proc. Soc. exp. Biol. (N. Y.) *95:* 583 (1957).

Purified platelet cofactor I, platelet factor 3 or the two together reduce the clotting time of hemophilic blood or recalcified plasma; but, not to the degree observed with normal blood or plasma. In the concentrations used platelet factor 3 was more effective than platelet cofactor I.

Assay of Antihemophilic Globulin in Treatment of Hemophilic Patients. Biggs, R., Dept. Path., Radcliffe Infirmary, Oxford, England, Lancet *273:* 311 (1957).

The author proposes a method for the assay of antihemophilic globulin which may easily be adapted in laboratories not especially devoted to work on coagulation. Although the method described is not precise, it has proved of great value in the control of therapy of hemophilic patients. If surgery has been undertaken with AHG level over 30%, bleeding has been controlled. If for any reason the level has failed to rise above 10—15%, subsequent bleeding has been predicted with irritating reliability.

The Toxicity and Fate of Injected Animal Antihemophilic Globulin. Sharp, A. A., Bidwell, E., Radcliffe Infirmary, Oxford, England, Lancet *273:* 359 (1957).

The fate of heterologous animal proteins containing antihemophilic globulin was determined by use of specific fluorescein-aconjugated antisera. Evidence has been obtained to suggest that these proteins are concentrated in the wound fibrin of the recipient. Their toxicity appears to be negligible except when given in very large doses. They are antigenic and may be expected to provoke varying allergic responses in a sensitized recipient.

Therapie schwerer Hämophilie-A-Blutungen mit frisch hergestellter Plasmafraktion I. Hörder, M. H., Med. Univ.-Klinik, Freiburg/Br., Germany, Klin. Wschr. *35:* 775 (1957).

The author reports results obtained with the administration of fresh plasma fraction I in cases of severe bleeding in hemophilia A. The administration of 1.5 to 2.5 g of the freshly prepared fracti on regularly resulted in a rise of AHG level of over 40%, with simultaneous normalization of coagulation time and prothrombin consumption. The hemostatic effect was satisfactory and no side-effects were noted. The only disadvantage is the large amount of blood (1600 ml) needed for the preparation of 2 g of fraction I. This difficulty however should not limit the use of fraction I as substitution therapy as long as no more active and more purified preparations of AHG are available.

i) Factor IX (Christmas Factor, PTC)

Christmas Disease in a Woman. Hardisty, R. M., Dept. clin. Path., Welsh. Nat. School of Med., Cardiff, England, Brit. med. J. no. 5026, 1039 (1957).

The case of a young woman with Christmas disease is reported, in which the presenting symptom was prolonged hemorrhage following tooth extraction. Her serum contained approximately 8% Christmas factor. The family history suggested that the patient's father and his uncle suffered from Christmas disease of a similar degree of severity. The genetic implication of these observations is that the gene for Christmas disease may be intermediate rather than completely recessive.

Christmas Factor Activity of Cord Blood. Barkhan, P., Dept. Med. Univ., Cambridge, England, Brit. J. Haemat. *3:* 215 (1957).

Cord blood from 27 newborns was examined for Christmas factor activity in a thromboplastin generation system. Normal sera gave an activity of 95 to 130%, cord sera 19 to 91%. The possible relationship of prothrombin, factor VII, Christmas factor and vitamin K is discussed.

Haemophilia B and its Treatment. Heni, F., Krauss, I., German med. Monthly *2:* 55 (1957).

3 patients with hemophilia B were studied, 2 were men, 41 and 30 years old and one was a 12-month-old boy. The treatment of severe hemorrhage in these patients consists of intravenous infusion of serum which is more effective than either fresh or stored whole blood. It was found that in hemophilia B, as in hemophilia A, antibodies against plasma thromboplastin may develop..

The Effect of Coumarin Drugs upon Plasma Thromboplastin Component. McElfresh, A. E., Oezge, A., St. Christopher's Hosp. for Children, Philadelphia, Pa., USA, J. Lab. clin. Med. *49:* 753 (1957).

Tromexan and dicumarol reduced the PTC content of normal plasmas as evidenced by their failure to correct the prolonged clotting time, the low prothrombin consumption, and the deficient generation of thromboplastin in the blood of a patient deficient in PTC. This reduction was evident within 24 to 48 hours and did not require prolonged administration.

k) Other Factors

Coagulation Defect in Horse Plasma. Sjolin, K. E., Biol. Inst., Carlsberg Foundation, Copenhagen, Denmark, Proc. Soc. exp. Biol. (N.Y.) *94:* 818 (1957).

The delayed thrombin generation of horse plasma indicates that the clotting defect of the horse plasma investigated is caused by lack of a factor similar to the Hageman factor. Blood platelets after washing or freezing, apparently substitute for the effect of the lacking plasma factor. The coagulation defects in horse plasma apparently reflect various types of hemophiloid deficiencies.

Über einen neuartigen kongenitalen Gerinnungsdefekt (Mangel an Stuart-Faktor). Bachmann, F., Duckert, F., Flückiger, P., Hitzig, W., Koller, F., Gerinnungsphysiol. Lab., Med. Univ.-Klinik, Zürich, Switzerland, Thromb. Diath. haem. *1:* 87 (1957).

In a newborn with a severe hemorrhagic diathesis the following coagulation defect has been found: Quick's prothrombin time increased, coagulation time with addition of Russel's viper venom prolonged, pathologic prothrombin consumption, factor VII 1% to 3%, factor IX 30%, thromboplastin generation using the patients serum highly pathologic. Normalization by addition of hemophilia B serum and serum of patients under beginning marcoumar therapy. Plasma and serum of the patient Stuart (Graham) and of this patient showed identical behaviour in all tests.

Stuart Clotting Defect. I. Segregation of an Hereditary Hemorrhagic State from the Heterogenous Group Heretofore Called "Stable Factor" (SPCA, Proconvertin, Factor VII) Deficiency. Hougie, C., Barrow, E. M., Graham, J. B., Dept. Path., Univ. N. Carolina, Chapel Hill, N. C., USA, J. clin. Invest. *36:* 485 (1957).

A patient was restudied who had been diagnosed previously as hypoproconvertinemia. The deficient factor was shown, not to be SPCA by cross-matching and is named Stuart factor. Stuart factor has been found to be essential for the formation of blood thromboplastin. It is required for optimal activity of tissue thromboplastin, cephalin and "Stypven". The characteristics of Stuart factor are discussed. The hemorrhagic state(s) previously classified as congenital factor VII deficiency (hypoproconvertinemia, SPCA-deficiency) are probably not identical diseases. There are at least 2 separable conditions included in this group.

Stuart Clotting Defect. II. Genetic Aspects of a "New" Hemorrhagic State. Graham, J. B., Barrow, E. M., Hougie, C., J. clin. Invest. *36:* 497 (1957).

Stuart factor deficiency has been studied in a large North Carolina kindred and shown to be inherited as a highly penetrant but incompletely recessive autosomal characteristic. The heterozygotes have been found to be only mildly affected and have a reduction in the level of this factor in the range of 20 to 52%. It is pointed out that carrier detection may be possible in many instances with fairly simple tests. It is emphasized that heterozygotes for the various hemorrhagic states, especially females, may be encountered as patients with abnormal operative bleeding, persistent gastrointestinal bleeding or menorrhagia with persistent anemia. Such symptoms, in the absence of clean-cut laboratory evidence, however, should not be assumed to represent heterozygotes.

A Case of Serious Clotting Defect, without Hemorrhagic Diathesis, Caused by PTA-Deficiency. Vreeken, D., Hoorweg, P. G., Centraal Lab., Bloedtransfusiedienst, Nederlansche Roode Kruis, Amsterdam, Holland, Nederl. T. Geneesk. *101:* 582 (1957).

A woman with a coagulation defect caused by PTA deficiency is described. This coagulation disorder was found by coincidence and did not cause a hemorrhagic diathesis. A nephew of the patient who suffered from hematuria, also appeared to have PTA deficiency. Some properties of PTA are discussed.

Déficit en Facteur Hageman. Larrieu, M. J., Soulier, J. P., Culot, Y., Centre National de Transfusion Sanguine, Paris XV^{e}, France, Sang *28:* 152 (1957).

The authors report the case of a 50-year-old woman with a latent hemostatic disorder caused by deficiency of the Hageman factor. Characteristics: No hemorrhagic manifestations, prolonged coagulation time, pathologic prothrombin consumption and disturbed thromboplastin formation. A small quantity of injected plasma normalized all tests of hemostasis. The relation between the Hageman factor and PTA needs further investigation.

l) Hemophilia, General Aspects

The Antihemophilic and Christmas Factor Activities of Ethanol Fractions of Brain Extract. Nour-Eldin, F., Wilkinson, F. J., Dept. Hematol., Royal Infirmary, Univ. Manchester, England, Nature (Lond.) *179:* 532 (1957).

Verschiedene Formen der Hämophilie (Übersicht). Deutsch, E., I. Med. Univ.-Klinik, Wien, Austria, Thromb. Diath. haem. *1:* 93 (1957).

The clinical picture of hemophilia may be caused by the deficiency of different factors involved in the formation of plasma thromboplastin (hypoprothromboplastinogenemias). The designation hemophilia A or B may only be applied to those sex-linked inherited hemorrhagic diseases which are exclusively caused by factor VIII and/or IX deficiency. A deficiency of factor VIII in patients with factor V deficiency is called concomitant hemophilia. A deficiency of factor VIII combined with a prolonged bleeding time is designated as vascular hemophilia.

The combined deficiency of factor VII and IX and their relation to the deficiency of Stuart factor are discussed. A comparison is done of the physical and chemical characteristics of the prothromboplastic factors and the possibilites of differential diagnosis are tabulated. With the knowledge on the properties of the clotting factors a more differentiated and more efficient treatment becomes possible.

Sur la valeur diagnostique du test de génération de la thromboplastine (TGT) dans l'hémophilie. Observations cliniques. Bianco, S., Crolle, G., Inst. Pathol. méd., Univ., Turin, Italy, Presse méd. *65:* 1076 (1957).

The authors examined the behaviour of thromboplastin generation in 9 hemophiliacs. In 8 cases they thus discovered a factor VIII deficiency and only in one case a deficiency of Christmas factor. In 4 cases coagulation time and prothrombin consumption were both normal and only the thromboplastin generation test revealed a hemophilic alteration corresponding to the clinical picture. As this thromboplastin generation test, according to the authors, yields pathologic results also in congenital or acquired factor V or VII deficiency, the measurement of prothrombin activity (Quick) is necessary for differentiation.

