

## Physiology and Pathology of Blood Coagulation

### A Review of the Literature of 1958 (Second Series)\*)

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\*) Papers appearing in Thromb. Diath. haem. will as a rule not be summarized, but only mentioned by their title.

### a) General Aspects

*The Coagulation of Horse Blood.* Fantl, P., Marr, A. G., Baker Med. Research Inst., Alfred Hosp., Melbourne, Australia. J. Physiol. (London) 142: 197 (1958).

Thromboplastin formation from plasma and serum components takes place at the same rate in human and horse blood.  $\alpha$ -Prothromboplastin (antihemophilic factor) and  $\beta$ -prothromboplastin (PTC) and prothrombin of horse plasma have activities similar to factors of human plasma. Horse as well as human brain extracts show some degree of species specificity in one-stage prothrombin tests. Prothrombin accelerator of horse plasma is more active than that of human plasma. Factor VII in horse serum is as active as that of human serum when acting in homologous systems. Thrombins isolated from mammalian plasmas give shorter clotting times with human than with horse plasma.

*Beobachtungen an Gerinnung und Fibrinolyse während chirurgischer Eingriffe am menschlichen Herzen in Unterkühlung oder mittels extrakorporalen Kreislaufes.* Kaulla, K. N. von, Swan, H., Kaulla, E. von, Dept. Med. and Surg., Univ. of Colorado Med. School, Denver, Col., USA. Klin. Wschr. 36: 1050 (1958).

Hypothermia does not lead to any decrease of coagulation activity in man. Cardiac surgery during hypothermia causes a progressive increase in prothrombin time with simultaneous increase of prothrombin consumption. Increased thrombin times may occur during surgery. Fibrinolytic activity does not increase significantly during surgery with hypothermia. Cardiac surgery performed by help of extracorporeal circulation may cause markedly increased thrombin times mostly in connection with cardiac or circulatory dysfunction. Increase of thrombin inhibitor alone or combined with fibrinolytic activity seem to be the main reason for hemorrhages occurring in connection with cardiac surgery.

*Der heutige Stand der Gerinnungsforschung.* Koller, F., Med. Abtg., Krankenhaus Neumünster, Zollikerberg, Zürich, Switzerland. Thromb. Diath. haem. 2: 407 (1958).

*Die Einwirkung von Leberautolysaten auf den Gerinnungshaushalt des menschlichen Blutplasmas.* Margraf, W., Greuer, W., Göttingen, Germany. Arzneim.-Forsch. 3: 127 (1958).

Liver autolysates from guinea-pigs inhibit the activity of prothrombin, factor VII, and thrombin inhibitor when mixed in vitro with human oxalated plasma. Factor V and antithrombin, on the other hand are activated. In the whole autolysates cause hypocoagulability.

*Veränderungen der Gerinnungsfaktoren nach chirurgischen Eingriffen in Ganglionblockade.* Holzknecht, F., Olbrich, E., Wilflingseder, P., Innsbruck, Austria. Med. Klin. 8: 296 (1958).

*Über eine intravasale Funktion der Blutgerinnung.* Witte, S., Erlangen, Germany. Medizinische 27/28: 1095 (1958).

The author reports results of experiments revealing a relation between blood coagulation and vascular permeability. Decreased blood coagulability leads to increased vascular permeability. The permeability of vessel walls for tagged plasma constituents is revealed by means of fluorescent microscopy. The results of this study suggest another physiologically important function of blood coagulation, namely the control over vascular permeability.

*Die Wirkung von Spasmolytica und Parasympatholytica auf das Gerinnungs-System des Menschen.* Schimpf, K., Petry, H. J., Lasch, H. G., Heidelberg, Germany. Dtsch. Arch. klin. Med. 205: 166 (1958).

In the healthy individual sympatholytica (hydergine, reserpine) produce an increase and parasympatholytica (atropin) a decrease of blood coagulability as measured by levels of prothrombin, factor V, VI and VII. In patients with parenchymous liver damage and in patients under marcoumar treatment, atropin however, increases the coagulative tendency.

*Über die Gerinnungsfaktoren in der Cantharidenblasenflüssigkeit.* Witte, S., Bressel, D., Erlangen, Germany. Dtsch. Arch. klin. Med. 205: 200 (1958).

*Klinik der Makroglobulinämie Waldenström. Beschreibung von 21 Fällen und Übersicht der Literatur.* Kappeler, R., Krebs, A., Riva, G., Med. Univ.-Klinik, Bern, Switzerland, *Helv. med. Acta* 25: 101a (1958).

The authors present a clinical survey of macroglobulinemia Waldenström, discussing in turn cytology, hematologic findings, blood coagulation alterations, diagnosis and nosology, therapy and prognosis. 21 own observations are discussed.

*Über den Einfluß von Frischblut und Konservenblut auf die Gerinnungsverhältnisse des Empfängers.* Schwenzer, A. W., Halberstadt, E., Univ.-Frauenklinik, Frankfurt/M., Germany. *Blut* 4: 143 (1958).

Coagulation studies were carried out in 50 patients receiving fresh blood transfusions and compared to 50 patients with transfusions of stored blood. Within 2 hours coagulation improved in about 75% of the patients with stored blood and only in about 30% of the patients with fresh blood transfusions. After 24 hours this improvement still persisted in 50% of the patients with stored blood and in 25% of the patients with fresh blood transfusions.

*Serum Lipoproteins and Blood Coagulation.* Goldrich, R. B., Whyte, H. M., Clin. Research Dept., Sydney Hosp., Sydney, Australia. *Nature (Lond.)* 182: 1744 (1958).

*Phosphatidyl Serine and Blood Coagulation.* Barkhan, P., Silver, M. J., da Costa, P. B., Tocantins, L. M., Jefferson Med. College, Philadelphia Pa., USA. *Nature (Lond.)* 182: 1031 (1958).

*Nouveaux aspects de la maladie hémorragique du nouveau-né.* Van Creveld, S., Clin. Infantile, Univ. Amsterdam, Holland. *Arch. franç. Pédiat.* 15: 721 (1958).

*Die Laboratoriumsdiagnostik der auf Störungen der Blutgerinnungsvorphase beruhenden Krankheitsbilder.* Rálk, K., I. Med. Klinik, Univ. Szeged, Hungary. *Z. ges. inn. Med.* 13: 347 (1958).

*Über die Bedeutung gerinnungsphysiologischer Untersuchungen bei akuten und chronischen Lebererkrankungen.* Broicher, H., Egli, H., Kessler, K., Oberhoffer, G., Physiol. Inst., Univ., Bonn, Germany. *Dtsch. Arch. klin. Med.* 205: 292 (1958).

The behaviour of prothrombin, antithrombin, and factors V, VII, IX and X has been studied in acute and chronic hepatitis, cirrhosis, obstructive jaundice and other liver disorders and compared to paper electrophoretic protein tests and results of some other protein lability tests. The results reveal that coagulation studies offer an additional possibility for diagnosis of functional liver disorders, provided that all coagulation factors are investigated.

*Die periphere Wirkung von Tannin auf Blutung, Blutgerinnung und Permeabilität der Blutgefäße.* Stefl, J., Eysselet, M., Brünn, CSR. *Arzneim.-Forsch.* 8: 662 (1958).

*Über Koagulopathien in der Frauenheilkunde.* Elsner, P., II. Univ.-Frauenklinik, Wien, Austria. *Wien. med. Wschr.* 108: 819 (1958).

*Accidents hémorragiques au cours du traitement par Cyclosérine.* Bertheau, M., Romeuf, J., *Rev. Tuberc. (Paris)* 22: 549 (1958).

*Oleandomycin und Blutgerinnung.* Künzer, W., Beck, B., Univ.-Kinderklinik, Würzburg, Germany. *Münd. med. Wschr.* 100: 1391 (1958).

Romicil was found to increase the coagulative tendency of blood as measured by decrease of recalcification time as well as increase of prothrombin, factor V, and VII. Prothrombin consumption is decreased by the drug.

*Regelvorgänge bei der Blutgerinnung.* Perlick, E., Med. Klinik, Med. Akademie, Magdeburg, Germany. *Acta biol. med. germ.* 1: 506 (1958).

The analysis of clinical material and animal experiments shows that a regulation similar to that observed for circulation of blood and for the neurovegetative system can be demonstrated for blood coagulation. This phenomenon and all influencing factors are discussed.

*Methods for the Investigation of the Coagulation Mechanism in Small Children.* Ashley, D. J. B., United Liverpool Hosps., Liverpool, England. J. clin. Path. 11: 399 (1958).

*The Kaolin Clotting Time.* Margolis, J., Pharm. Dept., Middlesex Hosp., Med. School, London, England. J. clin. Path. 11: 406 (1958).

*Zur Diagnostik kardial- und gefäßbedingter hämorrhagischer Diathesen sowie arterieller und venöser Gefäßschäden.* Heinrich, H. G., I. Med. Univ.-Klinik, Charité, Berlin, Germany. Dtsch. Gesundh.Wes. 13: 1309 (1958).

*Über Beziehungen zwischen Blutgerinnung und Kreislauffunktion.* Lasch, H. G., Mechelke, K., Nusser, E., Sessner, H. H., Med. Univ.-Klinik, Heidelberg, Germany. Z. ges. exp. Med. 129: 484 (1958).

*Blutungsbereitschaft und Gerinnungsstörung bei Urämie.* Gross, R., Nieth, H., Mammen, E., Med. Univ.-Klinik, Marburg/Lahn, Germany. Klin. Wschr. 36: 107 (1958).

Out of 90 patients with uremia, 28 were found with a general bleeding tendency. Abnormal values of coagulation time in 20%, of silicone coagulation time in 45%, of heparin tolerance test in 65%, of thrombelastography in 70%. 66% of the cases had hyperfibrinogenemia. No correlation between clinical severity and bleeding tendency was found. Only one third of the patients with coagulation factor deficiency showed liver function disorder. The markedly decreased heparin tolerance in uremia calls for extremely carefully heparinization of the patient for blood dialysis.

*Pathophysiology of Hemorrhagic Conditions.* Jorpes, E., Chemical Inst. II, Karolinska Inst., Stockholm, Sweden. Nord. Med. 59: 3 (1958).

A summary is given of the genesis of different hemorrhagic conditions including allergic thrombocytopenia, hemophilia A and B, fibrinogenolytic bleedings and defibrination following abruptio placentae. Referring to a case of hemophilia in a girl treated with AHG in connection with surgery (hysterectomy) the possibility of using AHG preparations for the treatment of hemophiliacs is discussed.

*Pathophysiology and Clinical Picture of Hemorrhagic Conditions.* Waldenström, J., Med. Clinic, Allmänna Hosp., Malmö, Sweden. Nord. Med. 59: 7 (1958).

The author presents some clinical observations in various coagulation defects and discusses their diagnoses and specific therapy.

*Über den Einfluß des Cholins auf die gesteigerte Gerinnungstendenz im lipämischen Blut.* Schimpf, K., Diedrichs, A., Med. Univ.-Klinik, Heidelberg, Germany. Klin. Wschr. 36: 682 (1958).

The activation of plasma thromboplastin by fat extract in vitro is inhibited by cholin-chloride. In vivo activation of the coagulation mechanism produced by a fatty meal is prevented by previous administration of cholin-chlorid.

*Lipæmia and Blood Coagulation. With Special Reference to the Stypven Technique.* MacLagan, N. F., Billimoria, J. D., Curtis, C., Dept. chem. Path., Westminster Med. School, London, S. W. 1, England. Lancet 2: 865 (1958).

When Stypven is added to plasma, lipolysis starts immediately and may exert a significant effect on the clotting time. The lipolytic action is confined to the phosphatide fraction of the plasma fats. If there is delay between the addition of Stypven and calcium, considerable amounts of lysophosphatides are produced which lengthen the clotting time. More lipolysis occurs with lipemic plasma than with fasting plasma, so that the accelerating effect of lipemia on the clotting time is partly masked by the lysophosphatides produced. Stypven and calcium are therefore better added simultaneously. Experiments with this "instantaneous" method on 9 volunteers showed that the effect of fat feeding was consistent with all types of fat tried. There was a significant positive correlation between the degree of lipemia and the drop in Stypven-time.

*The Hemorrhagic Syndrome Complicating Extracorporeal Shunting of Blood: An Experimental Study of its Pathogenesis.* Penick, G. D., Averette, A. D., Peters, R. M., Brinkhous, K. M., Depts. Path. and Surg., Univ. N. Carolina Med. School, Chapel Hill, USA. *Thromb. Diath. haem.* 2: 218 (1958).

*The Haemostatic Balance.* Astrup, T., Biol. Inst. Carlsberg Foundation, Copenhagen, Denmark. *Thromb. Diath. haem.* 2: 347 (1958).

*Adherence and Viscosity of Blood Contacting Foreign Surfaces, and the Plasmatic Zone in Blood Circulation.* Copley, A. L., Med. Research Labs., Charing Cross Hosp., London W. C. 2, England. *Nature (Lond.)* 181: 551 (1958).

The author describes a method for the measurement of adherence of blood and plasma. The effect of the nature of the surface on the adherence is discussed. From the author's observations it appears that the immobile layer of plasma at the blood vessel wall is not necessarily due to a suspension of red cells, but may as well exist when plasma alone flows through a living blood capillary, for example in plasma skimming. These observations may throw a new light on a number of problems related to the physiology of blood circulation as well as on certain vascular disorders associated with changes in the structure of the inner lining facing the lumen of the vessel.

*Diet, Blood Chemistry, Blood Coagulation and Fibrinolysis in Relation to Coronary Heart Disease: An Inter-Racial Study.* Merskey, C., Gordon, H., Ladener, H., Dept. Med. and Dept. Surg. Research, Univ., Cape Town, S. Africa. *S. Afr. med. J.* 32: 855 (1958).

It appears that phases of slow fibrinolysis are characteristic of the white race but the role that this may play in atherogenesis remains purely speculative. The Bantu is characterized by a greater fibrinolytic activity but whether this is the result of hepatic dysfunction, dietary custom or any other inherent of environmental factors is at present unknown.

*Bantu Haematology and Coagulation.* Merskey, C., Dept. Med., Univ., Cape Town, S. Africa. *Leech* 28: 45 (1958).

*On the Purposelessness of the Clinical Application of Coagulen.* Niewiarowski, S., Kopec, M., Inst. Hematol., ul. Chocimska 5, Warszawa, Poland. *Pol. Tyg. lek.* 13: 3 (1958).

*Effect of Ionizing Radiation on the Blood Clotting in vitro.* Latallo, Z., Danciewicz, A. M., Musialowicz, T., Nuclear Res., Warszawa, Poland. *Acta biochim. polon.* 5: 225 (1958).

The authors investigated the effect of in vitro radiation on the coagulation system. Recalcification time was slightly prolonged in irradiated platelet-poor serum, and irradiation of platelets and Christmas factor impaired thromboplastic functions. No appreciable effect of X-rays on the second coagulation phase was revealed. Inactivation of plasminogen was not confirmed. Neither were any differences revealed in the behaviour of the fibrinolytic system before and after irradiation.

*Comparison of Animal and Vegetable Fats in Increasing Blood Coagulability. Effect of Physical Activity on Increased Coagulability of Blood after Ingestion of High-Fat Meal.* McDonald, G. A., Fullerton, H. W., Aberdeen, Scotland. *Lancet* 2: 598 (1958).

*Fats and Blood Coagulation.* Poole, J. C. F., Oxford, England. *Brit. med. Bull.* 14: 253 (1958).

*Effect of Human  $\alpha_1$ -Acid Glycoprotein on Blood Coagulation.* Nilsson, J. M., Chem. Dept. II, Karolinska Inst., Stockholm, Sweden. *Nature (Lond.)* 181: 711 (1958).

The average amount of  $\alpha_1$ -acid-glycoprotein in normal plasma is 50 mgm/100 ml. On addition of  $\alpha_1$ -acid-glycoprotein to normal plasma the author noted a prolongation of coagulation time which prompted further investigation of such effects. It was found that the anticoagulant effect of acid glycoprotein could be attributed to an inhibition of the transformation of prothrombin to thrombin by thromboplastin in a competitive manner. As even normal concentration of  $\alpha_1$ -glycoprotein is sufficient to influence clotting time a more

significant effect of acid-glycoprotein can be expected in diseases associated with a decrease of prothrombin or an increase of acid-glycoprotein (cancer, inflammatory dermatoses).

*Blood Coagulation Before and After a Fatty Meal.* O'Brien, J. R., Portsmouth a. Isle of Wright Area Path. Service, Portsmouth, England. *Lancet* (Lond.) 1: 410 (1958).

*The Nonprotein Products of Plasma Coagulation.* Cohen, S. I., West Roxbury, Mass., USA. *Arch. Biochem. Biophys.* 77: 50 (1958).

After recalcification and coagulation of human plasma the release of a peptide as well as of arginin and glutamic acid has been noted.

*Blood Coagulation in Subjects with and without Clinical Evidence of Atherosclerotic Vessel Disease.* Mustard, J. F., Dept. Veterans Affairs, Sunnybrook Hosp., Toronto, Canada, *Canad. med. Ass. J.* 79: 554 (1958).

*Effect of Fat-Loading upon Blood Coagulation.* Mandel, E. E., Dept. Med., Chicago Med. School, Chicago, Ill., USA. *Amer. J. clin. Path.* 30: 11 (1958).

*In vitro and in vivo Effect of Different Fat Preparations on Blood Coagulation.* Mustard, J. F., Dept. Vet. Affairs, Sunnybrook Hosp., Toronto, Ont., Canada. *Canad. med. Ass. J.* 79: 818 (1958).

*Some Effects of Divalent Cations on the Clotting Mechanism and the Platelets of EDTA Blood.* Zucker, M. B., Borrelli, J., Sloan-Kettering Inst. for Cancer Research, New York City, N. Y., USA. *J. appl. Physiol.* 12: 453 (1958).

Metal EDTA chelates, the stability of which are higher than that of calcium, fail to act as anticoagulants, whereas magnesium and barium EDTA prevent clotting. SrEDTA is not an effective anticoagulant. Blood prevented from clotting by magnesium or barium EDTA, fails to show certain peculiar characteristics seen in disodium EDTA blood. These characteristic are: long thrombin clotting time, rapid factor V destruction, absence of clot retraction, spherical shaped platelets and diminished platelet adhesiveness to glass, and agglutinability. Addition of  $MgCl_2$ ,  $BaCl_2$ ,  $SrCl_2$ , or  $CaCl_2$  to disodium EDTA blood corrects the thrombin clotting time and clot retraction and diminishes factor V destruction.  $MgCl_2$  changes the spherical platelets to discs and increases platelet adhesiveness. The concentration of divalent cations required to correct the behaviour of disodium EDTA blood is much less than the concentration of calcium or strontium required to produce even trace fibrin formation. It is suggested that magnesium may normally be responsible for maintaining a short thrombin clotting time, platelet disc shape, and adhesiveness, and for slowing factor V destruction.

*Hemorrhage and Massive Transfusion.* Ulin, A. W., Seymour, W. G., Winchell, H. S., Ehrlich, E. W., Blood Coagulation Research Lab., Hahnemann Med. College, Philadelphia, Pa., USA. *J. amer. med. Ass.* 168: 1971 (1958).

Data on 38 patients receiving massive transfusion, including 16 "bleeders", show that massive transfusion was not sufficient in itself to produce hemorrhage. Massive transfusion may be, and probably in large part was, a result rather than a cause of bleeding. A common cause for bleeding was not evident for all cases. Thrombocytopenia was not sufficient to produce hemorrhage. Fibrinogenopenia and/or fibrinolysis was not impressive. The vasculature it as yet uninvestigated. Consequently hemorrhage cannot be blamed on compatible transfusion. Transfusion may initiate or aggravate the bleeding due to a defective mechanism or a system already primed for hemorrhage. Therefore every patient to undergo surgery who seems to show a likelihood of requiring transfusions should have a complete investigation of coagulation factors.

*Some in vitro Effects of Various Concentrations of Disodium Ethylenediamine Tetracetate, Potassium Oxalate, and Sodium Citrate on Coagulation of Blood.* Mustard, J. F., Dept. Vet. Affairs, Sunnybrook Hosp., Toronto, Ontario, Canada. *Amer. J. clin. Path.* 30: 498 (1958).



*Hemorrhagic States Secondary to Intravascular Clotting.* Penick, G. D., Dept. Path., Univ. N. Carolina Med. School, Chapel Hill, N. C., USA. Arch. Path. 66: 708 (1958).

*Effect of Polycarboxylic Acids on Blood Coagulation.* Gordon, E. E., Dept. Med., Harvard Med. School, Boston, Mass., USA. Proc. Soc. exp. Biol. (N. Y.) 99: 192 (1958).

Human blood was incubated in vitro with the sodium salts of a number of di- and tri-carboxylic acids and their effect on clotting time was noted. Cis-aconitate, trans-aconitate, isocitrate and tricarballoylate markedly increased clotting time of whole blood. Prolongation of clotting in the presence of isocitrate and cis-aconitate was dependent upon their concentration in blood. The possible mode of action of these metabolically active compounds and the implications of the findings were discussed.

*Dietary Fats and Blood Coagulation.* Hashim, S. A., Clancy, R. E., Dept. Nutrition, Harvard School of Public Health, Boston, Mass., USA. New. Engl. J. Med. 259: 1115 (1958).

*The Inadequacies of Routine Bleeding and Clotting Times.* Diamond, L. K., Porter, F. S., Dept. Pediatrics, Harvard Med. School, Boston, Mass., USA. New. Engl. J. Med. 259: 1025 (1958).

A strong plea is made for the abandonment of routine presurgery tests of bleeding and clotting times on the basis of such evident inherent limitations as the occurrence of false-positive reactions and the fact that a normal result in no way assures a normal bleeding and clotting status in the patient. A carefully taken family history and past history and an adequate physical examination, as well as the examination of a peripheral blood smear, are suggested as being far more informative and effective screening procedures. If reliable laboratory studies are indicated, accurate platelet estimations and the complete battery of clotting tests must be done.

*Polycythemia vera: Study of Coagulation Abnormalities, Both Thrombotic and Hemorrhagic.* Wilson, S. J. J. Kans. med. Soc. 58: 90 (1958).

