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Physiology and Pathology of Blood Coagulation

A Review of the Literature of 1958 (First Series)

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Index

As a rule articles appearing in Thromb. Diath. haem. will not be summarized, but only mentioned by their title.

a) General Aspects

Hemorrhagic Diathesis Due to Increased Capillary Fragility Secondary to Ovarian Deficiency. Wells, R., Dept. Med., General Hosp., Singapore. Lancet *1:* 886 (1958).

A case is described of a woman in whom a hemorrhagic diathesis developed owing to increased capillary fragility following oophorectomy; this responded well to oestrogen therapy. This syndrome resembles hereditary familial purpura simplex, which in turn resembles allergic Schönlein-Henoch purpura. Hereditary familial purpura simplex may also be found to respond to oestrogen therapy.

Dietary Restriction and Coagulability of the Blood in Ischaemic Heart Disease. McDonald, L., Edgill, M., Inst. Cardiology, National Heart Hosp., London W 1., England. Lancet *1:* 996 (1958).

Coagulability of the blood was studied in 34 patients with ischaemic heart disease, before and after half of them had maintained a rice-fruit diet for 4—5 weeks. A statistically significant decrease in platelet-stickiness was found after the diet, together with a statistically significant decrease in serum-cholesterol and other changes. No significant difference was found in thromboplastin generation, fibrinogen estimation, and prothrombin-time (Stypven).

The Separation and Properties of an Anticoagulant Principle from Russell's Viper Venom. Bowers, E. F., Hall, G. H., Univ. Coll. Hosp., London, England. Brit. J. Haematol. *4:* 220 (1958).

The observation that Russell's viper venom contains an anticoagulants as well as a coagulant substance is confirmed. The properties of the anticoagulant fraction are discussed. It prolongs the clotting times of normal, Dindevan or Christmas factor-deficient plasma. Neither coagulant nor anticoagulant fraction affects the thrombin-fibrinogen reaction. The coagulant fraction appeared to be homogenous in that its effects on plasma samples deficient in various clotting constituents were similar. The coagulant activity was completely removed from preparations which had been absorbed to aluminium hydroxide.

Neue gerinnungsanalytische Befunde beim Neugeborenen. Beller, F. K., Univ.-Frauenklinik, Tübingen, Germany. Geburtsh. u. Frauenheilk. *18:* 447 (1958).

The author was able to demonstrate a decreased antithrombin II level in the newborn, whereas the values of plasmin disintegration were found to be normal.

Leberdiagnostik mit der Blutgerinnungsanalyse. Jürgens, J., II. Med. Univ.-Klinik, Frankfurt/M., Germany. Medizinische *21:* 857 (1958).

Le alterazioni dell'emostasi e dell'emocoagulazione nelle leucemie. Manai, G., Mandelli, F., Ist. Clin. Med. Generale, Univ., Parma, Italy. G. Clin. med. *39:* 351 (1958).

Ist die Verkürzung der Blutgerinnungszeit nach alimentärer Fettbelastung medikamentös zu verhindern? Lasch, H. G., Med. Univ.-Klinik, Heidelberg, Germany. Medizinische 23: 944 (1958).

Die Steigerung der Kapillarpermeabilität durch Blutgerinnungsstörungen. Witte, S., Med. Univ.-Klinik, Erlangen, Germany. Thromb. Diath. haem. *4:* 146 (1958).

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

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

La coagulation du sang. Gaertner, H., 3e Clin. Maladies Int., Académie de Méd. Cracovie, Poland. Haematologica Cravoviensia *2:* 185 (1958).

The author presents historic data on the findings of coagulation factors and their repartition in blood cells, plasma and tissue. A description is given of platelet factors, plasmatic coagulation factors, the coagulation mechanism. The survey ends with a classification of hemostatic defects.

L'influence des états psychiques sur la coagulation sanguine. Gaertner, H., 3e Clin. Maladies Int., Académie de Méd., Cracovie, Poland. Méd. Lab. *8:* 35 (1958).

Die Therapie akuter Blutungen im Kindesalter. Haupt, H., Univ.-Kinderklinik, Bonn, Germany. Mschr. Kinderheilk. *106:* 245 (1958).

After discussing the main types of hemorrhagic diatheses the bleeding disorders of childhood are reported. Conservative therapy consists of 1. general and 2. local measures and of 3. direct approach of disturbed coagulation. The latter consisting in stimulation of production of coagulation factors, replacement of deficient factors, or inactivation of coagulation inhibitors. These methods of therapy are particularly effective and should be reserved for the severe cases together with local hemostasis and general therapeutical measures.

Blutgerinnung und Kreislauf. Perlick, E., Med. Klinik, Med. Akademie, Magdeburg, Germany. Dtsch. Arch. klin. Med. *205:* 118 (1958).

The author studied the effect of a decrease in blood volume on the coagulation system in 58 persons. Blood coagulation, heparin-like inhibitors, and fibrinolytic activity were analysed by thrombelastographic methods. Immediate decrease of blood volume induces decrease or increase of coagulative tendency, suggesting different regulation phases, which again guarantee regular correlation between circulation and intravasal coagulation.

Dextran and Prolonged Bleeding Time. Results of a Sixty-Gram, One-Liter Infusion Given to 163 Normal Human Subjects. Langdell, R. E., Adelson, E., Furth, F. W., Crosby, W. H., Dept. Hemat., Walter Reed Army Inst. of Research, Washington D. C., USA. J. Amer. med. Ass. *166:* 346 (1958).

The infusion of one liter of commercially available dextran solution into normal adult humans resulted in a hemostatic defect characterized by a prolonged bleeding time. The effect cannot be explained on the basis of simple increase in circulating blood volume, thrombocytopenia or fibrinogenopenia. The mode of action is not clear but the phenomenon appears to be due to interference with platelet activity. Dextran infusion would appear to be contraindicated in patients with a known bleeding tendency or to whom large transfusions of whole blood had been given. The use of large infusions of dextran alone also carries a risk of serious failure of the hemostatic mechanism.

Coagulation During Hypothermia in Man. Bunker, J. P., Goldstein, R., Anesthesia Lab., Harvard Med. School, Mass., General Hosp., Boston, Mass., USA. Proc. Soc. exp. Biol. (N. Y.) *97:* 199 (1958).

Clotting times, platelets, thromboplastin generation, prothrombin consumption, prothrombin time, and concentrations of prothrombin accelerator globulin, proconvertin, and fibrinogen were measured in 10 patients after the slow induction of hypothermia and later during surgery and transfusion. In contrast to previous studies in the dog, uncomplicated hypothermia in man was not associated with a fall in concentration of clotting factors. Moderate disturbances in coagulation with surgery and transfusion during hypothermia were in most regards similar to those observed during surgery and transfusion at normal body temperature. The one significant difference was a decrease in prothrombin consumption.

Influence of Soybean Phosphatide on Blood Coagulation and its Use in the Thromboplastin Generation Test. Connor, W. E., Carter, J. R., Dept. int. Med. and Path., Med. Coll., State Univ. of Iowa, Iowa City, Iowa, USA. Proc. Soc. exp. Biol. (N. Y.) *97:* 38 (1958).

By its use in a variety of blood clotting systems, soybean phosphatide has been shown to act as a partial thromboplastin in blood coagulation. In vitro, this substance displayed anti-heparin activity in human and dog blood and anti-protamine activity in human plasma. A simplified

thromboplastin generation test is described for the study of hemorrhagic disorders. Soybean phosphatide serves as a complete substitute for platelets in this test.

The Recalcification Time of Blood. Belko, J. S., Warren, R., Veterans Adm. Hosp., West Roxburry, Mass., USA. Arch. Surg. (Chicago) *76:* 210 (1958).

Blood Coagulation in Acute Iron Intoxication. Wilson, S. J., Heath, H. E., Nelson, P. L., Ens, G. G., Hemat. Section, Dept. Med., Univ. of Kansas Med. Center, Kansas City, USA. Blood *13:* 483 (1958).

Acute intestinal iron intoxication was produced in rabbits and the levels of serum were correlated with changes in blood coagulation. Acute intestinal iron intoxication resulted in a prolongation of the coagulation time or a complete absence of coagulation, thrombocytopenia, hypoprothrombinemia, and qualitative changes in the fibrinogen. Clot retraction was decreased or absent. Fibrinolytic studies revealed no increase in the lysis of the fibrin.

Changes in the Serum Cholesterol and Blood Clotting Time in Men Subjected To Cyclic Variation of Occupational Stress. Friedman, M., Mount Zion Hosp., San Francisco, Calif., USA. Circulation (N. Y.) *17:* 852 (1958).

Alimentary Lipemia and Coagulability of Blood. Sheehy, T., Dept. Hemat., Walter Reed Army Med. Center, Washington D. C., USA. Circulation (N. Y.) *17:* 927 (1958).

Further Experiences with Blood Coagulation after Fat Meals and Carbohydrate Meals. Borrero, J., Vascular Section, Med. Dept., Cornell Univ. Med. Coll., New York, N. Y., USA. Circulation (N. Y.) *17:* 936 (1958).

A Micromethod for Determining Clotting Time, Using Capillary Blood and Siliconized Tubes. Lewis, R. C., Glueck, H. I., Depts. Med. and Obst., College of Med., Univ. of Cincinnati, Cincinnati, O., USA. J. Lab. clin. Med. *52:* 299 (1958).

A New Theory of Interference with the Clotting Mechanism: The Complexing of Euglobulin with Factor V, Factor VII, and Prothrombin. Henstell, H. H., Kligerman, M., Inst. Med. Research, Cedars of Libanon Hosp., Los Angeles, Calif. Ann. intern. Med. *49:* 371 (1958).

Data are presented in support of a new theory to explain certain hemorrhagic and thrombotic disorders. It is suggested that under a variety of clinical conditions unusual plasma globulins are produced which complex with clotting factors, reducing the concentration of these factors and leading to hemorrhages. The clotting factor-globulin complexes result in an unstable clotting mechanism, leading to thromboses. The 3 cases presented were selected to illustrate clinical conditions in which the offending proteins were euglobulins. The clotting factors complexed with them were chiefly factor V and, secondarily, factor VII and prothrombin. The euglobulin-clotting factor reversible complex may be a normal mechanism for regulating the activity of factor V and possibly other factors.

b) Fibrinogen (Factor I), Fibrin, Fibrinolysis

Untersuchungen über die Fibrinolyse bei hämorrhagischen Diathesen. I. Med. Univ.-Klinik, Halle/Saale, Germany. Ärztl. Forsch. *12:* 157 (1958).

Thromboemboliebehandlung mit Pyrexal. Stamm, H., Eichenberger, E., Univ.-Frauenklinik, Basel, Switzerland. Geburts. u. Frauenheilk. *18:* 451 (1958).

Experimental and clinical observations confirm the effect of fibrinolytic treatment of thrombosis. The fibrinolytic agents cannot replace anticoagulants, but complete them.

Einfache Methoden zur Untersuchung von Fibrinolyseproblemen. Marbet, R., Forschungsabtg. F. Hoffmann-La Roche & Co. AG., Basel, Switzerland. Röntgen- u. Lab.praxis *11:* 3/4 (1958).

The author presents exact and simple methods for the determination of fibrinolysis, and in particular of its end-point. End-point of fibrinolysis which up to now has been difficult to determine is neatly marked by the sinking of some sand previously brought upon the surface of the clot. The significance of each factor influencing fibrinolysis is discussed.

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

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

Physiological Mechanism of Fibrinolysis. Cliffton, E. E., Clotting Mechanism Section, Sloan-Kettering Inst., New York, N. Y. USA. Acta haemat. *20:* 76 (1958).

Fibrinolysis as Mechanism of Hemorrhagic Tendency. Stefanini, M., Joseph Stanton Memorial Lab., Saint Elizabeth Hosp., Boston, Mass., USA. Acta haemat. (Basel) *20:* 85 (1958).

Intravascular clotting and fibrinolysis are often unsuspected causes of overt or occult bleeding tendency in many clinical and experimental conditions. Laboratory studies help to reveal their presence and to differentiate between them. Their relative importance varies from disease to disease. Intravascular clotting is probably the more significant of the two, and, in fact, is found in a large number of conditions with clinical bleeding. Fibrinolysis, on the other hand, appears significant in a few conditions such as acute leukemia, transfusion reactions, intrauterine fetal death, some cases of disseminated carcinoma, and more rarely, in polycythemia vera, and in the course of some types of surgery.

Etude statistique des cas de fibrinolyse observés pendant 5 ans dans un laboratoire d'étude de la coagulation. Revol, L., Centre Nat. Transfusion Sang., Paris, France. Sang. *29:* 62 (1958).

Afibrinogenämie und Aprothrombinämie bei vorzeitiger Lösung der Plazenta. Drescher, A., Landesfrauenklinik, Stuttgart, Germany. Zbl. Gynäk. *80:* 258 (1958).

The author reports a case of afibrinogenemia accompanied by aprothrombinemia occurring in abruptio placentae with nephropathia. The replacement of fibrinogen by a stored and dried fibrinogen preparation proved to be life-saving. Cause, diagnosis and treatment of this rare but very serious obstetrical complication are discussed.