Deficient Thromboplastin Formation in Man. Vertraete, M., Vandenbroucke, J., Physiopath. Lab., Dept. Med., Univ., Louvain, Belgium, Amer. J. Med. *22:* 624 (1957).
Intensive study of hemophilia and related disorders in many clinics is rounding out the clinical picture of deficiencies of AHG, PTC, and PTA, and is piecing together the complex mechanism involed. The authors describe their experience in this connection, including combined defects and association with circulating anticoagulants. They are particularly interested in the concept that AHG, PTC and calcium react in the earlier stages of thromboplastin formation to form an intermediate compound, and present some evidence in support of this view.

Electrophoretic Studies on the Serum Proteins in Hemophilia and Christmas Disease. Wilkinson, J. F., Turner, R. L., Bottomley, A. C., Dept. Hematol., Univ. and Royal Infirmary, Manchester, England, Acta med. scand. *156:* 457 (1957).

Serum electrophoretic studies were carried out in 46 cases of hemophilia and 9 cases of Christmas disease. No evidence of the Bernfeld/Stefanini anomaly was discovered. The hemophilic sera showed an increase in the gamma-globulin fraction which was significantly correlated with the clinical severity but not with the degree of the clotting defect. No evidence of liver dysfunction was found in the patients showing a gamma-hyperglobulinemia. The significance of the protein changes is briefly discussed.

Hemophilioid Factors: Acquired Deficiencies in Several Hemorrhagic States. Naeye, R. L., Dept. Path., Coll. of Physicians and Surg., Columbia Univ., New York City, N. Y., USA, Proc. Soc. exp. Biol. (N. Y.) *94:* 623 (1957).

Deficiencies of hemophilioid factors are not necessarily genetic in origin. Serum activities of PTA and PTC were depressed in 20 patients with a variety of hepatocellular disorders. They were also reduced in several patients who developed vit. K deficiency subsequent to inability to adsorb fats. PTC and PTA were depressed in a number of patients following administration of coumarin compounds and rapidly increased towards normal following administration of vitamin K analogue. Significant deficiency of AHF was not found in any of the above conditions.

On the Epidemiology of Hemophilia and Christmas Disease. Ratnoff, O. D., Margolius, A., Dept. Med., Western Reserve Univ. Med. School, Cleveland, O., USA, N. Engl. J. Med. *256:* 845 (1957).

Among 43 families of bleeders studied, 34 had hemophilia, and 9 Christmas disease. Analysis of the origin of these families indicates that 29 of the families with hemophilia but only 2 of the families with Christmas disease live in Metropolitan Cleveland. No adequate explanation for the geographic distribution of the 2 disorders has been found. One likely

possibility is that Christmas disease is much rarer than has heretofore been thought, and that subtle differences in the symptomatology of the diseases led patients with Christmas disease to these laboratories from the aerea outside Cleveland.

m) Combined Deficiencies

Sindrome emorragica plasmoangiopatica acquisita. Salamone, L., Ist. Med. del Lavoro, Univ., Palermo, Italy, Haematologica Arch. *42:* 129 (1957).

The author describes the case of a patient with an acquired hemorrhagic syndrome primary and sporadic, with the following characteristics: Hypofibrinogenemia of varying degree, sometimes leading to afibrinogenemia. Unstable anticoagulant activity of the antithromboplastin type, closely related to variations of alpha-2-globulin. Deficiency of PTC, slight hypoprothrombinemia, and marked vascular fragility. Clinical symptoms were most significantly aggravated with increasing hypofibrinogenemia. Therapy with blood and plasma transfusions, ACTH, cortisone, vitamin K, and with vasoprotective agents was unsuccessful. The patient died within 9 months. Concerning the pathogenesis of this disorder the author stresses the post mortem finding of an apparently essential alteration of the hystiocytes as revealed by bone marrow examination and by probably secondary impairment of the liver function.

Zur Problematik der Thrombopathia Willebrand-Jürgens der Pseudohämophilie bzw. weiblichen Hämophilie. Epikrise einer fast 20jährigen Beobachtung. Koch, F., Schultze, H. E., Schwick, G., Klees, E., Kuntze, E., Kinderklinik, Justus-Liebig-Hochschule, Gießen, Germany, Z. Kinderheilk. *79:* 449 (1957).

n) Platelets

The Effect of Oxalate and Citrate on the Platelet Count of Whole Blood and Plasma. Barkhan, P., Dept. Med., Univ., Cambridge, England, J. clin. Path. *10:* 26 (1957).

Platelet Antibiodies in Hodgkin's Disease. Elgvin, T., Med. Dept., Nordland County Hosp., Bodø, Norway, Acta med. scand. *158:* 35 (1957).

Case report.

Enzymveränderungen der Blutplättchen bei den hypoprothrombinämischen Morgagni-Laennecschen Leberzirrhosen. Pedrazzini, A., Salvidio, E., Med. Abtg., Kantonspital, Winterthur, Switzerland, Acta haemat. (Basel) *18:* 42 (1957).

In 25 cases of hypoprothrombinemic cirrhosis of the liver marked alterations of phosphatase activity of the platelets were demonstrated by micro-enzymologic methods. Such changes are the expression of functional platelet damage connected with diffuse liver damage and hypoprothrombinemia, and are possibly enhanced by the high estrogen level in cirrhotic patients. In 3 cases of obstructive jaundice, on the other hand, no marked changes were seen in the platelets in spite of hypoprothrombinemia.

Der Einfluß körperlicher Arbeit auf die Zahl der Thrombozyten und auf deren Haftneigung. Wachholder, K., Parchwitz, E., Egli, H., Kesseler, K., Physiol. Inst., Univ., Bonn, Germany, Acta haemat. (Basel) *18:* 59 (1957).

Strenuous physical exercise leads to an increase in platelet number and in their adhesiveness, and in a decrease of *r* (reaction time) as measured by thrombelastography. No alterations occur, on the other hand, when the person is fasting and resting throughout the whole morning. After an excercise easily managable by the person doing it, the observed changes rapidly return to normal. If the exercise, however, is excessive and followed by delayed normalization of the pulse rate, the alterations reach their maximum 20—30 mins. after the end of exercise and may return in waves for several hours. Acute nervous stress also induces increase of platelets. The origin of these alterations is discussed regarding stimulation of the sympathetic nervous system and production of adrenaline and noradrenaline, and their possible consequences are pointed out.

The Effect of Stored Blood Transfusions on the Platelet Levels in Patients Undergoing Surgical Procedures. Mustard, J. F., Dept. Med., Univ., Cambridge, England, Acta haemat. (Basel) *18:* 80 (1957).

About half of 62 patients receiving whole blood transfusions demonstrated a decrease in platelet level. This did not appear to be entirely due to the diluting effect of transfused blood. The patients with a platelet decrease were transfused with blood in which the thromboplastin factors had undergone changes similar to those occurring during coagulation. Transfusion of serum which contains similarly altered plasma factors consistently produced platelet decrease in the recipient. This suggests that when stored blood undergoes changes in the thromboplastin factors, a thrombocytopenic activity develops which causes platelet decrease in the recipient.

Acido jaluronico ed jaluronidasi nelle piastrine. Tropeano, L., Cacciola, E., Motta, L., Ist. Patol., Spec. Med., Univ., Catania, Italy, Haematologica *42:* 807 (1957).

The authors studied the hyaluronic acid — hyaluronidase system in intact and lysed platelets by turbidity determinations. The results seems to confirm that both hyaluronidase and hyaluronic acid exist in platelets.

Beiträge zu dem Mechanismus des Thrombozytenfalles bei allergischen Prozessen. Kovács, E., Pastinszky, S., Laboratorium, Károlyi Krankenhaus, Budapest, Hungary, Int. Arch. Allergy *10:* 233 (1957).

Alcuni aspetti di semeiologia funzionale delle trombopenie: la componente piastrinopatica delle trombopatie piastrinopeniche. Del Bono, N., Pasero, G., Ist. Clin. med. Generale, Univ., Pisa, Italy, G. Clin. med. *38:* 1 (1957).

Über einen besonderen Fall von Obstallergie unter dem Bild einer Thrombopenischen Purpura. Sonneck, H. J., Städt. Hautklinik, Karl-Marx-Stadt, Germany, Dtsch. Gesundhwes. *12:* 196 (1957).

A case of thrombocytopenic purpura caused by fruit allergy is reported.

Examen critique des méthodes immunologiques employées pour l'étude des purpuras thrombopéniques. Dausset, J., Malinvaud, G., Centre Nat. Transfusion Sang., Paris, France, Sang *28:* 1 (1957).

Trombopathie. Creveld, S. van, Kinderkliniek, Univ., Amsterdam, Holland, Maandschr. Kindergeneesk. *25:* 112 (1957).

Etudes immunochimiques sur la présence de fibrinogène dans des extraits de plaquettes humaines lavées et dans certains extraits leukocytaires. Seligmann, M., Goudemand, B., Janin, A., Bernard, J., Grabar, P., Serv. Chimie Microbienne, Inst. Pasteur, Paris, France, Rev. Hémat. *12:* 302 (1957).

By immunochemical methods it was demonstrated that human platelet extracts after frequent washing, and certain leukocyte extracts contain a substance with the antigenic specifity of fibrinogen and also with its characteristic properties. The significance of these findings is discussed and it is concluded that fibrinogen is intimately connected with the platelets and that it is most probably fixed on the platelet surface. Possible consequences regarding immunohematology, properties of platelets in vitro, and hemostasis are discussed.

Über die Gerinnungsaktivität und intravenöse Anwendung lyophil getrockneter Thrombozyten. Gross, R., Schwick, G., Med. Univ.-Klinik, Marburg/L., Germany, Klin. Wschr. *35:* 814 (1957).

5 healthy individuals, 21 thrombocytopenic patients, and 2 patients with dysthrombocytosis were given a total of 32 intravenous infusions of lyophilized thrombocytes suspended in isotonic salt or sugar solutions. These solutions contained factor 3 and 4 as well as platelet antifibrinolysin in unaltered quantities even after storage of several months. Platelet factor 1 and 2, and serotonin content were reduced to 40—90% of normal values. These platelet solutions had remarkably little influence on blood coagulation in vivo, whereas they produced normali-

zation of disturbed thromboplastin formation caused by platelets in vitro. No side-effects were noted after platelet infusions. Hemostasis was obtained in about half the cases of thrombocytopenic hemorrhage. Further experience with gaining, dosage and eventual ad-mixture of plasma factors, will most probably lead to more effective results.

Zur Nachweismethodik von antithrombozytären Substanzen im Plasma von Thrombopenie-Patienten. Wuilleret, B., Meyer, W., Blutspendezentrum d. Schweiz. Roten Kreuzes, Lausanne, Switzerland, Blut *3:* 192 (1957).

Out of 68 blood samples of thrombocytopenic patients, 17 were found to contain antithrombocytic substances. A "retraction-inhibitory-test" was used for this study. The substances were most frequently found in cases of essential thrombocytopenia and acquired hemolytic anemia. No inhibitor of plasma thromboplastin could be demonstrated in these cases.