*Effect of Glucose on Appearance of Plasma Clotting Accelerator Activity, Lactescence, and Plasma Lipids in Fat-Fed Dogs.* Tilden, J. H., Shipley, R. E., Lilly Lab. clin. Research, General Hosp., Indianapolis, Ind., USA. Circulation (N. Y.) Res. 6: 804 (1958).

The influence of glucose, given orally or intravenously, on the acceleration of plasma clotting and appearance of lipemia following the feeding of pea-nut oil was determined in dogs. Oral glucose blocked or masked the appearance of plasma lactescence and clotting accelerator activity, whereas intravenous administration tended to delay their appearance. In other experiments heparin abolished or reduced plasma lactescence without modifying clotting accelerator activity induced by fat feeding.

### **b) Fibrinogen (Factor I), Fibrin, Fibrinolysis**

*The Effect of Citrate on Euglobulin Methods of Estimating Fibrinolytic Activity.* Buckell, M., Clin. Research Lab., Charing Cross Hosp., London, England. J. clin. Path. 11: 403 (1958).

*Un caso di afibrinogenemia congenita con epistassi ripetute.* Orlando, E., Manara, E., Ist. Patol. Spec. med., Univ., Bologna, Italy. G. Clin. med. 39: 1216 (1958).

*Vergleichende Untersuchungen über die Bedeutung der Transaminasen- und Fibrinogenwerte im Serum für Differentialdiagnose und Prognose des Myokardinfarktes.* Lasch, F., Theinl, K., Landeskrankenhaus Villach, Austria. Med. Klin. 53: 1769 (1958).

*L'hyperfibrinémie dans la maladie de Hodgkin et les gangliopathies réticulaires malignes.* Croizat, P., Clin. Propédeutique, Fac. de Méd., Lyon, France. Presse méd. 66: 1471 (1958).

*Über die fibrinolytischen Vorgänge und ihre Auswirkung in klinischer Sicht.* Fonio, A., Poststraße 19, Chur, Switzerland. Medizinische 40: 1564 (1958).

*Das fibrinolytische Potential. I. Enzymologie, Pathologie und Klinik.* Halse, Th., München, Germany. Medizinische 50: 2044 (1958).

*Ipfibrinogenemia congenita con fibrinoastenia.* Imperato, C., Dettori, A. G., Ist. Clin. Paediatrica, Univ. Parma, Italy. *Helv. paediat. Acta* 13: 380 (1958).

*Uncontrollable Post-Operative Hemorrhage After Incompatible Blood Transfusion.* Moore, J. M., Hairmyres Hosp., East Kilbride, England. *Brit. med. J.* 5106: 1201 (1958).

A case is described in which there was fatal postoperative bleeding associated with afibrinogenemia, following a hemolytic transfusion reaction. Treatment is discussed and the following points may be of value in controlling such a condition: 1. Early recognition of the fact that a hemorrhagic state has developed. 2. Administration of large amounts of the fibrinogen fraction. 3. Fresh frozen plasma, or fresh blood, if there is a poor response to adequate fibrinogen. 4. Avoidance of dextran. 5. Corticotrophine, cortisone, or toluidine-blue dye intravenously, if not responding.

*Untersuchungen über die Inaktivierung von streptokinaseaktiviertem Plasmin.* Beller, F. K., Reinhardt, U.: Univ.-Frauenklinik, Tübingen, Germany. *Blut* 4: 367 (1958).

*The Estimation of Fibrinolytic Components by Means of the Lysis Time Method.* Lassen, M., Biol. Inst., Carlsberg Found., Copenhagen, Denmark. *Scand. J. clin. Lab. Invest.* 10: 384 (1958).

The lysis time method has been developed for the determination of activator, proactivator, and streptokinase. Streptokinase was found to be adsorbed on glass surfaces. Complete solution has been accomplished by addition of gelatin to the buffer.

*Fibrinolysis in Normal Pregnancy.* Biezanski, J. J., Moore, H. C., Rotunda Hosp. Lab., Dublin. *J. clin. Path.* 11: 306 (1958).

*The Acute Defibrination Syndrome in Obstetrics.* McBride, W. G., Sydney, Australia. *Med. J. Austr.* 54: 627 (1958).

*Hämorrhagische Diathesen in der Geburtshilfe.* Elsner, P., II. Univ.-Frauenklinik, Wien, Austria. *Wien. klin. Wschr.* 70: 726 (1958).

Fibrinogen deficiency is the cause of bleeding in obstetric hemorrhagic diatheses. The author presents schemes of coagulation and activation of the fibrinolytic mechanism. Therapy in obstetric hemorrhagic diathesis consists of emptying of the uterus cavum, restitution of lacking fibrinogen, normalization of the circulation and treatment of shock.

*The Turnover of Plasma Fibrinogen.* Korsgaard-Christensen, L., Gentofte Hosp., Lab. of Med. Dept. C, Copenhagen, Denmark. *Acta med. scand.* 162: 407 (1958).

The half-life turnover of fibrinogen was determined in 8 normal subjects. It was found to vary from 4.0 to 4.7 days. The fibrinogen survival time was found to be shorter in certain patients. An analysis of these cases shows what kind of information the method can yield. The experimental and theoretical difficulties inherent to the method are discussed.

*Recherches sur les inhibiteurs de la fibrinolyse. 1. Influence de l'antistreptokinase sur l'activation spontanée de la fibrinolyse.* Giacomazzi, G., Cassi, E., Visca, U., Inst. Path. Méd. et Méthodologie, Univ., Milano, Italy. *Haematol. lat.* 1: 233 (1958).

*Studies on the Mechanism of Action of Staphylocoagulase.* Rubinstein, H. M., London, England. *Brit. J. Haematol.* 326 (1958).

*Antigenic Studies on Human Plasminogen.* Meyers, W. M., Burdon, K. L., Riley, M. N., Houston, Texas, USA. *Experientia (Basel)* 14: 280 (1958).

*Über Fermenteffektoren der Fibrinolyse. II. Die Bedeutung der Erythrocyten für die Fibrinolyse.* Bayerle, H., Kammenhuber, K., Path. Inst., Univ., München, Germany. *Blut* 4: 78 (1958).

*Defibrinierungsblutungen post partum.* Finke, L., Mölln/Lauenburg, Germany. *Med. Klin.* 26: 1143 (1958).



*The Esterase Activity of the Fibrinolytic System.* Lassen, M., Biol. Inst., Carlsberg Found., Copenhagen, Denmark. Biochem. J. 69: 360 (1958).

*Fibrinolytic Activity in Some Human Body Fluids.* Albrechtsen, O. K., Biol. Inst., Carlsberg Found., Copenhagen, Denmark. Scand. J. clin. Lab. Invest. 10: 310 (1958).

*Hypofibrinogenic Bleedings in Obstetrics and Gynecology.* Zilliacus, H., Kvinnokliniken, Helsingfors, Finland. Nord. Med. 59: 16 (1958).

The clinical course of ablatio placentae ante tempus is described: hemorrhagic diathesis, shock, and later complications. The treatment of this condition as given at the University Hospital for Women in Helsinki, is discussed. It is pointed out that dextran is not suitable for treating shock associated with ablatio placentae. Fibrinolysis and fibrinogenolysis are briefly mentioned as well as coagulopathias that may ensue from gynecological conditions.

*Cushing's Syndrome with Cyclic Afibrinogenemia.* Scott, D., Med. afdeling B, Haukeland sykehus, Bergen, Norway. Nord. Med. 59: 30 (1958).

Case report.

*Zur Frage der Fibrinolyse an experimentellen Gerinnungs- und Abscheidungsthromben.* Sandritter, W., Huppert, M., Schlüter, G., Senckenbergisches Path. Inst., Univ. Frankfurt a. M., Germany. Klin. Wschr. 36: 651 (1958).

Experimentally produced thrombi in animals were treated with doses of 2 mg/kg of thrombocid. A melting of the fibrin structure was noted together with characteristic morphologic alterations. The fibrinolytic activity of the blood thus activated leads to complete disappearance of the thrombi. As the site of adherence of the thrombi consists of agglutinated platelets, and as these are not affected by the drug, the danger of mobilisation of the thrombus is neglectable.

*The Effect of Fibrinogen Concentration on Susceptibility of Clots to in vitro Clot Lysis with Plasmin.* Freiman, A. H., Clifton, E. E., Clotting Mechanism Section, Div. of Metabolism Enzyme Studies. Sloan Kettering Inst., New York, N. Y., USA. Thromb. Diath. haem. 2: 269 (1958).

*Fibrinolysis in Liver Disease. Study of 109 Cases by Means of the Fibrin Plate Method.* de Nicola, P., Soardi, F., Clinica Med., Univ. Pavia, Italy. Thromb. Diath. haem. 2: 290 (1958).

*Congenital Afibrinogenemia.* van Creveld, S., Liem Khe Hoo, Pediatric Clinic, Univ., Amsterdam, Holland. Maandschr. Kindergeneesk. 26: 227 (1958).

The development of hemorrhage after trauma or prolonged bleeding during tooth eruption are the chief manifestations of congenital afibrinogenemia. Congenital hypofibrinogenemia can be temporary or permanent. The permanent form has been ascribed to hereditary factors. The authors present the case of a female infant with healthy unrelated parents. They emphasize that in the blood of such a patient the antihemophilic factor is present in normal amounts notwithstanding the absence of fibrinogen. There exists, however, an increased instability of the antihemophilic factor and an increased prothrombin consumption. Transfusions of blood, plasma, or fibrinogen are promptly effective against the hemorrhagic diathesis of afibrinogenemia, but the effect is temporary only.

*Possibilité d'étude immunochimique de la fibrinolyse.* Seligman, M., Service, P. Grabar, Inst. Pasteur, Paris, France. Rev. franç. Etudes clin. et biol. 3: 1073 (1958).

The degradation products obtained from fibrinogen and fibrin by plasmin can be identified by immunochemical methods with anti-fibrinogen serum. Possible applications of these findings, both experimentally and clinically, are emphasized.

*La conservazione delle proprietà fibrinolitiche del plasma umano attivato.* Meneghini, P., Binda, B., Ist. Clin. med. Generale, Univ. Genova, Italy. Boll. Soc. ital. Ematol. 6: 5 (1958).

*Sex Differences in Plasma Fibrin, Fibrinolytic Capacity and Lipids as Influenced by Ingested Fat, Gonadectomy and Hormon Implants: Possible Implications for Pathogenesis of Coronary Occlusion.* Gillman, T., Naidon, S. S., Hathorn, M. Clin. Sci. 17: 393 (1958).

*Un nouveau cas de fibrinolyse hémorragique grave en obstétrique. Rôle d'une interruption de grossesse par immunisation antirhésus.* — Guerrison, Favre-Gilly, M. M., Devic, G. Lyon méd. 25: 921 (1958).

Case report.

*Etude statistique des cas de fibrinolyse observés pendant 5 ans dans un laboratoire d'étude de la coagulation.* Revol, L., Favre-Gilly, J., Thowverez, J.-P., Croizat, P. Sang. 29: 62 (1958).

Based on statistic studies the authors come to the conclusion that fibrinolysis is not a rare syndrome, as beside the well-known cases of severe hemorrhagic fibrinolysis namely in obstetrics, numerous cases of latent fibrinolysis have to be taken into consideration.

*Defibrination Syndrome in Pregnancy. Value of Various Diagnostic Tests.* Sharp, A. A., Howie, B., Biggs, R., Methuen, D. T., Radcliffe Infirmary, Oxford, England. Lancet 2: 1309 (1958).

Four cases of obstetric defibrination are described. Laboratory study of their blood showed that tests based on the reactivity of plasma to purified thrombin were more reliable than other methods for detecting the abnormality. The beneficial effects of concentrated purified fibrinogen has been confirmed. The defect in the early stages of this syndrome may consist of a qualitative alteration in the reactivity of fibrinogen to thrombin, rather than a simple quantitative depletion of fibrinogen.

*A Method of Preparing Fibrinogen Tagged with Radioactive Iodine.* Clement, E., McNicol, P. G., Univ. Dept. Med. of Med., Royal Infirmary, Glasgow, Scotland. Lancet 2: 1212 (1958).

A method of tagging fibrinogen with radioactive iodine is described. This simple method produces a material in which 89—94% of the radioactivity is coagulable. (Preliminary communication).

*Effect of Divalent Cations on Proteolysis of Fibrinogen.* Medart, W. S., Dept. Path., Washington Univ. Med. School, Saint Louis, Mo., USA. Proc. Soc. exp. Biol. (N. Y.) 97: 728 (1958).

The effects of various divalent cations on proteolysis of fibrinogen by trypsin and chymotrypsin were studied. Calcium, Mg, Mn, Co, Zn, and Cd were approximately equally effective in reducing the rate of proteolysis by trypsin. At levels as low as  $10^{-7}$  M, Ca began to decrease the rate of proteolysis by either trypsin or chymotrypsin, and 50% reduction of the rate occurred at about  $10^{-3}$  M. The effects of Ca on both tryptic and chymotryptic digestion appeared to yield the kinetics of a competitive inhibition, and the suggestion is made that Ca acts to affect an equilibrium between two forms of fibrinogen, the one susceptible, the other inhibitory, to proteolysis.

*The Fibrinogen Polymerization Test in Nonspecific Myocarditis and Pericarditis.* Fremont, R. E., Losner, S., Volk, B. W., Cardiovasc. Sec., Brooklyn Veterans Administration Hosp., Brooklyn, N. Y., USA. Arch. intern. Med. 102: 41 (1958).

*Fibrinolysis and Hemorrhage: A New Diagnostic and Therapeutic Approach.* Henson, J. C., Peers, W., Tagnon, H. J., Dept. Med. and clin. Invest., Institut Jules Bordet, Brussels, Belgium. Blood 13: 874 (1958).

The case of a patient is presented who underwent a cesarean section during which cardiac arrest occurred. Cardiac massage was successful. A severe hemorrhagic diathesis associated with fibrinolysis appeared during the period of shock associated with cardiac arrest. The plasma of the patient was able to digest its own fibrin as well as a substrate of casein marked with radioactive iodine. A new method of measurement of fibrinolysis based on the use of tagged casein is presented: the main advantage of this method is that the substrate is not contaminated with plasminogen or plasmin. In addition the products of the reaction are measured by their radioactivity. The proteolytic activity of the plasma from a patient with fibrinolysis was shown to be inhibited by the trypsin inhibitor from soy bean. The intravenous injection of trypsin inhibitor in this patient was followed by the disappearance of fibrinolysis in her blood.

*The Use of a Lyophilized Human Plasma Standardized for Blood Coagulation Factors in the Coagulase and Fibrinolytic Tests.* Turner, F. J., Schwartz, B. S., Dept. Microbiol., Warner-Lambert Research Inst., Morris Plains, N. J., USA. J. Lab. clin. Med. 52: 888 (1958).

A lyophilized human plasma standardized for blood clotting factors gave essentially the same results as freshly drawn human plasma in the coagulase test. A chart illustrating the types of clot formation in the coagulase tests and the influence and significance of the various plasmas on such clot formation is presented. The lyophilized plasma, when reconstituted in distilled water and diluted 1:5 in physiologic saline, gave consistently more uniform results in the fibrinolytic test than did unselected fresh human plasma. All lots of the lyophilized plasma tested were nonrefractory to fibrinolysis. The possible use of this lyophilized plasma in the detection and study of staphylokinase-producing *Staphylococcus pyogenes* strains is indicated.

*Occult Intravascular Clotting.* Quick, A. J., Hussey, C. V., Harris, J., Peters, K., Dept. Biochem., Marquette Univ. Med. School, Milwaukee, Wisc., USA. J. Lab. clin. Med. 52: 935 (1958).

The results of this study demonstrate that a state of hypocoagulability is induced in dogs by the intravenous injection of thrombin. No massive thrombin occurs, but the fibrinogen is gradually diminished. It appears probable that the chief cause of the hypocoagulability is the drastic reduction of labile factor and thromboplastinogen. These findings suggest that the defective hemostasis in acquired clinical hypofibrinogenemia may perhaps not be due primarily to the lack of fibrinogen but to the loss of other essential clotting factors.

*Application of Continuous Flow Electrophoresis to the Study of the Blood Coagulation Proteins and the Fibrinolytic Enzyme System. I. Normal Human Materials.* Lewis, J. H., Walters, D., Didisheim, P., Merchant, W. R., Dept. Med., Univ. of Pittsburgh, Pa., USA. J. clin. Invest. 37: 1323 (1958).

*Fibrinolysis. I. Fibrinolytic Activity of Extracts from Non-Pathogenic Fungi.* Stefanini, M., Marin, H., Joseph Stanton Memorial Labs., Saint Elizabeth Hosp., and Dept. Med. Tufts Univ., Boston, Mass., USA. Proc. Soc. exp. Biol. (N. Y.) 99: 504 (1958).

A study of properties of extracts from cultures of 160 non-pathogenic fungi has shown that 4 cultures produce non-protein materials able to lyse plasma clots and fibrin, of both human and bovine source; at least one shows some specificity against human plasma clots.

*Treatment of Thrombosis with Fibrinolysin (Plasmin).* Sokal, J. E., Ambrus, J. L., Ambrus, C. M., Roswell Park Memorial Inst., Univ. of Buffalo Med. School, Buffalo, N. Y. USA. J. Amer. med. Ass. 168: 1314 (1958).

Various preparations of fibrinolysin have been administered to patients with thrombotic disorders. Rapid resolution of signs and symptoms has been observed in patients treated within a few days of the apparent clinical onset of thrombosis. Fibrinolysin therapy was ineffective when started one week or more after the first manifestations of thrombosis. Several patients treated only with fibrinolysin suffered recurrence of thrombosis soon after the completion of therapy. The authors, therefore, believe that fibrinolysin treatment should be supported by

anticoagulant therapy to prevent such recurrent thrombosis. It must be emphasized that this approach to the therapy of acute thrombosis is still experimental.

*Occurrence of Fibrinolytic Activity Following Administration of Nicotinic Acid.* Weiner, M., Redisch, W., Steele, J. M., 3rd Med. Research Serv., Goldwater Memorial Hosp., New York, N. Y., USA. Proc. Soc. exp. Biol. (N. Y.) 98: 755 (1958).

It is concluded that a relatively simple non-enzymatic substance, nicotinic acid, can induce fibrinolytic activity in vivo.

*Fibrinolysis: Report of a Case and Clinical Review.* Cohen, S. N., Kupfer, H. G., Med. Serv., Veterans Administration Hosp., Richmond, Va., USA. New Engl. J. Med. 259: 1103 (1958).

The clinically important conditions associated with fibrinolysis include obstetric accidents, major surgical procedures on the thorax, pancreas, uterus and prostate, and disseminated carcinoma of the prostate, urinary bladder, stomach, and lung. Diagnosis depends on an awareness of fibrinolysis and is confirmed by appropriate tests demonstrating lysis of the blood clots and deficiencies in factor V and fibrinogen. Therapy is directed at the inactivation of fibrinolysin, replacement of the plasma fibrinogen, combating shock by replacement of blood loss and treating the underlying condition. The importance of differentiating the hypofibrinogenemia of intravascular coagulation from that of fibrinolysis is stressed. When excessive intravascular coagulation continues, fibrinogen administration may precipitate the formation of fibrin thrombi with disastrous results. Fibrinolysis, conversely, may demand large amounts of fibrinogen to inactivate the circulating fibrinolysin and arrive at a state homeostasis.

*The Use of Plasmin in the Treatment of Intravascular Thromboses.* Clifton, E. E., New York, USA. J. Amer. Ger. Soc. 6: 118 (1958).

Plasmin (Merck) or Plasminogen (Ortho Pharmaceut. Co.) were intravenously administered to 42 patients with thrombosis and embolism. In most cases this treatment resulted in surprisingly rapid decrease of pains and of the inflammatory process, and in some cases even to lysis of thrombi. Most significant results were obtained in cases of venous thrombosis and of thrombophlebitis, although even some cases of arterial thrombosis were favorably influenced by direct local injection of the enzymes.

*Action of Serotonin on Conversion of Fibrinogen to Fibrin.* Kato, L., Göszy, B., Inst. Microbiol., Univ., Montreal, Canada. Amer. J. Physiol. 195: 66 (1958).

Varying amounts of serotonin increased the coagulation time in vitro in the presence of thrombin. It is shown that serotonin inhibits the conversion of fibrinogen to fibrin.

*Equilibria in the Fibrinogen-Fibrin Conversion. IV. Kinetics of the Conversion of Fibrinogen to Fibrin Monomer.* Ehrenpreis, S., Laskowski, M., Donnelly, T. H., Scheraga, H. A., J. Amer. chem. Soc. 80: 4255 (1958).

*Measurement of the Rate of Plasmin Action on Synthetic Substrates.* Roberts, P. S., Div. Cancer Studies, Med. Coll. Virginia, Richmond, Va., USA. J. biol. Chem. 232: 285 (1958).

The Hestrin ester method was modified to fix the pH of the colored complex, to reduce the concentration of buffer and salts in the colored solution, and to decrease the concentration of ester from the amount needed in the ester-enzyme reaction to a convenient reading range. The rate of the reaction of p-toluenesulfonyl-L-arginine methyl ester (TAME) with alkaline hydroxylamine was found to be slower than that of L-lysine-methyl ester (LME), but it was complete in less than 20 mins. at room temperature with the reagents used here. The activities of a number of enzymes toward both TAME and LME were determined by this method. The enzymes used were plasminogen, as present in human plasma, in serum, or in the euglobulin fraction of the serum, each of which was activated with streptokinase, as well as bovine fibrinolysin and crystalline trypsin.

*Abruptio Placentae and Hypofibrinogenemia.* Pritchard, J. A., Depts. Obst. Gynec., Univ. of Texas, Southwestern Med. School, Dallas, Texas, USA. J. Obstet. Gynec. 76: 347 (1958).

*Studies on the Polymerization of Fibrin. The Role of the Globulin: Fibrin-Stabilizing Factor.* Lorand, L., Jacobson, A., Dept. Chem., Northwestern Univ., Evanston, Ill., USA. J. biol. Chem. 230: 421 (1958).