Studio della sintesi del fibrinogeno in un caso di afibrinogenemia congenita con l'impiego di tioaminoacidi S 35 marcati. Maurer, W., Imperato, C., Ist. Studi degli Isotopi, Univ., Köln, Germany. Minerva med. (Torino) *49:* 742 (1958).

Sulla terapia fibrinolitica mediante shock vaccinico nelle vasculopatie periferiche trombotiche. Terreni, F., Taddeucci, E., Ospedali Riuniti, Livorno, Italy. Minerva med. (Torino) *49:* 1368 (1958).

The Fibrinolytic Agents in Saline Extracts of Human Tissues. Albrechtsen, O. K., Biol. Inst., Carlsberg Found., Copenhagen, Denmark. Scand. J. clin. Lab. Invest. *10:* 91 (1958).

Saline extracts from different human organs contain fibrinolytic activity. This is caused by two different activators of plasminogen. One activator is labile and corresponds to the plasminogen activator in blood, the other is stable and corresponds to the stable tissue activator. There is reason to believe that the activity in the saline extracts reflects the immediate availability of the plasminogen activator for the organism.

Etude des antigènes plaquettaires et, en particulier, du fibrinogène. Salmon, J., Bounameaux, Y., Inst. Clin. Path. méd., Univ. Liège, Belgium. Thromb. Diath. haem. *2:* 93 (1958).

Fibrinolysis in Myocardial Infarction. Hume, R., Univ. Dept. Med., Royal Infirmary, Glasgow, Scotland. Brit. Heart J. *20:* 15 (1958).

This paper reports the results of measurement of fibrinolytic activity in patients following myocardial infarction. The fibrinolytic activity was studied in 10 patients for 28 days subsequent to the episode and compared with 10 controls. In the patients with myocardial infarction there was depression of the fibrinolytic activity and it did not reach normal levels for 8 days. It did not appear that the treatment received by the patients was responsible for this phenomenon, nor was it a nonspecific reaction to some severe physically disturbing incident.

Aktivierung der Fibrinolyse beim Menschen durch ein bakterielles Pyrogen. Der Einfluß von Phenylbutazon und Heparin auf Fibrinolyse, Blutgerinnung und Fieberreaktion. Hörder, M. H., Kicköfen, B., Wendt, F., Med. Univ.-Klinik, Freiburg/Br., Germany. Klin. Wschr. *36:* 164 (1958).

In healthy male individuals intravenous injection of lipopolysaccharide of S. abortus equi produced high temperature and fibrinolyses. The occurring alteration of temperature, fibrinolytic activity, coagulation time, factor V, and antithrombin II have been studied. It is shown that the increased blood coagulability occurring during fibrinolysis can be eliminated by heparin without influencing the fibrinolytic activity of the blood. High temperature and other side-effects were successfully taken care of by phenylbutazone, which also did not affect the activation of fibrinolysis.

Fibrinolytic Treatment of Thrombo-Embolic Diseases with Purified Bacterial Pyrogens. Meneghini, P., Med. Clin. Univ., Genova, Italy. Acta haemat. (Basel) *19:* 65 (1958).

The value of activation of fibrinolysis by bacterial lipopolysaccharides has been investigated in 58 thrombo-embolic conditions. The results are as satisfactory as those obtained with vaccines as reported previously. The author advocates combined therapy of anticoagulants with fibrinolysis activated by bacterial lipopolysaccharides.

Inhibition de la conversion du fibrinogène au cours d'un myélome. Larrieu, M. J., Beaumont, *J. L., Caen, J., Seligmann, M., Bernard, J.*, Centre d' Association Claude-Bernard, Hôp. St. Louis, Paris, France. Rev. franç. Etudes clin. Biol. *3:* 617 (1958).

A case of multiple myeloma is presented. Disturbed clot formation and an inhibition of fibrinogen—fibrin reaction were noted. Two possible causes of these phenomena are discussed: a) a protein disorder, and b) action of an anticoagulant found in the patient's blood.

Plasminogen Activator in Animal Meninges. Moltke, P., Biol. Inst., Carlsberg Foundation, Copenhagen, Denmark. Proc. Soc. exp. Biol. (N. Y.) *98:* 377 (1958).

Concentrations of plasminogen activator in the pia mater from pigs, horses, cows, monkeys, dogs, and rabbits were generally higher than recorded for any other organ in these animals. Different pia sections of the same animal showed different activator concentrations. Dura mater had lower activity than pia. The wall of the superior longitudinal sinus had higher activity than the dura adjacent to the skull.

The Fibrinolytic Enzyme System in Normal, Hemorrhagic and Disease States. Phillips, L. L., Skrodelis, V., Dept. Obst. Gynecol., Coll. Physicians a. Surg., Columbia Univ., New York, N. Y., USA. J. clin. Invest. *37:* 965 (1958).

A group of methods for investigating the factors of the human fibrinolytic enzyme system in plasma is presented. These factors include fibrinogen, active fibrinolysin, "free" and total profibrinolysin, and inhibitors. Normal obstetrical patients were studied during pregnancy, normal levels are compared with cases involving surgical hemorrhage and disease states. It was found that fibrinolysis is probably the principle cause of afibrinogenemia in hemorrhage following abruptio placentae and surgery of the liver.

Intravenous Protein-Free Pyrogen. A Powerful Fibrinolytic Agent in Man. Kaulla, K. N., Dept. Med. Univ. of Colorado Med. School, Denver, Col., USA. Circulation *17:* 187 (1958).

Thrombolysis with Fibrinolysis (Plasmin) — New Therapeutic Approach to Thromboembolism. Moser, K. M., District of Columbia General Hosp., Washington D.C., USA. J. Amer. med. Ass. *167:* 1695 (1958).

52 patients with various forms of thromboembolism were treated by intravenous infusions of fibrinolysin in doses up to 90 000 fibrinolytic units. 10 case histories illustrate the symptomatic relief that generally followed the infusion. Hemorrhagic complications have not occurred, fever followed the infusion in 25 patients, and delayed allergic skin reactions occurred in 2; these were the most significant side-effects. The results encourage further trials in cases of thromboembolic disease of peripheral, cerebral, and coronary vessels.

Thrombolysis with Fibrinolysin in Cerebral Arterial Occlusion. Sussman, B. J., Fitch, T. S. P. Div. Neurosurg. Muhlenberg Hosp., Plainfield, N. J., USA. J. Amer. med. Ass. *167:* 1705 (1958).

In a preliminary study, 3 patients with occlusive carotid or cerebral vascular disease were treated with fibrinolysin. Arteriography demonstrated the site of obstruction in all 3 cases. The authors are impressed with the possible advantageous action of fibrinolysin. It is believed that its prompt administration in cases of cerebral thrombosis or embolism may prove beneficial. It is not expected to benefit patients with progressive atherosclerotic occlusion in whom an actual thrombus does not occlude the lumen.

The Activation of Human Plasminogen. I. Spontaneous Activation in Glycerol. Alkjaersig, N., Fletcher, A. P., Sherry, S., Med. Section, Res. Inst., Jewish Hosp., St. Louis, Mo., USA. J. biol. Chem. *233:* 81 (1958).

Studies of the mechanism of spontaneous activation of plasminogen have been made by the use of a new method for the stabilization of plasminogen and newly formed plasmin. The results indicate that the mechanism is autocatalytic in nature, and it involves the release of a peptide moiety. These methods permit the preparation in a stable form of plasmin comparable in purity to the original starting material. Optimal conditions for the reaction are defined and evidence is offered which suggests that the action of glycerol is confined in its effect upon the stability of the reacting components.

II. *A Kinetic Study of Activation with Trypsin, Urokinase, and Streptokinase.* Current availability of sufficiently pure preparations of plasminogen and its activators has made it possible to obtain rigid kinetic data bearing on the activation process. The results show that the activators trypsin, urokinase, and streptokinase exert their effect through an enzymatic mechanism. Inhibition of the activation reaction by the addition of alternative activator substrates conform with the criteria for competitive inhibition. During the process of activation there is a release of a trichloroacetic acid-soluble moiety, equivalent in each case to some 25% of the original trichloroacetic acid-precipitable material. Attention is drawn to the similarity between the activation of plasminogen and the known behaviour of trypsinogen, chymotrypsinogen, and pepsinogen.

Physiochemical Studies on Human Plasminogen (Profibrinolysin) and Plasmin (Fibrinolysin). Shulman, S., Alkjaersig, N., Sherry, S., Dept. Bacteriol. and Immunol., Univ. of Buffalo Med. School, Buffalo, N. Y., USA. J. biol. Chem. *233*, 91 (1958).

Preparations of human plasminogen and plasmin have been examined for ultracentrifugal and electrophoretic homogeneity. Molecular weights and sedimentation rates are discussed. Isoelectric points were established and content of nitrogen, phosphorus, tyrosine, tryptophan, and hexose has also been measured.

Study on the Effect of Streptokinase-Activated Plasmin (Fibrinolysin) on Clots in Various Stages of Organization. Back, N., Ambrus, J. L., Simpson, C. L., Shulman, S., Roswell Park Memorial Inst., Buffalo N. Y., USA. J. clin. Invest. *37:* 864 (1958).

Experimental venous clots were produced in dogs. 5 daily treatments with 30 plasmin units/kg completely lysed clots less than 3 days old, but did not affect those older than

3 days. On the basis of these findings, it seems that better therapeutic results may be expected from intravenous treatment with plasmin in acute rather than chronic thromboembolic disorders. In the latter, results would appear to depend on the degree of organization of the clot.

The Inhibition of Plasmin by Toxic Phosphorus Compounds. Mounter, L. A., Shipley, B. A., Dept. Biophysics, Med. College of Virginia, Richmond, Va. J. biol. Chem. *231:* 855 (1958).

It has been demonstrated that plasmin, the proteolytic enzyme of serum, is inhibited by toxic organophosphorus compounds of the diisopropyl fluorophosphate type. Plasminogen, the inactive precursor of plasmin, is not affected by diisopropyl fluorophosphate. Differential inhibition provides additional distinction between plasmin and trypsin.

On the Occurrence of a Plasminogen-like Substance in Human Tissues. Kowalski, E., Kopec, M., Latallo, Z., Roszkowski, S., Sendys, N., Lab. clin. Biochem., Inst. of Hemat., Warsaw, Poland. Blood *13:* 436 (1958).

Evidence is presented for the occurrence of a plasminogen-like proenzyme in human tissues. The chemical features of tissue "plasminogen" are the same as of blood plasminogen. Tissue "plasminogen" occurs chiefly in organs rich in connective tissue, like the aorta wall, fascia etc. It is suggested that tissue "plasminogen" may be of significance in the pathogenesis of certain diseases of connective tissue, e. g. rheumatoid arthritis, in which proteolysis is postulated to be an important pathogenetic factor.

The Lysis of Artificially Induced Intravascular Clots in Man by Intravenous Infusions of Streptokinase. Johnson, A. J., McCarty W. R., New York, N. Y., USA. J. clin. Invest. *37:* 905 (1958).

The present studies were undertaken to demonstrate that intravascular clot lysis may be produced by the infusion of purified streptokinase in patients, under optimum biochemical conditions. Methods of administration, dosage, and results are discussed.

The Appearance of a Fibrinolysin Activator in the Blood of Patients with Enhanced Fibrinolytic Activity. Sherry, S., Lindemeyer, R. I., Fletcher, A. P., Alkjaersig, N., St. Louis, Mo., USA. J. clin. Invest. *37:* 931 (1958).

Increased fibrinolytic activity in the human circulation has been reported following electroshock therapy, pyrogen injections, intense exercise, epinephrine, and ischemia. Utilizing a variety of methods, a study has been made of the state of fibrinolytic activity in the blood of patients subjected to the various stresses mentioned above. The production of intense fibrinolytic activity in the blood of these patients was associated with the appearance of a fibrinolysin activator and without significant reduction in antifibrinolytic activity, profibrinolysin, or fibrinogen concentration.

Acquired Fibrinogenopenia. Bowman, H. S., Dept. Med., Harrisburg Hosp., Harrisburg, Pa., USA. Amer. J. Med. *24:* 967 (1958).

Two cases of acquired fibrinogenopenia are recorded. In one instance this blood coagulation abnormality was associated with amyloidosis of the liver, in the other with pregnancy and intrauterine fetal death. A simplified scheme for obtaining in vitro and in vivo evidence of severe fibrinogen deficiency is presented.

c) Prothrombin (Factor II), Thrombin

Een geval van congentale idiopatische hypoprotrombinemie. Radhakishun, K. S., Int. Abtg., Gemeente Ziekenhuis, Bergweg, Rotterdam, Holland. Ned. T. Geneeskd. *102:* 712 (1958).

The author describes the case of a 16-years-old patient whose hemorrhagic diathesis was due to congenital idiopathic hypoprothrombinemia. A study of blood coagulation in the family members indicated the presence of familial hypoprothrombinemia.

Comparison Between Micro-Modifications of Prothrombin-Proconvertin Determinations and of the Prothrombin Time Method. Dyggve, H., Pediatric Dept., Rigshospitalet, Copenhagen, Denmark. Scand. J. clin. Lab. Invest. *10:* 1 (1958).