Les thrombocythémies essentielles. Goudemand, M., Hutin, A., Lille, France, Sem. Hôp., Paris, *33:* 21 (1957).

Revêtement des plaquettes humaines et des globules rouges par les dextranes. Ponder, E., Nassau Hosp., Mineola, N. Y., USA, Rev. Hémat. *12:* 11 (1957).

Sur le mécanisme de la rétraction du caillot et de la métamorphose visqueuse des plaquettes. Bounameaux, Y., Gerinnungsphysiol. Lab., Med. Klinik, Univ., Zürich, Switzerland, Rev. Hémat. *12:* 16 (1957).

Platelets, fibrinogen and thrombin, glucose and assisting factors are necessary for clot retraction. These assisting factors can either be phosphate, phosphoric esters of glucose or fructose, glycerophosphate, or some others. Calcium also is necessary but available in sufficient amounts on human platelet surface. Viscous metamorphosis of platelets is induced in the presence of calcium and thrombin by the assisting factors mentioned. Various substances inhibiting clot retraction and viscous metamorphosis are discussed. Based on his results the author confirms that clot retraction results from viscous metamorphosis of platelets. The two phenomena are, however, not identical. Pathologic clot retraction can result only from insufficient thrombin formation or from specific platelet insufficiency. Deficiency of glucose or assisting factors is impossible in human beings.

Changes in the Platelet Levels of Non-transfused Patients Following Surgical Operations. Mustard, J. F., Sunnybrook Hosp., Toronto, Canada, Acta haemat. (Basel) *17:* 257 (1957).

There is an elevation of about 10% in the circulating platelet level of non-transfused patients immediately following mayor surgical operations. During the first 3 postoperative days the platelet level in most of these patients remains above the pre-operative level.

Über die Bedeutung der serologischen Reaktionen bei allergisch-medikamentös bedingten Thrombopenien, dargestellt an einem Fall von Chinidinpurpura. Spielmann, W., Gathof, A., Fritzche, W., Pfeiffer, E. F., I. Med. Univ.-Klinik, Frankfurt/M., Germany, Acta haemat. (Basel) *17:* 287 (1957).

In a case of quinidine purpura the following serological tests were repeatedly carried out: agglutination with and without the addition of allergen, direct and indirect Coombs test, anti-human-globulin fixation tests, hemagglutination tests and analytical tests of the clotting mechanism. The results of the serological examinations in the course of exposure to quinidine are graphically tabulated and the various methods used are critically evaluated.

The Detection of the Sensitizing Substance in Cases with Acute Thrombopenic Purpura by New "in vitro" Methods. Hoigné, R., Flückiger, P., Schmuziger, P., Mumenthaler, M., Dept. Int. Med., Univ., Zurich, Switzerland, Acta haemat. (Basel) *17:* 24 (1957).

A new serologic reaction for the detection of the sensitizing substance has been applied in 9 patients with acute or subacute thrombocytopenia. The method is shortly described. All but

one patient recovered within a few days to two months when exposure to the substance with the specific "in vitro" reaction was discontinued.

Dosaggio del fattore vasostrittore piastrinico (5-OH-triptamina) nel sangue conservato. Bracco, M., Ist. Patol. med., Univ., Genova, Italy, Minerva med. (Torino) *48:* 204 (1957).

Les thrombocytémies. Bousser, J., Benhamou, J.-P., Christol, D., Mas, M., Hôtel-Dieu, Paris, France, Presse méd. *65:* 347 (1957).

The principal aspects of thrombocythemia are rewieved with reference to 3 observations. Essential thrombocythemia occurs most frequently in patients over 50 years of age. It is characterized by hemorrhages, splenomegalia and vascular thrombosis. Platelet numbers vary between 1 and 3 millions, hyperleukocytosis is frequent, polyglobulia was noted in 20% of the cases. Hyperplasia of megakaryocytes is found. The treatment of choice consists in radioactive phosphorus (P 32). Prognosis is favorable, recidivation possible.

Le test d'activité plaquettaire du sérum. Alagille, D., Soulier, J.-P., Centre Nat. Transfusion Sanguine, Paris, France, Rev. franç Etudes clin. et biol. *2:* 231 (1957).

Normal serum contains a platelet-like property stimulating thrombin formation in a plasma that is platelet-free or has a low thrombin content (O'Brien). The authors have measured the kinetics of prothrombin consumption of a mixture of normal platelet-free plasma and different normal or pathologic sera. This has suggested a new test for measuring platelet activity of serum (APS). The details of this test are given and the results obtained in 204 patients with hemorrhagic disorders are presented. The test is both sensitive and narrowly specific for platelet abnormalities. The nature of platelet factor and its relation to platelet prothromboplastin are discussed. The APS test measures the residual prothromboplastic activity in serum, always abnormal, when this factor is absent in platelets.

The Influence of Blood Collecting Techniques on Platelet Numbers During Blood Storage. Mustard, J. F., Walker, C. B. V., Dept. Med. Univ., Cambridge, England, Brit. J. Haemat. *3:* 50 (1957).

The preservation of platelets during the storage of whole blood collected into acid-citrate-dextrose anticoagulant (ACD) is related to the number of platelets lost during collection. Platelet preservation during storage is improved if platelet loss during collection is minimized. The type of surface used in the blood taking set is an important factor. Silicone-coated and plastic surfaces minimize platelet loss during collection. The increased blood-air interface caused by the blood frothing when collected into vacuum bottles does not produce a greater platelet loss than in blood collected by gravity.

Dosage des facteurs de coagulation contenus dans l'atmosphère plasmatique des plaquettes humaines. Bounameaux, Y., Gerinnungsphysiol. Labor., Med. Univ.-Klinik, Zürich, Switzerland, Rev. franç. Etudes clin. et biol. *2:* 52 (1957).

Human platelets contain adsorbed unto their surface, several coagulation factors which play a part in maintaining around platelets the "plasmatic" atmosphere", as described by Roskam. Evidence is given for the presence of prothrombin and factors V, VII, VIII, IX, and X in this atmosphere. No antithrombin was found. These factors disappear progressively with repeated washing of platelets. The importance of this "plasmatic atmosphere" is discussed. Platelets washed by the usual methods cannot be considered completely free of plasma.

Durée de vie des plaquettes. Maupin, B., Centre de Transfusion et Réanimation de l'Armée, Clamart, France, Rev. franç. Etudes clin. et biol. *2:* 72 (1957).

The life-span of platelets has been studied. The different methods of studying circulating platelets are described and the results compared critically. The most accurate methods are those with in vivo labelling, unfortunately of limited application, and by in vitro labelling with radio-active chromium. Both in man and other mammals studied the platelet survival time is about 5 days, with a theoretical maximum of 8 to 9 days. Factors affecting survival of transfused platelets are reviewed as well as the fate of insufficient platelets.

Studien zur Thrombozytenbildung an Megakaryozyten in menschlichen Knochenmarkkulturen. Albrecht, M., II. Med. Klinik, Städt. Krankenhaus Moabit, Berlin, Germany, Acta haemat. (Basel) *17:* 160 (1957).

Megakaryocytes from human bone marrow samples in living tissue cultures were studied cinematographically. The investigation indicated several possibilities of platelet formation. Megakaryocytes showed lively amoeboid movements of their cytoplasm. In some cases the whole megakaryocytes dissolved into platelets, in others individual platelets were given off. Platelets originating in cultures are often forming chains, possibly because the culture medium has a high content of substances enhancing coagulation.

A Technical Improvement of Direct Platelet Counting by Phase Contrast Microscopy: A Special "Thin Bottom" Counting Chamber. Marmot, A. M., Giacca, S., Med. Clin. Univ. Genova, Italy, Acta haemat. (Basel) *17:* 169 (1957).

After briefly exposing the advantages and optical requirements of platelet enumeration by phase contrast microscopy, the authors present a specially designed counting chamber with a thin, flat bottom allowing an optical phase contrast effect. Counts were performed according to the Feissly-Lüdin cocaine technic and to the Brecher-Cronkite ammonium oxalate method. Excellent results were obtained by both methods; but the former proved more satisfactory in thrombocytopenic states, as it gives higher concentrations of enumerable platelets.

La dystrophie thrombocytaire hémorragipare congénitale. Bernard, J., Caen, J., Maroteau, P., Hôp. Hérold, Paris, France, Rev. Hémat. *12:* 222 (1957).

Hemorrhagic thrombocytic dystrophy is characterized as follows: It is a congenital thrombopathy with recessive heredity. Size and shape of platelets are abnormal. Disturbance of thromboplastic function of platelets. Agglutination, adhesiveness, clot retraction are normal. Serotonin markedly descreased. The platelet function is corrected by the addition of platelets from a case of Willebrand's disease. The findings are in favor of the existence of more than one prothromboplastic platelet factor, one deficient in platelet dysthrophy, the other in Willebrand's disease.

Le porpore trombocitopeniche idiopatiche, da anticorpi antipiastrinici. Grasso, E., Ist. Clinica pediatr., Univ., Bari, Italy, Minerva pediat. (Torino) *9:* 87 (1957).

Die Wirkung der Thrombozyten des Thrombins und des Calciums auf das 2. und 3. Stadium der Blutgerinnung. I. Die Rolle des Thrombins und der Blutplättchen in der Retraktion des Blutkuchens. Tsamboulas, N., Lazanas, G., Med. Propadeut. Klinik, Univ. Athen, Greece, Dtsch. Arch. klin. Med. *204:* 81 (1957).

The retraction of fibrin following addition of thrombin to oxalated plasma has been studied. Conclusions: The capacity of blood platelets to retract fibrin in oxalated plasma remains active for a period less than 48 hours. To obtain fibrin retraction after coagulation active platelets are imperative. It is assumed that during the period previous to coagulation a net is formed by platelets which together with the other formed blood elements is contained in the gel of fibrinogen. The retraction of the clot means a "dying" of the platelets. Thrombin alone cannot induce retraction of clotted fibrinogen.

Thrombopenie nach Reserpintherapie. Schmidt, K., III. Med. Abtg., Wilhelminenspital, Wien XVI, Austria, Wien. klin. Wschr. *69:* 27 (1957).

Glycolytic Intermediates of Human Platelets: Their Separation and Identification. Campbell, E. W., Small, W. J., LoPilato, E., Dameshek, W., New England Center Hosp., Boston, Mass., USA, Proc. Soc. exp. Biol. (N. Y.) *94:* 505 (1957).