When fibrinogen is clotted by fibrin in the presence of calcium ions and the fibrin-stabilizing factor of plasma, a clot is obtained which resembles the "plasma clot" in every respect. It cannot be dissolved in urea or in monochloroacetic acid, in contrast to the soluble and mechanically weaker clot formed in the absence of the factor. A method is described for the preparation of highly purified fibrin-stabilizing factor from bovine plasma. The activity is shown to lie in a globulin fraction. All the evidence indicates that the sulfhydryl groups of fibrin-stabilizing factor are important for its biological activity. The insoluble clot, which in the case of bovine and human species, is probably the only naturally occurring one, was shown to be a copolymer of fibrin and the fibrin-stabilizing factor in definite stoichiometric proportions.

*Circulating Fibrinolysin in a Case of Prostatic Carcinoma with Bony Metastases.* Bergen, S., Schilling, F. J., Dept. Med., St. Luke's Hosp., New York, N. Y., USA. Ann. intern. Med. 48: 389 (1958).

A case is presented of prostatic carcinoma with bony metastasis and a demonstrable circulating fibrinolysin causing hypofibrinogenemia. The mechanism and possible effect of this enzyme are discussed.

*Two Possible Cases of Acquired Hypofibrinogenemia in the Newborn.* Boyd, J. F., Path. Dept., Western Infirmary, Glasgow, Scotland. Surg. Gynec. Obstet. 106: 176 (1958).

*Methods for the Evaluation of Human Fibrinolysis.* Kaulla, K. N. von, Schultz, R. I., Dept. Med., Univ. of Colorado Med. School, Denver, Col., USA. Amer. J. clin. Path. 29: 104 (1958).

*Fibrinolysis and Changes in Fibrinogen in Multiple Myeloma.* Sirridge, M. S., Lab. Serv., Hosp., Veterans Administration Center, Wadsworth, Kan., USA. Arch. intern. Med. 101: 630 (1958).

*Effects of Intravenous Human Plasmin on the Blood Clotting Mechanism of the Dog.* Coon, W. W., Duff, I. F., Depts. Surg. and Med., Univ. of Michigan Med. School, Ann. Arbor, Mich., USA. J. Lab. clin. Med. 51: 381 (1958).

These studies suggest that plasmin in sufficient concentration may alter all 3 phases of the clotting mechanism in vivo. The changes are discussed with respect to the clotting abnormality associated with excessive fibrinolysis seen in some patients with a hemorrhagic diathesis. Satisfactory time-dosage infusion data for cautious administration to humans are presented. If satisfactory proteolytic degradation of intravascular clots can be safely obtained with plasmin, it may prove to be a valuable therapeutic agent in certain cases of thromboembolism.

*Experience with a Blood Fibrinogen Bank.* Paxson, N. F., Philadelphia County Med. Soc., Philadelphia, Pa., USA. Amer. J. Obstet. Gynec. 75: 618 (1958).

An analysis of the first 76 obstetrical patients who received fibrinogen from the bank established in Philadelphia shows that there were 67 recoveries and 9 deaths. The fibrinogen was a decisive factor in the recovery of these patients. Fibrinogen, as produced for the American Red Cross, is a relatively safe product as the incidence of hepatitis was only 5%. A supply of 10 gm of fibrinogen should be enough to meet the demands of any case that may develop. This supply might well be pooled by a community of several hospitals for reasons of economy.

*Anticoagulant Effect of Incubated Fibrinogen.* Triantaphyllopoulos, D. C., Dept. Physiol. Pharm., Univ. of Alberta, Edmonton, Alberta, Canada. J. Biochem. Physiol. 36: 249 (1958).

### c) Prothrombin (Factor II), Thrombin

*Blood Prothrombin in Acute Gastro-Intestinal Haemorrhage.* Ofstad, J., Med. afdeling, Fylkesjukehuset, Kristiansund, Norway. Nord. Med. 60: 1754 (1958).

Blood prothrombin time was studied in 16 cases of acute gastro-intestinal hemorrhage. In several cases a transient reduction of the prothrombin activity in connection with the bleeding was demonstrated. The significance of the observation is discussed. A temporary impairment of the liver function seems to be the most probable explanation of the phenomenon.

*The Mode of Action of Thrombin.* Laki, K., Gladner, J. A., Folk, J. E., Kominz, D. R., Nat. Inst. Arthritis and Metabolic Disease, Nat. Inst. of Health, U.S. Dept. Health, Education and Welfare, Bethesda, Md., USA. Thromb. Diath. haem. 2: 207 (1958).

*Action of Thrombin on Plasma Digested Fibrinogen.* Wallen, P., Bergström, K., Stockholm, Sweden. Acta chem. scand. 12: 574 (1958).

*The Synthesis of Prothrombin and Proconvertin in the Reticulo-Endothelial System. An Experimental Study on Rats.* Slätis, P., IV Med. Univ. Clinic, Maria Hosp., Helsingfors, Finland. Scand. J. clin. Lab. Invest. 10, suppl. 33 (1958).

*Comparative Kinetic Behaviour of Thrombin, Plasmin, and Trypsin Toward Synthetic Substrates.* Scheraga, H. A., Dept. Chem., Cornell Univ., New York, N. Y., USA. Nature (Lond.) 182: 461 (1958).

*Bemerkungen zur Bestimmung der Gerinnungsvalenz nach Quick und zum Thrombokinaseproblem.* Kranz, H., Würzburg, Germany. Ärztl. Wschr. 13: 882 (1958).

*Die Reaktion zwischen Hirudin und Thrombin.* Markwardt, F., Walsmann, P., Pharm. Inst., Univ., Greifswald, Germany. Hoppe Seyler's Z. physiol. Chem. 312: 85 (1958).

*Prothrombinverbrauch und Bromsulphaleintest bei Blutkrankheiten. II. Mitteilung.* Brichta, G., Kühböck, J., Reimer, E. E., Wien, Austria. Dtsch. Arch. klin. Med. 204: 310 (1958).

*Zur Frage der Existenz zweier Aktivitätsformen des Prothrombins.* Schröder, H., Würzburg, Germany, Pflügers Arch. ges. Physiol. 268: 53 (1958).

*Über das thrombinähnlich wirkende Prinzip von Jararacagift.* Habermann, E., Pharm. Inst., Univ. Würzburg, Germany. Naunyn-Schmiedeberg's Arch. exp. Path. Pharm. 234: 291 (1958).

*Zur Anwendung der Thrombinpräparate.* Mlzoč, R., II. Chir. Univ.-Klinik, Wien, Austria. Wien. med. Wschr. 108: 848 (1958).

*Activation of Prothrombin.* Landaburu, R. H., Seegers, W. H., Dept. Physiol. and Pharm., Wayne State Univ. Coll. of Med., Detroit, Mich., USA. Amer. J. Physiol. 193: 169 (1958).

In experiments with purified biotrombin it was found that strong solutions of sodium citrate or protamine sulfate or purified platelet factor 3 depress the esterase activity and leave the clotting power unaltered. Apparently a depression of esterase activity is beneficial for the autocatalytic activation of purified prothrombin. In protamine sulfate solution, prothrombin gradually becomes thrombin. Prothrombin also depresses the esterase activity of biotrombin, and itself serves as a substrate for the enzyme thrombin. When prothrombin becomes an inactive derivative it can nevertheless be changed to thrombin with the use of thrombin as a catalyst. Thrombin as activator of prothrombin can account for all observed conditions of prothrombin activation. Other factors support the production and enzymic function of thrombin, they are called procoagulants as opposed to anticoagulants.



*Activation of Prothrombin with Thrombin.* Fukutake, K., Min, H. Cho, Seegers, W. H., Dept. Physiol. and Pharm., Wayne State Univ. Med. Coll., Detroit, Mich., USA. *Amer. J. Physiol.* 194: 280 (1958).

Mixtures were made consisting of purified prothrombin as substrate and purified thrombin as activator. During an observation time of 90 mins. prothrombin activates and some thrombin is formed. If purified platelet factor 3, or purified platelet co-factor I, or the lipid portion of platelet factor 3, or a certain lipid preparation are also added separately all of the prothrombin substrate becomes thrombin. Each substance is a procoagulant in the sense of functioning in support of prothrombin as activator. Each procoagulant is more active together with Ac-globulin (factor V), and even with the latter present sphingosine inhibits the activation of prothrombin by thrombin.

*Action of Erythrocyte Extract on the Prothrombin Consumption Test.* Stanski, F., Quicke, A. J., Dept. Biochem., Marquette Univ. Med. School, Milwaukee, Wisc., USA. *Amer. J. Physiol.* 194: 527 (1958).

The addition of human erythrocyte extract to blood or plasma before coagulation increases prothrombin consumption markedly, except in platelet-poor rabbit plasma. If stored serum is simultaneously added to platelet-poor rabbit plasma prothrombin consumption increases too. This effect of stored serum is also noted with stored hemophilia A serum but is lacking in serum of a patient with hemophilia B.

*An Analysis of Human Prothrombin by Starch Block Electrophoresis.* Lachantin, G. F., Los Angeles, Calif., USA. *Amer. J. Physiol.* 194: 7 (1958).

Based on experiments with starch block electrophoresis it is concluded that a prothrombin-like factor is also needed for the transformation of human prothrombin to thrombin.

*Residual Serum Thrombin Activity.* Weiner, M., New York, USA. *Clin. Chem.* 4: 271 (1958).

The author describes a method of residual serum thrombin activity determination. In cases of prothrombin deficiency, of acute pancreatitis, and in patients with 2 daily injections of "Varidase" the residual thrombin was decreased. In one case of hypofibrinogenemia the residual thrombin activity was markedly increased.

*The Feasibility of Using Finger Blood for Prothrombin Determinations.* Reich, C., New York, N. Y., USA. *Amer. J. clin. Path.* 30: 19 (1958).

*Thrombin and its Interaction with Fibrinogen.* Scheraga, H. A., Dept. Chem. Cornell Univ., Ithaca, N. Y., USA. *Ann. N. Y. Acad. Sci.* 75: 189 (1958).

Thrombin, like trypsin, has hydrolytic activity toward arginyl and lysyl ester and peptide bonds in several synthetic and protein substrates. In fibrinogen, the action of thrombin appears to be specific for two arginyl-glycine bonds to liberate peptide material and "expose" the donor groups required for the subsequent polymerization. Thrombin does not take part in the polymerization steps. Hydrogen bonding between side-chain polar groups plays an important role in the various equilibria in the fibrinogen-fibrin conversion.

*Experience with the TAME Assay During Anticoagulant Therapy.* Auscott, P. M., Koppel, J. L., Olwin, J. H., Coagulation Lab., Dept. Surg., Presbyterian-St.-Luke's Hosp., Chicago, Ill., USA. *J. Lab. clin. Med.* 51: 805 (1958).

Two-stage and TAME prothrombin determinations have been carried out on plasmas from patients on 8 different anticoagulant drugs. For clinical purposes, the results obtained with the TAME assay have been found to compare favorably with those provided by the two-stage technic regardless of which of the 8 drugs was used. The concept of "effective thrombic activity" has been introduced and discussed in regard to the possible accelerator and/or inhibitor content of the thromboplastin preparation used in the TAME assay.

*Further Studies on the Purification of Thrombin.* Seegers, W. H., Dept. Physiol. Pharm., Wayne State Univ., Detroit, Mich., USA. *Canad. J. Biochem. Physiol.* 36: 603 (1958).

*Is Thrombin the Only Enzyme Involved with Prothrombin Activation?* Seegers, W. H., Dept. Physiol. and Pharm., Wayne State Univ. Med. Coll., Detroit, Mich., USA. *Ann. N. Y. Acad. Sci.* 75: 182 (1958).

#### d) Thromboplastin (Factor III)

*The Inactivation of Plasma Thromboplastin,* Deutsch, E., Mammen, E., Central Coagulation Lab., First Med. Dept., Univ. of Vienna Med. School, Vienna, Austria. *Thromb. Diath. haem.* 2: 324 (1958).

*Use of Different Tissue Thromboplastins in the Control of Anticoagulant Therapy.* Verstraete, M., Clark, P. A., Wright, I. S., Vasc. Sec. Dept. Med., New York Hosp., New York, N. Y., USA. *Thromb. Diath. haem.* 2: 462 (1958).

*Thromboplastic Activity of the Plasma in Paroxysmal Nocturnal Haemoglobinuria.* McKellar, M., Dacie, J. V., Dept. Haematol., Postgraduate Med. School, London, England. *Brit. J. Haematol.* 4: 404 (1958).

The liberation of "non-hemolytic thromboplastic activity" from paroxysmal nocturnal hemoglobinuria red cells during incubation is described and the nature and significance of this activity is discussed. The abnormality, although characteristic of PNH, is not confined to this disease. Similar changes have been observed in sickle-cell anemia and in congenital non-spherocytic hemolytic anemia. Redcell hemolysates possess potent thromboplastic properties in vitro, and it is possible that products of hemolysed red cells together with the "non-hemolytic thromboplastic activity" here demonstrated are important in relation to the occurrence of thrombosis in vivo in PNH and possibly in other hemolytic disorders. Their importance probably depends upon the quantity of material liberated and the rate of its liberation into the circulation.

*Diathèses hémorragiques et déficience thromboplastique.* Verstraete, M., Lab. Physiopath., Serv. de Méd. int., Univ. Louvain, Belgique. *Sem. Hôp. Paris* 34: no. 53 (1958).

Hemorrhagic diatheses due to delayed or incomplete thromboplastin formation can have a variety of causes: 1. decreased level of factor VIII in man or homozygote females. 2. deficiency of factor IX. 3. deficiency of PTA. 4. combined deficiency of factor VIII and IX. 5. presence of circulating anticoagulant in one of the mentioned forms of hemophilia. 6. the presence of an anticoagulant in the non-hemophilic male. 7. circulating anticoagulant in the normal or the pregnant woman. 8. factor VIII deficiency of spontaneous occurrence in the female, usually combined with a vascular disorder. 9. decreased number or dysfunction of platelets. The relative frequency of these various disorders, their characteristics, the tests for their differential diagnosis and the methods used are described and discussed.

*Zur chemischen Konstitution des Lipoids der Gewebethrombokinase.* Kuhn, R., Klesse, P., Max-Planck-Inst. für med. Forsch., Heidelberg, Germany. *Hoppe Seyler's Z. physiol. Chem.* 312: 214 (1958).

*Thromboplastic and Fibrinolytic Activity of Human Synovial Membrane and Fibrous Capsular Tissue.* Astrup, T., Sjölin, K. E., Biol. Inst., Carlsberg Foundation, Copenhagen, Denmark. *Proc. Soc. exp. Biol. (N. Y.)* 97: 852 (1958).

Human synovial tissue and fibrous capsular tissue contain no or only traces of tissue thromboplastin. An activator of plasminogen of the tissue type is present in low (but varying) concentrations in both tissues.

*The Effect of Protamine on Thromboplastin Generation.* Shanberge, J. N., Barlas, A., Regan, E. E., Dept. Path., Harvard Med. School, Boston Mass., USA. J. Lab. clin. Med. 52: 744 (1958).

Protamine sulfate markedly inhibits the formation of plasma thromboplastin activity as measured in the thromboplastin generation test. Protamine has less effect on "formed thromboplastin" after the point of optimum generation. The inhibition of thromboplastin generation by protamine appears to be due to interference with PTC activity. The inhibition of thromboplastic activity by protamine can be counteracted by heparin. Twice as much heparin is required to neutralize the protamine effect before generation is started than is required to correct thromboplastic activity after beginning generation in the presence of protamine.

*Purification and Identification of Brain Phospholipides Associated with Thromboplastic Activity.* Theriault, D., Nichols, T., Jensen, H., Biochem. Dept., United States Army Med. Research. Lab., Fort Knox, Ky., USA. J. biol. Chem. 233: 1061 (1958).

Phosphatidyl serine and lecithine have been isolated from beef brain tissue by means of countercurrent distribution and identified. Neither phosphatidyl serine nor lecithine alone possesses any appreciable thromboplastic activity. When lecithine and phosphatidyl serine are dissolved together in chloroform, however, a potent thromboplastic substance results.

*The Coagulation of Blood by Russell's Viper Venom.* Peden, J. C., Peacock, A. C., Clin. Path. Dept., Nat. Insts. of Health, Bethesda, Md., USA. J. Lab. clin. Med. 52: 101 (1958).

*Thromboplastin: Nomenclature and Preparation of Protein-Free Material Different from Platelet Factor 3 or Lipid Activator.* Hecht, E. R., Min, H. Cho, Seegers, W. H., Dept. Physiol. and Pharm., Wayne State Univ. Med. Coll., Detroit, Mich., USA. Amer. J. Physiol. 193: 584 (1958).

A method was developed for obtaining a highly active fraction from rabbit brain tissue which meets all the requirements of a complete thromboplastin. This lipid fraction contains no protein. When the brain thromboplastin is combined with Ac-globulin and calcium ions, purified prothrombin changes to biotrombin, but such a change does not occur when purified platelet factor 3 or lipid activator replaces the brain thromboplastin. The characteristics of this thromboplastin are discussed.

*Phospholipid Structure and Thromboplastic Activity. I. The Phosphatide Fraction Active in Recalcified Normal Human Plasma. II. The Fatty Acid Composition of the Active Phosphatidyl Ethanolamines.* Rouser, G., White, S. G., Schloredt, D., Duarte, Calif., USA. Biochim. Biophys. Acta 28: 71 and 81 (1958).

Among various phospholipids phosphatidyl acid and phosphatidyl ethanolamine were found to enhance coagulation of platelet-poor recalcified human plasma. It is demonstrated that the activation of thromboplastin is indirectly proportional to the saturation of the fatty acid of the phosphatidyl ethanolamine.

*Effect of Intravenous Blood Thromboplastin Intermediates on Clotting in Rats.* Spaet, T. H., Kropatkin, M., Dept. Hemat., Montefiore Hosp., New York City, N. Y., USA. Amer. J. Physiol. 195: 77 (1958).

Following the intravenous injection of 2 cc of thromboplastin or product II (Bergsagel and Hougie) in rats a defibrination syndrome occurred. On the other hand, the intravenous injection of single elements of thromboplastin had no effect on coagulation.

### f) Factor V (and VI)

*Déficit congénital en proaccélérine (Facteur V). Quelques données nouvelles.* Soulier, J. P., Wartelle, O., Weilland, C., Ménaché, D., Centre National Transfusion Sang., Paris, France. Thromb. Diath. haem. 2: 250 (1958).

*Experimentelle und klinische Untersuchungen bei isoliertem Faktor-V-Mangel.* Hörder, M. H. Klin. Wschr. 36: 1173 (1958).

Experiments with the plasma of a case of congenital factor V deficiency showed that factor V is essential for the formation of blood thromboplastin and that the so-called platelet factor I probably consists of factor V adsorbed by platelets. Factor V thus takes part twice in the process of coagulation: late in the phase of blood thromboplastin formation and in the formation of thrombin from prothrombin. The following characteristics of factor V deficiency were established: The disease occurs in both sexes and part of the family members also show decreased factor V levels. First signs of bleeding appear predominantly during childhood. Joint bleedings are very rare.

*Function of Ac-Globulin Utilizing TAME Synthetic Substrate Assay Method for Determination of Prothrombin.* Glueck, H. I., Cincinnati, O., USA. Amer. J. Physiol. 194: 285 (1958).

*Role of Plasma Accelerator — Globulin and Serum Accelerator — Globulin in Conversion of Prothrombin.* Johnston, B. R., Jensen, H., Fort Knox, Kentucky, USA. Amer. J. Physiol. 194: 1 (1958).

### g) Factor VII

*Über den Erbgang bei kongenitalem Faktor-VII-Mangel.* Zollinger, W., Hitzig, W. H., Gerinnungsphysiol. Labor., Med. Univ.-Klinik, Zürich, Switzerland. Helv. med. Acta 25: 475 (1958).

Factor VII deficiency was demonstrated in a 5-days-old girl suffering from a hemorrhagic diathesis. 1% of normal factor VII activity was found. The girl's elder brother had died at the age of one following intestinal hemorrhage. In the girl transfusions of whole blood and of plasma as well as injection of a concentrated factor VII preparation (Acc 76) were successful, whereas vitamin K<sub>1</sub> had no effect. Family history revealed consanguinity of the parents. 19 of 100 family members showed factor VII levels around 50% of normal values. Factor VII deficiency is found to be inherited as an autosomal characteristic with normal homozygotes, and pathologic heterozygotes and homozygotes, whereby clinically factor VII deficiency is found to be a recessive disease.

*Congenital Deficiency of Factor VII.* Pitney, W. R., Dept. Hematol., Royal Perth Hosp., Western Australia. Aust. Ann. Med. 7: 15 (1958).

Laboratory investigations are described in a female patient who suffers from congenital factor VII deficiency. The patient provides the 8th recorded case of factor VII deficiency with the following characteristic findings: Prolonged one-stage prothrombin time with brain extract, and normal with viper venom. All tests of the intrinsic coagulation mechanism, including thromboplastin generation, were normal. Evidence is presented indicating that factor VII consists of at least 2 compounds. The factor VII component deficient in the patient described is reduced early in "Dindevan" therapy. The patient has 3 children, all with reduced factor VII levels. It is suggested that the children represent the heterozygous state of factor VII deficiency and that the defect is transmitted in recessive manner.

*Il deficit congenito del fattore VII.* Vanacore, C., Grifoni, V., Visca, U., Ist. Patologia Spec. Med., Univ. Milano, Italy. Haematol. lat. 1: 265 (1958).

A case of hemorrhagic disease due to congenital factor VII deficiency has been studied. The available literature on the subject is reviewed.

*Congenital Hypoproconvertinemia.* Creveld, S. van, Veder, H. A., Pediatric Clinic, Univ. Amsterdam, Holland. Ann. paediat. 190: 316 (1958).

The authors describe a second family with two boys suffering from congenital factor VII deficiency with fatal cerebral hemorrhage. Consanguinity was established in parents. The

necessity of differentiation between Stuart factor deficiency and hypoprothrombinemia is pointed out.

*Activation of Factor VII by Asbestos in Beef Plasma and Serum.* *Israel, L. G.*, Dept. Biochem., Univ. of Manitoba, Winnipeg, Manitoba, Canada. *Canad. J. Biochem. Physiol.* 36: 953 (1958).

#### **h) Factor VIII (Antihemophilic Globulin)**

*Primi risultati sulla separazione della globulina anti-emofilica dal fibrinogeno nella frazione I di Cohn da plasma umano normale.* *Conte Marotta, R., Rostiglione, F., Romano, E., Giardiello, G.*, Ist. Semeiotica med., Univ., Napoli, Italy. *Haematol. lat.* 1: 132 (1958).