Comparison of Quick's, Owren's, and Ware's Techniques for the Control of Anticoagulant Therapy. Toohey, M., Anticoagulant Unit, New End Hosp., London N.W. 3, England. J. clin. Path. *11:* 56 (1958).

The Mode of Action of Thrombin. Laki, K., Gladner, J. A., Folk, J. E., Kominz, D. R., Nat. Inst. Arthritis and Metabolic Diseases, Public Health Serv., US Dept. of Health, Education and Welfare, Bethesda, Md., USA. Thromb. Diath. haem. *2:* 205 (1958).

The Determinant of the Prothrombin Time in Normal Human Plasma. Quick, A. J.: Dept. Biochem., Marquette Univ. Med. School, Milwaukee, Wisc. USA. Thromb. Diath. haem. *2:* 226 (1958).

The Role of the Bone Marrow in Prothrombin and Proconvertin Synthesis. Gordin, R., IVth Med. Clinic, Maria Hosp., Univ. Helsingfors, Finland. Acta haemat. (Basel) *19:* 341 (1958).

In a series of patients with various diseases the prothrombin and proconvertin concentrations in the peripheral blood and in bone marrow punctates were compared. In contrast to the results of other investigators higher values were found in the peripheral blood in the majority of cases. The results seem to constitute evidence against the view that the bone marrow plays an essential part in the production of prothrombin and proconvertin.

Prothrombin Measurement by Two-stage Technique with Hemolyzed Whole Blood Thromboplastin. Dreskin, O. H., Dept. int. Med. and Path., Jewish Hosp., Cincinnati, Ohio, USA. J. Lab. clin. Med. *51:* 312 (1958).

A new two-stage method of measuring prothrombin activity is described. The method is based on the use of a natural thromboplastin derived from hemolyzed red blood cells. A high yield of prothrombin is obtained and measured by a relatively simple method employing a minimum of reagents.

Prothrombin Activation Cycle. Cho, M. H., Seegers, W. H., Dept. Physiol. and Pharm., Wayne State Univ. Med. Coll., Detroit, Mich., USA. Proc. Soc. exp. Biol. *97:* 642 (1958).

The prothrombin activation cycle consists of a sequence described by the following: Prothrombin (sensitive to calcium + Ac-globulin + lung thromboplastin) ⟶ prothrombin derivative I (not sensitive to calcium + Ac-globulin + lung thromboplastin) ⟶ prothrombin derivative II (sensitive to calcium + Ac-globulin + lung thromboplastin) ⟶ thrombin. Solutions of prothrombin standing at 4° C go through most of this cycle, the prothrombin molecule alone possessing the peculiar properties that enables it to this.

Chromatographic Isolation of Plasma Prothrombin and Trans-α-Glycosylase. Miller, K. D., Div. Labs. and Research, N. Y., State Dept. of Health, Albany, N. Y., USA. J. biol. Chem. *231:* 987 (1958).

Prothrombin is stable on and quantitatively recovered from columns of Amberlite ICR-50. Separation of prothrombin and trans-α-glucosylase from each other and from contaminants is highly efficient. Chromatographically purified prothrombin is homogenous.

d) Thromboplastin (Factor III)

Synergistic Action of Russell Viper Venom and Tissue Thromboplastin Extracts. Georgatsos, J. G., Hussey, C. V., Quick, A. J., Dept. Biochem., Marquette Univ. Med. School, Milwaukee, Wisc., USA. Proc. Soc. exp. Biol. (N. Y.) *97:* 674 (1958).

As measured by one-stage prothrombin time, mixtures of various body tissues may have thromboplastic activity greater than that of either of the tissues in the mixture. A marked

synergistic action as to thromboplastic activity occurs between body tissue extracts and Russell viper venom. This effect is absent if the plasma lacks either prothrombin or factor V. The thromboplastic activity of Russell viper venom is not influenced by the lack of factor VII in contrast to the high sensitivity observed with rabbit brain thromboplastin.

Untersuchungen über den Thrombokinasebildungstest. Egli, H., Klesper, R., Physiol. Inst. Univ. Bonn, Germany. Thromb. Diath. haem. *2:* 39 (1958).

(Ein Beitrag zur Methodik und zur Reaktionskinetik der Thrombokinasebildung).

Über die Thrombokinase-Aktivität der Blutgefäße. Witte, S., Bressel, D., Med. Univ.-Klinik, Erlangen, Germany. Folia haemat. *2:* 236 (1958).

The authors investigated aqueous extracts of human blood vessels in order to determine their thromboplastic activity. A significant thromboplastic activity was found regularly. There was no difference between the activity of the intima as compared to the activity of total vascular tissue extract. By dilution an antithromboplastic factor could be demonstrated in all preparations, its activity varied considerably. The results are discussed regarding their physiological importance and it is pointed out that vascular thromboplastin may be of great importance in the pathogenesis of arteriosclerosis.

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

Inhibition of Thromboplastin Generation by Hyaluronidase Preparations and Reversal by Lyophilized Platelet Material and Derivatives. Djerassi, I., Klein, E., Farber, S., Children's Cancer Res. Found., Harvard Med. School, Boston, Mass., USA. Proc. Soc. exp. Biol. (N. Y.) *97:* 481 (1958).

Bovine testicular hyaluronidase preparations inhibited formation of thromboplastin in absence of platelets or equivalent materials. This effect was not due to distruction of an essential component of the coagulation mechanism. Inhibition was prevented or reversed by platelets, thromboplastin-generating components extracted from platelets and tissues, and by defatted platelet material.

A Modification of the Thromboplastin Generation Test. McMillan, R. L., Med. Serv. Toronto General Hosp., Toronto, Canada. Amer. J. med. Sci. *235:* 437 (1958).

The thromboplastin generation test was modified by substituting dilute plasma for serum as a source of Christmas factor. This modification may broaden the scope of the test and may make it possible to assess increased as well as diminished activity of thromboplastin formation. The method may be used as a quantitative measure of Christmas factor activity. The test may prove valuable in demonstrating an increased tendency towards thrombosis as well as measuring anticoagulant effectiveness. In both Christmas disease and in Dicumarol treated patients the plasma has diminished activity in thromboplastin generation. The test demonstrates a distinct difference between the 2 conditions.

Therapeutic Attempts with Cephalin Fraction of Bovine Brain in Thrombocytopenia and Classical Hemophilia. Gobbi, F., Stefanini, M., Boston, Mass., USA. J. clin. Invest. *37:* 897 (1958).

It is concluded that cephalin at varying doses completely corrects the coagulation defect of thrombocytopenia and classical hemophilia in vitro. Cephalin of bovine origin is not antigenic and may be administered safely to humans. Significant, total or partial correction of the coagulation defect in classical hemophilia and thrombocytopenia may thus be achieved in vivo with the use of material of origin other than human.

e) Calcium (Factor IV)

Nouvelle méthode du dosage du calcium ionisé utilisant un système coagulant. Soulier, J. P., Crosnier, J., Centre Nat. Transfusion Sang., Paris, France. Rev. franç. Etudes clin. Biol. *3:* 157 (1958); Presse méd. *66:* 617 (1958).

A new method for the determination of ionized calcium is described. A clotting system is used containing amberlite-treated plasma, to which magnesium is added and diluted thromboplastin. Normal values: Serum 57 mg per 1000 ml, cerebrospinal fluid 40 mg. This simple micromethod is precise and rapid.

f) Factor V (and VI)

Factor V in Blood Coagulation in Vitro, and a Report of a Case of Factor V Deficiency. O'Brien, J. R., Portsmouth and Isle of Wight Area, Path. Service, Portsmouth, Hants., England. Brit. J. Haematol. *4:* 210 (1958).

An isolated case of apparently complete factor V deficiency has been studied and the findings of previous workers confirmed. Factor V accelerates the speed of thromboplastin formation and may increase the quantity formed. The phospholipid of platelets appears to determine the quantity of thromboplastin formed, and also to increase the speed of its formation. The effect of phospholipid on the speed of thromboplastin formation is independent of the accelerating effect of factor V. When plasma clots in the presence of Russell's viper venom, factor V and the venom interact first in a time-consuming reaction. Calcium and platelet phospholipid are involved later in an apparently instantaneous reaction. It is possible that the same order of reactions occur in the absence of Russell's viper venom.

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

g) Factor VII

Zur Differentialdiagnose des angeborenen Faktor-VII-Mangels. Burmeister, A., Elisabeth-Kinderkrankenhaus, Oldenburg i. O., Germany. Z. Kinderheilk. *81:* 88 (1958).

The authors report a case of a 9-years-old girl with congenital factor VII deficiency. Based on this case the author discusses differential diagnosis of deficiencies of coagulation factors of the first phase, such as factor V and Stuart factor and factor VII.

Kongenitaler Faktor-VII-Mangel. Familienuntersuchung und physiologische Studien über den Faktor VII. Hitzig, W. H., Zollinger, W., Univ.-Kinderklinik, Zürich, Switzerland. Helv. paediat. Acta *13:* 189 (1958).

Two cases of congenital factor VII deficiency in brother and sister, are described. The severe hemorrhagic diathesis was characterized clinically by the early manifestation of the disease, by the exclusive involvement of skin and mucous membranes, and by the absence of cerebral or intraarticular hemorrhage. In the course of a family study, consanguinity of the parents was detected. The way of the pathologic gene was traceable as the recessive transmitters had significantly diminished factor VII levels. Factor VII metabolism studies revealed its halftime to be 2 to 3 hours, that of the factor VII complex 4 to 8 hours. This short survival is in contrast with the clinical remission lasting 5 to 14 days following transfusion. An attempt is made in order to explain this phenomenon.

Studies on the Turnover Rate of Stable Prothrombin Conversion Factor in Man. Frick, G. P., Dept. Metabolism, Div. Med., Walter Reed Army Inst. Research, Washington D. C., USA. Acta haemat. (Basel) *19:* 20 (1958).

The disappearance and turnover rate of stable prothrombin conversion factor (factor VII) in man was studied after blocking factor VII synthesis with a large single dose of Warfarin

sodium and after infusion of normal plasma in individuals whose factor VII level was severely depressed by the same drug. The various factors which may influence the data obtained in this study are discussed. The half-life of factor VII in normal man ranges from 5.5 to 10.8 hours. The hourly turnover rate is at least 6.4% of the total body pool of factor VII.

Hemarthrosis Due to Proconvertin Deficiency. Tveten, H. T., Med. Avdeling B, Haukeland Sykehus, Bergen, Norway. Nord. Med. *59:* 565 (1958).

A case of hemarthrosis due to factor VII deficiency is reported. The patient had previously suffered from tuberculous hilar adenitis, and hemarthrosis affecting both knees and shoulders had for several years been thought to be of same etiology. Tourniquet test, whole coagulation time and bleeding time were normal. The coagulation defect was revealed by Owren's P and P test, Quicks thromboplastin time, and specific factor VII determination.

Blood Clotting Substances with "Factor VII" Activity: A Comparison of Some Congenital and Acquired Deficiencies. Dische, F. E., Dept. Hemat., St. George's Hosp. Med. School, London, England. Brit. J. Haematol. *4:* 201 (1958).

Coagulation tests have been performed on mixtures of blood from cases with congenital factor VII deficiency and persons treated with Dindevan. The results confirm that serum contains 2 factors which accelerate the conversion of prothrombin by brain extract. One of these factors is factor VII, the other 'Prower-Stuart factor'. The administration of Dindevan causes a rapid fall in factor VII, followed sometimes by a rise. The level of the Prower-Stuart factor, however, drops only after several days. These effects must be taken into account when matching tests with Dindevan plasma are used as an aid to the diagnosis of factor VII deficiency.

L'hypoconvertinémie constitutionelle. Gillot, F., Centre de Transfusion Sanguine, Alger. Arch. franç. Pédiat. *15:* 506 (1958).

Congenital Serum Prothrombin Conversion Accelerator (SPCA) Deficiency. Dann, H. A., Fisher, H. M., Burnett, L., Briggs, D., Dept. Med. New York Univ. Post-Graduate Med. School, New York, N. Y., USA. Ann. intern. Med. *49:* 459 (1958).

A case of congenital SPCA (Factor VII) deficiency is presented. The methods employed in diagnosing the condition are discussed.

h) Factor VIII (Antihemophilic Globulin)

Vergleichende Bestimmungen des antihämophilen Globulins bei beiden Geschlechtern. Fischer, J., Landbeck, G., Lenz, W., Univ.-Kinderklinik, Hamburg-Eppendorf, Germany. Klin. Wschr. *36:* 20 (1958).

Average values and deviations of AHG activity are similar in boys and girls. The hypothesis that normal deviation of AHG activity be caused by X-chromosomal allele series is not in conformity with these findings. Female carriers of hemophilia probably show slightly diminished AHG activity. This observation sustains the theory that hemophilia is not only caused by AHG deficiency, but also by a functionally deficient gene product.

Acute Renal Failure Associated with Massive Hemorrhage in a Haemophiliac. D'Almero Kok, Barkhan, P., Dept. Med., Univ. of Cambridge, England. Brit. med. J., no. 5068, 434 (1958).