Presence of active degree of carbohydrate metabolism and identification and separation of some intermediates of this system has been directly demonstrated in human platelets. The use of radioactive phosphorus to determine specific activity of some fractions has yielded important additional data. Preliminary studies have indicated quantitative and qualitative alterations in carbohydrate metabolism during storage of normal platelets and particularly in platelets obtained from certain hematologic disorders, notably chronic granulocytic leukemia.

Thromboplastic Cell Component, the Lipoprotein of Erythrocytes and Platelets. Shinowara, G. Y., Dept. Path., The Ohio State Univ., Columbus, O., USA, J. biol. Chem. *225:* 63 (1957).

A highly purified lipoprotein fraction prepared by differential ultracentrifugation of human blood cell homogenates consists of peptide, free cholesterol, and phospholipide in about equal proportions. The lipoprotein has thromboplastic cell component activity; 0.034 gamma can quantitatively convert 1 unit of prothrombin into 1 unit of thrombin (NIH) in the presence of thromboplastic plasma component and ionic calcium. This activity is associated in normal human blood with both erythrocytes and platelets.

Thyrotoxicosis Associated with Thrombocytopenia and Hypersplenism, Report of a Case. Girsh, L. S., Myerson, R. M., Med. Serv. Veterans Administration Hosp., Philadelphia, Pa., USA, Amer. J. clin. Path. *27:* 328 (1957).

Platelet Cothromboplastin: A Platelet Factor(s) Related to the Blood Clotting Mechanisms. Lee, P. H., Johnson, S. A., Seegers, W. H., Dept. Physiol. and Pharm., Wayne State Univ. Med. Coll., Detroit, Mich., USA, Thromb. Diath. haem. *1:* 16 (1957).

Bovine platelets contain a factor(s) that greatly enhances the capacity of lung extract thromboplastin to convert purified prothrombin to biothrombin. It also may function with Russel's viper venom in the activation of prothrombin. The activity is destroyed below pH 4 or above pH 11 or at temperatures above 52° C. Concentrates of the activity have been obtained in a fraction of platelets that consists predominan tely of carbohydrate and protein.

Thrombotic Thrombocytopenic Purpura: Report of a Case with Some Unusual Characteristics. Báez-Villasenor, J., Ambrosius, K., Hosp. de Enfermedades de la Nutricion, México 7 D. F., México, Ann. intern. Med. *46:* 378 (1957).

A case is presented of a 43 year old woman in whom final diagnosis of thrombotic thrombocytopenic purpura was established. There were episodes of purpura for 8 years, and the 3rd one was accompanied by jaundice. The same association occurred in the final exacerbation, which, in addition was characterized by the presence of neurologic manifestations. The laboratory findings demonstrated the thrombocytopenic nature of the purpura and the presence of hemolytic anemia, with macrospherocytosis and a positive Coomb's test. The postmortem examination showed the presence of arteriolar thrombotic formations in the myocardium, spleen brain, stomach, pancreas, adrenals, and subcutaneous tissue. The chronicity of the disease, the absence of fever and the positive Coomb's test are mentioned as unusual findings in thrombotic thrombocytopenic purpura.

Effects of Varying Concentrations of Platelets and their Lyophilized Derivatives on Generation of Thromboplastin. Klein, E., Fiorentio, R., Children's Cancer Research Found., Children's Med. Center, Harvard Med. School, Boston, Mass., USA, Proc. Soc. exp. Biol. (N. Y.) *94:* 357 (1957).

High concentrations of fresh and lyophilized platelet materials inhibit the generation of plasma thromboplastin. Lyophilized platelet material, at the approximate equivalent of physiological concentrations, produces a normal level of plasma thromboplastin activity. Thromboplastin generation is not activated excessively at any concentration of these preparations.

A Thrombasthenic Syndrome Associated with Hyperheparinemia. Bell, W. N., Imber, I., Div. Hematol., Dept. Med., Univ. Hosp., Jackson, Miss. USA, Ann. Intern. Med. *46:* 537 (1957).

The authors described 27 patients with a thromasthenic syndrome characterized by a normal clotting time and venous platelet count, low adhesive platelet count, prolonged oil clot retraction time, decreased serum prothrombin time, frequently prolonged bleeding time and abnormal tourniquet test. These patients have an increased blood heparin titer during hemorrhagic phases. Females were more commonly affected than males, and all ages may be affected. The syndrome may show a familial tendency, may occur spontaneously, or may develop in the presence of other diseases. Protamine sulfate and desoxycorticosterone acetate were found to be valuable therapeutic agents in these patients.

Hemorrhagic Disease in Osteogenesis Imperfecta. Study of Platelet Function Defect. Siegel, B. M., Friedman, I. A., Schwartz, S. O., Hematol. Lab., Cook County Hosp., Chicago, Ill., USA, Amer. J. Med. *22:* 315 (1957).

An interesting case is reported and a discussion of the presence of a deficiency in the thromboplastic function of platelets, with associated bleeding tendency, in a patient with osteogenesis imperfecta is added. It is suggested that this occurrence of 2 rather rare anomalies, both representing mesenchymal defects, is not altogether coincidental.

Serotonin Changes in Platelets and Brain Induced by Small Daily Doses of Reserpine: Lack of Effect of Depletion of Platelet Serotonin on Hemostatic Mechanisms. Haverback, B. J., Dutcher, T. F., Shore, P. A., Tomich, E. G., Terry, L. L., Brodie, B. B., Clinic of General Medicine, Bethesda, Md., USA, New Engl. J. Med. *256:* 343 (1957).

The daily administration of 1 mg of reserpine to man virtually depleted serotonin of platelets within one week. After depletion of serotonin bleeding time, coagulation mechanism or capillary fragility were not significantly altered. It is concluded that serotonin in the platelets of man has no obvious role in hemostasis.

Transient Hemolytic and Thrombocytopenic Episode (Acute Transient Thrombohemolytic Thrombocytopenic Purpura), with Probable Meningococcemia: Report of a Case. Nussbaum, M., Dameshek, W., Dept. Med., Tufts Univ. Med. School, Boston, Mass., USA, New Engl. J. Med. *256:* 448 (1957).

An unusual case of probable meningococcemia with the clinical and hematologic picture of thrombohemolytic thrombocytopenic purpura is presented. It is suggested that a transient disturbance identical or similar to thrombohemolytic thrombocytopenic purpura developed during the course of meningococcemia.

Attempted Passive Transfer of Thrombotic Thrombocytopenic Purpura. Brittingham, T. E., Chaplin, H., Dept. Int. Med., Div. Hematol., Washington Univ. Med. School, St. Louis, Miss., USA, Blood *12:* 480 (1957).

Transfusion of 300 ml of plasma from a patient with thrombotic thrombocytopenic purpura produced no hematologic change in a healthy recipient; 10 months after the infusion there has been no evidence of transmission of any disease.

Thrombotic Thrombocytopenic Purpura with Extensive Hemorrhagic Gangrene of the Skin and Subcutaneous Tissue. Luttgens, W. F., Med. Serv., Madigan Army Hosp., Tacoma, Wash., USA, Ann. intern. Med. *46:* 1207 (1957).

Case report.

Platelet Transfusions in Pediatrics. McGovern, J. J., Hematol. Lab., Children's Med. Serv., Mass. General Hosp., Boston, Mass., USA, New Engl. J. Med. *256:* 123 (1957).

A simplified method of preparing platelet concentrates, without refrigeration or special anticoagulants is described. Brief clinical sumaries are given of 3 patients with severe chronic thrombocytopenia who received platelet transfusions before major surgery and 2 patients who received repeated platelet transfusions in the course of acute reversible thrombocytopenia. Development of platelet antibodies was not observed in this series.

Purpura. Israels, M., Practitioner *178:* 191 (1957).

The author gives a general survey of purpura, discussing in turn, pathogenesis, various forms, and therapy, including splenectomy.

Studies on Thrombopoiesis. I. Thrombocytopoiesis in Vitro: Experiments with Animal and Normal Human Material. Izak, G., Nelken, D., Gurevitch, J., Dept. Med. B, Hadassah Univ. Hosp., Jerusalem, Israel, Blood *12:* 507 (1957).

Thrombocyte production from megakaryocytes of healthy humans, dogs, guinea pigs and mice was observed continuously for 1 to 6 days in tissue culture. About 70% of the explanted megakaryocytes broke down to give rise to numerous platelets, while the remaining 30%

remained unchanged. The newly formed platelets were separated from the bone marrow tissue, counted and their serotonin — absorbing capacity determined. There was invariably a gradual increase in both the number of platelets and in their serotonin — absorbing capacity during the 1 to 6 days of observation.

II. Thrombocytopoiesis in Vitro from the Bone Marrow of Patients with Idiopathic Thrombocytopenic Purpura. Izak, G., Nelken, D., Blood *12:* 520 (1957).

Thrombocytopoiesis was studied in tissue cultures of bone marrows taken from 3 patients with chronic ITP and from normals following the addition of a potent anti-platelet serum to the culture media. The process of platelet production was similar in these 2 conditions and in bone marrow cultures of healthy individuals. The breakdown of megakaryocytes of patients with ITP and those treated with anti-platelet serum was greatly accelerated. No morphologic evidence of injury to the megakaryocytes was present. The platelets produced showed degenerative changes, they were agglutinated and underwent phagocytosis by the myeloid elements. Reticulum cells were present in the cultures.

Circulating Rat Platelets in Lethally X-radiated Mice Given Rat Bone Marrow. Smith, L. H., Makinodan, T., Congdon, C. C., Biol. Div., Oak Ridge Nat. Lab., Oak Ridge, Tenn., USA, Cancer Res. *17:* 367 (1957).

Congenital Amegakaryocytic Thrombocytopenia with Congenital Deformities and a Leukemoid Blood Picture in the Newborn. Emery, J. L., Gordon, R. R., Rendle-Short, J., Varadi, S., Warrack, A. J. N., Children's Hosp., Sheffield, England, Blood *12:* 567 (1957).

Two case reports. Both infants with absent radii and hemorrhagic manifestations which occurred within 24 hours of birth, and from which they eventually died. The most important hematologic feature was absence of megakaryocytes in the bone marrow.

Relationship of Platelet Serotonin to Disturbance of Clotting and Hemostasis. Weiner, M., Udenfriend, S., 3rd Med. Div., Goldwater Memorial Hosp., New York, N. Y., USA, Circulation (N. Y.) *15:* 353 (1957).

Platelet serotonin content was measured in normal subjects and in a variety of diseases by a spectophotofluorimetric method. It was not disturbed in any of the clinical groups studied, including hypertensive patients. Capillary fragility was not correlated with platelet serotonin. Platelet serotonin tended to be reduced in patients with markedly elevated urea nitrogen or severe anemia. With abnormally high platelet counts the concentration per platelet was also low. In man, reserpine in doses commonly used clinically caused a marked and prolonged depletion of platelet serotonin without influencing the clotting mechanism or hemostasis. Serotonin added in vitro was found to be without effect on coagulation, clot retraction, or fibrinolysis.

o) Spontaneous Anticoagulants

Über Hemmkörperhämophilie bei Pemphigus vulgaris. Ein pathologisch-anatomischer Beitrag. Gasser, H., Pathol. Inst. Univ. Bonn, Germany, Dtsch. Arch. klin. Med. *203:* 617 (1957).