The different attempts made, as reported in the literature, to separate fibrinogen and antihemophilic globulin, are discussed. The first data obtained by the authors with a careful thermocoagulation of fibrinogen of human Cohn fraction I are illustrated. The new preparation obtained possessed satisfactory activity in vitro as it corrected coagulation time, prothrombin consumption and thromboplastin generation of hemophilic blood. Primary fraction I, devoid of coagulation factors absorbable on barium sulfate, maintained its capacity of correcting coagulation time and prothrombin consumption of hemophilic blood.

#### **i) Factor IX (Christmas Factor, PTC)**

*The Christmas Factor Deficiency in Coumarin Therapy.* *Douglas, A. S., Mair, K.*, Univ. Dept. Med., Royal Infirmary, Glasgow, Scotland. *Clin. Sci.* 17: 445 (1958).

Evidence is described indicating a deficiency of the Christmas factor as part of the defect in coumarin drug therapy. The deficiency has been demonstrated by the impaired ability of phenindione plasma to correct the prolonged recalcification time and the defective prothrombin consumption of recalcified Christmas disease plasma. There is impaired ability of the phenindione serum to correct the thromboplastin generation of Christmas disease serum and the thrombin-thromboplastin generation from Christmas disease plasma. This deficiency of Christmas factor is well established 48—72 hours after the commencement of treatment.

*The Demonstration of the Carrier State in Christmas Disease.* *Firkin, B. G.*, Clinical Research Unit, Royal Prince Alfred Hosp., Sydney, Australia. *Med. J. Aust.* 45: 557 (1958).

A slight modification of the thromboplastin generation test enabled the detection of a subnormal level of Christmas factor in the serum of 5 Christmas disease carriers who were examined. The demonstration of subnormal levels of Christmas factor in 2 of 3 patients with liver disease suggests that Christmas factor is synthesized in the liver. It is unrelated to the synthesis of the factors concerned with a normal prothrombin time.

*The One-Stage Method for the Assay of Antihemophilic Factor B.* *Stapp, W. F.*, Inst. for Thrombosis Research, Dept. Med., Univ. Hosp., Oslo, Norway. *Scand. J. clin. Lab. Invest.* 10: 169 (1958).

*Die Fertilität im Bluterstamm von Tenna (Hämophilie B).* *Rosin, S., Moor-Jankowski, J. K., Schneeberger, M.*, Zool. Inst., Univ. Bern, Switzerland. *Acta genet. (Basel)* 8: 1 (1958).

An attempt has been made to calculate the fitness of bleeders and female carriers belonging to the kindred of hemophiliacs (B) originating from Tenna. The fitness of the bleeders ( $f = 0.64$ ) is considerably higher than values reported by Haldane or Vogel. The fitness of the female carrier is  $g = 1.22$ . It is shown that a fitness of bleeders of 0.64 can be balanced by a fitness of female carriers of 1.22 without the occurrence of mutations. The order of magnitude of fitness values in the Tenna kindred leads to the conclusion that the selection in the bleeders could be countered by the increased number of children of the female carriers. If similar results were obtained by further investigations on other kindreds with hemophilia B, it could mean that the rate of mutation is much lower than reported so far.

**k) Other Factors (Stuart, PTA, Hageman etc.)**

*Role of Hageman Factor in the Initiation of Clotting by Glass. Evidence that Glass Frees Hageman Factor from Inhibition.* Ratnoff, O. D., Rosenblum, J. M., Dept. Med., Western Reserve University Med. School, Cleveland, O., USA. Amer. J. Med. 25: 160 (1958).

Evidence is presented that the clot-promoting effect of glass or of certain other adsorbents upon normal human plasma requires the presence of Hageman factor. Human or duck plasma, deficient in Hageman factor, inhibited the clot-promoting effect of glass or barium carbonate upon normal human plasma. The clot-promoting property of normal human plasma, once activated, deteriorated rapidly, apparently as the result of enzymatic destruction. These observations suggest that the fluidity of blood within blood vessels may be maintained by inhibitors directed against Hageman factor.

*Surface Activation of Plasma Clotting.* Johnston, C. L. Ferguson, J. H., O'Hanlon, F. A., Dept. Physiol., Univ. N. Carolina, Chapel Hill, N. C., USA. Proc. Soc. exp. Biol. (N. Y.) 99: 197 (1958).

Asbestos treatment of plasma produced activation (clotting time acceleration) in normal and AHF, PTC, proconvertin, prothrombin, proaccelerin and Stuart deficient plasma, Hageman deficient plasma was not activated by comparable treatment. Purified Hageman factor preparations from normal sera simulated activation, whereas preparations from sera of Hageman trait patients were inactive in the same test system. The phenomenon of surface activation resulted from Hageman factor activation and was not due to inhibitor adsorption. Asbestos treatment of plasma may be used as a presumptive test for Hageman trait.

*Evidence that Glass Increases Plasma PTA Activity.* Rapaport, S. I., Dept. Med., Univ. of California Med. Center, Los Angeles, Calif., USA. J. Lab. clin. Med. 52: 624 (1958).

Plasma from 3 patients with PTA deficiency was shaken with glass beads to make a glass-activated substrate plasma. The prolonged partial thromboplastin time of this PTA-deficient substrate plasma was effectively shortened by glass-activated normal plasma but not by normal plasma that had been exposed only to silicone-coated surfaces. This is strong evidence that exposure to glass increases plasma PTA activity, and suggests that PTA may exist in circulating plasma largely, if not entirely, in an inactive state.

*Der Gerinnungsdefekt beim kongenitalen PTA-Mangel.* Bachmann, F., Duckert, F., Fisch, U., Streuli, F., Gerber, D., Koller, F., Gerinnungsphysiol. Lab., Med. Univ.-Klinik, Zürich, Switzerland. Schweiz. med. Wschr. 88: 1037 (1958).

Two patients with moderate PTA deficiency are described. Neither patient suffered from spontaneous bleeding, but both manifested definite hemorrhagic tendency after surgical intervention and tooth extraction. The most significant features of the clotting defect were prolonged clotting time, highly pathologic prothrombin consumption, and defective thromboplastin generation in the combination of serum and plasma from the patient. By means of paper electrophoresis a protein fraction could be obtained containing minimal amounts of all known clotting factors but high PTA activity. These results suggest that PTA is an entity. Various experiments lead to the hypothesis that PTA acts on a very early stage of blood thromboplastin formation and is necessary for the activation of factor IX.

*The Properties of Thrombinogen.* Ronwin, E., Dept. Pharm., Univ. S. California, School of Med., Los Angeles, Calif., USA. Canad. J. Biochem. Physiol. 36: 75 (1958).

Evidence is given which demonstrates the existence of an intermediate, designated thrombinogen, during the conversion of prothrombin to thrombin. The conversion of prothrombin to thrombinogen requires thromboplastin. The conversion of thrombinogen to thrombin requires thrombin, though other tryptic enzymes can replace thrombin. The properties of thrombinogen have been studied.



*Neue Möglichkeiten für die Abklärung von Gerinnungsstörungen.* Fisch, U., Duckert, F., Koller, F., Gerinnungsphysiol. Lab., Med. Univ.-Klinik, Zurich, Switzerland. Schweiz. med. Wschr. 88: 1045 (1958).

Separation of serum clotting factors was obtained by means of paper electrophoresis. Stuart-Prower factor is distinctly separated from factor VII and from the other serum factors. A new clotting factor necessary for blood thromboplastin formation was found. It is clearly separated from Stuart-Prower factor but not completely from factor VII. This factor, as measured with a one-stage assay method, showed factor IX-like activity. Further experiments indicated that it acts only on the rate of thromboplastin formation and that it could not normalize the clotting defect of factor IX-deficiency (hemophilia B). This new clotting factor is called "Prephase Accelerator".

*Hageman Factor in Plasma Foreign Surface Reactions.* Margolis, J., Pharm. Dept., Middlesex Hosp., Med. School, London W 1, England. Nature (Lond.) 182: 1103 (1958).

*Peculiar Disorder of Plasma Thromboplastin Production.* Nour-Eldin, F., Dept. Hemat., Royal Infirmary, Manchester, England. Nature (Lond.) 181: 989 (1958).

*Déficit en facteur Stuart. Etude biologique.* Caen, J., Beaumont, J., Serv. Jean Bernard, Hôp. Saint-Louis, Paris, France. Rev. franç. Etudes clin. biol. 3: 161 (1958).

The authors have restudied the blood of the child previously diagnosed as a case of congenital hypoconvertinemia. They found that the patient actually suffered from Stuart factor deficiency as described by Hougie, Barrow and Graham.

*Un nuovo fattore della emocoagulazione (fattore Stuart) e la sua importanza in campo pediatrico.* Vecchio, F., Ist. Clin. Ped., Univ., Napoli, Italy. Pediatria (Napoli) 66: 169 (1958).

*Electrophoretic Studies of The Prower Factor; A Blood Coagulation Factor which Differs from Factor VII.* Denson, K. W., Path. Dept., St. Pancras Hosp., London N.W. 1, England. Brit. J. Haematol. 4: 313 (1958).

A female patient (Prower) suffering from a congenital hemorrhagic disease has been restudied and is now considered to be deficient in both Prower factor and factor VII. Prower factor and factor VII are both deficient in patients treated with Dindevan, and Russell's viper venom acts as an incomplete thromboplastin in the absence of Prower factor. The characteristics of the Prower factor are discussed. Differentiation of Prower factor- and factor VII-deficiency is outlined. The Prower factor is probably concerned with the formation of an intermediate product of thromboplastin, and it is probably identical with factor X and the Stuart factor.

*Activation of a Permeability Factor in Plasma by Contact with Glass.* Margolis, J., Pharm. Dept., Middlesex Hosp., Med. School, London W 1, England. Nature (Lond.) 181: 635 (1958).

### 1) General Aspects of Hemophilia

*The Hemophilic Syndrome: A Review of 27 Cases.* Thomas J. W., Whitelaw, D. M., Perry, W. H., Canad. med. Ass. J. 79: 100 (1958).

The authors examined 24 patients with AHG deficiency and 3 patients with Christmas factor deficiency, in order to evaluate and correlate the results of the thromboplastin generation test and the new methods of assaying the AHG defect with the clinical picture in patients with the hemophilic syndrome. The thromboplastin generation test made differentiation between the 2 deficiencies in all cases possible. The percentage of thromboplastin generated varied from 3 to 38%. The antihemophilic globulin level varied from 0.1 to 6%. The authors believe that the percentage of thromboplastin generated is of the greatest value in the diagnosis and differentiation of hemophilic disorders.

*Lipoprotein-Bound Cholesterol in Hemophilic Serum.* Barkhan, P., Dept. Med., Univ. of Cambridge, England. *Lancet* 1: 773 (1958).

The amounts of total and lipo-protein-bound cholesterol in the serum were determined in healthy people and in hemophiliacs. The mean total cholesterol level in the hemophiliacs was significantly lower than that in healthy people. The percentage of cholesterol in the beta-lipoprotein of the hemophiliacs was not significantly different from that of healthy people.

*The Secondary Bleeding Time. A New Method for the Differentiation of Hemorrhagic Diseases.* Borchgrevink, C. F., Waaler, B. A., Inst. of Thrombosis Research, Univ. Hosp., Rikshosp., Oslo, Norway. *Acta med. scand.* 162: 362 (1958).

A method for estimation of the secondary bleeding time is described. The secondary bleeding time is prolonged when the intrinsic blood clotting system is disturbed such as in hemophilia and proaccelerin (V) deficiency. In these conditions the primary bleeding time is almost normal. In thrombocytopenia both the primary and secondary bleeding time are prolonged. In the estimation of both bleeding times cuts of 12—14 mm length are recommended as smaller cuts will not yield the same clear results. With the exception of hemophilia the prevalence of deficiencies in clotting factors essential to the intrinsic clotting system is very low. The secondary bleeding time may thus be used as a diagnostic test in hemophilia. As such it is fairly sensitive, disclosing even mild cases.

*Hemophilia and Related Conditions: A Survey of 187 Cases.* Biggs, R., Macfarlane, R. G., Dept. Path., Radcliffe Infirmary, Oxford, England. *Brit. J. Hematol.* 4: 1 (1958).

187 unrelated patients with constitutional hemorrhagic diathesis are reviewed. Of these 138 had hemophilia A, 20 had Christmas disease, 2 developed circulating anticoagulants, 3 had Rosenthal's syndrome, 11 had v. Willebrand's disease and in 13 instances the type of anomaly was not identified. Study of hemophilia reveals an apparent excess of affected male patients. Of the hemophilic patients, 48 were moderately or mildly affected with AHG levels from 1 to 40%. Information about Christmas disease is much less complete than that about hemophilia. A high proportion of the patients studied were mildly affected. Quantitative tests have not proved as useful in assessing the effects of treatment as in hemophilia. Some female carriers of hemophilia and Christmas disease have given abnormal laboratory tests. The level of AHG was reduced in 11 patients with v. Willebrand's disease.

*Rapports entre hémostasie et tests de la coagulation dans l'hémophilie.* Introzzi, P., Pavia, Italy. *Schweiz. med. Wschr.* 88: 1044 (1958).

*Les altérations articulaires dans l'hémophilie. Images radiologiques tomographiques et agrandis directement.* Svoboda, M., Maly, V., Inst. Hématol. et de la Transfusion sang., Prague. *J. Radiol. Electrol.* 39: 610 (1958).

*Síndrome de Volkmann en un hemofílico. Tratamiento por la operacion de Page-Scaglietti.* Izarn, P., Inst. Hematol., Montpellier, France, *Sangre* 3: 143 (1958).

*Die hämophilen Syndrome (AHG, PTC, PTA) und ihre Behandlung.* Schmutzler, R., Med. Univ., Rostock, Germany. *Z. ges. inn. Med.* 13: 841 (1958).

*Observations on Hemophilia, Parahemophilia, and Coexistent Hemophilia and Parahemophilia. Alterations in the Platelets and the Thromboplastin Generation Test.* Seibert, R. H., Margolius, A., Ratnoff, O. D., Dept. Med., Western Reserve Univ. Med. School, Cleveland, Ohio, USA. *J. Lab. clin. Med.* 52: 449 (1958).

Cases of parahemophilia and coexistent hemophilia and parahemophilia are described. The coexistence of these 2 defects suggests a common step in the syntheses of antihemophilic factor

and proaccelerin. That hemophilic platelets are deficient in antihemophilic activity and parahemophilic platelets in proaccelerin-like activity has been confirmed. These defects are correctible by incubating the abnormal platelets with normal plasma. The defect measured in the thromboplastin generation test was exaggerated in parahemophilia by the use of parahemophilic platelets and a substrate of parahemophilic plasma. The significance of these observations in relationship to the mechanism measured by this test is discussed.

*Properdin Assay and Levels in Various Blood Diseases.* DeWitt, H., Hill, J. M., Dallas, Texas, USA. Amer. J. clin. Path. 29: 128 (1958).

The authors describe a simple and accurate method for the determination of properdin. Properdin levels, as measured by this method, were markedly decreased in serum of patients with chronic or acute leukemia, but normal in cases of hemophilia or pregnancy anemia.

*Diagnosis and Control of the Hemophiloid States with the Partial Thromboplastin Time (PTT) Test.* Rodman, N. F., Dept. Path., Univ. N. Carolina, Chapel Hill, N. Carolina, USA. Amer. J. clin. Path. 29: 525 (1958).

### m) Combined Deficiencies

*Hemorrhagic Capillary Disorder Associated with Antihemophilic Globulin Deficiency.* Valberg, L. S., Brown, G. M., Medicine (Baltimore) 37: 181 (1958).

*Schwere transitorische hämorrhagische Diathese in der Gravidität. Thrombokinasintoxikation durch vorzeitige Abruption placentae bei familiärer Purpura simplex.* Marx, R., Pfaller, G., I. Med. Univ.-Klinik, München, Germany. Blut 4: 212 (1958).

*Dominante, milde Hämophilie AB mit verlängerter Blutungszeit — Untergruppe der Pseudo-hämophilien.* Marx, R., Frubmann, G., I. Med. Univ.-Klinik, München, Germany. Klin. Wschr. 36: 1109 (1958).

The authors report upon a family (61 members) with a dominant, hereditary hemorrhagic diathesis characterized by nose bleeding, a combined mild deficiency of factor VIII und IX, and prolonged bleeding time. It is interesting to note that among the members single individuals with normal bleeding time and others with only factor VIII deficiency and temporarily increased bleeding time were found. The ancestor of this family was found to have 16 living children (11 bleeders) and 22 living grandchildren (6 bleeders).

*Etudes sur la coagulation sanguine chez le nouveau-né. Apport de la thrombélagraphie.* Venezia, R., Alger. Pédiatrie 13: 571 (1958).

Normal newborns, on term or premature, show characteristic alteration of blood coagulation, namely hypoprothrombinemia and hypoproconvertinemia. Factor V, normal or even increased in the mature newborn, is slightly decreased in the premature. The authors furthermore found a deficiency of antihemophilic factor (A or B?). These deficiency can clearly be demonstrated by thrombelastography.

*Hemorrhagic Diathesis in Carcinoma of the Stomach: A Case Report.* Biben, R. L., Tyan, M. L., Dept. Med., Univ. California Med. School, San Francisco, California, USA. Ann. intern. Med. 49: 917 (1958).

A case is presented of carcinoma of the stomach complicated by an acute bleeding diathesis due to thrombocytopenia, hypofibrinogenemia, hypoprothrombinemia and decrease in stable and labile prothrombin conversion factors. A brief review of the literature and discussion of possible mechanism involved are presented.

*Deletion of Plasma Thromboplastin Factor D Deficiency.* Spaet, T. H., Ratnoff, O. D., Graham, J. B., Schulman, I., Rosenthal, R. I., Dept. Hemat., Lab. Div., Montefiore Hosp., New York, N. Y., USA. J. Lab. clin. Med. 52: 634 (1958).

A patient previously reported to be deficient in plasma thromboplastin D (PTF-D) has been found to have mild PTC (Factor IX) deficiency probably associated with a circulating anticoagulant.

*Über eine Gerinnungsstörung bei einem Patienten mit multiplem Myelom.* Benda, L., Deutsch, M., Mammen, E., Med. Univ.-Klinik Wien, Austria. Wien. klin. Wschr. 70: 559 (1958).

The authors report upon the case of a 63-year-old man with multiple myeloma and hemorrhagic diathesis. In vitro native blood of the patient showed rapid sedimentation of the red cells whereas the supernatant gelatinized. No retraction occurred although number of platelets was normal. High-speed centrifugation yielded only minimum quantities of serum. This points to a disorder of the second phase of coagulation. Thrombin coagulation time was markedly increased. Antithrombin II was markedly increased and could be normalized with protamine sulfate. It was found that the pathologic myeloma protein inhibited the coagulation of normal serum. Comparison with other cases of myeloma reveals a characteristic disturbance of coagulation: Gelatinized clots without retraction, prolonged thrombin time, pathologic values of thrombin inhibitor, inhibition of thrombin time in normal serum following addition of patient's plasma. Slight increase of coagulation time in glass and of recalcification time. Decreased heparin tolerance. Various other factors may be diminished.

*Normalisierung der Blutungszeit durch Traumatisierung des Gewebes bei Patienten mit der äländischen Blutungskrankheit (v. Willebrand-Jürgens).* Wegelius, O., IV. Med. Univ.-Klinik, Helsingfors, Finland. Thromb. Diath. haem. 2: 342 (1958).

*Simultaneous Occurrence of Moderate Hemophilia and Thrombopathy in One Family.* van Creveld, S., Everts-Coster, C., Veder, H. A., Pediatric Clinic, Amsterdam, Holland. Ned. T. Geneesk. 102: 1493 (1948).

The authors studied a family in which a form of moderate hemophilia occurred. With regard to the hereditary transmission of the disease, however, this form differed from that of classical hemophilia. When a man from this family married a woman from a family in which some of the members had constitutional thrombopathy, the result was a child with both these hemorrhagic disorders.

*Bridge Anticoagulant in v. Willebrand's Syndrome.* Wilkinson, J. F., Nour-Eldin, F., Israels, M. C. G., Dept. Hematol., Royal Infirmary, Manchester, England. Lancet 2: 115 (1958).

The authors describe 3 cases of v. Willebrand's syndrome with factor VIII deficiency as measured by the thromboplastin generation test. The so-called bridge anticoagulant always present in hemophilia A and B, was also missing in the plasma. The authors come to the conclusion that v. Willebrand's syndrome is not a variety of classical hemophilia but a disease in itself.

*Zur Frage der Nomenklatur bei hämophilieähnlichen hämorrhagischen Diathesen.* Lehmann, W., Kiel, Germany. Medizinische 15: 598 (1958).

*Zur Methode des Thromboplastin-Generations-Tests an Thrombozyten bei erblicher Thrombopathie.* Jürgens, R., Hiepler, E., Wiss. Abtlg., F. Hoffmann-La Roche, Basel, Switzerland. Med. Klin. 20: 895 (1958).

In 7 patients with thrombopathia (Åland island) the authors found factor VIII deficiency and markedly delayed thromboplastin formation, as measured by a modification of the original test as described by Biggs and MacFarlane. The authors come to the conclusion that in hereditary thrombopathia v. Willebrand-Jürgens the hemorrhagic diathesis is caused by dysfunction of platelets, capillary damage, and factor VIII-deficiency.

*Hämorrhagische Diathese bei kongenitaler Herzkrankheit. Einfluß der Operation unter Hypothermie und Vollbluttransfusion.* van Creveld, S., Univ. Kinderklinik, Amsterdam, Holland. Ann. paediat. 190: 342 (1948).

A latent or manifest hemorrhagic diathesis may exist in cyanotic heart disease. It can be caused by thrombocytopenia, fibrinogenopenia, or decrease of prothrombin and factor VII. These coagulation factors should be controlled before surgery. Hypothermia induces transitory alteration of various coagulation factors and of the thrombelastogram. Normalization occurs following normalization of the body temperature. During massive blood transfusion, especially with hypothermia, an acute danger of thrombocytopenia exists. This danger is of particular importance in small children. The author suggests the use of fresh blood collected in siliconized glass-ware with addition of minimal amounts of heparin.