Acute renal failure, with complete recovery, is reported in a hemophiliac after massive hemorrhage into the abdominal wall. Treatment included transfusion with large volumes of fresh plasma and blood. Potassium citrate was given intravenously for a time, and was found to produce local pain when a treshold concentration was exceeded.

Treatment of Hemophilia A with Human Antihemophilic Globulin. Blombäck, M., Nilsson, I. M., Chem. Dept. II., Karolinska Inst., Stockholm, Sweden. Acta med. scand. *161:* 301 (1958).

Human fraction I—0, was given to 12 patients with severe hemophilia A in connection with appendectomy, gastrointestinal and renal hemorrhage, hemarthrosis, and tooth extraction. By

increasing the AHG level to 40—80% and by maintaining it at 20—30% the necessary surgical operations could safely by performed. No side reactions were observed and no antibodies could be demonstrated. The purification of the antihemophilic activity per mg protein in fraction I—0 as compared to fresh human plasma is about 20 fold; 50 fold purification has occasionally been obtained.

Fundamental Aspect of Hemophilia. Quick, A. J., Marquette Univ. Med. School, Milwaukee, Wisc., USA. Acta haemat. (Basel) *20:* 115 (1958).

By means of the prothrombin consumption test modified by the addition of erythrocyte extract to the blood before coagulation, the concentration of thromboplastinogen A can be quantitatively determined. Plasma from a severe hemophiliac serves as the assay medium. The present studies, in agreement with the findings of others, support the conclusion that the coagulation defect is caused by the lack of a specific clotting factor, thromboplastinogen A, and not by an inhibitor.

Physiopathology of Hemophilia. Brinkhous, K. M., Univ. N. Carolina, Chapel Hill, N. C., USA. Acta haemat. (Basel) *20:* 125 (1958).

The author discusses the 2 main hypotheses regarding the nature of the plasma defect in hemophilia: 1) Deficiency of antihemophilic factor, and 2) excess of an inhibitor. Re-examination of some of the most important findings which have lead to divergent hypotheses regarding the nature of hemophilia is made. Data which heretofore suggested an excessive inhibitor are actually in accord with the deficiency hypothesis. The experiments also emphasize that test-tube experiments alone may be misleading; in vivo testing of coagulant effects may be needed.

The Inhibitory Effect of Hemophilic Plasma. Biggs, R., Dept. Path., Radcliffe Infirmary, Oxford, England. Brit. J. Haematol. *4:* 192 (1958).

In two coagulation systems based on the thromboplastin generation test it has been found that undiluted hemophilic plasma produces a longer clotting time than diluted hemophilic plasma. In comparing undiluted with diluted plasma it is necessary to maintain a constant concentration of trisodium citrate and an optimum concentration of calcium chloride. The inhibitory effect of undiluted plasma is in part caused by the fact that the optimum concentration of phospholipid required by the test system depends on the concentration of plasma to which it is added. Similar inhibitory effects are produced by $Al(OH)_3$-adsorbed normal serum and $Al(OH)_3$-adsorbed hemophilic plasma.

In Vivo Study on the Relation Between Bridge Anticoagulant and Antihemophilie Globulin. Nour-Eldin, F., Wilkinson, J. F., Dept. Haemat., Royal Infirmary, Manchester, England. Brit. J. Haematol. *4:* 292 (1958).

Owing to the presence of Bridge anticoagulant, the levels of AHG in hemophilic plasma, before or after transfusion cannot be precisely estimated. A new method which provides a clearer picture of the fundamental changes in the clotting defect in hemophilia has been applied to the study of the effect of pig AHG. Assay of Bridge Anticoagulant demonstrated different levels in hemophilic patients. In 11 cases the degree of benefit derived from AHG was mainly determined by the concentration of this blood clotting inhibitor. Amounts equivalent to 4—16 litres of normal plasma may be required for the correction of the hemophilic defect. One of 6 patients who received multiple transfusions developed a refractory phase, an event attributable to a transient rise in Bridge Anticoagulant level.

Classic Hemophilia in a Negro Infant. Boyles, P. W., Univ. of Miami Med. School, Miami, Fla., USA. Amer. J. med. Sci. *235:* 452 (1958).

A case of proven hemophilia due to specific deficiency of AHG has been described in a negro infant. This report emphasizes the fact that hemophilia can occur in the American negro, and probably with greater frequency than has been suspected from the literature.

Antihemophilic Globulin Assay Following Plasma Infusions in Hemophilia. Douglas, A. S., Univ. Dept. Med., Royal Infirmary, Glasgow, Scotland. J. Lab. clin. Med. *51:* 850 (1958).

AHG has been assayed in hemophiliacs following the administration of 1 litre of plasma. In 30 observations, using the thromboplastin generation test as a method of AHG assay, a mean level of 14% AHG was attained on completion of the infusion. The half-life of the administered AHG was approximately 9 hours and less than 1% was demonstrable after 24 hours. Similar levels of AHG were found using a thrombin generation method and a prothrombin consumption technic. The observations suggested that the levels of AHG attained by these infusions probably provided some hemostatic effect in hematuria and tooth extraction in hemophiliacs.

Antihemophilic Factor Deficiency in the Female. McGovern, J. J., Steinberg, A. G., Dept. Pediatrics, Harvard Med. School, Boston, Mass., USA. J. Lab. clin. Med. *51:* 386 (1958).

Case report.

i) Factor IX (Christmas Factor, PTC)

Zur Therapie der Hämophilie B. Birk, G., Med. Univ.-Klinik, Münster/Westf., Germany. Klin. Wschr. *36:* 240 (1958).

Préparation d'un réactif artificiel permettant de doser le facteur antihémophilique B (PTC, Christmas Factor). Wartelle, O., Centre Nat. Transfusion Sanguine, Paris, France. Rev. Hémat. *13:* 100 (1958).

The author worked out an artificial reagent for the measurement of antihemophilic factor B. This reagent can replace hemophilia B plasma in the determination method described by Soulier and Larrieu. It consists of equal parts of chicken plasma and absorbed oxalated human serum. It is specific and extremely sensitive towards variations of antihemophilic factor B content, thus permitting the diagnosis of hemophilia B.

Changes in the Blood Clotting Defect in Christmas Disease after Plasma and Serum Transfusions. Nour-Eldin, F., Wilkinson, J. F., Dept. Hemat., Royal Infirmary, Manchester, England. Clin. Sci. *17:* 303 (1958).

Changes in the blood clotting defect following plasma and serum transfusions in patients with Christmas disease have been studied and compared with in vitro tests. The influence of plasma on blood clotting, prothrombin consumption, and thromboplastin generation was apparent in vivo and in vitro, but injections of serum failed to correct the defective plasma thromboplastin formation. Plasma stored at 4° C for periods less than 5 days is recommended for the treatment of Christmas disease, since no deleterious effect on the Christmas factor activity was noticed during this period. The improvement in the production of plasma thromboplastin ceases within 24 hours.

Heparin and Christmas Factor. O'Brien, J. R., Central Lab., Milton Road, Portsmouth, Hampsh., England. Nature (Lond.) *181:* 1801 (1958).

The author's experiments lead to the conclusion that the inhibition of the early stages of blood coagulation in vitro by heparin might be due to the action of heparin on Christmas factor. Since the intima of blood vessels may be lined by mucoitin, an acidic, muco-polysaccharide like heparin, and since Christmas factor is involved at an early stage in blood coagulation, these tentatative conclusions may be related to the inception of thrombosis in vivo. Further investigations are in progress.

Klinische, genetische und gerinnungsphysiologische Aspekte der Hämophilie B bei den Blutern von Tenna, mit einem Beitrag zur Genetik der Gerinnungsfaktoren. Huser, M. J., Moor, J. K., Troug, G., Geiger, M., Inst. Génétique méd., Univ. Genève, Switzerland. Acta genet. (Basel) *8:* 25 (1958).

Inherited hemorrhagic diatheses are discussed. Coagulation factors and corresponding literature regarding heredity are tabulated. Autosomal, partially dominant, partially recessive and partially

intermediary processes as occurring in the majority of hemorrhagic disorders are opposed to the recessive sex-linked hereditary process of classical hemophilia A and B. Based on studies of sibblings of the hemophilia B tribe of Tenna the clinical manifestation of the hemophilia B gene is discussed. 67 individuals were investigated, among them 10 bleeders and 11 carriers were found. Factor IX levels in the bleeders varied from 2.5 to 6%, the clinical manifestations however varied widely. Carriers showed no increased bleeding tendency. No coupling of Daltonism with hemophilia was found. An examination of the ability to smell cyanide solutions, showed a dominant, probably autosomal heredity.

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

Familiärer Faktor-X-Mangel. Oehme, J., Schwick, G., Schultze, H. E., Univ.-Kinderklinik, Marburg/Lahn, Germany. Klin. Wschr. *36:* 521 (1958).

The authors describe the case of a 14-months-old child with a slight hemorrhagic diathesis characterized by increased activation time as measured by the chromboplastin generation test, thus indicating a factor X deficiency as described by Koller. Normalization of Biggs'test was obtained by normal serum, hemophilia B serum, Stuart factor deficiency serum, but not by $BaSO_4$-adsorbed serum, by $Al(OH)_3$-adsorbed serum nor by normal platelets. The identity of factor X and Stuart factor is, therefore, rejected by the authors. The same disorder was found in the father and two brothers, whereas mother and sisters showed normal coagulation mechanism. As the heredity of this affection is not similar to that of hemophilia A and B, and as hemarthrosis is lacking in this case, the authors suggest the term hemophilia C.

Déficit en 3ème facteur prothromboplastique plasmatique. Rapports entre le PTA et le facteur Hagemann. Soulier, J. P., Larrieu, M. J., Centre Nat. Transfusion Sanguine, Paris, France. Thromb. Diath. haem. *2:* 1 (1958).

The Stuart-Prower Factor Assay and its Clinical Significance. Bachmann, F., Duckert, F., Koller, F., Gerinnungsphysiol. Lab., Med. Univ.-Klinik, Zurich, Switzerland. Thromb. Diath. haem. *2:* 24 (1958).

Der Stuartfaktor während der Cumarintherapie. Hörder, M. H., Med. Univ.-Klinik, Freiburg/Br., Germany. Thromb. Diath. haem. *2:* 170 (1958).

Congenital Coagulation Deficiency of Stuart Factor Activity. Gonyea, L. M., Krivit, W., Dept. Med. Technology and Pediatrics, Univ. of Minnesota, Minneapolis, Minn., USA. J. Lab. clin. Med. *51:* 398 (1958).

A patient with a coagulation deficiency first reported as idiopathic hypoprothrombinemia and later as factor VII deficiency, was restudied. Her deficiency appeared to be Stuart factor deficiency. The prolonged Quick time was corrected by plasma of Owren's proconvertin deficiency but not by serum of Hougie's Stuart factor deficiency. Amount of prothrombin was normal but conversion delayed. This was corrected by normal plasma and serum, and proconvertin deficient plasma, but not by $BaSO_4$-adsorbed plasma or Stuart factor deficient serum. Abnormal thromboplastin generation was corrected by normal serum and by hemophilia B serum but not by $BaSO_4$-adsorbed plasma or Stuart factor deficient serum. The prolonged "Stypven time" was corrected by normal plasma and by proconvertin deficient plasma, but not by Stuart factor deficient serum.

Déficit en facteur de Hageman. Caen, J., Bernard, J., Centre de l'association Claude-Bernard, Hôp. St. Louis, Paris, France. Rev. Hémat. *13:* 154 (1958).

The authors present a typical case of Hageman's trait in a 6-year-old girl. They discuss arguments in favour of Hageman factor being a contact factor, intervening primarily in the activation of antihemophilic factor B (IX). The hypothesis of recessive heredity of the trait is confirmed, without consanguinity among the heterozygote parents the girl being a homozygote.

Defects in the Early Stages of Blood Coagulation: A Report of Four Cases. Biggs, R., Sharp, A. A., Margolis, J., Hardisty, R. M., Stewart, J., Davidson, W. M., Dept. Path., Radcliffe Infirmary, Oxford, England. Brit. J. Haematol. *4:* 177 (1958).

A report of 4 cases is given: 3 of the patients have a coagulation defect identified as Rosenthal's syndrome; the fourth has no clinical hemorrhagic state and is thought to have Hageman trait. Investigation showed a delay in platelet viscous metamorphosis, and an abnormal reaction to glass contact in blood samples from all 4 cases. Blood samples from the patients diagnosed as PTA deficiencies showed some delay in the activation of the Christmas factor. Experiments in which the degree of exposure to glass was standardized suggest that the reactions involved in glass contact may take place in two stages.

The Probable Identity of Glass Factor with Hageman Factor. Lewis, J. H., Merchant, W. R., Pittsburgh, Pa., USA. J. clin. Invest. *37:* 911 (1958).

Blood in contact with glass clots more rapidly than when in contact with a nonwettable surface. This increased ability has been ascribed to one or more of the various plasma coagulation factors or to removal of an inhibitor. This glass-activated accelerator effect, called glass factor, was lacking in a patient with Hageman factor deficiency and a stored-frozen sample from a PTA deficiency had only minimal accelerating action. When normal plasma was fractionated some of the 32 fractions obtained showed the ability to accelerate the clotting of normal silicone plasma. The distribution of this "glass factor" corresponded almost exactly to that of the Hageman factor. On the other hand, when Hageman factor deficient plasma was so fractionated, neither Hageman factor nor glass factor activities were found in any of the fractions.