The author reports the autopsy findings of a case of "Hemmkörper"-hemophilia with pemphigus vulgaris. The significance of the occurrence of "Hemmkörper"-hemophilia together with pemphigus is discussed.

Das Verhalten der blutgerinnungshemmenden Faktoren im Verlauf der alimentären Lipämie. Witte, S., Schmidt, B., Med. Univ.-Klinik, Erlangen, Germany, Klin. Wschr. *35:* 301 (1957).

The authors studied the effect of alimentary lipemia on the activity of thrombin inhibitor and of antithrombin in 45 patients. The average showed an increase of the thrombin inhibitor whereas no alteration of plasma antithrombin could be noticed. The results indicate an endogenous secretion of heparin into circulating blood occurring during the course of intake of large amounts of fat.

Neue Bestimmungsmethoden und Bedeutung der Antithrombine für die Klinik. Jürgens, J., II. Med. Univ.-Klinik, Frankfurt a. M., Germany, Klin. Wschr. *35:* 303 (1957).

The author describes simple methods for the determination of thrombin inhibitor (heparin antithrombin) and of serum antithrombin (antithrombin III). The clinical significance of these determinations is discussed.

Influenza della bile e dei biliari sull'emocoagulazione "in vitro" con particolare riguardo all'attività antitrombinica. Garagnani, A., Facchini, G., Ist. Clin. med., Univ., Bologna, Italy, Arch. Patol. Clin. med. *33:* 203 (1957).

Un inhibiteur de la maladie de Christmas. O'Brien, J. R., Portsmouth and Isle of Wright Area Path. Serv., Portsmouth, England, Rev. Hémat. *12:* 294 (1957).

The case is reported of a man having received numerous transfusions for a hemorrhagic tendency. It is demonstrated that there exists in the plasma and serum an inhibitor with an activity maintained unaltered for 2 years following the last transfusion. The action of this inhibitor can be neutralized by an excess of Christmas factor, it cannot be adsorbed by aluminum and is precipitated by 25% saturated ammonium sulfate; whereas Christmas factor is adsorbable by aluminum and is precipitated by ammonium sulfate from 33 to 55% saturation. It is concluded that Christmas factor and its specific inhibitor are proteins of entirely different nature. It was also found that the inhibitor more readily neutralizes plasmatic Christmas factor than Christmas factor in serum.

Heparin in Blood. Eiber, H. B., Danishefsky, I., Gilman Lab., New York Med. College, New York, USA, Proc. Soc. exp. Biol. (N. Y.) *94:* 801 (1957).

The presence of heparin in normal blood is demonstrated by the "carrier" technic, using radioactive sulfate as precursor. It appears to be found in blood in a combined form so that preliminary decomposition of the complex is required before it can be isolated.

Anti-AcG: Specific Circulating Inhibitor of the Labile Clotting Factor. Ferguson, J. H., Johnston, C. L., Howell, D. A., Dept. Physiol., Univ. N. Carolina, Chapel Hill, N. C., USA, Proc. Soc. exp. Biol. (N. Y.) *95:* 567 (1957).

The data described demonstrate an exceptionally interesting and unsusual case, namely, a specific inhibitor of AcG (labile factor, factor V), occurring in a human subject. It presence satisfactorily explains the anomalies of a number of clotting tests and accounts for the clinical hemorrhagic syndrome.

Anti-Heparin Activity of Erythrocyte Hemolysate. Rapaport, S. I., Ames, S. B., Dept. Med. Univ. of Carolina Med. Center. Los Angeles, Calif., USA, Proc. Soc. exp. Biol. (N. Y.) *95:* 158 (1957).

Erythrocyte hemolysate possesses anti-heparin activity that can correct the prolonged thrombin time and impaired prothrombin consumption of heparinized blood. This makes erythrocyte hemolysate a useful reagent to detect heparinemia and to permit the evaluation of plasma clotting factor activities in heparinized blood. Erythrocyte hemolysate also produces some shortening of the thrombin time of plasma not containing added heparin.

Hypergammaglobulinemia, Circulating Anticoagulant, and Biologic False Wassermann Reaction. Laurell, A. B., Nilsson, I. M., Bacteriol. Inst., Univ., Lund, Malmö, Sweden, J. Lab. clin. Med. *49:* 694 (1957).

An anticoagulant with antithromboplastin effect was found in 2 patients who had hypergammaglobulinemia and hemorrhagic diathesis and whose sera gave false biologic reactions for siphilis. After electrophoretic separation of the sera both Wassermann reagins and antithromboplastin were localized to the same regions in the gamma-globulins. On absorption with lipid antigen ist was possible to remove both from the active, separated fractions, but none of them from unfractionated sera. On absorption of the sera with thromboplastin, the antithromboplastin effect decreased by about 50% while the titer of the Wassermann reagins persisted unchanged. The relationship between the abnormal components is discussed.

Humoral Aspects of Tissue Mast Cells. Fulton, G. P., Maynard, F. L., Riley, J. F., West, G. B., Dept. Biol., Boston Univ., Boston, Mass., USA, Physiol. Rev. *37:* 221 (1957).

Tissue mast cells are involved in physiological processes by the formation and release of humoral agents. The presence of heparin in mast cells is now well established. It remains to be determined whether or not the release of heparin represents the primary function of the mast cell. Mast cells are also rich in histamine and they may produce hyaluronic acid. Production and release of 5-hydroxytryptamine is a possibility. The physiological significance of these facts is uncertain, but the evidence suggests an important role in adjustment of the microcirculation to the needs of tissue cells, especially during trauma or stress.

Tissue Heparin and Mastcells in Rats and Rabbits. Marx, W., Marx, L., Rucker, P., Ruggeri, L., Freeman, L., Dept. Biochem. and Nutr., Univ. of S. California Med. School, Los Angeles, Calif., USA, Proc. Soc. exp. Biol. (N. Y.) *94:* 217 (1957).

Tissue heparin contents and mast cell counts were determined on liver, lung, intestine, kidney, spleen and thymus of male rats and rabbits. In most instances, distribution of heparin and mast cells did not follow the same pattern. Rat organs showed higher heparin values, but lower mast cell numbers than the corresponding rabbit tissues.

p) Vitamin K

Doses of Water-Soluble Vitamin K Analogues in Hemorrhagic Disease of the Newborn. Council on Drugs, Report of the Council, J. Amer. med. Ass. *164:* 1331 (1957).

It is important to emphasize more generally the danger of high doses of the water-soluble vitamin K analogues administered to infants. There is ample evidence that a single dose of a water-soluble analogue equivalent to 1 mg of synthetic vitamin K is adequate to prevent hemorrhagic disease in the newborn. This would correspond to a dose of 3 mg of Synkavite. Therefore, since this vitamin can cause severe metabolic changes, it is unwise to exceed this dose level.

q) Heparin and Heparin-like Substances

Inibizione della fase tromboplastinica della coagulazione da parte dell'eparina. Marcacci, M., Ist. di Semeiotica, Univ., Napoli, Italy, La Sintesi *1:* 106 (1957).

Based on activity curves of factor V and VIII of blood of heparinized subjects, the author demonstates the inhibitory action of heparin on the first phase of blood coagulation (formation of thromboplastin).

Subcutaneous Heparin With and Without Hyaluronidase. Hollman, A., Nagle, R. E., Brit. med. J., no. 5038, 182 (1957).

The clotting time has been compared following the subcutaneous injection of heparin mixed with hyaluronidase, of subcutaneous heparin alone, and of heparin given intravenously. Hyaluronidase hastened the absorption of heparin from the skin to a significant extent in only 15% of the cases and did not diminish local bruising. Eight-hourly subcutaneous injection of heparin, with or without hyaluronidase, satisfactorily maintained the clotting time at 2 to 3 times normal after an initial delay averaging 14 hours. Severe local bruising occurred in 25% of the cases.

Gerinnungsaktivität und Toxizität bei Heparinen und Heparinoiden. Hardegg, W., Hartert, H., Hieronymi, G., Physiol. Inst., Univ., Heidelberg, Germany, Klin. Wschr. *35:* 778 (1957).

Erfahrungen mit einem neuen Heparinkörper in der Gynäkologie. Klahn, J., Frauenklinik, Städt. Krankenanstalten, Wiesbaden, Germany, Ther. d. Gegenw. *96:* 96 (1957).

Verhalten des Heparintoleranztestes unter gerinnungshemmenden Maßnahmen mit Dicumarol (analogen). Matis, P., Chir. Univ.-Klinik, Tübingen, Germany, Zbl. Chir. *82:* 599 (1957).

Les variations de la coagulabilité appréciées in vitro par le test à l'héparine de Marbet et Winterstein en fonction des valeurs de Quick et des différentes concentrations plaquettaires. Pettavel, J., Wuilleret, B., Serv. univ. de Chir., Lausanne, Switzerland, Helv. chir. Acta *24:* 39 (1957).

Zum Wirkungsmechanismus des Heparins als Antithrombin und zur Dynamik der Fibrinbildung. Amann, R., Werle, E., Wiss. Labor., Chir. Klinik, Univ., München, Germany, Klin. Wschr. *35:* 22 (1957).

The authors studied the solubility of thrombin in the presence of heparin and sodium chloride, and the behaviour of heparin mixed with thrombin in paper electrophoresis. The influence of increasing amounts of protamin, 48/80 (histamin releaser), and of spermin on the coagulation time of a purified fibrinogen-thrombin system was determined. Results: Heparin and thrombin form an easily dissociable complex. It is suggested that heparin, because of its strong negative charge, acts as an inhibitor of thrombin in the fibrinogen-thrombin system. Protamine, 48/80, and spermin in high concentrations inhibit the coagulation of fibrinogen by thrombin; lower concentrations activate thrombin.

Heparin and Sympathetic Block in Treatment of Venous Thrombosis. Experimental Investigations. Rudowski, W., I. Surg. Clinic, Academy of Med., Warsaw, Poland, Brit. med. J. no. 5019, 626 (1957).

The intravenous injection in dogs of a 50% solution of sodium salicylate results in thrombosis 6—12 hours later. The administration of heparin 6—24 hours after production of thrombosis prevents the development of the thrombotic process. Heparin given after 3 days does not prevent its development. Microscopically symptoms of the fibrinolytic action of heparin are absent. The application of procaine block less than 6 hours from the production of the thrombosis prevents the full development of the thrombus. Procaine block applied after 24 hours does not disperse the existing thrombus. The degree of organization of the thrombosis in dogs treated with heparin or with procaine block is approximately the same. The proliferation of endothelial cells is more marked in thrombosis after heparin treatment.