*Thrombopathie constitutionnelle pseudo-hémophilique de Willebrand-Jürgens avec présence d'une substance anticoagulante et d'une ostéo-arthropathie.* Roth, H. W., Cohn, M. L. Praxis 47: 558 (1958).

The authors report a case of constitutional pseudo-hemophilic thrombopathy v. Willebrand-Jürgens complicated by an anticoagulant (immunologic antibody) and hemophilia-like osteoarthropathia.

*Malattia emorragica da turba associata di tipo emofilico e vascolare. (Vascular hemophilia).* Ronconi, G., Ospedale Civile, Rep. Pediatrico, Vicenza, Italy, Minerva pediat. (Torino) 10: 538 (1958).

A case of hemorrhagic disease due to combined factor VIII and IX deficiency and associated vascular defect with constant prolongation of the bleeding time is presented. This condition is defined as vascular hemophilia according to American terminology.

*Diathèse hémorragique par héparinémie avec thrombocytopénie au cours d'une lupo-érythémato-viscérée.* Favre-Gilly, J., Normand, J., Guillot, A., Thouverez, J.-P., Gonin, A., Froment, R., Clin. méd., Lyon, France. Lyon méd. no. 50: 1 (1958).

*Thrombopathie Willebrand-Jürgens oder Angiohämophilie?* Beller, F. K., Univ.-Frauenklinik, Tübingen, Germany. Medizinische 15: 601 (1958).

The author reports the case of a girl with prolonged bleeding time, decreased factor VIII, thrombopathia with normal to slightly increased coagulation time, normal thrombelastogram. The terms hemophilia, thrombopathia, and angiohemophilia are discussed. In the above mentioned case the authors suggest the diagnosis "v. Willebrand-Jürgens syndrome". Therapy consists of blood transfusions, and infusion of fibrinogen. Bleeding time was normalized by high doses of cortisone.

*Inherited Autosomal Hemorrhagic Diathesis with Antihemophilic Globulin Deficiency and Prolonged Bleeding Time.* Nilsson, I. M., Med. Clinic, Allmänna sjukhuset, Malmö, Sweden. Nord. Med. 59: 403 (1958).

The author reports upon 5 female patients (from 4 different families) with congenital hemorrhagic diathesis. Laboratory studies revealed decreased AHG level and prolonged bleeding time but normal platelets. The disease was inherited but not sex-linked. An especially purified human fraction I containing AHG corrected the clotting defect of all cases in vitro. One patient was treated with an intravenous AHG preparation and normalization was obtained. The AHG preparation corrected not only the AHG deficiency but also the prolonged bleeding time and the capillary bleeding tendency. The bleeding disorder is believed to represent an inherited

hemorrhagic diathesis different from v. Willebrand's thrombopathy and also from classical hemophilia A. The prolonged bleeding time is thought to be due to the lack of a plasma factor rather than to a damaged capillary wall.

*Familial Hemophilia and Factor VII Deficiency.* Constandoulakis, M., Group Lab., St. Mary Abbots Hosp., London, England. J. clin. Path. 11: 412 (1958).

*Déficit en facteur A associé à un temps de saignement allongé.* Ducos, C., Biermé, R., Centre Régional de Transfusion sang., Toulouse, France. Sang. 29: 595 (1958).

*Antihemophilic Factor Deficiency Associated with Prolonged Bleeding Time. Report of Two Cases in Females.* Fukui, H., Majima, T., Tagawa, N., Dept. Pediatrics, Nara Med. Coll., Nara, Japan. Acta haem. jap. 21: 608 (1958).

Two cases of antihemophilic factor deficiency associated with prolonged bleeding time in the female are reported. The laboratory tests revealed markedly prolonged bleeding, and recalcification time. All clotting factors and platelet factors except factor VIII were found to be normal. Factor VIII content according to the Douglas method was 25—50% in case 1 (9-year-old girl) and 2.5% in case 2 (baby girl of 9 months).

*Hemorrhagic Diathesis due to a Deficiency of an AHF-like Factor (Nishimine factor) Associated with a Qualitative Platelet Dysfunction.* Yoshida, K., Umegaki, K., Yoshioka, K., Fukui, H., Majima, T., Dept. Pediatrics, Nara Med. Coll., Nara Japan, Acta haemat. jap. 21: 874 (1954).

A case of hemorrhagic diathesis in a 3-year-old boy which is considered to be due to a previously undescribed clotting anomaly is presented. The patient had prolonged recalcification time, reduced prothrombin consumption, prolonged bleeding time and slightly increased capillary fragility. Platelet count, clot retraction and prothrombin time were normal. The platelets were morphologically abnormal. Thromboplastin generation test with the patient's plasma and platelets was abnormal. Mixture of the patient's plasma and hemophilic BaSO<sub>4</sub>-plasma yielded correction of thromboplastin generation test. It is suggested that the substance deficient in the patient's plasma is different from AHG. Like AHG the substance is consumed during coagulation, not adsorbed by BaSO<sub>4</sub>, stable to heat and labile on storage.

*Thrombocytopathia of Glanzmann Type Associated with Serum Factor Deficiency. A Case Report.* Yoshida, K., Fukui, H., Majima, T., Dept. Pediatrics, Nara Med. Coll., Nara, Japan. J. Nara Med. Ass. 9: 241 (1958).

A case of thrombocytopathia of Glanzmann type associated with factor VII deficiency, occurring in a 5-year-old boy, is presented. Clinical symptoms: Uncontrollable gum bleeding of two days' duration.

## n) Platelets and Clot Retraction

*Vergleichende Untersuchungen über die Einwirkungen von Demecolcin auf die Thrombocytenbildung, Mitosehemmung und Zellbewegung (durchgeführt an Knochenmarkkulturen).* Albrecht, M., Kretschmer, V., Berlin, Germany. Ärztl. Wschr. 23: 508 (1958).

*The Effect of 2,4-Dinitrophenol and of Potassium on the Uptake of 5-Hydroxytryptamine by Platelets.* Born, G. V. R., Gillson, R. E., Oxford, England. J. Physiol. 141: 39 (1958).

*Serological Studies of Human Blood Platelets.* Lundevall, J., Inst. of Forensic Med., Univ., Oslo, Norway. Scand. J. clin. Lab. Invest. 10, suppl. 34 (1958).

Part 1. The unspecific clumping of platelets. — Part 2. Platelet antigens and antibodies.



*Technique de séparation des leucocytes et des plaquettes à partir du sédiment globulaire mixte recueilli sur les bols des séparateurs centrifuges.* Maupin, B., Dausset, J., Baudot, C., Centre nat. Transfusion sang., Paris, France. Vox sang. 3: 178 (1958).

*Test direct de consommation de l'antiglobuline sur les leucocytes et les plaquettes de certains malades atteints de pancytopenies idiopathiques.* Dausset, J., Brecy, H., Centre nat. Transfusion sang., Paris, France. Vox sang. 3: 197 (1958).

The direct antiglobulin consumption test was found to be regularly positive with the leukocytes and the platelets of a case of chronic idiopathic pancytopenia. The test was also positive in a number of patients with leukocytopenia and thrombocytopenia.

*Experimenteller Beitrag zur Pathogenese der allergischen medikamentösen Agranulocytose und Thrombopenie.* Pearl, A., Med. Poliklinik, Universität, Basel, Switzerland. Blut 4: 86 (1958).

*Chronic Idiopathic Thrombocytopenia in the Bantu.* Kramer, S., Dept. Med., Barawanath Hosp., Johannesburg, South Africa. S. Afr. med. J. 32: 617 (1958).

*Ein Fall von Thrombopenie-Hämangiom-Syndrom bei einem jungen Säugling.* Nöller, H. G., Freundt, K. J., Univ.-Kinderklinik, Heidelberg, Germany. Arch. Kinderheilk. 157: 258 (1958).

*Etude immunoélectrophorique des antigènes plaquettaires humains.* Salmon, J., Genève, Switzerland. Schweiz med. Wschr. 88: 1047 (1958).

*Antihistaminiques de synthèse et rétraction du caillot.* Bounameaux, Y., Lab. Physiopath., Univ., Liège, Belgique. Arch. int. Pharmacodyn. 116: 252 (1958).

*Neue Befunde zur Retraktion des Fibringerinnsels.* Kuhnke, E., Phys. Inst., Univ., Bonn, Germany. Pflügers Arch. ges. Physiol. 268: (1958).

*Elektronenoptische Untersuchungen über die Veränderung der Thrombozyten und des Fibringerinnsels im Verlaufe der Gerinnung unter besonderer Berücksichtigung der Retraktion.* Kuhnke, E., Physiol. Inst. Univ., Bonn, Germany. Pflügers Arch. ges. Physiol. 268: 87 (1958).

*Cortison und Prednison bei allergischer, thrombozytopenischer Purpura.* Krüger, H. U., Inn. Abtg., Bezirkskrankenhaus, Schwerin, Germany. Dtsch. Gesundh.Wes. 13: 1015 (1958).

*Purpura thrombopénique post-varicelleux.* Revue de la littérature à propos d'une observation. Beyer, P., Serv. Méd. Infantile, Hôp., Mulhouse, France. Arch. franç. Pédiat. 15: 920 (1958).

*Thrombopenia unter Doriden-Medikation.* Kirchmair, H., Med. Univ.-Klinik, Innsbruck, Austria. Med. Klin. 53: 1683 (1958).

*Hémorragies et thromboses au cours de la thrombocythémie essentielle (à propos de 3 observations personnelles).* Wassermann, L. R., Mount Sinai Hosp., New York, N. Y., USA. Sang. 29: 560 (1958).

*Effet hémostatique des transfusion de plasma sec concentré dans les hémorragies des thrombopathie.* Biermé, R., Ducos, J., Centre Régional de Transfusion sang., Toulouse, France. Sang. 29: 591 (1958).

*Purpura thrombotique thrombocytopénique (syndrome de Moschcowitz) précédé pendant deux ans par des accidents neurologiques répétés et régressifs. Remarques sur les formes prolongées de la maladie et sur la valeur de la poikilocytose.* Dreyfus, B., Centre Départ. de Transfusion Sanguine, Hôp. St. Antoine, Paris, France. Rev. franç. Etudes clin. and biol. 3: 1062 (1958).

A case of Moschcowitz syndrome is described. The clinical history was unusual with 2 years of isolated neurological involvement. The diagnosis only became apparent when purpura occurred, shortly followed by the characteristics of the disease and the fatal issue. The published cases of this disease are discussed. The claims that curable forms of this disease exist are discussed. The characteristic appearance of many deformed red cells is of great importance in the diagnosis.

*Experimentelle Untersuchungen über das Verhalten der Thrombozyten im Kreislauf.* Witte, S., Schricker, K. T., Med. Univ.-Klinik, Erlangen, Germany. *Klin. Wschr.* 36: 1119 (1958).

The intravascular behaviour of platelets has been studied by means of electronic flash microphotography of rat mesenteric tissue. Normal behaviour as well as experimentally produced alterations are discussed with regard to intravascular coagulation.

*Elektrophorese der Blutplättchen.* Donner, L., Mach, O., Brabcova, S., II. Med. Univ.-Klinik, Prag, CSR. *Acta haemat. (Basel)* 20: 369 (1958).

The protein and lipid fractions of lipo-proteins in isolated platelets were estimated by means of paper electrophoresis. It was found that the coagulative activity of platelets lies predominantly in zone D of the lipoprotein fractions. By precipitation methods it was found that the protein fraction of the lipoprotein of platelets consists of alpha 1-globulin. There is no significant difference between the total amounts of protein and lipid fractions of the lipo-proteins of platelets from healthy people and from patients with thrombocytopenia, thrombocythemia, or thrombasthenia.

*Demonstration of Some Properties of Human Thrombopoietin in Thrombocythemic Sera.* Kelemen, E., Cserhati, I., Tanos, B., I. Belgyogyszati Clinic, Univ. Med. School, Szeged, Hungary. *Acta haemat. (Basel)* 20: 350 (1958).

Intravenously administered human thrombocythemic serum induces thrombocytosis in mice. The increase in platelet count ranges from 50 000 to 250 000/cmm. The active substance is heat-sensitive, non-dialyzable, destroyable by trypsin and runs with the beta-globulin area in paper electrophoresis. The activity is inhibited by normal serum. It is concluded that the biological assay used in these experiments indicates the equilibrium between serum thrombopoietin and its biological inhibitor(s) and that this equilibrium is markedly disturbed in some pathologic conditions as in thrombocythemia and thrombocytosis.

*Viscous Metamorphosis of Blood Platelets: A Study of the Relationship to Coagulation Factors and Fibrin Formation.* Sharp, A. A., Dept. Path., Radcliffe Infirmary, Oxford, England. *Brit. J. Haematol.* 4: 28 (1958).

Viscous metamorphosis of platelets has been analysed in hemophilia, Christmas disease, congenital factor V-deficiency, induced factor VII-deficiency, PTA-deficiency, v. Willebrand's disease, in the presence of a circulating anticoagulant, in heparinized blood, and in thrombocytopenia. The results obtained suggest that viscous metamorphosis is independent of antihemophilic globulin, Christmas factor, factor V or VII and probably precedes these factors in the sequence of blood coagulation. Viscous metamorphosis did not occur normally in the absence of PTA.

*Die Bedeutung des Serum-Proteingehaltes in der Testung auf antithrombozytäre Antikörper.* Schmid, H. J., Med. Poliklinik, Univ., Basel, Switzerland. *Vox sang.* 3: 162 (1958).

*Thrombocytopenic Purpura Due to Quinidine.* Schen, R. J., Rabinovitz, Dept. int. Med. C, Hadassah Municipal Hosp., Tel-Aviv, Israel. *Brit. med. J.* no. 5111: 1502 (1958).

A case of quinidine purpura is described. It is shown that the diagnosis can be made in the ward by a simplified version of the clot retraction test. A simplified method for demonstrating platelet agglutination is described. The prodromal symptoms of quinidine purpura are described and their importance is stressed. It is shown that many of the drug-induced thrombocytopenias conform to a definite clinical pattern, and certain criteria are proposed for classification.

*Hemorrhagic Thrombocythemia. Report of 2 Cases Treated with Radioactive Phosphorus.* Fountain, J. R., Dept. Med., General Infirmary, Leeds, England. Brit. med. J. no. 5089: 126 (1958).

The clinical and hematological features of hemorrhagic thrombocythemia are described and 2 further examples reported. Hemorrhagic thrombocythemia is usually associated with other myeloproliferative disorders or splenic atrophy. It may follow splenectomy but is rarely primary in that it is unassociated with other pathological processes. Case 1 belongs to the latter category, while case 2 followed splenectomy. The mechanism of the bleeding tendency is unknown. The bleeding time is occasionally prolonged, but other routine tests of hemostatic function are invariably normal. The deficiency of platelet factor as evidenced by the normal thromboplastin generation tests was detected in either of the above patients. In both patients the platelet count returned to normal and bleeding ceased after treatment with radioactive phosphorus.

*La serotonina piastrinica nelle leucemie.* Polli, E. E., Bianchi, P. A., Crosti, P. F., Ist. Clin. med. Generale e Terapia med., Univ., Milano, Italy. Haematol. lat. 1: 250 (1958).

The serotonin content of platelets of normal persons over 70 was significantly lower than that of platelets of normal subjects aged from 20 to 50. Platelet serotonin of 12 leukemic subjects was reduced in comparison to that of normal subjects. No clear correlation between the reduction of platelet serotonin in leukemic subjects and hemorrhagic phenomena was revealed.

*Mikroangiopathia thrombotica. (Thrombotische thrombozytopenische Purpura).* Kornfeld, M., Zagreb, Poland. Med. Klin. no. 32, 1375 (1958).

Over 50 cases of thrombotic thrombocytopenic purpura (TTP) have been described. All are characterized by hemolytic anemia, thrombocytopenic purpura and transitory neurologic complications. The author describes 2 own observations and stresses the importance of biopsy of the skin, muscles and bone marrow for intravital diagnosis of the disease.

*The Relationship between 5-hydroxytryptamine and Adenosine Triphosphate in Blood Platelets.* Born, G. V. R., Ingram, G. I. C., Stacey, R. S., London, England. Brit. J. Pharmacol. 12: 62 (1958).

In normal human blood platelets the serotonin concentration is proportional to the adenosine triphosphate content. Patients treated with reserpine and patients suffering from leukemia show decreased serotonin content of the platelets but normal ATP level.

*Changes in the Distribution of Phosphorus in Platelet-Rich Plasma During Clotting.* Born, G. V. R., Oxford, England. Biochem. J. 68: 695 (1958).

During coagulation of platelet-rich plasma the ATP content decreases in the ethanol-chloroform extract and increases in the residue. Later on the ATP content of the extract increases and it decreases in the residue. These alterations do not occur, or only to a minimal extent, in the absence of platelets. It is assumed that a phospholipoprotein is formed during coagulation and later again disappears and that it might possibly be plasma thromboplastin.

*Einst und Jetzt: Die essentielle Thrombopenie nach 40 Jahren.* Frank, E., Istanbul, Turkey. Münch. med. Wschr. 100: 940 (1958).

*Thrombopathie familiale.* Hemmeler, G., Clin. méd. univ., Lausanne, Switzerland. Schweiz. med. Wschr. 88: 1018 (1958).

Description of a hemorrhagic diathesis due to thrombocytopathia. The platelets often are of abnormal size, their protoplasm is usually colourless and contains few or no granulation. Their number is normal. It is assumed that the hemorrhagic tendency is due to a lack of factor 3 in platelets, as this factor might normally be contained in the protoplasmic granulation.

*Platelet-Agglutinating Factor in Glandular Fever Complicated by Jaundice and Thrombocytopenia.* Freeman, T., Wakefield, G. S., Dept. clin. Chem. St. Mary's Hosp., London W. 2, England. *Lancet* 2: 883 (1958).

A man with glandular fever showed impaired liver function and thrombocytopenia. The thrombocytopenia was thought to be due to a factor in the blood that agglutinated group-P platelets to a high titre. This factor was shown not to be the same as the heterophil antibody, but no further evidence as to its nature was found. The disorder responded dramatically to cortisone therapy. After two and a half years the platelet-agglutinating factor was not present in the patient's serum.

*Retraktographie: Eine neue Methode zur fortlaufenden Messung der Retraktion des Blutkuchens.* Hartert, H., Med. Univ.-Klinik, Heidelberg, Germany. *Klin. Wschr.* 36: 1084 (1958).

Description of a new method for the measurement of clot retraction.

*A New Approach to the Thrombocytopathys.* Thrombocytopathy A. Johnson, S. A., Monto, R. W., Caldwell, M. J., *Thromb. Diath. haem.* 22 279 (1958).

*Die Ultrastruktur der Thrombozyten bei der konstitutionellen Thrombopathie (v. Willebrand-Jürgens) mit einem Beitrag zur submikroskopischen Orthologie der Thrombozyten.* Schulz, H., Jürgens, R., Hiepler, E., *Path. Inst., Med. Akademie, Düsseldorf, Germany. Thromb. Diath. haem.* 2: 300 (1958) and *Med. Klin.* no. 20, 892 (1958).

*Predni-steroidi e porpore trombocitopeniche idiopatiche.* Marmont, A., Fusco, F. A., *Ist. Clin. med. gener., Univ., Genova, Italy. Haematol. lat.* 1: 3 (1958).

Prednosteroid administration is the therapy of choice for thrombocytopenic purpura, idiopathic and symptomatic. The authors present a 2 years-follow-up study of 9 cases of ITP treated with prednisolone. They point out that although the hemostatic action of the drug is considered effective in every type of thrombocytopenia, the best clinical results are obtained in the so-called megakaryocytic forms. Prednosteroid treatment may be applied generally in acute self-limiting cases, as preparatory procedure to splenectomy, and, finally, as a remedy for post-splenectomy relapses. The authors present a few hypotheses as to the mechanism of action of these compounds in ITP.

*Attività lisozimica, ialuronidasi ed antieparinica delle piastrine.* Tropeano, L., Cacciola, E., *Ist. Patol. Med., Univ., Catania, Italy. Haematol. lat.* 1: 90 (1958).

The authors, in an attempt to correlate the biochemical characteristics of platelets and their coagulative function, and based on the facts that platelets contain lysozyme and hyaluronidase, advance the hypothesis that these enzymes may be responsible for the anti-heparin activity of platelets, their structure being similar to that of heparin.

*Posizione attuale dei prednisteroidi nel trattamento delle porpore trombocitopeniche idiopatiche.* Marmont, A., *Ist. Clin. Med. Generale, Univ. Genova, Italy. Boll. Soc. ital. Ematol.* 6: 18 (1958).

*Ulteriori osservazioni sulla agglutinazione e lisi piastrinica a frigore nei soggetti affetti da sclerodermia. Possibili rapporti del fenomeno con alcune manifestazioni della malattia.* Bianchi, V., Barisone, D., *Ist. Patol. Spec. Med., Univ. Genova, Italy. Boll. Soc. ital. Ematol.* 6: 20 (1958).

*Studies on the Thrombocyte in Tuberculosis. Report 2. Clinical Part (I).* Yasuoka, H., 2nd Med. Clinic, Med. Faculty, Kyoto Univ., Japan. *Jap. Arch. int. Med.* 5: 606 (1958).

*The Reaction of the Thrombocytes to Intravenously Injected Suspensions of Submicroscopic Particles.* Bloom, G., Swenson, A., Div. Occupational Med., Karolinska Sjukhuset, Stockholm, Sweden. *Acta med. scand.* 162: 423 (1958).

After intravenous injections of suspensions of particles of synthetic amorphous silica, of titanium dioxide and of water-soluble starch a rapid reduction in the number of platelets circulating in the blood was noted. This reduction reached a maximum after 4 to 8 minutes and was followed by a slow increase. Injections of colloidal solutions of an iron preparation and of methylene blue did not cause such a reaction.

*Phosphatides as Platelet Substitutes in Blood Coagulation.* Schulman, I., Currimbhoy, Z., Smith, C. H., Dept. Pediatrics, The New York Hosp.-Cornell Med. Center, New York, N. Y., USA. Ann. N. Y. Acad. Sci. 75: 195 (1958).

A soybean cephalin has been found to demonstrate thromboplastic and fibrinoplastic effects similar to those of platelets. Despite the absence of 4 of the 6 known platelet functions, the lipid holds promise in the therapy of thrombocytopenic states.