Caractères différentiels des facteurs Hageman et PTA. Rôle du contact dans la phase initiale de la coagulation. Soulier, J. P., Wartelle, O., Menache, D., Centre Nat. Transfusion Sanguine, Paris, France. Rev. franç. Etudes clin. biol. *3:* 263 (1958).

PTA deficiency and Hageman trait mutually correct each other, whether native blood and plasma or plasmas are mixed. Some of the data presented suggest the presence of a weak inhibitor of contact factor in Hageman trait. The specifity of this inhibitor is discussed. Hageman trait plasma does not respond to activation by glass but to addition of glass-activated contact factor. PTA deficient plasma, on the other hand can be activated by glass but does not respond to the addition of glass-activated contact factor. It is concluded that the contact factor in normal blood is Hageman factor, but activated Hageman factor needs PTA to form a third prothromboplastic factor. The apparent activation by glass of factor IX actually depends on the activation by glass of Hageman factor. Chicken plasma has the characteristics of Hageman trait but it is also deficient in PTA.

Epistaxis intermittente avec permanence d'une mauvaise consommation de la prothrombine. Discussion d'une maladie de Rosenthal. Chevallier, P., Centre Nat. Transfusion Sang., Paris, France. Sang *29:* 75 (1958).

Een zeldzaam gefal van hemorrhagische diathese veroorzaakt door tekort aan Plasma Thromboplastin Antecedent: Wijffels, M., Kinderkliniek St. Canisius Ziekenhuis, Nijmegen, Holland. Ned. T. Geneesk. *102:* 815 (1958).

Description of a case of hemorrhagic diathesis due to PTA deficiency in a boy who from the age of 18 months had shown discoloured bruising. Severe melaena was observed during an acute infection and ecchymoses increased in number and in size. PTA deficiency was then established and disappeared after recovery from the infectious disease. A sister was also found to be deficient in PTA. Some characteristics of the disorder are discussed.

Über einen neuen Accelerator der Blutthrombokinasebildung. Fisch, U., Gerinnungsphysiol. Lab., Med. Univ.-Klinik, Zürich, Switzerland. Thromb. Diath. haem. *2:* 60 (1958).

An Enzyme in Plasma Inactivating Hageman Factor. Ratnoff, O. D., Cleveland, O., USA. J. clin. Invest. *37:* 923 (1958).

The following tentative hypothesis is suggested: The fluidity of blood is partly maintained by inhibitors directed against Hageman factor. Exposure to glass converts Hageman factor to an active form, presumably releasing it from inhibition. The freed Hageman factor then initiates clotting. Once active, Hageman factor is enzymatically destroyed, preventing its continued action. The enzyme is present in normal plasma, 56° C-heated plasma, delipidized plasma and plasma in patients deficient in Hageman factor. Its action is uninfluenced by glass or decalcification. The enzyme is concentrated in a fraction of plasma soluble successively at half-saturation with an ammonium sulfate and upon dialysis at pH 5.2, ionic strength 0.02; it is found in Cohn's fraction IV—4.

l) General Aspects of Hemophilia

La ponction sternale dans l'hémophilie vraie. Renseignements donnés par le medullogramme dans 11 cas. Fiehrer, A., Clin. Maladies du Sang, Hôp. Broussais, Paris, France. Acta haemat. (Basel) *19:* 129 (1958).

A recent paper by Bernheim et al. suggested the importance of an increase of plasma cells in the bone marrow as early evidence of an immunological disorder. The sternal marrow findings in 11 patients with hemophilia are recorded. No plasma cell increase was found in the marrow. In several cases direct immunologic investigations revealed negative results. It is, therefore, reasonable to assume that no immunologic mechanism is involved in hemophilia. Cytological examination of the marrow of these patients merely revealed variable marrow hyperplasia in half the number of cases. The lesions in the marrow are probably chance findings in hemophilia.

Diagnosis of the Hemophiloid States. Biggs, R., MacFarlane, R., G., Radcliffe Infirmary, Oxford, England. Acta haemat. (Basel) *20:* 118 (1958).

187 Patients with constitutional hemorrhagic states are discussed and separated into categories. The system used for differential diagnosis is explained. The series includes cases of hemophilia A, B, of circulating anticoagulants, PTA deficiency, and of Hageman defect.

Hemostatic Data in Relatives of Hemophiliacs A and B. Didisheim, P., Ferguson, J. H., Lewis, J. H., Dept. Med., Univ. Pittsburgh Med. School, Pittsburgh, Pa, USA. Arch. intern. Med. *101:* 347 (1958).

Evidence for Modifying the Classical Sex-Linked Recessive Theory.

63 obligatory carriers of hemophilia A and 14 of hemophilia B were studied by means of the available tests of blood coagulation. Of the hemophilia A carriers 8 were abnormal on the basis of 2 or more of the tests used or on two or more occasions. By the same criteria, 4 of the 14 hemophilia B carriers were abnormal. The coagulation defect is constant at repeated tests over a year's time. 52% of the obligatory carriers whose laboratory tests were abnormal have had significant hemorrhagic symptoms, usually milder in nature. Genetic implications of these findings are discussed. In some cases the genes h^a for hemophilia A and h^b for hemophilia B appear to be only partially recessive.

m) Combined Deficiencies

Über Pseudohämophilie, Angiohämophilie, v. Willebrand-Jürgensscbe Krankheit und verwandte hämorrhagische Diathesen. Gross, R., Mammen, E., Med. Univ.-Klinik, Marburg/Lahn, Germany. Klin. Wschr. *36:* 112 (1958).

A survey of papers concerning "pseudohemophilia" reveals the confused nomenclature in this group of diseases. The authors come to the conclusion that hemorrhagic diatheses designed as

— angiohemophilia — vascular hemophilia — v. Willebrand-Jürgens thrombopathia — and v. Willebrand's angiopathia are all one disease characterized by probably dominant heredity with optional disorder of capillaries, platelets, and plasma factors VIII and IX. The authors propose the name "v. Willebrand-Jürgens-syndrome". The clinical symptoms and characteristic coagulation disorders are discussed.

Über eine hereditäre hämorrhagische Diathese mit verlängerter Blutungszeit, partiellem Mangel an antihämophilem Globulin A und einer funktionellen Störung einzelner Thrombozytenfaktoren. Koch, F., Schultze, H. E., Schwick, G., Kinderklinik, Justus-Liebig-Univ., Gießen, Germany. Blut *4:* 19 (1958).

The authors report upon a family where the mother showed a slight, and 2 of the 6 children a severe hemorrhagic tendency. The mother had a slight and the 2 children a marked decrease of factor VIII (85%, 8%, 11% respectively) together with a deficiency of certain platelet factors but normal capillary microscopical results. The remaining children also showed coagulation disorders, however, without hemorrhagic symptoms. The autors discuss differential diagnosis regarding v. Willebrand-Jürgens' thrombocytopathy (deficiency of factor VIII with pathologic vascular alterations) and classical hemophilia A as well as therapy of this syndrome.

Kongenitaler, familiärer Faktor-VII-Mangel mit zusätzlichem Defekt in der Thromboplastinbildung. Hörder, M. H., Med. Univ.-Klinik, Freiburg/Br., Germany. Acta haemat. (Basel) *19:* 30 (1958).

The cause of a hemorrhagic diathesis in a woman of 27 was found to be factor VII deficiency with additional defect in autogenous thromboplastin formation. The clotting defect was also found in a less severe form without obvious bleeding tendency in the patient's family members. Factor VII did not influence autogenous thromboplastin formation. The deficient thromboplastic factor was not Christmas factor, but rather resembled factor X.

Hemophilia-Like States in Girls. Quick, A. J., Hussey, C. V., Marquette Univ. Med. School, Milwaukee, Wisc., USA. Lancet *1:* 1294 (1958).

Four girls with congenital bleeding conditions characterized by defective production of thromboplastin are reported. Case 1 is undistinguishable from classical hemophilia, expect that the family history is negative. Case 2 has, in addition to defective consumption of prothrombin and defective thromboplastin generation, a prolonged prothrombin time. Her disease is similar or probably identical with "Stuart clotting defect". Cases 3 and 4 have a normal prothrombin time but a prolonged bleeding time, defective consumption of prothrombin, and faulty thromboplastin generation. The name "pseudohemophilia B" has been tentatively accepted to designate this disease. The differential diagnosis of these diseases is discussed, and their clinical and genetic aspects are presented.

Thrombopathic States. Report of Twenty-Four Patients. McIlvanie, S. K., Dept. Med., Rockwood Clinic, Spokane, Wash., USA. J. Amer. med. Ass. *166:* 2114 (1958).

A clinical approach to the evaluation of the mild or questionable bleeder has been studied in 24 patients with thrombopathic states. A searching history is the best screening test. A positive family history was obtained in two-thirds of the patients and was usually manifested as a simple dominant trait. A prolonged bleeding time was the most frequent laboratory finding, whereas a history of excessive bleeding after tooth extraction was the most important anamnestic observation. Approximately one half of the patients at some time had abnormal prothrombin consumption and/or thrombin generation. The cases in general fit the so-called thrombopathic state of von Willebrand and include abnormalities of labile prothrombin accelerator, platelet prothrombin accelerator, and platelet co-thromboplastin defect. Therapy is discussed.

n) Platelets

Die Thrombocytopathie Glanzmann-Naegeli. Pathogenese der Blutungsbereitschaft. Bucher, U., Baumgartner, W., Med. Abtg., Bezirksspital, Interlaken, Switzerland. Schweiz. med. Wschr. *88:* 753 (1958).

This paper contains a detailed report of a typical case and a general survey of the clinical features of the type of thrombopathia described by Glanzmann and Naegeli (thrombasthenia). This congenital disease associated with bruises and recurrent bleeding from mucous membranes, is characterized by impaired clot retraction, prolonged bleeding time, increased capillary fragility, decreased agglutination and adhesiveness of platelets. It is attempted to explain these features on the grounds of a single platelet factor deficiency, namely Lüscher's protein "S". Careful study of the case suggested that the protein "S" content of platelets was normal, but that its release was impaired due to a defect in platelet disintegration or so-called viscous metamorphosis. Bleeding tendency can momentarily be controlled by transfusion of concentrated normal platelets. Increased vascular fragility is reduced by administration of steroid hormones.

The Treatment of Idiopathic Thrombocytopenic Purpura. (Review of 93 Cases). Watson-Williams, E. J., Macpherson, A. I. S., Sir Stanley Davidson, Dept. Med., Univ., Edinburgh, Scotland. Lancet *2:* 221 (1958).

93 cases of idiopathic thrombocytopenic purpura are reviewed. The response to various types of therapy is discussed. Recommendations for the management of patients with idiopathic thrombocytopenic purpura are made.

Study on the Thrombocytes in Tuberculosis. I. A Research on Fonio's Method. Yasuoka, H., 2nd med. Clinic, Med. Faculty, Univ. Kyoto, Japan. Jap. Arch. int. Med. *5:* 364 (1958).

Discussion of Fonio's method for determination of platelet number.

Modifications des cellules sanguines après injections de protamines chez le lapin. Ardoino, A. L., Inst. Pathol. Générale, Univ. Palermo, Italy, Rev. Hémat. *13:* 311 (1958).

A New Approach to the Thrombocytopathies. Thrombocytopathy A. Johnson, S. A., Monto, R. W., Caldwell, M. J., Thromb. Diath. haem. *2:* 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).

Les thrombopathies associées aux cardiopathies congénitales. (Etude de l'hémostase dans 50 cas). Alagille, D., Heim, R., Guéry, J., Centre Chir., Centre Nat. Transfusion Sanguine, Paris, France. Rev. franç. Etudes clin. biol. *3:* 322 (1958).

The incidence of impaired hemostasis is significantly higher in patients with congenital heart disease. If cyanosis and erythremia are present, an isolated deficiency of pro-accelerin may be found resulting of increased proteolytic activity. The most frequent disorder in congenital heart disease is qualitative platelet deficiency without thrombocytopenia. The platelet abnormality is possibly due to a congenital platelet defect. The hemostatic disorder may often, but not always, be corrected by cortisone administration before operation.

Un cas atypique de la thrombopénie idiopathique. Gaernter, H., Tutajowa, L., 3ième Clin. Maladies int., Académie de Méd., Cracovie, Poland. Haematologica Cracoviensia *2:* 221 (1958).

The authors present an atypical case of morbus Werlhof, characterized by normal bleeding time, normal clot retraction, and deficient thromboplastic and antiheparinic platelet activity. The exact analysis of this atypical case demonstrated the existence in platelets of different factors and hemostatic functions.

Aspeti della funzionalità piastrinica nelle epatopatie. Fachini, G., Ist. Clinica Med. Generale, Univ., Bologna, Italy. G. Clin. med. *39:* 370 (1958).