Über die Wirkung des Heparins bei der Behandlung von atherosklerotisch bedingten Verschlußereignissen am arteriellen Netzhautgefäßsystem. Stark, H., Augenklinik, Allgem. Krankenhaus Barmbek, Hamburg, Germany, Klin. Mbl. Augenhlk. *130:* 72 (1957).

Acute Thrombosis of the Portal Vein. Posey, E. L., Long, J. W., Stephenson, S. L., S. Afr. med. J. *50:* 8 (1957).

The characteristics and clinical symptoms of portal vein thrombosis are discussed as well as its etiological factors. A case is presented illustrating the successful results of heparin therapy. The patients is in excellent health 2 years after recovery.

A Clinical Study of Anticoagulants in Acute Myocardial Infarction with Particular Reference to Early Heparin Therapy. Eastman, G. L., Cook, E. T., Shinn, E. T., Dutton, R. E., Lyons, R. H., N. Y. State Univ. Med. Coll., Syracuse, N. Y., USA, Amer. J. med. Sci. *233:* 647 (1957).

The experience with anticoagulant therapy in acute myocardial infarction were analyzed in retrospect. Cases were divided into 3 groups: untreated, treated with dicumarol, and those given early heparin plus dicumarol. The mortality rate was higher in untreated cases but the differences are of no significance unless the early deaths are counted. Group 3 had a higher mortality rate than group 2. The difference, however, is not significant. There was a lower incidence of thromboembolism in group 2 and 3 than in group 1. Hemorrhagic phenomena occurred in treated cases 4 times as often as in group one. In group 3 they were 7 times as frequent. Superficial examination of these data would suggest that anticoagulants are of benefit. Comparison of the severity of illness in each group, however, suggests that untreated cases in these series were more seriously ill, and differences in death rates may conceivably be due to that factor. The addition of heparin to anticoagulant therapy seems unprofitable.

r) Other Anticoagulants

Influence des dérivés coumariniques sur le "Christmas Factor". Verstraete, M., Vandenbroucke, J., Lab. de Physiopathologie, Univ. Louvain, Belgium, Arch. int. Pharmacodyn. *59:* 429 (1957).

During treatment with coumarin derivatives prothrombin, factor VII, and Christmas factor are diminished. Decreased thromboplastin activity, as measured by the thromboplastin generation test using normal platelets and adsorbed plasma but serum from a patient under coumarin treatment, is primarily caused by diminished Christmas factor activity. The significance of these findings is discussed in relation to its importance in coumarin therapy of thromboembolism.

Clinical Evaluation of Three Anticoagulants in Thrombo-Embolic Disease. Neilson, J. McE., Mollison, A. W., Dept. Med. and clin. Biochem. Stobhill General Hosp., Glasgow, Scotland, Brit. med. J. no. 5029, 1214 (1957).

The properties of cyclocoumarol as an anticoagulant are reviewed on the findings obtained in its use in 57 patients. The results are compared with those obtained in 125 patients given ethyl-biscoumacetate and 179 given phenindione under similar conditions. The results are evaluated and it is concluded that phenindione is a more satisfactory and more easily controlled anticoagulant than either biscoumacetate or cyclocoumarol.

The Effect of Thyroid Function on the Prothrombin Time Response to Warfarin in Rats. Lowenthal, J., Fisher, L. M., Dept. Physiol., Univ. Saskatchewan, Saskatoon, Canada, Experientia (Basel) *13:* 253 (1957).

The effect of the dicumarol-like anticoagulant warfarin is increased in hyperthyroid and decreased in hypothyroid rats.

Sintrom, ein neues kurz wirkendes, gerinnungshemmendes Monocumarinderivat. Deutsch, E., Zentrales Gerinnungslabor, I. Med. Univ.-Klinik, Wien, Austria, Wien. klin. Wschr. *69:* 40 (1957).

Über die Verwendung von seltenen Salzen seltener Erdmetalle (Neodym + Praseodym) als Thromboseprophylaktikum. Osten, W., Chir. Abtlg., Rudolf-Virchow-Krankenhaus, Berlin N 65, Germany, Ärztl. Wschr. *12:* 107 (1957).

Vermeidung der Gefahren bei Behandlung von Thrombosen und Myokardinfarkten mit Antikoagulantien (Heparin, Cumarine) durch erfolgreiche Anwendung von Butazolidin. Müller, K., Med. Klinik, Nordstadtkrankenhaus, Hannover, Germany, Schweiz. med. Wschr. *87:* 617 (1957).

Following the discussion of the various risks and danger of anticoagulant therapy (heparin and cumarins) in cases of thrombosis, embolism, and myocardial infarction, the author demonstrates his success in treatment of these conditions with butazolidine. Based on these results the Nordstadt Hospital in Hannover now treats all its cases of infarction, thrombosis, or embolism with butazolidine.

Grenzen der Thrombose- und Embolieprophylaxe. Buser, P., Chir. Abtlg., Kantonsspital, Winterthur, Switzerland, Schweiz. med. Wschr. *87:* 1020 (1957).

On the basis of 700 patients treated with Sintrom and 250 with Panthesine-Hydergine (PH 203) an attempt is made to summarize the possibilities of avoiding postoperative thromboembolic complications. The favorable influence of specific prophylaxis on the incidence of mortal embolism is particularly emphasized, complete avoidance of complications seems not to be possible yet. The drugs available for prophylaxis and therapy, such as cumarin derivatives, heparin and heparinoids, as well as PH 203 are to be prescribed individually. The organization of centralized prophylaxis in clinical service is highly recommended.

Erhöhte Kapillardurchlässigkeit bei Antikoagulantientherapie und beim postthrombotischen Syndrom. Stamm, H., Frauenklinik, Univ., Basel, Switzerland, Ther. Umsch. *14:* 144 (1957).

Experiments were carried out in order to decrease capillary permeability in cases of hemorrhage caused by anticoagulants and of postthrombotic edema by protamine sulfate, vitamin K, and P-factors. It was found that in anticoagulant bleeding only normalization of coagulation

by protamine sulfate and vitamin K1 can abolish the capillary defect. The increased permeability of capillaries in the posthrombotic syndrome can clinically be normalized by vitamin K and P-factors. The sealing effect of vitamin K seems also to be reproducable experimentally.

Postoperative Blutungen durch Antikoagulantien. Thies, H. A., Chir. Univ.-Klinik, Hamburg-Eppendorf, Germany, Chirurg *28:* 196 (1957).

Klinischer Beitrag zur Genese und Therapie der Antikoagulantienblutung. Stamm, H., Hertig, H., Univ.-Frauenklinik, Basel, Switzerland, Schweiz. med. Wschr. *87:* 53 (1957).

The sealing mechanism of the capillary wall between blood and tissue is still partly unexplained. Clinical observations postulate, beside other sealing factors, a mechanism connected with coagulation. Hemorrhagic incidences during anticoagulant therapy are a consequence of a destruction of this sealing mechanism. Clinical studies revealed that only little compensation for the destroyed fibrin sealing is obtained by activation of the remaining mechanisms such as P-factors and vitamin E. As even a small increase in the therapeutic range of anticoagulants is desirable, the authors as a rule administer capillary wall sealing substances simultaneously with anticoagulants.

Place des Anticoagulants dans le traitement des embolies pulmonaires. Soulier, J. P., Centre Nat. de Transfusion Sanguine, Paris, France, Presse méd. *65:* 66 (1957).

Anticoagulant therapy should systematically be applied in all cases of pulmonary embolism in order to prevent very frequently fatal recurring embolism. The prophylaxis against thromboembolic complications must be considered in every particular case. As long as the indication is sound and the control of therapy reliable, prophylactic treatment yields very satisfactory results.

Ricerche sperimentali istopatologiche sulla tossicità degli anticoagulanti indiretti. Colli, A., Bevilacqua, M., Ist. Clin. Med. Generale, Univ. Pavia, Italy, Haematologica *42:* 1 (1957).

The authors studied the toxicity of the so-called indirect anticoagulants. Survival time of the rats and alterations appearing in liver, kidney, and spleen following administration of toxic dose of the drugs were investigated. Based on their results the authors come to the conclusion that tromexan was the least toxic preparation studied. Marcoumar and G 23350 and cumopyran have much more toxic activity, whereas dicumarol and phenylindanedione exert an intermediate activity between the 2 other groups of anticoagulants.

The Effect of Permanent Anticoagulant Therapy on Symptoms and Mortality in Angina Pectoris. Waaler, B. B., Med. Dept. A, Univ. Hosp., Oslo, Norway, Acta med. scand. *47:* 289 (1957).

Permanent anticoagulant therapy has been given for an average of 2½ years to 275 patients with angina pectoris, probably caused by coronary atherosclerosis. The mortality was significantly reduced. The frequency of myocardial infarction during treatment was significantly lower than in a corresponding period before treatment. The anginal distress improved greatly in 38% and showed some improvement in another 12%. The frequency of clinically significant bleedings, caused by anticoagulants alone, was about 1 per 27 patient-treatment years.

Complications thrombo-emboliques, traitement anticoagulant et tests de laboratoire. Pettavel, J., Serv. univ. Chirurgie, Lausanne, Switzerland, Schweiz. med. Wschr. *87:* 167 (1957).

The author discusses the difficulties in diagnosis of thromboembolic complications. The various dangers of anticoagulant therapy, in particular the danger of hemorrhage, are mentioned. The advantages and error margin of a number of heparin tests are compared and the technic described by Marbet and Winterstein is recommended.

2-p-chlor-phenyl-1,3-indanedione (G 25766) in Treatment of Thromboembolic Conditions, Especially Thrombophlebitis. Lund, E., Kommunehosp., Med. Dept. VII, Copenhagen, Denmark, Acta med. scand. *157:* 39 (1957).

G 25766 (Geigy) has been used in treatment of 19 patients with thrombophlebitis, and one patient with endoarteritis obliterans, and prophylactically during digitalization or diuretic

therapy in 5 cases of cardiac insufficiency. It was as a rule easy to adjust the prothrombin-proconvertin value. In one patient with recurrent hemorrhagic complications the bleeding stopped after i.v. injection of 20 mg of vitamin K1. G 25766 is considered a reliable drug suitable for anticoagulant therapy.

Thrombo-Embolie-Prophylaxe ohne Bestimmung der Gerinnungsfaktoren. Hartenbach, W., Chir. Univ.-Klinik, München, Germany, Münch. med. Wschr. *99:* 335 (1957).