*A Survey of Some Platelet Enzymes and Functions: The Platelets as the Source of Normal Serum Acid Glycerophosphatase.* Zucker, M. B., Borrelli, J., Sloan-Kettering Inst. for Cancer Research, New York, N. Y., USA. Ann. N. Y. Acad. Sci. 75: 203 (1958).

The literature on platelet function, enzymes and chemical constituents is reviewed. Platelets contain sufficient lactic dehydrogenase and acid glycerophosphatase to account for all the activity in normal serum. However, serum lactic dehydrogenase is the same whether clotting does or does not occur in the presence of platelets. In contrast, serum activity against glycerophosphate, at acid pH is absent in serum obtained from platelet-poor plasma but is normal when serum is obtained from plasma with normal platelet count. Thus, normal serum acid glycerophosphatase appears to come from platelets. In contrast to normal individuals, acid glycerophosphatase activity was found in serum from platelet-poor plasma obtained from 2 patients with metastatic carcinoma of the prostate, suggesting that a more sensitive test for pathologic elevation of acid phosphatase in prostate carcinoma is provided when the contribution of acid phosphatase from the platelets is avoided.

*Chemical Studies of Mucopolysaccharides of Rat Blood Platelets.* Anderson, B., Odell, T. T., Biol. Div., Oak Ridge Nat. Lab., Oak Ridge, Tenn. USA. Proc. Soc. exp. Biol. (N. Y.) 99: 765 (1958).

Two mucopolysaccharide fractions have been extracted from blood platelets of rats. Paper electrophoresis and paper chromatography of the intact MPS of fraction 1 and paper chromatography of its hydrolysis products show it to be similar to chondroitin sulfate. Fraction 2 is probably a uronic acid-free mucopolysaccharide.

*Comparative Effectiveness of Fresh and Lyophilized Platelets in Controlling Irradiation Hemorrhage in the Rat.* Fliedner, T. M., Sorenson, D. K., Bond, V. P., Cronkite, E. P., Jackson, D. P., Adamik, E., Med. Research Center, Brookhaven Nat. Lab., Upton, N. Y., USA. Proc. Soc. exp. Biol. (N. Y.) 99: 731 (1958).

*Clinical Section: Transfusion of Platelets and Platelet Substitutes; Transplantation of Bone Marrow. Discussion. Participants:* Harrington, W. J., Smith, C. H., Cronkite, E. P., Conley, C. L., Gardner, F. H., Tocantins, L. M. Blood 13: 1089 (1958).

*Thrombotic Thrombocytopenic Purpura: Report of a Case and Review of the Literature.* Kingsley, J. W., Aquino, R., Dept. Med., Alexander Blain Hosp., Detroit, Mich. USA. Ann. intern. Med. 49: 934 (1958).

Thrombotic thrombocytopenic purpura is a disease of unknown etiology characterized by thrombocytopenia, hemolytic anemia and bizarre neurologic manifestations. The diagnosis is not difficult if the typical clinical picture is recognized. An illustrative case is described and the recent literature on the subject reviewed. It is suggested that earlier diagnosis, administration of cortisone or related steroids, and splenectomy may forestall the usual rapidly fatal progression of the disease.

*Survival of Blood Platelets Labeled with Chromium<sup>51</sup>*. Aas, K. A., Gardner, F. H., Richard C. Curtis, Hemat. Lab., Peter Bent Brigham Hosp., Boston, Mass., USA. J. clin. Invest. 37: 1257 (1958).

A standardized technic has been developed to evaluate the life span of transfused blood platelets in normal recipients. In vitro measurements indicate that radioactive sodium chromate will bind to human blood platelets suspended in plasma. The factors related to time, temperature and concentration of sodium chromate for labeling platelets in vitro have been presented. It was found that transfused platelets have a survival period of 9 to 11 days. No relabeling of the recipient's platelets or other blood elements was observed.

*Platelets. Glutamic Pyruvic Transaminase Activity of Human Platelets*. Tsitouris G., Stefanini, M., Joseph Stanton Memorial Labs., Saint Elizabeth's Hosp., Boston, Mass., USA. Proc. Soc. exp. Biol. (N. Y.) 99: 40 (1958).

Platelets are a source of glutamic oxalacetic transaminase in human blood. Platelets, however, contain only traces of glutamic pyruvic transaminase in normal and pathologic conditions. This finding is not explained by presence of enzyme inhibitors or by lack of a co-enzyme. The significance of the dissociation between GO-T and GP-T activity in platelets, as for other tissues, remains obscure.

*Platelet Factor I Related to Prothrombin Activation*. Fell, C., Seegers, W. H., Dept. Physiol. and Pharm., Med. Coll., Wayne Univ., Detroit, Mich., USA. Canad. J. Biochem. Physiol. 36: 645 (1958).

Concentrates of platelet factor I were made from bovine platelets. Being bound to fine particles, the activity was not obtained in solution. The concentrates accelerate the clotting of whole blood, and also the activation of prothrombin either to form thrombin or a non-thrombin derivative. Activation of purified prothrombin occurred under several different circumstances, and different end products formed. Platelet factor I concentrates appear to have a general property of accelerating alterations in the prothrombin molecule independently of these variants.

*Enzyme and Nucleic Acid Content of Thrombocytes from Normal and Thrombocytopenic Calves*. Mizuno, N. S., Sautter, J. N., Schultze, M. O., Div. Veterinary Path. and Parasitol., Coll. of Veterinary Med., Univ. of Minn., St. Paul, Minn., USA. Proc. Soc. exp. Biol. (N. Y.) 98: 42 (1958).

Bovine thrombocyte concentrations contained acid phosphatase, beta-D-glucuronidase, alylsulfatase, aliesterase and acetyl-cholinesterase but no alkaline phosphatase. Benzoylcholine was not hydrolyzed by thrombocytes. There was no significant difference in these enzyme activities of thrombocytes from normal or thrombocytopenic calves. There was no significant quantity of deoxypentose nucleic or pentose nucleic acid in bovine thrombocyte concentrates from either normal or thrombocytopenic calves. Thrombocytes released by hypoplastic bone marrow could not be differentiated from normal thrombocytes by the tests used.

*Platelet Counts in the Rat After Hypophysectomy, Gonadectomy or Thyroidectomy*. Lawrence, A. M., Contopoulos, A. N., Inst. exper. Biol., Univ. California, Berkeley, Calif., USA. Proc. Soc. exp. Biol. (N. Y.) 98: 738 (1958).

Removal of pituitary gland, or of thyroid resulted in decrease in number of circulating blood platelets. Decrease in clot retraction observed in these animals was consistent with reduced platelet counts. Gonadectomy had no effect on post-operative platelet counts or clot retraction.

*Thrombopenic Purpura as a Complication of Mumps*. Kolars, C. P., Spink, W. W., Dept. Med., Univ. Minnesota, Minneapolis, Minn., USA. J. Amer. med. Ass. 168: 2213 (1958).



The present report indicates that steroid therapy is also effective in thrombocytopenia occurring as a complication of mumps. In 2 of the 3 patients steroid therapy was insufficient to correct the platelet deficiency but did control the bleeding tendency. In a third patient with orchitis and thrombocytopenic purpura, steroid therapy alone controlled both complications. It is suggested that mumps should be considered as a possible causative factor in cases of "idiopathic" thrombocytopenic purpura. The clinical course of these 3 patients suggests that splenectomy was not definitive in terminating the thrombocytopenic state. Steroids did control the bleeding tendency.

*Purpura Due to Chlorothiazide (Diuril).* Jaffe, M. O., Kierland, R. R., Section of Dermatol., Mayo Clinic, Rochester, Minn., USA. J. Amer. med. Ass. 168: 2264 (1958).

Previously reported undesirable side-effects of Diuril therapy have been primarily those related to fluid and electrolyte imbalance. At this clinic, two cases of purpura, only one with decreased platelet count (94 000), resulted from the administration of this drug.

*Platelet Phosphatides: Their Separation, Identification, and Clotting Activity.* Marcus, A. J., Spaet, T. H., Dept. Hematol., Div. of Labs., Montefiore Hosp., New York, N. Y., USA. J. clin. Invest. 37: 1836 (1958).

Crude phospholipid extracts of human platelets have been subjected to paper and column chromatography on silicic acid. The components resolved were phosphatidioethanolamine, phosphatidylserine, lecithin, sphingomyelin and inositol phosphatide. Phosphatidylserine obtained by column chromatography could replace platelets in thromboplastin generation and prothrombin consumption tests. An unidentified fraction showed thromboplastic activity. The role of phosphatidylethanolamine could not be clarified by this study. Lecithin and sphingomyelin, obtained as a single fraction, were inactive. High concentrations of the various phosphatides appeared to act as anticoagulants.

*Simultaneous Placental Transfer of Factors Responsible for L.E. Cell Formation and Thrombocytopenia.* Nathan, D. J., Snapper, I., Med. Serv., Beth-El Hosp., Brooklyn, N. Y., USA. Amer. J. Med. 25: 647 (1958).

Placental transfer of L.E. cell factor and platelet agglutinins was demonstrated in the premature child of a mother with systemic lupus erythematosus.

*Thrombocythemia and Pulmonary Intra-Alveolar Coagulum in a Young Woman.* Levinson, B., Jones, R. S., Wintrobe, M. M., Cartwright, G. E., Depts. Med. and Path., Coll. of Med., Univ. of Utah, Salt Lake City, Utah, USA. Blood 13: 959 (1958).

A description is given of the clinical course and findings at autopsy in a 19-year-old girl with a myeloproliferative syndrome characterized primarily by thrombocythemia. This was associated with an unusual pulmonary disorder in which the alveoli were filled by a non-cellular exudate comprised of carbohydrate, fat and protein which resembled in some respects pneumonia attributed to *Pneumocystis carinii*. The possible interrelationship of the thrombocythemia and the intra-alveolar coagulum is discussed.

*Osmotic Fragility of Human Blood Platelets: Phase Contrast and Electron Microscopic Studies.* Gurevitch, J., Nelken, D., Danon, D., Dept. clin. Microbiol., Hebrew Univ.-Hadassah Med. School, Jerusalem, Israel. Blood 13: 773 (1958).

Phase contrast and electron-microscopic studies on the morphologic changes of platelets in various hypotonic salt solutions are presented.

*Inhibition of Lipemia Clearing Activity by Human White Blood Cell and Platelet Components.* Fekete, L. L., Lever, W. F., Klein, E., Research Labs., Dept. Dermatology, Harvard Med. School, Boston, Mass., USA. J. Lab. clin. Med. 52: 680 (1958).

Extracts of white blood cells and of platelets inhibited the heparin-induced clearing activity of serum in vitro. The extracts reversed the anticoagulant action of heparin. White blood cell and platelet material inhibited clearing activity in vivo. Some of the inhibitory activity of the white cell and of the platelet extracts seems to be associated with proteins.

*The Effect of Heparin on the Platelet Count in vitro. With Particular Reference to the Collection of Blood for Extracorporeal Circulation.* Perkins, H. A., Osborn, J. J., Gerbode, F., Dept. Med., Stanford Univ. Med. School, San Francisco, Calif., USA. Amer. J. clin. Path. 30: 397 (1958).

The fall in platelet count that occurs when fresh blood is added to heparin in vitro is greater the less the anticoagulant. Most of the loss occurs in the first 5 mins. Loss of platelets is as great and as rapid in siliconed glass containers and polyethylene vials as in uncoated glass. Platelets are lost primarily by clumping and disintegration rather than by adherence to the foreign surface. Loss of platelets is minimized by having the containers filled to near capacity. This explains why loss of platelets is slight under the conditions in which donor blood is collected for extracorporeal circulation.

*Acquired Thrombocytopathy. Observations on the Coagulation Defect in Uremia.* Johnson, S. A., Monto, R. W., Caldwell, M. J., Div. of Hematol., Henry Ford Hosp., Detroit, Mich., USA. Amer. J. clin. Path. 30: 507 (1958).

*Binding and Transport of Serotonin in Rabbit Blood Platelets and Action of Reserpine.* Sano, I., Dept. Neuropsych., Univ. Med. School, Osaka, Japan. Amer. J. Physiol. 195: 495 (1958).

*Massive Corticosteroid Therapy in the Management of Resistant Thrombocytopenic Purpura.* Weisberger, A. S., Subrland, L. G., Dept. Med. Univ. Hosp., Cleveland, O., USA. Amer. J. med. Sci. 236: 425 (1958).

*Immunothrombocytopenia Induced by Novobiocin.* Day, H. J., Moore, J. E., Temple Univ. Hosp., Philadelphia, Pa., USA. Amer. J. med. Sci. 236: 475 (1958).

*Thrombocytopenia Following Gold Therapy with Successful Treatment.* Hazlett, B., Yendt, E. R., Toronto, Canada. Canad. med. Ass. J., 79: 31 (1958).

Report of a case of chronic rheumatism treated with gold (total of 485 mg) who after 6 months developed thrombocytopenic purpura. Cortisone and ACTH were without effect whereas repeated therapy with Dimercaprol resulted in normalization.

*Evaluation of Thrombocythemia by the Thromboplastin Generation Test.* Hyun, B. H., Dawson, E. A., Custer, R. P., Philadelphia, Pa., USA. Amer. J. clin. Path. 29: 539 (1958).

### **o) Spontaneous Anticoagulants**

*Una rara associazione di anemia emolitica e di anticoagulina anomala in circolo in un caso di lupus eritematosi acuto disseminato.* Doni, A., Cioni, P., Ist. Patol. Spec. Med. Univ., Firenze, Italy. Boll. Soc. ital. Ematol. 6: 82 (1958).

*Purpura hémorragique mortel avec héparinémie, au cours d'une lupo-érythémato-viscéríte.* Thiers, H., Favre-Gilly, J., Fayolle, J., Colomb, D., Chassard, A., Thouverez, J.-P., Clin. méd., Lyon, France. Lyon méd. no. 50 (1958).

Case report.

*Circulating Anticoagulants and Bullous Dermatoses (Including a Case Report of Senear-Usher's Syndrome with a Hemophilia-like Condition).* Björnberg, A., Gothenburg, Sweden. Acta dermat.-venerol. (Stockh.) 38: 251 (1958).

*Ricerche sulla tolleranza eparinica e sulla eparinemia nell'immaturo.* Arditi, E., Nigro N., Clin. Pediatrica, Univ., Torino, Italy. Minerva pediat. (Torino) 10: 868 (1958).

*Diathèse hémorragique féminine avec présence dans le sang d'une antithrombine du type de l'héparine.* Favre-Gilly, R., Lab. D'Hématol., Inst. Pasteur, Lyon, France. Sang 29: 398 (1958).

*Existence and Significance of a Physiological Anticoagulating System.* Kudrjashov, B. A., Ulytina, P. D., Faculty of Biol. and Soil Science, State Univ. Moscow, UdSSR, Natur (Lond.) 182: 396 (1958).

The authors' experiments lead to the hypothesis that the problem of thromboses should be approached not from the point of view of an excess of coagulating components in the circulating blood nor of the pathology of the vessel wall but through an analysis of the physiological state of the anticoagulating system present outside the vascular bed.

*Plasma Antithrombin Elevations in Buccal Varidase-Treated Patients.* Innerfield, I., Dept. Med., New York Med. Coll., Metropolitan Med. Center, New York City, N. Y., USA. Surgery 43: 956 (1958).

*Synthesis and Metabolism of Radioactive Heparin.* Eiber, H. B., Danishefsky, I., Dept. Med. N. Y., Med. Coll., New York, USA. Arch. intern. Med. 102: 189 (1958).

Heparin is a sulfated mucopolysaccharide which is normally present in animal tissues and blood. Its activity as an anticoagulant makes it a compound of basic interest in medicine, and, consequently, a firm understanding of its biochemical and pharmacological action is extremely important. By means of radioactive isotopes it was shown that heparin is synthesized from glucose antiorganic sulfate. The availability of radioactive heparin allows for the study of its metabolism and pharmacological action. It appears that the optimum dosage for an adult of 150 lb. weight is 50 mg every 4 hours when given intravenously. Larger doses would not proportionally increase the heparin effect and are unwarranted. Heparin is a normal constituent of blood in concentrations of 0.5 mg/100 ml.

*Relationship of Blood Heparin Levels to Serum Lipoproteins and Cholesterol Levels in Fasting Subjects.* Yasugi, T., Gofman, J. W., de Lalla, O., Tamplin, A. R., Oshima, K., Biophysics Univ. of California, Berkeley, Calif., USA. Proc. Soc. exp. Biol. (N. Y.) 98: 46 (1958).

A highly reproducible modification of the Bassiouni method for determining spontaneously occurring blood heparin-like substances is described and evaluated. A mean level of 3.07 mg/100 ml of blood heparin-like substances was determined for a sample of 105 schizophrenic males 40 to 50 years old. This sample group showed lipoprotein and cholesterol values very close to those characteristic for other samples of males previously studied. Highly significant negative correlations were demonstrated for the following pairs of variables,  $S_t^0$  0—12 lipoproteins versus blood "heparin",  $S_t^0$  12—20 lipoproteins versus blood "heparin", and serum cholesterol versus blood "heparin".

#### p) Vitamin K

*Gerinnungsfaktoren und Leberfunktion.* Koller, F., Med. Klinik, Krankenhaus Neumünster, Zollikerberg/Zürich, Switzerland. Med. Klin. 8: 327 (1958).

The author discusses the relationship between coagulation factors and their behaviour in liver cell damage. If intravenous administration of 10 mg of Konaktion does not within 24 hours lead to prothrombin and factor VII levels above 20—30% very severe parenchymous liver damage is to be considered and acute liver atrophy may occur.

*Synthese und Isolierung von Vitamin K<sub>2</sub> und isoprenologen Verbindungen.* Isler, O., Rüegg, R., Chopard-dit-Jean, L. H., Winterstein, A., Wiss. Abtg. F. Hoffmann-La Roche, Basel, Switzerland. Helv. chim. Acta 41: 786 (1958).

*The Action of Synkavit (Sodium Salt of 2-Methyl-1,4-Napthohydroquinone Diphosphate) on the Conversion of 3-Hydroxyanthranilic Acid into Quinolinic Acid.* Quagliariello, E., Auricchio, S., Barone, B., Napoli, Italy. *Ital. J. Biochem.* 7: 35 (1958).

*Action de la vitamine K<sub>1</sub> de synthèse au cours des atteintes hépatiques de la petite enfance.* Sarrony, C., Clausse, J., De Peretti, E., *Pédiatrie* 13: 91 (1958).

15 children with a variety of liver affections accompanied by hypoprothrombinemia were given daily doses of 20 mg of Konaktion i.m. over a period of 5 to 15 days. In 10 patients marked improvement of the condition occurred together with normalization of prothrombin values. The other unaffected 5 cases showed no improvement either clinically nor regarding prothrombin levels.

*Vitamin K<sub>1</sub> bei tuberkulösen Lungenblutungen.* Rossellit, G., *Ärzt. Praxis* 10: 639 (1958).

*A Brief Review of Blood Coagulation and Methods for the Control of Hemorrhage.* Archer, R. K., Miller, W. C., Newmarket, England. *Vet. Rec.* 70: 357 (1958).  
(Vitamin K and K<sub>1</sub>.)

*Über Wirkungen und Nebenwirkungen von Vitamin-K-Präparaten bei der Anwendung im Neugeborenenalter.* Haupt, H., Krebs, H., Bonn, Germany. *Z. Kinderheilk.* 81: 330 (1958).

*Methyl-Napthochinon-Gaben und Gelbsucht bei unreifen Neugeborenen.* Gleiss, J., Düsseldorf, Germany. *Mshr. Kinderheilk.* 106: 58 (1958).

*Synkavit-Ikterus und Vitamin-K-Prophylaxe beim Neugeborenen.* Wespi, H. J., Kinderspital, Aarau, Switzerland. *Gynaecologia (Basel)* 145: 341 (1958).

*Der Einfluß von Napthohydrochinonderivaten (wasserlöslichen Vitamin-K-Ersatzpräparaten, Synkavit) auf Erythrozytenabbau und -regeneration bei Frühgeburten und auf das Glukuronidierungsvermögen der Leber in vitro.* Vest, M., Univ.-Kinderklinik, Basel, Switzerland. *Schweiz. med. Wschr.* 88: 969 (1958).

Administration of Synkavit in doses of 30 mg or more to premature infants is followed by a reduction of the hemoglobin concentration and the red cell count. This did not occur in the control group which was given 1 mg of Synkavit. Furthermore the group of premature infants given high doses showed an increase of reticulocytes and Heinz bodies. According to these results high doses of Synkavit cause an increased break-down of erythrocytes in premature infants. This explains their high serum bilirubin values. In vitro experiments with rats showed that high doses of Synkavit impair glucuronide formation. Since bilirubin is excreted as a glucuronide, a direct disorder of the excretory mechanism is conceivable as cause of bilirubin accumulation in the serum.

*Der Wirkungsmechanismus der K-Vitamine.* Martius, C., Lab. f. Biochem., ETH, Zürich, Switzerland. *Dtsch. med. Wschr.* 83: 1701 (1958).

*Vergleichende Untersuchungen eines wasserlöslichen und eines öllöslichen Vitamin-K-Präparates auf ihre Schädlichkeit bei Frühgebornen.* Yalcindag, S., Univ.-Kinderklinik, Freiburg/Br., Germany. *Arch. Kinderheilk.* 158: 228 (1958).

*Studies on "Prothrombin Derivatives" in Vitamin K Deficiency.* Spaet, T. H., Kropatkin, M., Dept. Hemat., Div. Labs., Montefiore Hosp., New York, N. Y., USA. *Arch. intern. Med.* 102: 558 (1958).

Coagulation studies were performed on a patient with an intestinal malabsorptive syndrome resulting in vitamin K deficiency. Initially there was a depression of prothrombin, factor VII and Stuart factor. Plasma thromboplastin component (factor IX) was not affected. Intravenous

vitamin K was followed by rapid restoration of all depressed factors. The data conform with the view that prothrombin and the "serum factors" are chemically and metabolically related compounds.

*Possible Role for Vitamin K for Electron Transport.* Weber, M. N., Dept. Bacteriol., Harvard Med. School, Boston, Mass., USA. *Science* 128: 897 (1958).