Thrombopathia. Creveld, S. van, Liem Khe Ho, Veder, H. A., Pediatric Clinic, Univ., Amsterdam, Holland. Acta haemat. *19:* 199 (1958).

Platelet function was investigated in 36 cases of thrombopathia and in patients recovering from thrombocytopenia. In thrombopathia it was possible, on the basis of disturbed platelet function, to discern several groups of different combinations of these functions. The impossibility of classification of thrombopathias on this basis is explained. It is recommended to classify thrombopathias by the platelet function which is found to be disturbed. The behaviour of platelet functions in patients recovering from thrombocytopenia appeared to vary markedly. Complete recovery of platelet functions usually took place slowly, and did not parallel normalization of the platelet count.

Intermediate Stages in Platelet Alterations During Coagulation. Setna, S. S., Rosenthal, R. L., Labs. of J. and H. Yeamans Levy Found., Beth Israel Hosp., New York, N. Y., USA. Acta haemat. (Basel) *19:* 209 (1958).

A pattern of blood platelet changes during coagulation is described. The chromomere and the hyalomere of the platelet revealed different physiological behaviour. Early in coagulation, the platelets clumped together by means of their excentric chromomere, formed "rosettes". This preceded the formation of fibrin which became attached to the fused chromomere substance. Observations were made on AHG, PTC, PTA and fibrinogen-deficient samples. The findings are discussed in relation to the clotting mechanism.

Effect of Physical and Chemical Agents on Platelet Morphology in Relation to Coagulation. Setna, S. S., Rosenthal, R. L., Labs. J. and H. Yeamans Levy Found., Beth Israel Hosp., New York, N. Y., USA. Acta haemat. (Basel) *19:* 222 (1958).

Platelets subjected to various types of treatment were studied from the standpoints of morphology, viscous metamorphosis, and clot retraction. Freezing and thawing, washing and storage eliminated clot retraction by producing signet-ring platelet forms, which did not clump or adher to the fibrin network during coagulation. Effects of acetone, chloroform, ether and electricity on platelet chromomere and hyalomere are reported.

A Platelet Defect in a Case of Scurvy. Cetingil, A. I., Ulutin, O. N., Karaca, M., Guraba Hosp., Istanbul, Turkey. Brit. J. Haematol. *4:* 350 (1958).

Secondary thrombopathy was demonstrated in a case of scurvy by a prolonged bleeding time, positive tourniquet test, prolonged heparin clotting time, defective agglutinability and adhesiveness of platelets, and by an abnormal thromboplastin generation test. The patient's platelets did not release the phospholipid factor on treatment with distilled water; this is considered to be pathognomonic of secondary thrombopathy. The literature on secondary thrombopathia is reviewed and it is concluded that the bleeding tendency in scurvy, which has been considered to be of vascular origin, is due to a platelet defect.

The Influence of Serotonin on Clot Retraction and the Thrombelastogram. Deutsch, E., Martiny, K., Central Coagulation Lab., Ist. Med. Dept., Univ., Vienna, Austria. Thromb. Diath. haem. *2:* 111 (1958).

Über den Einfluß von 5-Hydroxytryptamin (Serotonin), 5-Hydroxytryptophan und von Serotoninantagonisten auf die Retraktion von Blutgerinnseln. Gross, R., Staufenberg, E., Med. Klinik, Univ. Marburg/Lahn, Germany. Thromb. Diath. haem. *2:* 125 (1958)

Histologische Untersuchungen über die Retraktion. Benthaus, J., Grünberg, H., Med. Univ.-Poliklinik, Bonn, Germany. Thromb. Diath. haem. *4:* 140 (1958).

Elektronenmikroskopische Untersuchungen zur Funktionsmorphologie der Thrombozyten und zum Gerinnungsablauf im normalen menschlichen Nativblut. I. Frühe Veränderungen der Thrombozyten. Köppel, G., I. Med. Univ.-Klinik, München, Germany. Z. Zellforsch. *47:* 401 (1958).

By means of electronmicroscopic pictures the author demonstrates the extravasal alterations of platelets in native blood at room temperature. The different stages are described based on the photographic pictures which show the morphology of agglutination, adhesion and extension of the platelets. Observations regarding viscous metamorphosis are discussed. It is concluded that a substantial exchange exists between blood plasma and hyalomere of platelets, and between the vacuoles of platelets and blood plasma; the possible meaning of this results regarding the enzymatic process of blood coagulation is discussed.

Les thrombo-anticorps. Dausset, J., Centre Nat. Transfusion Sanguine, Paris, France. Acta haemat. (Basel) *20:* 185 (1958).

The Significance of Platelet Antibodies. With Special Reference to Platelet Agglutinins. Stefanini, M., Mele, R. H., Joseph H. Stanton Memorial Lab., Saint Elizabeth Hosp., Boston, Mass., USA. Acta haemat. (Basel) *20:* 195 (1958).

Athrombie transitoire. Inceman, S., 3e Clinique int., Univ. Istanbul, Turkey. Sang *29:* 256 (1958).

The author presents 5 cases of hemorrhagic diathesis caused by insufficient platelet agglutination and adhesiveness. Hemorrhages disappeared when the patients had recovered from the primary disease: Platelet number was not decreased in any of the cases. The author suggests the name of "transitory athrombia" for these forms of thrombopathia.

Phospholipids, Proteins, and Platelet-lipoid. O'Brien, J. R., Central Lab., Milton Road, Portsmouth, Hampshire, England. Nature (Lond.) *181:* 420 (1958).

Traitement d'une thrombocytopénie essentielle par désensibilisation spécifique sous protection de prédnisone. Hofstetter, J. R., Policlinique méd., Univ., Lausanne, Switzerland. Praxis *47:* 95 (1958).

Un cas de télangiectasies hémorragiques avec hépatosplénomégalie et thrombopénie héréditaire. (Maladie de Osler). Dupasquier, E., Inst. Anatomie pathol., Univ., Lausanne, Switzerland. Rev. méd. Suisse rom. *74:* 77 (1958).

Hemolytic Anemia Following Thrombocytopenic Purpura. Harris-Jones, J. N., McLellan, D. M., Owen, G., Royal Hosp., Sheffield, England. Brit. med. J. 5071: 624 (1958).

Case report.

Les accidents thrombopéniques avec hémorragie dus à la quinidino-thérapie. Perrin, P., Dauphin, G., Nantes, France. Presse méd. *66:* 481 (1958).

Immunothrombozytopathien. Miescher, P., Med. Univ.-Poliklinik, Basel, Switzerland. Dtsch. med. Wschr. *83:* 651 (1958).

Thrombozytär bedingte hämorrhagische Diathesen. I. Teil. Schäfer, K. H., Fischer, K., Landbeck, G., Univ.-Kinderklinik, Hamburg-Eppendorf, Germany. Dtsch. med. Wschr. *83:* 695 (1958). II. Teil Dtsch. med. Wschr. *83:* 756 (1958).

The role of platelets in coagulation and hemostasis is reviewed. The authors' own observations are discussed and 12 cases of essential thrombocytopenia and 17 cases of thrombocytopenia with unknown etiology and 15 families with 26 cases of hereditary coagulation disorders are presented. It is shown that in addition to the determination of platelet factor 3 activity, the direct Coombs' test, recalcification time, retraction time and prothrombin consumption

provide the best information. A case is presented of a boy with a familial thrombocytopenic hemorrhagic diathesis accompanied by thrombocytopenia caused by autoantibodies due to coincidental development of Hodgkin's disease. This probably unique case forms the basis of a suggested new classification of thrombocytopenias along pathogenetic and if possible etiologic lines.

Das morphologische Substrat der idiopathischen thrombopenischen Purpura im Lichte neuer pathogenetischer Erkenntnisse. Cleve, H., Heckner, F., Schoen, R., Med. Univ.-Klinik, Göttingen, Germany. Schweiz. med. Wschr. *88:* 323 (1958).

Cytological studies of bone marrow smears in idiopathic thrombocytopenic purpura before and after splenectomy and in smears of the removed spleens reveal certain morphological alterations and lead to the conclusion that platelet agglutinins exist as the pathogenetic mechanism. The morphologically identified function of the spleen consists in sequestration of platelets and in antibody production. The effect of prednisone therapy in idiopathic thrombocytopenic purpura as observed clinically as well as cytologically supports this view.

Increase of 5-Hydroxytryptamine in Blood Plateletes by Isopropyl-isonicotinic Acid Hydrazide. Pletscher, A., Bernstein, A., Med. Research Dept. F. Hoffmann-La Roche & Co., Basel, Switzerland. Nature (Lond.) *181:* 1133 (1958).

Une nouvelle source de leucocytes et de plaquettes: Le sédiment globulaire mixte recueilli sur les bols des séparateurs centrifuges. Maupin, B., Centre de Transfusion Réanimation de l'Armée, Clamart, Seine, France. Sang *29:* 74 (1958).

Eine empfindliche Methode zur Messung der Thrombozytenfaktor-3-Aktivität im Thromboplastin-Generation-Test. Achenbach, W., Klesper, R., Maurer, K., Hoppe, G., Med. Univ.-Poliklinik, Köln, Germany. Klin. Wschr. *36:* 585 (1958).

The authors describe a sensitive method for the determination of platelet factor 3 activity.

Sérotonine sérique et maladies hémorragiques. Quivy, D., Caen, J., Bernard, J., Lab. Physiopath., Faculté de Méd., Hôp. St. Louis, Paris, France. Rev. franç. Etudes clin. biol. *3:* 477 (1958).

In 7 cases of thrombocytopenia, 7 cases of thrombocytopathia, and in one case of thrombocythemia, the authors have found very low serum serotonin levels. The results seem to parallel the platelet prothromboplastic deficiency. Serum serotonin level can also be markedly decreased in cases of deficient prothromboplastic activity, such as hemophilia A and B, and Hageman trait.

Purpura thrombopénique et néphropathies. Debré, R., 5, rue de l'Univ., Paris, France. Arch. franç. Pédiat. *15:* 289 (1958).

Studies on Platelets. XX. Further Characterization of the Electrophoretic Anomaly in Serum of Patients with Idiopathic Thrombocytopenic Purpura. Stefanini, M., Moschides, E., Dept. Med., Tufts Univ. Med. School, Boston, Mass., USA. J. Lab. clin. Med. *51:* 842 (1958).

Electrophoretic studies show an increase of total carbohydrate staining material as compared to normal values and its accumulation in the albumin fraction in the serum of patients with the acute or chronic variety of ITP. Chemical studies confirm these resultats as well as the presence of hexoses and of glucosamine in the albumin fraction of ITP serum. The eluted albumin fraction of normal serum migrates as a uniform component, under similar conditions the albumin fraction from serum of patients with ITP divides into 2 components. These findings may be related to the presence in patients with ITP of an autoimmune state against platelets.

Platelet Thromboplastic Factor: Its Chemical Nature, In Vitro Activity, and the Identification of Similar Thromboplastic Substances in Red Blood Cells. Troup, S. B., Reed, C. F., Rochester, N. Y., USA. J. clin. Invest. *37:* 937 (1958).

A Cause of the Thrombocytopenia and Leukopenia that Occur in Dogs During Deep Hypothermia. Villalobos, T. J., Adelson, E., Riley, P. A., Crosby, W. H., Dept. Hemat., Walter Reed Army Med. Center Washington, D. C., USA. J. clin. Invest. *37:* 1 (1958).

Investigations have been made into the mechanisms of the thrombocytopenia and leukopenia that occur in hypothermic dogs. By tagging platelets with P^{32}, the thrombocytopenia was shown to be caused by sequestration rather than destruction of platelets. It was demonstrated that the major site of platelet sequestration is in the portal circulation. By extirpation it was shown that the liver and spleen play a major role in the sequestration. However, since hepatectomized-splenectomized dogs still develop some thrombocytopenia, other areas must also be sites of sequestration.

Calcium-Lipid Complexes in Human Platelets. Hoelzl Wallach, D. F., Surgenor, D. M., Steele, B. B., Dept. Biol. Chem., Harvard Med. School, Boston, Mass., USA. Blood *13:* 598 (1958).

Carefully washed human platelets contain calcium in an unusual state of chemical combination. Platelet calcium is non-ionic and is not exchangeable with ionic Ca^{45}. On extraction of platelets with lipid solvents, the calcium separates with the phospholipids. The calcium-lipid complex thus obtained does not undergo any exchange with radioactive calcium. Study of other properties of platelets reveals that the clot-promoting activity of platelets also separates into the lipid fraction. Preliminary observations are reported on the nature of platelet lipids as revealed by paper chromatography and paper electrophoresis in solvents of low dielectric constante. Small amounts of proteolipid have been isolated from the lipid extracts. The unique calcium-lipid complex is thought to originate in the cell membrane of the platelet.

Platelet Adsorptive Properties and Platelet Extracts in Thromboplastin Generation. Perry, S., Craddock, C. G., Dept. Med., Univ. California Med. Center, Los Angeles, Calif., USA. Blood *13:* 177 (1958).