According to the author's experience, the post-operative alarm reaction favors the development of thrombosis. This is due mostly to an alteration of the metabolism of minerals with loss of sodium and blood fluid, and to an increase of thrombocytes. Prophylaxis (the author uses Thrombodym) should therefore be instituted immediately after operation and should include compensation of the above mentioned deficiency by administration of sufficient amounts of sodium and fluid.

Recurrent Hypoprothrombinemia Due to Poisoning with a Dicumarol-Containing Rat-Killer. Nilsson, I. M., Med. Clinic, Allmänna Sijukhuset, Malmö, Sweden, Acta haemat. (Basel) *17:* 176 (1957).

A case of recurrent hypoprothrombinemia in a woman of 73 is reported. Clotting studies and subsequent detailed inquiry into the case revealed that the hypoprothrombinemic episodes were induced by a daughter-in-law having admixed a rat killer containing Warfarin to the patient's cough-syrup. As the patient had as many as 7 recurrences, it was possible to compare the effects of various forms of therapy. Synthetic water-soluble vitamin K preparations had no effect on the prothrombin regeneration rate.

Early Use of Anticoagulants in Treatment of Myocardial Infarction. Wright, I. S., Dept. Med., Cornell Univ. Med. Coll., New York, N. Y., USA, J. Amer. med. Ass. *163:* 918 (1957).

In this paper practical points are emphasized rather than experimental and statistical studies. The report of the committee on anticoagulants and many others are available for the readers reference. The decision as to which patients should receive any form of therapy must rest on the judgement of the physician. His decision, however, should be based on all available facts. It is hoped that this brief outline will aid physicians to come to sound conclusions regarding this form of therapy.

Limited Use of Anticoagulants in Acute Myocardial Infarction. Analysis of 1000 "Good Risk" Cases. Russek, H. I., Zohman, B. L., Cardiovasc. Research, U.S. Public Health Service Hosp., Staten Island, N. Y., USA, J. Amer. med. Ass. *163:* 922 (1957).

Effect of Oral Anticoagulant (Marcumar) on Prothrombin and Related Components in Blood Coagulation. Johnson, S. A., Caldwell, J., Priest, E. M., Dept. Labs., Henry Ford Hosp., Detroit, Mich., USA, Circulation Res. *5:* 252 (1957).

A detailed analysis of the effect of the oral anticoagulant marcoumar on the plasma and serum levels of the coagulation factors has shown that while prothrombin and autoprothrombin I (factor VII) are decreased very much, autoprothrombin II (Christmas factor) remained almost unchanged.

Studies on the Anticoagulant Phenindione. Drinan, F. W., Tufts Med. Serv. and Anticoagulant Lab., Boston City Hosp., Boston, Mass., USA, Amer. Heart J. *53:* 284 (1957).

The Anticoagulant Effect of a New Coumarin Derivative-Sintrom-(Geigy) and its Control by Standardized Clotting Time. Mayer, G. A., Conell, W. F., Dept. Med., Queen's Univ., Kingston, Ont., Canada, Canad. med. Ass. J. *76:* 272 (1957).

Long-Term Anticoagulant Therapy of the Ambulatory Patient Following Myocardial Infarction Tanzi, F., Van Ness, A. L., Dept. Med., Univ. of Chicago, Chicago, Ill., USA, Med. Clin. N. Amer., Chicago Number, p. 25, jan. 1957.

The mortality rate of 6.1% in a group of unselected patients who have been on anticoagulant therapy for an average of 72.9 weeks per patient is considerably lower than that

generally reported in patients not on anticoagulant therapy after myocardial infarction. The protection given by continuous anticoagulation against fatal thromboembolic complications appears definitely to warrant their use, accepting the risk of hemorrhage. The proper time to stop therapy is still a matter of opinion. Only the accumulation of data from patients with adequate records will, in time, determine the proper answer.

Profund Bleeding After Dental Extractions During Dicumarol Therapy. Ziffer, A. M., Scopp, I. W., Medical and Dental Serv., N. Y. Veterans Administration Hosp., New York, N. Y., USA, New Engl. J. Med. *256:* 351 (1957).

Two cases are reported in which dental extraction, performed during dicumarol therapy, was followed by excessive and serious bleeding. It is suggested that long-term anticoagulation be discontinued briefly at the time of oral surgery. The risk of recurrent embolism is less to be feared than the hazard of serious postoperative bleeding. Prompt resumption of therapy, when hemostasis is certain, produces minimal interruption of anticoagulation.

Long-Term Dicumarol Administration as a Therapeutic Trial in Sicklemia. Report of a Case. Adelson, H. T., Med. Service, Roger Williams General Hosp., Providence, Rhode Island, USA, New Engl. J. Med. *256,* 353 (1957).

A trial course of long-term anticoagulant therapy in a case of sickle-cell anemia is reported. The apparently beneficial and encouraging results are described. It is suggested that this therapeutic approach justifies further trial and evaluation.

The Failure of Anticoagulant Therapy to Prevent Myocardial Infarction in Patients with Premonitory Symptoms of Impending Coronary Occlusion. Schlachman, M., N. Y., Med. Coll. Metropolitan Med. Center, New York, N. Y., USA, Ann. intern. Med. *46:* 728 (1957).

Three cases with premonitory symptoms of an impending coronary occlusion are presented in whom adequate anticoagulant therapy failed to prevent the occurrence of a myocardial infarction. No conclusions are reached as to the effectiveness of anticoagulants during this stage, but it is hoped that others will have an opportunity to apply anticoagulant therapy during this period so that sufficient data determine its value as preventive treatment.

Influence of Anticoagulants on Experimental Canine Cerebral Infarcts. Moyes, P. D., Millikan, C. H., Wakim, K. G., Sayre, G. P., Whisnant, J. P., Dept. of Neurosurg., Mayo Foundation, Rochester, Minn., USA, Proc. Mayo Clin. *32:* 124 (1957).

Cerebral infarcts were produced in dogs by injection of vinyl-acetate into the surgically exposed internal carotid artery. The dogs were given anticoagulants after operation. 11 of 13 dogs with cerebral infarcts surviving at least 31 hours had infarcts that were more hemorrhagic than those in dogs that died less than 31 hours after the operative procedure. These infarcts were also more hemorrhagic than were those of a control series of dogs which were not given anticoagulants. In most cases, the hemorrhage apparently did not extend beyond the margins of the infarct. The degree of hemorrhage appeared to be approximately proportional to the extent of the infarct.

The Technic of Permanent Anticoagulant Treatment. Owren, P. A., Rikshosp., Oslo, Norway, Postgrad. Med. *21:* 83 (1957).

Clinical Experience with 3-(1-Phenylpropyl)-4-Hydroxycoumarin. Fairbairn, J. F., Estes, J. E., Section of Med., Mayo Clinic, Rochester, Minn., USA, Proc. Staff. Mayo Clin. *32:* 342 (1957).

From this study it is concluded that marcoumar is an effective anticoagulant agent suitable for clinical use. However, it is not believed that it has any significant advantages over dicumarol. Achievement of therapeutic levels of plasma prothrombin activity might be hastened by combining a single "priming" dose of tromexan with the initial dose of marcoumar.

Permanent Anticoagulation Therapy in Cardiovascular Disease. Owren, P. A., Rikshosp., Oslo, Norway, Northwest Med. *56:* 298 (1957).

s) Thrombosis and Thrombelastography

Arteriosklerose und Thrombogenese. Koller, F., Med. Abtlg. Krankenhaus Neumünster, Zürich, Switzerland, Bull. Schweiz. Akad. med. Wiss. *13:* 81 (1957).

Arteriosclerosis favors the formation of thrombi for the following reasons: 1. by decreasing the lumen of the vessels and thus decreasing speed of blood flow in the vicinity of the stenosis. 2. by inducing lesions in the vessel walls which are apt to start the process of coagulation, especially when combined with an endothelial defect. The exact mechanisms of these two points as well as their consequences are discussed.

Erfahrungen in der Thromboembolieprophylaxe mit besonderer Berücksichtigung von Butazolidin. Schweiz. med. Wschr. suppl. 24 (1957).

This special issue of the Schweiz. med. Wschr. is totally concerned with "Results in Prophylaxis of Thromboembolism with Special Regard to The Use of Butazolidin". The experiences collected in this number represent a co-work of 6 Swiss hospitals and the following authors: Aeppli, H., Baerlocher, W., Binswanger, J. Bloch, H. R., Egli, E., Jenny, J., Kaufmann, P., Koller, Th., Küng, H. L., Kym, O., Müller, E., Rageth, S., Schmidlin, S., Sigg, K., Stamm, H., Triebold, H., Willenegger, H. In various articles the following problems are dealt with: A general part covers nomeclature, diagnosis and survey of prophylaxis of venous thromboembolism. The clinical investigations lead to the following conclusion: Butazolidin administered prophylactically, distinctly reduces the occurrence of superficial phlebitis. The figures available for deep thrombosis and embolism, on the other hand, are not conclusive. An interesting result is the beneficial influence of Butazolidin on the patient's general condition after operation or parturition, the patient's stay at the hospital may thus be markedly shortened. No-untoward side-effects were noted, and no increase in bleeding was observed. The results, as a whole, show that Butazolidin is a potent anti-inflammatory agent possessing concomitant antipyretic and analgesic properties, and has valuable characteristics as a complement to the usual prophylactic measures against thromboembolic disorders.

Über das Verhalten einzelner Gerinnungsfaktoren bei obturierenden Gefäßkrankheiten. Nolte-Billaudelle, R., Med. Klinik, Städt. Krankenhaus, Darmstadt, Germany, Klin. Wschr. *35:* 726 (1957).

Factor V, VII, and prothrombin levels were studied in venous and arterial occlusive disorders. A statistically highly significant increase of factor V was found in these patients. These results were obtained not only in cases of thromboembolism but also in endo-angiitis and occlusive arteriosclerosis. No difference could be found between arterial and venous disorders and therefore, no etiologic conclusions can be drawn. Therapeutical consequences of these findings are pointed out.

Diet and Coronary Thrombosis. Hypothesis and Fact. Yudkin, J., Queen Elizabeth Coll., Univ. of London, England, Lancet *273:* 155 (1957).

A consideration of some of the more readily available data on the incidence of coronary deaths and on food consumption makes difficult to support any theory which supposes a single or major dietary cause of coronary thrombosis. It is suggested that relative over-consumption of food, associated with reduced physical exercise, may be one of several causes of the disease.

Massive Thrombophlebitis. Catchpole, B. N., Univ. of Sheffield, England, Lancet *272:* 343 (1957).