### q) Heparin and Heparin-like Substances

*Rectal and Sublingual Heparin.* Ghanem, M. H., *Lancet* 2: 907 (1958).

Various investigations revealed that rectal or sublingual administration of heparin does not prolong the coagulation time.

*Heparin und Embolektomie.* Dick, W., Chir. Univ.-Klinik, Tübingen, Germany. *Wien. med. Wschr.* 108: 786 (1958).

The author advises the injection of 25 000 units of heparin as preoperative measure in cases of embolism in the extremities. For postoperative treatment other anticoagulants such as dicumarol derivatives may be used.

*Erfahrungen mit der Heparinbehandlung ohne Blutgerinnungskontrolle.* Runge, H., Hartert, I., Frauenklinik, Univ. Heidelberg, Germany. *Münch. med. Wschr.* 100: 1416 (1958).

Heparin can be used without control of coagulation. In cases of deep venous thromboses in the leg immediate injection of 25 000 units of heparin and of 3 cc of phenylbutazone followed by 6 hourly administration of 15 000 units of heparin are recommended. Maintenance dose over a period of 10 to 12 days consists of 15 000 units of heparin.

*Messung der Heparintoleranz mit dem Thrombelastographen.* Strobel, E., Erlangen, Germany. *Z. ges. exp. Med.* 130: 381 (1958).

*Influence de l'héparine sur la fibrinolyse activée par la streptokinase.* Giacomazzi, G., Inst. de Path. méd., Univ. Milano, Italy. *Sang.* 29: 614 (1958).

*Titrage de la coagulabilité plasmatique par l'héparine.* Paleirc, G., Inst. d'Hématol., Montpellier, France. *Sang.* 29: 627 (1958).

*Intracranial Venous Thrombosis in the Puerperium.* Dalle Ore, G., Ruberti, R., Policlinico 65 894 (1958).

(Heparin treatment).

*A propos de la toxicité du sulfate de dextrane, anticoagulant synthétique du type héparinique.* Sasaki, S., Takeomoto, T., Oka, S., Nagoya, Japan. *C. R. Soc. biol.* 151: 1799 (1958).

*Über klinische Erfahrungen mit dem Antikoagulans Eleparon.* Trautmann, H., Gelsenkirchen-Buer, Germany. *Münch. med. Wschr.* 100: 1037 (1958).

Eleparon (= Elheparin) has been used by the author for 2 years in patients with extended thrombosis, embolism and infarctions. Its value as "immediate" anticoagulant is considered ideal. The author reports 3 cases in details.

*Permeabilizing Effects of Heparin and Heparin-like Substances.* Capraro, V., Marro, F., Valzelli, G., Milano, Italy. *Nature (Lond.)* 182: 603 (1958).

*Experimental Data on the Heparin-Neutralizing Effect of Intravenously Administered Calcium.* Geszti, O., Wei-Chi, T., Tien-Huang, L., Peking, China. *Acta physiol. hung.* 13: 341 (1958).

*Die wichtigsten Sofortmaßnahmen bei Lungenembolie.* Gross, R., Marburg/Lahn, Germany. Med. Klin. 5: 182 (1958).

Among the most important immediate measures in cases of pulmonary embolism the author recommends the administration of heparin intravenously. Coumarin drugs should not be used before the 3rd or 4th day.

*Ein Zwischenfall in der Heparinbehandlung.* Heinrich, P., Chir. Klinik, Bezirkskrankenhaus, Görlitz, Germany. Zbl. Chir. 83: 1293 (1958).

*The Effect of Heparin on Components of the Human Fibrinolytic System.* von Kaulla, K. N., McDonald, T. S., Dept. Med., Univ. Colorado Med. School, Denver, Col., USA. Blood 13: 811 (1958).

It was demonstrated with human urokinase, human fibrinolytic euglobulins and human pyrogen plasma as enzyme source, and with bovine fibrin plates and human plasma plates as substrate, that high heparin concentrations inhibit fibrinolysis of preformed fibrin, in contrast to small ones which may enhance this phenomenon, provided albumin is present. No interference could be observed in the absence of plasma, serum or albumin fraction. Albumin or substances associated with the albumin fraction are required for interference of heparin with fibrinolysis. This interference probably takes place with the action of plasmin on fibrin.

*Effects of Heparin on Body Temperature and Plasma Lipids Following Intravenous Administration of Fat Emulsion in Man.* Shoulders, H. H., Meng, H. C., Tugle, S., Dept. Physiol., Vanderbilt Univ. Med. School, Nashville, Tenn., USA. J. Lab. clin. Med. 52: 559 (1958).

*Massive Venous Thrombosis Associated with Incoagulability of the Blood.* Rosenberg, N., Zullo, R. J., Surg. 76: 981 (1958).

Case report (Heparin).

*Coagulation Mechanism and Effect of Heparin in Hemorrhagic Shock.* Smith, J. J., Grace, R. A., Hussey, C. V., Dept. Biochem., Marquette Univ., Med. School, Milwaukee, Wisc., USA. Amer. J. Physiol. 193: 593 (1958).

Intravenous injection of 10 mg/kg of heparin in dogs with hemorrhagic shock decreased mortality as compared to a group of untreated dogs and increased survival time. Heparin, however, did not completely protect the dogs from decrease of prothrombin activity and disturbed blood coagulability.

*The Effect of Heparin upon the Total Oxygen Consumption of Artherosclerotic Individuals.* Engelberg, H., Beverly Hills, Calif., USA. Amer. J. med. Sci. 236: 175 (1958).

### r) Other Anticoagulants

*Die Antikoagulantien in der Prophylaxe und Therapie thrombo-embolischer Erkrankungen. Bericht über eine Umfrage.* Gordonoff, T., Ther. Umsch. 15: 83 (1958).

*Verlauf und Prognose des rudimentären Herzvorderwandinfarktes.* Kubicek, F., Wien, Austria. Cardiologia (Basel) 32: 257 (1958).

The author gives a detailed report of 35 cases of rudimentary cardiac infarction. Characteristics of the disease and evaluation of electrocardiogram are discussed. Long-term anticoagulant therapy is advocated. Patients were treated with marcoumar alone, or initially with heparin and later with marcoumar.

*Studies in Detoxication. The Metabolism of Hydroxycoumarins. The Metabolism of Coumarin and of o-Coumaric Acid.* Mead, J. A. R., Smith, J. N., Williams, R. T., London, England. Biochem. J. 68: 61 (1958).



*Ausgedehnte Gewebsnekrose nach postoperativer Embolieprophylaxe mit Marcoumar.* Augustin, E., Karlsruhe, Germany. *Geburts- und Frauenheilk.* 18: 461 (1958).

Petechial hemorrhage on the right thigh occurred in a 45-year-old woman on 4th day of marcoumar therapy for massive thrombophlebitis. In spite of discontinuation of the drug the petechia increased and finally lead to deep tissue necrosis making skin transplantation necessary. Hospitalization lasted for 115 days.

*Zur intravenösen Antikoagulantientherapie mit Marcoumar.* Kranz, H., Würzburg, Germany. *Ärztl. Wschr.* 35/36: 789 (1958).

Intravenous administration of marcoumar was tested in 30 healthy individuals. After one injection of 30 mg therapeutic level of prothrombin time was attained within 30 hours *e. i.* 10 to 14 hours earlier than with oral administration.

*Antikoagulantienbehandlung peripherer arterieller Embolien.* Karges, O., Marburg/Lahn, Germany. *Ärztl. Wschr.* 32: 707 (1958).

*Hirudin. Der blutgerinnungshemmende Wirkstoff des medizinischen Blutegels.* Marwardt, F., Pharm. Inst., Univ., Greifswald, Germany. *Blut* 4: 161 (1958).

*Occurrence of Coumarin Analogues in Lemon Juice.* Bernhard, R. A., Dept. Food Technol., Univ. of California, Davis, Calif., USA. *Nature (Lond.)* 182: 1172 (1958).

*Metabolism of Coumarin and Related Compounds in Cultures of Penicillium Species.* Bellis, D. M., Dept. Pharm. Univ., Manchester, England. *Nature (Lond.)* 182: 806 (1958).

*Hemorrhage During Phenindione Therapy.* Mickerson, J. N., London, England. *Brit. med. J.* p. 1522 (1958).

In 7 of 92 patients treated with phenindione severe hemorrhage occurred. One patient died of the complications. The author stresses the importance of early blood transfusions in cases of severe hemorrhage occurring during this therapy.

*Herzinfarkt.* Kaiser, K., Düsseldorf, Germany. *Dtsch. med. Wschr.* 83: 1140 (1958).

The author discusses briefly diagnosis and therapy of myocardial infarction. Liquemin and marcoumar are mentioned among anticoagulants in use.

*Pathologisch-anatomische Demonstrationen.* Walthard, B., Schweiz. med. Wschr. 88: 294 (1958).

Report of complications occurring under marcoumar and butazolidin in a patient with repeated femoral venous thrombosis. Severe hemorrhagic diathesis occurred following anticoagulant therapy, hemorrhages appeared in the skin, lungs, kidneys with multiple ulcers in the mouth and intestines. In a case of cor pulmonale with femoral vein thrombosis hemorrhagic diathesis with hemorrhagic infarction of the right hand and one toe occurred together with hemorrhagic anemia.

*Betrachtungen zur Therapie und Prognose des frischen Herzinfarktes.* Jasinski, B., Kantonsspital Winterthur, Switzerland. *Schweiz. med. Wschr.* 88: 264 (1958).

*Kritische Betrachtungen zur Therapie des Myokardinfarktes.* Bayer, O., Maring, H., Schmitt-Rohde, J. M., Berlin-Moabit, Germany. *Dtsch. med. Wschr.* 83: 792 (1958).

*Uricosuric Effect of Dicumarol.* Hansen, O. E., Holten, C., Aarhus, Denmark. *Lancet* I: 1047 (1958).

Initial doses of 500 to 750 mg of dicumarol in patients with myocardial infarction in a majority of the cases lead to marked decrease of uric acid concentration in serum. In healthy subjects dicumarol also decreased uric acid level in serum and increased its elimination.

*Schlechte Eigenschaft langwirkender Coumarine oder für deren Kontrolle ungeeignete Thrombo-kinase.* Loeliger, A., Gerinnungsphysiol. Lab., Med. Univ.-Klinik, Leiden, Holland. Schweiz. med. Wschr. 88: 639 (1958).

It has been shown that the control of anticoagulant therapy with long acting coumarin derivatives can be inaccurate if the "prothrombin time" test is performed with an thrombo-plastin that is not entirely sensitive to factor VII levels. The reason for this is found in the fact that the effectiveness of the therapy during the first few days of coumarin administration is indicated by the rate of factor VII decrease.

*Mikroskopische Untersuchungen über die Wirkung des Antikoagulans Marcoumar auf die Gefäß-permeabilität.* Witte, S., Med. Klinik, Univ. Erlangen, Germany. Folia haemat. 2: 366 (1958).

*Observations sur l'action thérapeutique de Sintrom.* Gaertner, H., Szmigiel, Z., Tutajowa, L., III<sup>e</sup> Clin. Maladies Int., Académie de Méd., Cracovie, Poland. Haematologica Cracoviensia 2: 236 (1958).

A study on the anticoagulant Sintrom (Geigy) revealed that the preparation has very strong anticoagulant action in spite of the small doses needed (20 to 4 mg/die) and that it is not cumulative. Prothrombin values normalize within 24 to 48 hours following discontinuation of the drug. The authors mention the general difficulty of fixing proper daily dosage in order to maintain therapeutic prothrombin values.

*Results in the Treatment of Myocardial Infarction with Anticoagulants.* Kushelevsky, B. P., Yasakova, O. I., Terp. Arkhiv 30: 3 (1958). (Moscow). (In Russian.)

*Über eine neue Kontrollmethode der Antikoagulantientherapie.* Zollikofer, H., v. Schulthess, P., Pugatsch, I., Med. Abtg., Krankenhaus Neumünster, Zollikerberg, Zürich, Switzerland. Helv. med. Acta 25: 465 (1958).

The authors suggest Stuart factor determination as a method of control of anticoagulant therapy as this factor is more likely to indicate a bleeding tendency than does the widely used Quick test.

*Der Gerinnungsdefekt bei Marcoumar-Abusus.* Kaufmann, G., Bachmann, F., Streuli, F., Wegmann, T., Med. Klinik, Kantonsspital, St. Gallen, Switzerland. Helv. med. Acta 25: 470 (1958).

The authors report 3 cases of self-intoxication with marcoumar. In every case of unidentified bleeding the abuse of anticoagulants by mistake or other reasons (simulation, suicide) should be taken into consideration. Diagnosis of intoxication by coumarin derivatives or phenylindanedione can be established by typical coagulation deficiency, absence of previous bleeding episodes, of severe liver damage, of obstructive jaundice or of severely disturbed fat metabolism.

*Distribution of Phenylindanedione in Blood and Tissues after Oral and Intravenous Administration.* Millar, G. J., Mersereau, M. O., Lowenthal, J., Jaques, L. B., Dept. Physiol. and Pharm. Univ. of Saskatchewan, Saskatoon, Canada. Thromb. Diath. haem. 2: 236 (1958).

*Biochemie und Pharmakologie der Antikoagulantien.* Winterstein, A., Wissenschaftl. Abtg., F. Hoffmann-La Roche, Basel, Switzerland. Thromb. Diath. haem. 2: 428 (1958).

*Methoden zur Kontrolle der Antikoagulantienwirkung.* Loeliger, A., Med. Univ.-Klinik, Leiden, Holland. Thromb. Diath. haem. 2: 441 (1958).

*Anticoagulant Protection in Surgery.* Storm, O., Rikshospitalet, Copenhagen, Denmark. Thromb. Diath. haem. 2: 484 (1958).

*Long Term Treatment with Anticoagulants in Coronary Artery Disease.* Owren, P. A., Rikshospitalet, Oslo, Norway. Thromb. Diath. haem. 2: 492 (1958).

*The Use of Anticoagulants in Cardiology.* Formijne, P., Afdeling Int. Ziekten, Wilhelmina Gasthuis, Amsterdam, Holland. *Thromb. Diath. haem.* 2: 505 (1958).

*Probleme der Antikoagulantienbehandlung.* Deutsch, E., Benda, L., Zischka, W., I. Med. Univ.-Klinik, Wien, Austria. *Thromb. Diath. haem.* 2: 510 (1958).

*Control of Anticoagulant Treatment.* Winterstein, A., Wissenschaftl. Abtg., F. Hoffmann-La Roche, Basel, Switzerland. *Thromb. Diath. haem.* 2: 546 (1958).

*Abortive Hemorrhagic Cutaneous Necrosis Following Dicumarol.* Mikkelsen, M., Amtssygehuset, Hobro, Denmark. *Nord. Med.* 60: 1758 (1958).

A 67-year-old woman with coronary thrombosis treated with dicumarol for a week developed several hemorrhagic subcutaneous infiltrations which probably represented an abortive form of the more severe cutaneous necrosis of which some 26 cases have been published since 1954. The case described here is the first one reported in connection with coronary thrombosis, the main disease in all other cases being venous thrombosis. Histologic examination gave no evidence of allergic origin, but was more compatible with the common conception that the complication is caused by a specific toxic effect of dicumarol on the capillaries, an effect independent of the prothrombin decreasing effect of dicumarol.

*Anticoagulant Therapy in Acute Myocardial Infarction.* Richards, R. L., *Scottish med. J.* 3: 235 (1958).

*Expérimentation clinique de la pommade anticoagulante "Pindione" dans quelques cas de phlébites et de périphlébites.* Rousselle, J., *Praxis* 47: 1078 (1958).

The author reports upon 25 cases of superficial phlebitis treated with the anticoagulant ointment "Pindione". The results were excellent, and the drug is highly recommended.

*The Significance of Hemorrhage During the Treatment of Patients with the Coumarin Anticoagulants.* Peyman, M. A., Charing Cross Hosp., London, England. *Acta med. scand.* 162: suppl. 339 (1958).

The mechanism of hemorrhage in patients treated with coumarin anticoagulants is discussed. The literature is reviewed and evidence presented which suggests that although the most obvious action of these drugs is an interference with blood coagulation, other effects such as damage to the capillary walls and reduction of platelet adhesiveness may also be important in the production of hemorrhage. The advantages and the limitations of the one-stage prothrombin time in the management of these patients are discussed. The clinical features of coumarin-induced hemorrhages are discussed. Microscopic hematuria was the most common sign of coumarin overdosage. Daily examination of the urine by a sensitive test is suggested as a useful safety measure which should be adopted in addition to regular estimation of prothrombin time. Contraindication to coumarin drugs are discussed. It is concluded that effective coumarin treatment is now practicable both on a short and a long term basis. In this series most of the hemorrhages were minor and none were fatal. All the out-patients were able to continue their normal activities. Although minor hemorrhages are always liable to occur, there is now abundant evidence that the fear of hemorrhage should not preclude the use of the coumarin drugs in clinical medicine.

*Probleme der Antikoagulantienbehandlung.* Jordan, F. L. J., Utrecht, Holland. *Thromb. Diath. haem.* 2: 582 (1958).

*Side-Effects and Contraindications of Anticoagulants.* Koller, F., Med. Abtg., Krankenhaus Neumünster, Zollikerberg, Zürich, Switzerland. *Thromb. Diath. haem.* 2: 604 (1958).

*Dicumarol and Serum Uric Acid.* Hansen, O. E., Holten, C., Aarhus, Denmark. *Ugeskr. Laeg.* 120: 974 (1958).

An uricosuric effect of dicumarol has been observed. In most of the 40 patients given anticoagulant treatment with heparin and dicumarol, there was a reduction of over 20% in the

serum uric acid value. The question is raised as to what extent the improved prognosis in ischemic cardiac disorder after treatment with anticoagulants depends only on the prolonged coagulation time, or whether the effect of these agents on the uric acid metabolism may be significant.

*Armchair Treatment with and without Anticoagulants in Cardiac Infarction.* Helander, S., Med. Dept. I, Karolinska Sjukhuset, Stockholm, Sweden. *Acta med. scand.* 162: 351 (1958).

The material consists of 112 cases treated in an armchair and given anticoagulants (mortality 10%); 100 cases treated in an armchair without anticoagulants (mortality 15%); and 80 cases with bed-rest and anticoagulants (mortality 26%). Armchair treatment seems to constitute a good prophylactic measure against embolic complications and it seems probable that it is sufficient to treat only the bad prognostic risks with anticoagulants i.e. patients with arrhythmia, heart block and cardiac failure (Dicumarol).

*Clinical Experience with Warfarin Sodium.* Toohey, M., New End Hosp., London, England. *Brit. med. J.* 5101: 892 (1958).

Warfarin sodium was used in the treatment of 175 patients with thromboembolic diseases. It is a rapidly acting drug and 95% of all patients reached a therapeutic prothrombin time in 36 hours. Warfarin proved extremely easy to control and it is also very useful for long-term anticoagulant therapy.

*Long-Term Anticoagulant Therapy for Coronary Thrombosis.* Toohey, M., New End Hosp., London, England. *Brit. med. J.* 5094: 472 (1958).

117 patients were treated with long-term anticoagulant therapy for 6 months or longer. The results, technic, control of this type of treatment are discussed.

*Antikoagulantien und Blutgruppenreaktionen.* Dotzauer, G., Hamburg, Germany. *Ärzt. Wschr.* 37: 814 (1958).

*Intérêt et limites de la thrombéléastographie dans la surveillance des traitements anticoagulants en cardiologie.* Mouquin, M., Marchal, G., Sawvan, R., Samama, M., Seroux, M., Richon, J., *Presse méd.* 66: 1703 (1958).

*Prévention des accidents thrombo-emboliques chez les opérés par le traitement anticoagulant pré- et postopératoire précoce et la correction des troubles hydroélectrolytiques.* Eurin, Brunet, *Presse méd.* 66: 1727 (1958).

*Die Antikoagulantien in der Prophylaxe und Therapie thrombo-embolischer Erkrankungen.* Hartert, H., Med. Univ.-Klinik, Heidelberg, Germany. *Ther. Umsch.* 15: 258 (1958).

(Heparin and marcoumar).

*Terapia anticoagulante con il fenilindanedione. Schemi di terapia piu opportuni. Terapia prolungata.* Gardi, L., Biffani, G., Reparto cardiol., Ospedali Riuniti, Roma, Italy. *Minerva med.* 49: 2252 (1958).

*Blutunfallsfall bei Thromboseprophylaxe mit Sintrom nach Sectio caesarea.* Deimel, H., Univ.-Frauenklinik, Saarbrücken. *Geburtsh. und Frauenheilk.* 18: 1028 (1958).

*The Problem of Interpretation of Results Obtained by Long-Term Anticoagulant Treatment in Myocardial Infarction.* Jordan, F. L. J., Punt, K., Med. Dept. Univ. Hosp., Utrecht, Holland. *Acta med. scand.* 162: 137 (1958).

*Erfahrungen mit genereller Thromboseprophylaxe. Ein Bericht über 3000 mit Hydroxycoumarin-Derivaten behandelte Patienten (Marcoumar).* Cramer, W., Pohlhaus, E., Chir. Klinik, Freie Univ., Berlin, Germany. *Brun's Beitr. klin. Chir.* 196: 1 (1958).

General prophylactic treatment against thrombosis included early rising on the first postoperative day and on the 2nd or 3rd day after major operations, exercises in bed and administration of anticoagulants. 3194 thus treated received Marcoumar as an anticoagulant. Comparative studies revealed that the incidence of thrombosis and pulmonary embolism, and particularly that of fatal pulmonary embolism, was definitely reduced by anticoagulant therapy. Emphasis is put on the fact that not every occurring hemorrhage is due to the administration of anticoagulants but that great care must be taken to determine the Quick values immediately when inspection of the operative wound reveals recent substanceous blue discoloration. On the whole the general prophylaxis has proved valuable.

*Efficiency and Limitations of Anticoagulant Therapy in Arterial Thrombosis. Panel Discussion.* 6th Congress Europ. Soc. Hematol., Copenhagen (1957, Cardiol. Suppl. fasc. 8 (1958).

*Anticoagulation Treatment.* Owren, P. A., Rijkshosp., Oslo, Norway. T. norske Laegeforen. 78: 571 (1958).