Incubation of normal platelets in saline for 10 mins. at 37° C markedly diminishes their activity in the thromboplastin generation test. This is due to the removal of a factor(s) from the platelet, and the lost activity is present in the saline extract. These "attenuated" platelets retain their effect on the recalcification time, prothrombin consumption, and clotting time of whole blood. Attenuated platelets as well as qualitatively defective platelets regain normal activity in the TGT after incubation in normal plasma or in plasmas from patients with qualitative platelet defects. Attenuated platelets in contrast to qualitatively defective platelets, are restored to normal, after treatment with saline extracts of normal platelets. Attenuated platelets, however, do not function normally after incubation with saline extracts of qualitatively defective platelets. The possible mechanisms involved are discussed, and it is concluded that the phenomenon involves the adsorption of plasma factor(s) by the platelets. The nature of the plasma factor(s) is not known.

Hemorrhagic Diathesis Related to Quinidine Therapy. Hunt, J. C., Anderson, M. W., Hanlon, D. G., Sec. Med., The Mayo Clinic, Rochester, Minn., USA. Proc. Mayo Clinic *33:* 87 (1958).

Four case reports with purpuric manifestations developing as an apparent consequence of idiosyncrasy to quinidine.

Fatal Acute Hemolytic Anemia, Thrombocytopenic Purpura, Nephrosis and Hepatitis, Resulting from Ingestion of a Compound Containing Apiol. Lowenstein, L., Ballew, L. H., Hemat. Service, Dept. Med., Royal Victoria Hosp., Montreal, Canada. Canad. med. Ass. J. *78:* 195 (1958).

Treatment of Idiopathic Thrombocytopenic Purpura (ITP) with Prednisone. Dameshek, W., Rubio, F., Mahoney, J. P., Reeves, W. H., Burgin, L. A., Dept. Med., Tufts Univ. Med. School, Boston, Mass., USA. J. Amer. med. Ass. *166:* 1805 (1958).

Thrombotic Thrombocytopenic Purpura: A Review of the Literature with Report of a Case. Antes, E. H., Fort Belvoir, Va., USA. Ann. intern. Med. *48:* 512 (1958).

A review of the literature has been made in order to elucidate further the clinical pattern of thrombotic thrombocytopenic purpura, a disease which has only recently been recognized as a clinical entity. A case in a 24-years-old man has been added to the literature. This case suggests the probability of an antigen-antibody response following the injection of influenza vaccine, tending to confirm the present theory in regard to the genesis of this disease.

Essential Thrombocythemia. Kupfer, H. G., Ebbels, B. J., Miller, J. N., Thoma, G. W., Russi, S., Med. College of Virginia, Richmond, Va., USA. Ann. intern. Med. *48:* 685 (1958).

A case of essential thrombocythemia with autopsy findings and brief review of the literature is presented. The possible mechanisms of altered platelet function, with emphasis on the probability of qualitative platelet variations, are discussed. Laboratory studies, including prothrombin consumption and thrombin generation are presented. The authors' reasons for considering the condition a myeloproliferative disorder of a primary nature are listed.

Effects of 5-Hydroxytryptamine on Some Aspects of Hemorrhagic State in Radiation-Induced Thrombocytopenia. Djerassi, I., Klein, E., Farber, S., Palmer, D., Children's Med. Center, Harvard Med. School, Boston, Mass., USA.. Proc. Soc. exp. Biol. (N. Y.) *97:* 552 (1958).

Synthetic serotonin increased vascular resistance and shortened the duration of traumatic bleeding in irradiated thrombocytopenic guinea pigs and mice, respectively. These effects were of short duration and were observed only when large doses of serotonin were given rapidly. Transient pulmonary distress was associated with the administration of effective doses to guinea pigs.

Thrombohemolytic Thrombocytopenic Purpura. Case Report and Review of Literature. Wasserman, E., Dept. Med., St. Vincent's Hosp., Bridgeport, Conn., USA. Amer. J. Med. Sci. *24:* 648 (1958).

Case report.

The Effect of Prednisolone on Circulation. Antibody Formation in Animals Immunized with Human Platelet Antigen. Suhrland, L.-G., Arquilla, E. R., Weisberger, A. S., Cleveland, Ohio, USA. J. Lab. clin. Med. *51:* 724 (1958).

Thrombocytopenia and Leukopenia Associated with Use of Sulfamethoxypyridazine. Schwartz, M. J., Norton, W. S., Dept. Med., St. Luke's Hosp., New York, N. Y., USA. J. Amer. med. Ass. *167:* 457 (1958).

Two cases of thrombocytopenia were associated with the use of sulfamethoxypyridazine. In the second case leukopenia was also noted.

Studies on Thrombocytosis. I. Hyperkalemia Due to Release of Potassium from Platelets During Coagulation. Hartmann, R. C., Auditore, J. V., Jackson, D. P., Dept. Med. Vanderbilt Univ. Med. School, Nashville, Tenn., USA. J. clin. Invest. *37:* 699 (1958).

Elevated serum potassium concentrations were noted in 4 of 13 patients with thrombocytosis in the absence of symptoms of hyperkalemia. This represented a spurious hyperkalemia due to release of potassium from platelets during coagulation, since serum prepared from platelet-free plasma had a normal potassium concentration. The mean potassium content of normal platelets was found to be 69.1 mEp/kg of platelets (wet weight) or 86.4 mEq/litre of platelet water. It is concluded that the hyperkalemia present in thrombocytosis was mainly due to an increased platelet mass per unit volume of blood or plasma, and only slightly due to increased platelet potassium concentration. Platelets were found to have a water content of approximately 80% and to contain small amounts of sodium. The method employed provides a means of measuring platelet cations under the most physiological conditions possible.

Macroscopic Studies of Platelet Agglutination; Nature of Thrombocyte Agglutinating Activity of Plasma. Brinkhous, K. M., Leroy, E. C., Cornell, W. P., Brown, R. C., Dept. Path., Univ. N. Carolina, Chapel Hill, N. C., USA. Proc. Soc. exp. Biol. (N. Y.) *98:* 379 (1958).

Optimal conditions for platelet agglutination were determined in the dog by macroscopic test. Most rapid agglutination was observed with Mg^{++} or Mg^{++}, undiluted plasma, and a platelet concentration above 200 000/cmm. Frozen or heated platelets were not agglutinable. The thrombocyte agglutinating factor (TAg) found in plasma was thermolabile and nondialyzable. Under optimal conditions it caused gross platelet clumping in 5—15 secs. This factor was active in the absence of fibrin coagulation, Ca^{++}, AHF, fibrinogen, prothrombin and related coagulant factors, suggesting the TAg may act independently of the coagulation process.

Thrombotic Thrombocytopenic Purpura Occurring in the Puerperium. Associated Pancreatic Islet-Cell Necrosis. Harrison, H. N., Path. Serv., Fitzsimons Army Hosp., Denver, Col., USA. Arch. intern. Med. *102:* 124 (1958).

A case of thrombotic thrombocytopenic purpura is presented occurring in the puerperium with a total clinical course of 70 hours. Selective pancreatic islet-cell necrosis is stressed as a cause of epigastric pain, a symptom of some frequency in this disease.

o) Spontaneous Anticoagulants

Natürlich vorkommende Koagulationsinhibitoren. Deutsch, E., Fuchs, H., Gerinnungslaboratorium, I. Med. Univ.-Klinik, Wien, Austria. Acta haemat. *20:* 97 (1958).

The highly active reaction products of the coagulatory system, namely thrombin, thromboplastin and convertin, are balanced by several inhibitors. These inhibitors can be separated into categories: lipoids or lipoproteins, inhibitors originating in immunologic reactions, and inhibitors localized in cells. The lability of factor V and VIII in human plasma might also be caused by a corresponding inhibitor. In normal blood, however, no inhibitors of the stable coagulation factors, namely prothrombin, proconvertin, and fibrinogen, have as yet been found.

Détection thrombélastographic d'anticoagulants circulants. Valeur et sensibilité de cette méthode comparées à celles des testes classiques. Sokal, G., Masure, R., Moriau, M., Lab. d'Hématol., Clinique méd. A, Univ. Louvain, Belgium. Acta haemat. (Basel) *19:* 327 (1958).

Several methods used to demonstrate circulating anticoagulants were investigated and compared. 6 different methods were used; 3 of them were new thrombelastographic procedures. Comparison of the results showed that thrombelastographic methods are superior in several respects to the classical methods. Thrombelastography also helps in the differentiation of several types of antibodies.

An Atypical Circulating Thromboplastin Inhibitor. Douglas, A. S., Univ. Dept. Med., Royal Infirmary, Glasgow, Scotland. Brit. J. Haematol. *4:* 302 (1958).

A case is described of a 33-years-old male with ankylosing spondylitis, who developed a hemorrhagic state due to an atypical circulating thromboplastin inhibitor. The whole-blood clotting time was prolonged and prothrombin consumption defective. Plasma from the patient shortened the recalcification time of hemophilic and Christmas disease plasma and, in small additions, did not prolong the recalcification time of normal plasma. The thromboplastin generation tests when used with diluted adsorbed plasma and serum gave normal results, but when these reagents were used undiluted the inhibitor was readily demonstrated. The results are interpreted as due to a circulating thromboplastin inhibitor, the effect of which was readily removed by dilution.

Les diathèses hémorragiques par anticoagulant inhibitant la formation ou l'action de la thromboplastine. (A propos d'un cas personnel, observé au cours d'une polyarthrite chronique évolutive). Favre-Gilly, J., Thouverez, J. P., Tourniaire, M., Clinique méd., Lyon, France. Sang *29:* 1 (1958).

Case report.

Un nouvel anticoagulant dérivé du fibrinogène. Niewiarowski, S., Kowalski, E., Lab. Biochem. clin., Inst. Hématol., Varsovie, Poland. Rev. Hémat. *13:* 320 (1958).

The authors describe an anticoagulant appearing in the course of proteolytic degradation of fibrinogen and fibrin by plasmin or trypsin. The anticoagulant inhibits the action of thrombin on fibrinogen. The authors studied some properties of the anticoagulant: It is precipitated with ammonium sulfate at 50% and with aceton. The partially purified anticoagulant is destroyed by plasmin and by heating to 60° C for one hour. It is neutralized by protamine and toluidine blue. The authors suggest that the anticoagulant is a product of fibrin degradation with a fairly high molecular weight.

Ricerche sulle attività antithromboplastinica ed antithrombinica nell' immaturo. Arditi, E., Clin. Pediatrica, Univ. Torino, Italy. Minerva pediat. (Torino) *10:* 493 (1958).

Circulating Anticoagulant after Pregnancy and its Response to ACTH. Nilsson, I. M., Skanse, B., Gydell, K., Dept. Med. Malmö General Hosp., Malmö, Sweden. Acta haemat. (Basel) *19:* 40 (1958).

The authors describe a hemorrhagic diathesis in a woman of 32 appearing 3 months following her first pregnancy. The clotting defect was caused by a circulating anticoagulant which inhibited antihemophilic globulin. The anticoagulant was electrophoretically seperated from gamma globulins, although no increase of this protein fraction was evident. ACTH therapy induced complete clinical and hematological recovery while cortisone was found to be ineffective.

Plasma Heparin Levels in Man Following Intravenous Fat Emulsions. Engelberg, H., Div. Labs., Dept. Med., Cedars of Lebanon Hosp., Los Angeles, Calif., USA. Proc. Soc. exp. Biol. (N. Y.) *97:* 304 (1958).

Plasma heparin levels were determined in 18 individuals before, during and after intravenous infusions of cottonseed oil emulsion, and in 14 of the group after control injection without fat. There was an average increase of 22% in circulating heparin in 12 of the 18 subjects after the fat emulsion; an average increase of 18% in 4 of 14 patients after non-fat emulsion. The results indicate that fat intake is a stimulus for the release of heparin into the blood stream.

Bridge Anticoagulant: A Hitherto Unrecognized Blood Clotting Inhibitor in Hemophilic and Christmas-Disease Plasma. A Simple Method for its Demonstration. Nour-Eldin, F., Wilkinson, J. F., Dept. Hematol., Royal Infirmary, Manchester, England. Brit. J. Haematol. *4:* 38 (1958).

A method is described for the demonstration of an anticoagulant in the plasma of patients with hemophilia or Christmas disease. This "Bridge Anticoagulant" is associated with the deficiency in either antihemophilic globulin or Christmas factor, respectively. It is a congenital anomaly and was demonstrated in 109 patients with hemophilia and 14 with Christmas disease. The properties of the anticoagulant and its action on the stages of plasma thromboplastin formation have been studied. The inconsistency observed between the results obtained after transfusing hemophilic patients with normal plasma or antihemophilic globulin and those expected from in vitro tests is discussed in the light of this anticoagulant. Taking into consideration the presence of this anticoagulant a titration method has been devised for the determination of the amount of normal plasma or antihemophilic globulin required for the correction of the defect of each hemophilic patient.

De antitrombineproef bij acute pancreatitis. Walpot, L., Int. afdeling, St. Canisius Ziekenhuis, Nijmegen, Holland. Ned. T. Geneesk. *102:* 811 (1958).

Eight cases of acute pancreatitis seen by the authors confirmed the observations made by others that the antithrombin level remains abnormal long after diastase levels in blood and urine have returned to normal. Especially in the later stages of acute pancreatitis the antithrombin test may be of considerable diagnostic value.