5 cases of massive thrombophlebitis (massive venous thrombosis, phlegmasia caerulea dolens) are described. The rarity of the condition has undoubtedly been over-emphasized, with the result that it is often tardily diagnosed and inadequately treated. The pathology of the condition has been briefly outlined and the diagnosis and clinical course discussed. The urgent need for vigorous treatment early in the fulminating type of the disease to prevent or overcome shock and to avert a speedy death is emphasized. Attempts to induce vasodilatation are contra-indicated and initial anticoagulant therapy should be avoided. Exercise is advocated to

pump blood from the congested tissues, if it is not feasible to remove the offending blood clot surgically. Any tissue necrosis which results should be treated with conservatism.

Hirnabszesse und zerebrale venöse Thrombose bei kongenitalen Herzfehlern. Weber, G., Neurochir. Klinik, Kantonsspital, Zürich, Switzerland, Schweiz. med. Wschr. *87:* 159 (1957).

Lungenembolie und Lungeninfarkt. Beitrag zur Pathogenese, Klinik und Therapie unter Berücksichtigung von 130 Fällen der medizinischen Abteilung des Kantonsspitals Winterthur aus den Jahren 1951 — 1955. Wick, A., Med. Klinik, Kantonsspital, Winterthur, Switzerland, Helv. med. Acta *23:* 663 (1957) und *24:* 100 (1957).

Pulmonary embolism and pulmonary infarction. A contribution to pathogenesis, clinic and therapie. With special regard to 130 cases from the medical department of the Kantonsspital Winterthur during the years 1951 to 1955.

Thromboseprophylaxe während der Schwangerschaft. Sigg, K., Stamm, H., Univ.-Frauenklinik, Basel, Switzerland, Medizinische 1957: 421.

A propos de la thrombose cardiaque à forme massive intracavitaire. Houcke, E., Lille, France, Arch. Mal. Coeur *50:* 104 (1957).

Pathogenese und Therapie der Thrombophlebitis und Thrombose. Heinrich, H. G., I. Med. Univ.-Klinik, Charité, Berlin, Germany, Z. ges. inn. Med. *12:* 145 (1957).

Cavernous Sinus Thrombophlebitis. Taylor, P. J., Thomas's Hosp., London, England, Brit. J. Ophtal. *41:* 228 (1957).

Unfall — Varizen — Thrombose. Neuere Gesichtspunkte zur Pathogenese und Behandlung. Eysholdt, K. G., Chir. Univ.-Klinik, Göttingen, Germany, Dtsch. med. Wschr. *82:* 818 (1957).

Der Elastoplast-Kompressionsverband zur Prophylaxe und Therapie der Thromboembolie. Hajek, O., An der Schleifmühle 82, Bremen, Germany, Zbl. Gynäk. *79:* 649 (1957).

Unfall und Thrombose. Hasse, G., Chir. Univ.-Klinik, Jena, Germany, Münch. med. Wschr. *99:* 14 (1957).

The author points out that there exist extremely few studies concerning the problem of accident and thrombosis, and that there exist no data on the incidence of post-traumatic thrombosis. The following questions are discussed: a) What is the cause of post-traumatic thrombosis? A brief survery on genesis of post-traumatic thrombosis is given. b) How frequent is post-traumatic thrombosis? 1.5% of the 1027 accidents studied developed embolism. Post-traumatic embolism occurred most frequently following fractures of the extremities. The therapy with anticoagulants is briefly outlined, and their superiority to conservative measures is emphasized.

Thromboseprophylaxe mit Magnesium. Schnitzler, B., Landesfrauenklinik, Karlsruhe, Germany, Münch. med. Wschr. *99:* 81 (1957).

After referring to the decisive significance of platelet disintegration in the origin of intravasal thrombosis, the author discusses the stabilizing effect of magnesium on thrombocytes. It is emphasized that only general prophylaxis can bring about satisfactory results. Prophylaxis with anticoagulants is considered complicated and not without danger. Since no coagulation tests are necessary prophylaxis of thrombosis and embolism with magnesium is economical and undangerous. Prophylaxis with magnesium as performed in the author's clinic over a period of 18 months yielded favorable results.

Zur Prophylaxe der Thromboembolischen Komplikationen in der Chirurgie mit PH 203 (Panthesin und Hydergin). Hausamann, E., Chirurg. Abtg., Inselspital Bern, Switzerland, Schweiz. med. Wschr. *87:* 219 (1957).

PH 203 (4 cc contain 400 mg panthesin and 0.3 mg hydergin, Sandoz A.G. Basel) was found to be an effective preparation for prophylaxis of postoperative and posttraumatic

thrombosis. The frequency of this incidence was significantly lowered. The few cases of thromboembolism which occured in spite of this prophylactic treatment were characterized by their unsevere course and were easily cured by further treatment with PH 203. No fatal embolism occurred in this group of patients. The application of this therapy is easy as no laboratory control is necessary. The total absence of hemorrhagic complications allows administration before or immediately after operation. No contraindications were noted.

Erfahrungen mit PH 203 zur Prophylaxe und Therapie der Thromboembolien. Morger, R., Bezirksspital Laufenburg, Switzerland, Praxis *46:* 331 (1957).

The author reports results obtained in over 100 cases of thromboembolism with the combined preparation PH 203 (panthesin + hydergin). The advantage over anticoagulants consists in the absence of hemorrhagic danger, and subsequently of laboratory control. The prophylactic value of this therapy could not be ascertained in these few cases whereas the therapeutic effect is considered satisfactory. In particular is the preparation recommended in cases of pulmonary embolism where its effect is rapid and reliable (i.v. infusions).

Zur Wirkung des Butazolidins auf die peripheren Gefäße und seine Eignung in der Behandlung von Thrombophlebitiden und Thrombosen. Ratschow, M., Thüre, D., Med. Klinik, Darmstadt, Germany, Medizinische no. 10, 359 (1957).

Die Behandlung der Thrombophlebitis mit dem Pyrazolderivat Butazolidin und dessen Einfluß auf das Blutgerinnungsystem. Heinrich, G. H., I. Med. Univ.-Klinik, Charité, Berlin, Germany, Z. ges. inn. Med. *12:* 49 (1957).

Ergebnisse der Röntgenbehandlung der chronischen Thrombophlebitis. Fuchs, G., Hofbauer, J., Zentral-Röntgeninst., Kaiser-Franz-Josef-Spital, Wien, Austria, Wien. med. Wschr. *107:* 197 (1957).

Die Bedeutung einiger Vitamine für die Behandlung der Thromboembolie. Naegeli, Th., Matis, P., Tübingen, Germany, Internat. Z. Vitaminforschg. *27:* 324 (1957).

Considerazioni anatomo-cliniche sulla evoluzione di un caso di trombosi della vena cava inferiore. Infranzi, A., Ist. Clin. chir. Generale, Univ., Napoli, Italy, Minerva chir. *12:* 115 (1957).

Eine gute Thromboseprophylaxe während Schwangerschaft, Geburt und Wochenbett sowie bei Operationen kann die Thromboembolie verhüten. Sigg, K., Kantonsspital Liestal, Basel, Switzerland, Münch. med. Wschr. *99:* 611 (1957).

(Butazolidin, compression badages, sclerosing therapy of large varicous veins, early rising after delivery.)

Massive Thrombophlebitis. Catchpole, B. N., Univ. of Sheffield, England, Lancet *272:* 343 (1957).

The Diagnosis of Traumatic Main Vessel Thrombosis. Mayor, G. E., Royal Infirmary, Aberdeen, Scotland, Brit. J. Surg. *44:* 337 (1957).

Was leisten Gerinnungsbestimmungen zur Erkenntnis der Thrombosegefährdung? Imdahl, H., Chir. Univ.-Klinik, Bonn, Germany, Ärztl. Wschr. *12:* 202 (1957).

The author shows that no test of coagulability, especially not Quick's method, is adequate for the estimation of the threat of thrombosis, since no method reproduces the intravital conditions, furthermore, since an increase in coagulability is not a necessary factor of thrombogenesis. Despite years of study on the action of dicumarol it is still not possible to evaluate the intricate process of coagulation in its entirety. It cannot be assumed that thrombogenesis is governed by the same factors, but in reversed values to those that are decisive in hemorrhagic diathesis. Thrombosis cannot be explained merely from the viewpoint of coagulation, but it is a vital and intravasal process with many interlocking modifying factors. The liver plays an important part, and recent investigations suggest close connections between functional disturbance of the liver and pancreas, and the development of thrombosis.

Occluding Thrombus of the Right Atrium. Intermittend Tricuspid Occlusion in a Case of Atrial Infarction with Mural Thrombosis. Pellegrino, E. D., Olmstead, E. V., Tompkins, G. B., Dept. and Path., Hunterdun med. Center, Flemington, N. J., USA, Amer. J. Med. *22:* 151 (1957).

A case is presented of atrial infarction with mural thrombus formation producing the syndrome of tricuspid valve occlusion by virtue of its size and position. The clinical syndrome produced was sufficiently striking so that antemortem diagnosis of both lesions was possible. Only 3 previous cases of occluding thrombi of the right atrium have been reported, none in association with atrial infarction. The clinical pictures of tricuspid and mitral valve occlusion are contrasted and their practical importance is emphasized.

Renal Vein Thrombosis in Newborn Infants of Diabetic Mothers. Report of Two Cases. Avery, M. E., Oppenheimer, E. H., Gordon, H. H., Dept. Pediatrics and Path., John Hopkins Univ. Med. School, Baltimore, O., USA, New Engl. J. Med. *256:* 1134 (1957).

The Natural History of Cerebral Thrombosis. Pincock, J. G., Dept. Neurol, Deer Lodge Hosp., Winnipeg, Manitoba, Canada, Ann. intern. Med. *46:* 925 (1957).

A series of 117 cases of cerebral thrombosis has been tabulated and analyzed at the end of an 8 year period following their initial episode. The results are discussed and presented in order that some base-line can be established upon which to gauge the values of new modes of treatment.

Cerebral Thrombangiitis Obliterans. Miller Fisher, C., Neurol. Serv., Mass. General Hosp., Boston, Mass., USA, Medicine (Baltimore) *36:* 169 (1957).

Rilievi trombelastografici nel neonato a termine e nell'immaturo. Fumarola, D., Li Moli, S., Ist. Patol. Generale, Univ., Bari, Italy, Haematologica *42:* 711 (1957).

Thrombelastographic studies in normal newborns, 20 cases, yielded the following results: moderate increase of reaction time "r" with normal values of the other thrombelastographic factors, besides slight hypoprothrombinemia and hypoconvertinemia. In the immature infant a distinct and constant prolongation of "r" and "k" was found, and in come cases also alterations of maximum elasticity of thrombus. A marked deficiency of the prothrombin complex was found and thought to be responsible for the thrombelastographic alterations.

Inhalts- und Sachverzeichnis liegt der 1. Ausgabe des Bandes II bei. — Index will be annexed to the 1st issue of volume II. — La table des matières sera jointe au 1er numéro du volume II.