All anticoagulant treatment is in its nature prophylactic and should be introduced at an early stage. Permanent anticoagulant treatment affords protection against renewed embolization in patients with rheumatic heart disease, considerably reduces the mortality in myocardial infarction and has a marked prophylactic effect in angina pectoris if the interval between diagnosis and treatment in angina pectoris is less than a year. The treatment has little if any effect on the mortality in patients with angina pectoris of more than 2 years' duration before treatment.

*Sintrom Long-Term Therapy in Angina Pectoris.* Wirecki, M., Center f. Anticoagulant Therapy, Int. Clinic, Warsaw, Poland. Cardiol. 33, suppl. (1958).

In 50 cases of angina pectoris, 25 patients without previous infarction, and 25 with one or several previous infarctions, the effect of long-term Sintrom therapy has been tested. The results were compared to those obtained in a similar group of 50 patients treated by classical methods. The average observation period was 15.2 months in the Sintrom group and 14.52 months in the controls. Average maintenance dose of Sintrom was 2.66 mg. The duration and the incidence of anginal attacks in the Sintrom group were reduced to a much greater degree and in many more patients than in the control group. Long-term therapy with "prothrombin"-reducing drugs is a valuable therapeutic method in angina pectoris, both with and without cardiac infarction. Sintrom shows, in the group of anticoagulant drugs, a marked superiority for its therapeutic efficiency and lack of toxicity.

*Ervaringen met het indirect werkende anticoagulans Marcoumar bij de trombosedienst.* Kettenborg, H. K., Stichting "Amsterdamse Trombosedienst", Amsterdam, Holland. Nederl. Geneesk. 102: 2269 (1958).

*Risiken der Thrombosetherapie.* Deutsch, E., I. Med. Univ.-Klinik, Wien, Austria. Wien. Z. inn. Med. 39: 387 (1958).

*Über ein neues Sofort-Antikoagulans zur Therapie bei Durchblutungsstörungen, Embolien und Thrombosen.* Mehl, H., Inn. Abtg., Städt. Krankenanstalten, Eßlingen/Neckar, Germany. Med. Klin. 53: 1911 (1958).

*The Uricosuric Action of Bishydroxycoumarin (Dicumarol).* Dreyfuss, F., Czaczkes, Dept. Med. A. Rothschild Hadassah Univ. Hosp., Jerusalem, Israel. Arch. intern. Med. 102: 389 (1958).

The influence of dicumarol on renal uric acid clearance has been examined. 111 clearance periods were studied. It was found that doses of 25 to 200 mg of this drug definitely increased uric acid clearance. This effect is proportionate to the dose administered. It can only be demonstrated when a particular clearance period is related to a dose of the drug given a number of hours before the beginning of this period. The role of this uricosuric action of dicu-

marol is briefly discussed with reference to those cases of coronary artery disease that exhibit an elevated uric acid level of their blood.

*Acute Myocardial Infarction in a City Hospital: I. Clinical Review of 264 Cases.* Malach, M., Rosenberg, B. A., Kings County Hosp., Brooklyn, N. Y., USA. *Amer. J. Cardiol.* 1: 682 (1958).  
*II. Experience with Anticoagulants.* Rosenberg, B. A., Malach, M., *Amer. J. Cardiol.* 2: 71 (1958).

There are 3 points of view with regard to the use of anticoagulants in acute myocardial infarction: 1) they should be used routinely, 2) they should be used selectively, and 3) they should not be used at all. This report deals with the use of anticoagulants in patients with acute myocardial infarction discharged from the King's County Hospital, Brooklyn. Of a total of 264 such patients, 66 received anticoagulants, while 198 did not. Anticoagulants did not improve the survival rate in this series. There was but one major hemorrhagic complication and this did not contribute to the death of the patient. The authors observed cardiac rupture in 3 patients who did not receive anticoagulants.

*Effects of Certain Anticoagulants on Serum Enzyme Activity.* Wroblewski, F., Manso, C., Dept. Med., Sloan-Kettering Inst., New York, N. Y., USA. *J. Amer. med. Ass.* 167: 18 (1958).

When serum enzymes are employed as indices of cardiac tissue necrosis, the effect of certain anticoagulant drugs on the serum transaminase activity must be taken into account. The administration of dicumarol in doses employed clinically to an individual without liver disease usually results in little or no change in serum transaminase activity, in a patient with liver disease it may be accompanied by an increase. The administration of dicumarol and tromexan to a patient with acute myocardial infarction may result in serum enzyme activity elevations independent of the changes resulting from myocardial necrosis.

*Peripheral Arterial Emboli.* McGarity, W. C., Logan, W. D., Cooper, F. W., *Surg. Gynec. Obst.* 106: 399 (1958).

The authors present a survey of therapy in 86 cases of peripheral arterial embolism. Conservative treatment is indicated only if the patient is in very poor condition. Immediate anticoagulation is important in any case. In all other cases the authors advocate embolectomy. Dicumarol-like drugs should be administered for months postoperatively. The authors come to the conclusion that in cases of occlusion of the aorta or the illiaca surgical intervention must be stated individually in every case.

*Anticoagulant Action of Protamine Sulphate.* Hougie, C., Dept. clin. Path., Univ. of Virginia, Charlottesville, Va., USA. *Proc. Soc. exp. Biol. (N. Y.)* 98: 130 (1958).

Protamine sulphate in low concentrations affects both rate and yield of blood thromboplastin but has no effect on formed thromboplastin. Relatively higher concentrations inhibit a reaction between blood thromboplastin, prothrombin and calcium.

*The Uricosuric Effect of Certain Oral Anticoagulant Drugs.* Thompson, G. R., Mikkelsen, W. M., Willis, P. W., Ann Arbor, Mich., USA. *J. Lab. clin. Med.* 52: 950 (1958).

The anticoagulant drugs Tromexan and Dicumarol have recently been shown to have uricosuric properties. Salicylates have long been known to have both anticoagulant and uricosuric effects. The uricosuric action of single oral doses of tromexan and acenocoumarin, of anisindione and phenylidanedione was compared to the effect of one single oral dose of probenecid. Thus Tromexan, probenecid and phenylidanedione were found to have uricosuric action, while anisindione and acenocoumarin lacked this effect in the doses employed.

*Long-Term Anticoagulant Therapy in Coronary Atherosclerosis.* Nichol, E. S., Keyes, J. N., Borg, J. F., Coogan, T. J., *Amer. Heart J.* 55: 142 (1958).



A compilation of the results of the pooled clinical investigation of 1091 patients with coronary atherosclerosis treated with long-term anticoagulants by a number of widely separated clinicians is presented. Of this group 4.2% developed non-fatal thromboembolism and 12.0% died while on the regimen, mostly from cardiac disease. Hemorrhage of significant character occurred at some time during treatment in 220 patients, but in only 6 could hemorrhagic complications be incriminated as causing death. 319 patients abandoned anticoagulants for one reason or another. Follow-up studies of these showed that 28.2% died within 4 years, chiefly due to cardiac disease. 417 patients not given anticoagulants were used as controls. Of this group 37.4% died, the majority from cardiovascular disease. The authors believe that the data of this study warrant the conclusion that the continuing administration of anticoagulants does prevent recurrent attacks of myocardial infarctions.

*Clinical Experience with the Anticoagulant Warfarin Sodium ("Coumadin Sodium").* Porter, R. R., Richardson, D., Page Mauck, H. Virginia med. Month. 85: 465 (1958).

*Theory and Practice in Acute Venous Thrombosis. A Reappraisal.* Wessler, S., Deykin, D., Med. Res. Dept., Beth Israel Hosp., Boston, Mass., USA. Circulation (N. Y.) 18: 1190 (1958).

The purpose of this review is to outline the basis for proposing, and the details for implementing, a rational and consistent plan of therapy for the management of acute venous thrombosis. Various aspects of the therapeutic approach are described in detail and illustrated by selected case studies.

*Subdural Hematoma Related to Anticoagulation Therapy.* Nathanson, M., Cravioto, H., Cohen, B., Depts. Neurol., N. Y. Univ. College of Med., New York, N. Y., USA. Ann. intern. Med. 49: 1368 (1958).

Two patients are reported who developed subdural hematoma in relation to anticoagulation therapy. In one case the hematoma was discovered at postmortem examination, in the other relatively early in the course of the illness and successfully removed. The need for consideration of subdural hematoma as a complication of dicumarol treatment is emphasized whenever mental and neurologic signs develop during the course of anticoagulation. "Trivial" or "minor" head trauma during anticoagulant therapy cannot be fully eliminated as a possible initiating factor.

*Hemorrhagic Effect of ACTH with Anticoagulants.* Van Cauwenberge, H., Jaques, L. B., Dept. Pharm., Univ. of Saskatchewan, Saskatoon, Sask., Canada. Canad. med. Ass. J. 79: 536 (1958).

The simultaneous administration of dicumarol or phenylindanedione and ACTH to rabbits lead to fatal bleeding in 25 to 30% of the cases. In connection with these results the authors report the case of a woman with severe gastrointestinal hemorrhage caused by combined therapy with ACTH and tromexan. The same patient had previously received tromexan only and no complications had occurred.

*Treatment of Cardiac Infarction with Oral Anticoagulants.* Manson, D. I., Aberdeen, Scotland. J. Amer. Ger. Soc. 6: 754 (1958).

Oral anticoagulants (ethyl-biscoumacetate and phenindione) reduced the mortality rate in a group of 162 patients with cardiac infarction as compared to an untreated control group. Thromboembolic complications are the most frequent death cause following cardiac infarction. To reduce the number of fatal cases intravenous injection of heparin is advised during the first 24 hours e.i. until oral anticoagulants are effective.

*Comparative Study of two Anticoagulants (Heparin vs. Dicumarol) in Acute Complicated Myocardial Infarction.* Griffith, G. C., Zinn, W. J., Engelberg, H., Dooley, J. V., Anderson, R., Los Angeles, Calif., USA. Circulation (N. Y.) 18: 728 (1958).

The authors compared the effect of heparin and of dicumarol in cases of acute myocardial infarction. The heparin group (100 patients) which contained more severe cases had a lethality

of 28%, and the dicumarol group of 63 patients a letality of 38%, although dicumarol had been combined with heparin during the first 2 to 3 days.

*Clinical Evaluation of Acenocoumarol (Sintrom), an Anticoagulant of Intermediate Range.* Rullo, F. R., Bartels, C. C., Evans, J. A., Boston, Mass., USA. J. Amer. med. Ass. 168: 743 (1958).

Acenocoumarol (Sintrom, Geigy) was found to be a reliable and compatible anticoagulant in 100 cases of thrombosis. The average initial dose was 21 mg, maintenance dose 6.6 mg daily.

*Management of Acute Venous Thromboembolism.* Anlyan, W. G., De Laughter, G. D., Fabrikant, J. I., Sullenberger, J. W., Durham, N. C., USA. J. Amer. med. Ass. 168: 725 (1958).

The authors present a survey of etiology, diagnosis, prognosis and therapy of venous thromboembolism.

*The Influence of Anticoagulant Therapy on the Occurrence of Cardiac Rupture and Hemopericardium Following Cardiac Infarction.* Aarseth, S., Lange, H. F., Dept. VII, Ulleval Hosp., Oslo, Norway. Amer. Heart J. 56: 250 and 275 (1958).

Among 1303 cases of cardiac infarction (94% autopsy) 89 cases with hemopericardium were found: 81 cases of cardiac rupture, 3 aortic rupture, 5 without recognizable rupture, all 5 under anticoagulant therapy. After exclusion of cases with prothrombin levels below therapeutic levels, 69 cases remained with effective anticoagulation. Comparison with 72 cases of cardiac infarction without anticoagulant treatment revealed that hemopericardium and cardiac rupture are twice as frequent under anticoagulation.

*Studies on the Possible Relationship of Tolbutamide to Dicumarol in Anticoagulant Therapy.* Chaplin, H., Cassell, M. Amer. J. med. Sci. 235: 706 (1958).

After a 1 week therapy with dicumarol two patients received additional tolbutamide for slight diabetes. 24 to 48 hours after administration of the two drugs an unusually marked prolongation of hitherto stable prothrombin level occurred asking for immediate withdrawal of dicumarol. It is assumed that tolbutamide has an anticoagulant effect or that it enhances the effect of dicumarol. Experiments in animals and in vitro did, however, not confirm this.

*Clinical Experience with Orally Administered Warfarin Sodium.* Danford, H. G., Juergens, J. L., Barker, N. W. Proc. Mayo Clin. 33: 359 (1958).

*Heart Lesions in Mice Caused by Treatment with Dicumarol.* Dessau, F. I., Klein, S., Lipchuck, L., O'Grady, J., Tsalikis, J., Pearl River, N. Y., USA. J. Pharm. exp. Ther. 122: 18A (1958).

The addition of 0.02% of dicumarol to the fodder lead to cardiac lesions in mice. This effect could be prevented by adding 0.04% of vitamin K. Vitamin E had no protective effect.

*Phenprocoumon (Marcoumar). An Agent for Short-Term Anticoagulant Therapy.* McCall, Priest, E., Pauli, H. G., Detroit, Mich., USA. Amer. J. Cardiol. 2: 61 (1958).

The authors report favorable results obtained with marcoumar in 134 patients with myocardial infarction, coronary insufficiency and thrombophlebitis. Bleeding occurred in 3.7% of the patients and was immediately controlled by Vitamin K.

*Clinical Experience with Intramuscular Warfarin Sodium (Coumadin Sodium).* Trumble, K. A., Dept. Med., Univ. of Wisconsin Med. School, Madison, Wisc., USA. Surg. Gynec. Obstet. 107: 303 (1958).

### s) Thrombosis

*Thrombotische Mikroangiopathie.* Frick, P., Ziegler, W., Gubler, R., Med. Klinik, Path. Anat. Inst., Univ., Zürich, Switzerland. Helv. med. Acta 25: 454 (1958).

The clinical features and the pathologic aspects of thrombotic microangiopathy are illustrated by means of two cases with intra vitam diagnosis.

*Organization of the "Thrombosis Service" in the Netherlands.* Jordan, F. L. J., Utrecht, Holland. *Thromb. Diath. haem.* 2: 527 (1958).

*Organization of the Thrombosis Service in the Netherlands.* de Vries, S. I., Amsterdam, Holland. *Thromb. Diath. haem.* 2: 633 (1958).

*Bilateral Thrombophlebitis After a Single Dose of Ergotamine Tartrate for Migraine.* Carter, E. R., Runcorn, Cheshire, England. *Brit. med. J.* 5110: 1452 (1958).

Three case reports.

*Thrombosis of the Major Pulmonary Arteries.* Amos, J. A. S., Dept. Path., St. George's and Southampton Group Hosps., London, England. *Brit. med. J.* 5097: 659 (1958).

Discussion of 19 cases.

*Lungenembolie.* Seitz, W., München, Germany. *Dtsch. med. Wschr.* 83: 1407 (1958).

The author presents a brief survey of diagnosis and therapy of pulmonary embolism.

*Butazolidine et phlébite superficielle. Considérations cliniques et thérapeutiques.* Bourde, M. M. C., Bernard, P., Marseille, France. *Presse méd.* 66: 1268 (1958).

*Spätresultate nach konservativ behandelte tiefer Thrombose der unteren Extremitäten.* Djelali, D., Basel, Switzerland. *Gynaecologica (Basel)* 145: 167 (1958).

*Fünf Jahre Thromboembolie-Prophylaxe mit Hirudoid.* Daniel, W., Somloi, L., Wien, Austria. *Wien. med. Wschr.* 24: 512 (1958).

*Thromboembolic Lung Lesions.* Bang, N., Iversen, K., Schmidt, H., Med. afdeling 2, Kommunehosp., Copenhagen, Denmark. *Nord. Med.* 60: 1413 (1958).

*Prophylaxie des accidents thrombo-emboliques en chirurgie gynécologique. Essai d'un nouveau médicament: le PH 203.* Decrausaz, H., Rossel, G., Clin. univ. d'obstétrique et de gynécologie, Lausanne, Switzerland. *Praxis* 47: 993 (1958).

During a period of 6 months the authors controlled simultaneously the number of thromboembolic complications occurring postoperatively in 2 groups of patients, one of the two having received prophylactic treatment with PH 203 (panthesin + hydergin). This preparation has no effect on blood coagulability, and can therefore, be administered immediately before or after operation. No laboratory control is necessary. In the group of patients without medication the normal average amount of complications occurred, whereas in the group prepared with PH 203 no thrombosis or pulmonary embolism were found. Although the number of patients investigated is too small to allow for conclusions, the results seem favorable, and PH 203 prophylaxis in operated patients endangered with thromboembolism indicated.

*Maladie thrombotique artériolocapillaire du rein chez l'enfant.* Habib, R., Mathieu, H., Royer, P., Centre d'Etude des Maladies du Métabolisme chez l'Enfant, Hôp. des Enfants-Malades, Paris, France. *Rev. franç. Etudes clin. and biol.* 3: 891 (1958).

A review of 60 fatal cases of renal disease in infants has revealed 6 cases with an acute renal lesion characterized by a) thrombotic lesion of the small vessels confined to the kidneys, b) a hemolytic anemia with distortion and shrinking of the red cells, c) a inconstant thrombocytopenic purpura and d) a renal lesion either with anuria, a nephrotic syndrome or most commonly, with hematuria and normal amount of urine, with hyponatremia, hypokalaemia and nitrogen retention.

*Die Ätiologie der Venenthrombose.* McLachlin, J., Paterson, J. C., Westminster Hosp., London, Ont., Canada. *Klin. Wschr.* 36: 645 (1958).

The authors present their various observations on the problem of venous thrombosis. The most frequent site of origin of venous thrombosis was found to be basin more than calf veins. Venous stasis in basin veins and in veins of lower extremities is more decisive for the origin of thrombosis than primary alterations of vein walls or abnormal coagulation. Surgical ligation of vena femoralis in pulmonary embolism as prophylactic or therapeutic measure does not seem to be effective according to the authors' observation.

*Thrombose des Ductus arteriosus Botalli mit Aortenverschuß.* Grosse, H., Bezirkskrankenhaus „Am Sund“, Stralsund, Germany. *Z. Kreisl.Forsch.* 47: 983 (1958).

Case report of a 21-day-old male child which died of thrombosis of the ductus arteriosus and connecting aorta of the breast.

*Über den Einfluß von Butazolidin auf das Blutgerinnungssystem, seine Verträglichkeit bei der Behandlung thrombophlebitischer Zustände.* Heinrich, H. G., Berlin, Germany. *Ärzt. Wschr.* 13: 839 (1958).

*Neuere Wege der Thrombophlebitisprophylaxe.* Feiks, F. K., Wien, Austria. *Wien. med. Wschr.* 108: 815 (1958).

A daily oral or parenteral dose of 600 mg of phenylbutazone is recommended for prophylactic treatment of thrombosis.

*Die thromboembolische Krankheit während Schwangerschaft und Wochenbett. Die Häufigkeit ihres Vorkommens in Fällen von chronischer Nephritis, Präeklampsie und Eklampsie.* Kese, G., Frauenklinik, Cluj, Rumania. *Zbl. Gynäk.* 80: 1299 (1958).

*Zur Genese der Koronarthrombose.* Jürgens, R., Wiss. Abtg., F. Hoffmann-La Roche, Basel, Switzerland. *Wien. Z. inn. Med.* 39: 313 (1958).

*Therapie der akuten Koronarthrombose.* Matthes, K., Univ.-Klinik, Heidelberg, Germany. *Wien. Z. inn. Med.* 39: 328 (1958).

*Die arterielle Embolie.* Dick, W., Chir. Univ.-Klinik, Tübingen, Germany. *Wien. Z. inn. Med.* 39: 882 (1958).

*Serumdiagnose der Koronarthrombose.* Weissel, W., III. Med. Abtg., Wilhelminenspital, Wien, Austria. *Wien. Z. inn. Med.* 39: 365 (1958).

*Neuere Aspekte in der Blutgerinnung und der Fibrinolyse und ihren Beziehungen zur Koronarthrombose und Koronarsklerose.* Astrup, T., Biol. Inst., Karlsberg-Stiftung, Kopenhagen, Denmark. *Wien. Z. inn. Med.* 39: 373 (1958).

*La thrombélastographie chez les cardiaques.* Raynaud, R., Clin. théér. méd., Univ., Alger. *Presse méd.* 66: 1969 (1958).

*Thrombotic Microangiopathic Hemolytic Anemia.* Robinson, M. J., Austin Hosp., Heidelberg, Melbourne, Australia. *Arch. Dis. Childh.* 33: 520 (1958).

*Mesenteric Vascular Thrombosis.* Robertson, R. W., Haley, W. B. *J. Kentucky med. Ass.* 56: 568 (1958).

*Arterial Thrombosis with Gangrene After Use of Promazine (Sparine) Hydrochloride.* Opinsky, M., Serbin, F., Rosenfeld, J. E., Hartford, Conn., USA. *J. Amer. med. Ass.* 168: 1224 (1958).  
Two case reports.

*Variations in a Plasma Enzyme Activity with Special Reference to Patients with Thrombo-embolic Tendencies.* Arscott, P. M., Koppel, J. L., Olwin, J. H., Chicago, Ill., USA. J. Lab. clin. Med. 52: 962 (1958).

*Thrombophlebitis in Patients with Severe Poliomyelitis.* Ferris, B. G., McNichol, B. Sutin, G., Dept. Physiol., Harvard School of Public Health, Boston, Mass., USA. New Engl. J. Med. 259: 971 (1958).

Thrombophlebitis occurred during convalescence in the lower limbs of 9 severely paralyzed patients. Thrombophlebitis usually developed during the first 6 weeks of the illness. It is suggested that circulatory stasis and hemoconcentration of even mild degree are important in the development of this complication. Dehydration, hypoventilation and possibly other factors are implicated, and hence adequate hydration and ventilation should be maintained during the acute illness.

*Multiple Thrombotic Episodes with Death Following a Reaction to Miokon.* Clinicopathologic Conference, Washington University School of Med. Amer. J. Med. 25: 950 (1958).

*Acute Thrombosis of the Anterior Tibial Artery.* Albanese, A. R., Av. Callao 137 2nd and 3rd A., Buenos Aires, Argentina. Angiology 9: 172 (1958).

*A Clinical Evaluation of Parenteral Trypsin in Thrombophlebitis.* Marino, D. J., Philadelphia, Pa., USA. Antibiotic Med. 5: 553 (1958).