Influenza della bile e dei sali biliari sull'emocoagulazione "in vitro" con particolare riguardo all'attività antitrombinica. Garagnani, A., Facchini, G., Ist. Clin. Med. e Terapia, Univ., Bologna, Italy, Arch. Patol. Clin. med. *33:* 203 (1958).

Demonstration of a Circulating Anticoagulant in Plasma Thromboplastin Antecedent Deficiency. Josephson, A. M., Lisker, R., Dept. Hemat. Res., Med. Res. Inst. Michael Reese Hosp., Chicago, Ill., USA. J. clin. Invest. *37:* 148 (1958).

The demonstration of a circulating anticoagulant in PTA deficiency is described for the first time. The anticoagulant could only be demonstrated by the use of the thromboplastin generation test after incubation of the patient's plasma with either normal sera or plasma. The anticoagulant activity is confirmed to the patient's plasma.

A Circulating Inhibitor (Anti-AcG) Specific for the Labile Factor V of the Blood Clotting Mechanism. Ferguson, J. H., Johnston, C. L., Howell, D. A., Dept. Physiol., Univ. N. Carolina, Chapel Hill, N. C., USA. Blood *13:* 382 (1958).

Study of the present hemorrhagic disorder establishes, without doubt, the presence of a powerful specific anti-AcG. The deprivation of AcG due to this inhibitor confirms the view that the labile factor plays a key role in the blood clotting system in at least two phases, namely during thromboplastin generation and later, during the conversion of prothrombin to thrombin. AcG is an essential component of many special clotting-test-systems.

p) Vitamin K

Die prognostische und differentialdiagnostische Bedeutung des Vitamin-K-Tests. Pestalozzi, H., Med. Abtg., Krankenhaus Neumünster, Zollikerberg, Switzerland. Schweiz. med. Wschr. *88:* 402 (1958).

The vitamin K test as introduced by Koller in 1940 is based on the response of various forms of jaundice and liver damage to the administration of vitamin K. The sensitivity of this test has since been increased by the determination of single clotting factors, replacing Quick's prothrombin time. The author reports the results obtained in over 200 patients suffering from liver disorders. The results obtained and the conclusions drawn are discussed.

Study on Plasma Prothrombin Time and Fluctuation of Plasma Prothrombin Index Following Vitamin K Loading Test in Healthy Persons. Obigata, H., Ist. Med. Clinic, Med. Faculty, Univ., Kyoto, Japan. Japan. Arch. int. Med. *5:* 381 (1958).

Some Observations on the Coagulation Defect in Vitamin K Deficiency. Douglas, A. S., Univ. Dept. Med., Royal Infirmary, Glasgow, Scotland. J. clin. Path. *11:* 261 (1958).

Evidence is described indicating a deficiency of Christmas factor as part of the coagulation defect resulting from lack of vitamin K. The reduced concentration of prothrombin and factor VII in vitamin K deficiency is confirmed. The facets of the vitamin K defect — prothrombin —, factor VII —, serum thromboplastin-defect, and the inability of serum to correct the Christmas serum thromboplastin-defect — are the same as those resulting from the administration of cumarin drugs. These components of the vitamin K defect all respond at similar rates to the administration of vitamin K.

Correction of Defects in Clotting Accelerator Activity by Administration of Methionine and Vitamin K and of New Sulfhydryl-Substituted Methyl-naphtho-Quinone, Vitamin K—S (II). Carter, J. R., Warner, E. D., Dept. Path., State Univ. Iowa, Iowa City, Iowa, USA. J. clin. Invest. *37:* 70 (1958).

Analysis of the experimental and clinical data indicates that accelerator activity (factor V and VII) in blood coagulation is influenced by the concomitant administration of methionine and vitamin K and by vitamin K—S (II). These compounds would appear to be useful, at times even specific, therapeutic measures in the treatment and management of accelerator deficiencies. Determination of the extent of applicability of these measures must await further clinical trial.

q) Heparin and Heparin-like Substances

Le traitement à l'héparine des angiopathies. Brauner, R., Sorin, E., et al., Clin. méd., Hôp. Brincovenesc, Bucarest, Rumania. Presse méd. *66:* 257 (1958).

Heparin Tolerance Test During Dehydration of Patients with Congestive Heart Failure. Holger-Madsen, T., Copenhagen County Hosp., Gentofte, Denmark. Acta med. scand. *160:* 109 (1958).

Effect of Heparin on Pathologically Decreased Serum Esterase in Carcinoma. Skorepa, J., 4th Med. Clinic, Charles Univ., Prague, CSR. Nature (Lond.) *181:* 908 (1958).

Die Anwendung von El-Heparin bei einer schweren arteriellen Embolie. Klein, O., Chir. Abtg., St. Josefs-Krankenhaus, Heidelberg, Germany. Med. Mschr. *12:* 31 (1958).

Nouvelle méthode de mesure de la tolérance à l'héparine "in vitro". Beaumont, J. L., Service, J., Lenègre, Hôp. Boucicaut, Paris, France. Rev. franç. Etudes clin. biol. *3:* 268 (1958).

The in vitro heparin tolerance test has been modified in order to eliminate errors due to centrifugation and inaccurate reading of the clotting time.

Über die Beziehungen zwischen Wirksamkeit und Toxizität bei Nativheparinen und Heparinoide. Goossens, N., Gastpar, H., Setz, W., Med. Poliklinik, Univ., München, Germany. Klin. Wschr. *36:* 524 (1958).

Beeinflussung der Gerinnungswirkung von Heparin durch Serotonin und Tryptamin. Keller, R., Inst. Hygiene und Arbeitsphysiol., ETH, Zürich, Switzerland. Experientia (Basel) *14:* 181 (1958).

Treatment of Fat Embolism with Heparin. Sage, R. H., Tudor, R. W., Selly Oak Hosp., Birmingham, England. Brit. med. J. 5080: 1160 (1958).

Heparin Neutralization with Polybrene Administered Intravenously. Weiss, W. A., Gilman, J. S., Catenacci, A. J., Osterberg, A. E., Dept. Anesthesiol., Hahnemann Med. Coll., Philadelphia Pa., USA. J. Amer. med. Ass. *166:* 603 (1958).

Three heparin-neutralizers (protamine, toluidine-blue, and polybrene) were compared. All three cause disagreeable side-effects in some patients, but polybrene, injected intravenously in proper dilution at the prescribed rate, did not cause either the methemoglobinemia and hypoxia seen after toluidine blue or the dangerous degrees of hypotension seen after protamine. Given in the recommended dose of 0.7 mg of polybrene to 1 mg of heparin, the polybrene promptly and completely neutralized the anticoagulant action of heparin.

Arterial Embolism Occurring During Systemic Heparin Therapy. Weismann, R. E., Tobin, R. W., Dartmouth Med. School, Hanover, N. H., USA. Arch. Surg. (Chicago) *76:* 219 (1958).

Effect of Heparin on Serum Lipids Following Intravenous Administration of Fat Emulsion in Dogs. Meng, H. C., Youmans, J. B., Dept. Physiol. and Med., Vanderbilt Univ. Med. School, Nashville, Tenn., USA. Proc. Soc. exp. Biol. (N. Y.) *97:* 691 (1958).

Physiological Disposition of Heparin. Eiber, H. B., Danishefsky, I., Borrelli, F. J., Gilman Lab., New York Med. College, New York City, N. Y., USA. Proc. Soc. exp. Biol. (N. Y.) *98:* 672 (1958).

After intravenous administration of heparin-S^{35} to dogs, it is rapidly cleared from the blood stream. The highest radioactivity is found in liver and lung. However, no measurable radioactivity is detected in any organ after 48 hours.

The Treatment of Thromboembolism with Aqueous Heparin. Harrower, H. W., Providence Rh. I., USA. Surg. Gynec. Obstet. *106:* 293 (1958).

r) Other Anticoagulants

Anticoagulant in Myocardial Infarction. Toohey, M., New End Hosp., London, England. Brit. med. J. 5065: 252 (1958).

Voorkomen en behandelen van tromboflebitis. Verstraete, M., Dienst f. Inwendige Geneeskunde B., Leuven, Belgium. Belg. T. Geneesk. 3: 115 (1958).
(Sintrom, Marcoumar, Heparin).

Die Prophylaxe der Thrombose und Embolie. Dick, W., Chir. Univ.-Klinik, Tübingen, Germany. Medizinische 14: 543 (1958).

Über die Beeinflussung der Blutgerinnung durch ein neues Antikoagulans aus Salzen der seltenen Erden. Bierstedt, P., Chir. Klinik, Städt. Krankenhaus, Friedrichshain, Berlin, Germany. Dtsch. med. J. *9:* 39 (1958).
(Helodym 88, by Helopharm AG, Berlin = Neodym + Praseodym + beta-acetyl-propion-acid.)

Permanent Anticoagulant Therapy; Complications and Rate of Mortality. Oedegaard, E. A., Univ. Hosp., Outpatient Dept. int. Med., Oslo, Norway. Acta med. scand. *160:* 105 (1958).

Hemorrhagic Cutaneous Necrosis in Phenylindanedione Treatment. Keyrilainen, A. O., Inre-medicinska Kliniken, Universitetet, Abo, Finland. Nord. Med. Ark. *59:* 567 (1958).
The author describes a complication occurring during phenylindanedione therapy. The clinical picture was similar to the previously reported hemorrhagic cutaneous necrosis associated with the use of dicumarol and its derivatives.

Prophylaxe und Therapie mit dem Antikoagulans Sintrom in der Gynäkologie und Geburtshilfe. Uebelhart, R., Stäubli, P., Frauenklinik, Kantonsspital, Winterthur, Switzerland. Schweiz. med. Wschr. *88:* 269 (1958).
Sintrom has been used in prophylaxis and treatment of thrombosis and embolism in 200 obstetric-gynecological cases. The practical advantages of the drug are described. After discussing the results and demonstrating 6 typical cases the authors conclude that Sintrom is an efficient and safe anticoagulant.

Alopecia Following Treatment with Dextran Sulphate and other Anticoagulant Drugs. Tudhope, G. R., Dept. Pharm. Ther., Univ. Sheffield, England. Brit. med. J. 5078: 1034 (1958).

La thrombo-élastographie dans la surveillance des traitements anticoagulants. Raynaud, R., Brochier, M., Alger. Sem. Hôp. Paris *34:* 977 (1958).

Owren's Method for the Control of Anticoagulant Therapy. Allington, M. J., Dept. Haemat., Radcliffe Infirmary, Oxford, England. J. clin. Path. *11:* 62 (1958).
A description is given of the P and P (prothrombin and proconvertin) method of Owren as used routinely in this department for the control of anticoagulant therapy. The method has been found to be more sensitive and subject to less random variation than Quick's one-stage method and to be particularly suitable for the control of long-term anticoagulant therapy.

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. Pharm. Univ. Saskatchewan, Saskatoon, Sask., Canada. Thromb. Diath. haem. *2:* 236 (1958).

Die Thromboembolie. Unter besonderer Berücksichtigung der Antikoagulantien. Zukschwerdt, L., Thies, H. A., Univ.-Klinik, Hamburg, Germany. Dtsch. med. Wschr. *83:* 1001 (1958).
Modern theories on cause and development of thrombosis, fate of thrombi, reaction of venous walls and physiological studies of the post-phlebitic chronic edema are reviewed. Incidence of embolism and cause of death are discussed. Determination of clotting factors is considered of little value whereas clinical signs should thoroughly be considered. The use of anticoagulants is advocated and the pros and cons of the various types are discussed, as well as surgical treatment of thromboembolism. Anticoagulant activity should have its onset 3 to 4 days postoperatively and be continued for one week as a prophylactic measure.

Bronchodilator Action of the Anticoagulant Warfarin Sodium. Blumberg, H., et al., Research Labs., Endo Labs. Inc., Richmond Hill, N. Y., USA. Science *127:* 188 (1958).

A New Coumarin. Delage, J. M., Dept. Med., Lab. of Hemat., Saint Sacrament Hosp., Quebec, Canada. Canad. med. Ass. J. *78:* 43 (1958).

Experience with Outpatient Anticoagulant Therapy. Grant, W. G., Dept. Med., Univ., Toronto, Canada. Canad. med. Ass. J. *78:* 317 (1958).

59 out-patients with various types of thrombotic disease received Dicumarol for an average period of 11 months. One-stage prothrombin times were measured every 2 to 3 weeks. To minimize the risk of bleeding it is suggested that the prothrombin time be kept within a range of 20 to 25 seconds (normal value 14 to 15 seconds). Bleeding was a serious problem, 18 episodes being encountered. No conclusions could be drawn about effectiveness of treatment. There is an urgent need for carefully controlled studies.

Effect of Dicumarol on Bleeding Time. Cauwenberge, H. van, Jaques, L. B., Dept. Physiol. and Pharm., Univ. of Saskatchewan, Saskatoon, Canada. Proc. Soc. exp. Biol. (N. Y.) *98:* 599 (1958).

Rabbits were treated with dicumarol and dicumarol plus ACTH and prothrombin times and bleeding times determined. A slight increase in bleeding time was observed after 3 days on dicumarol, in 50% of the rabbits. Half the rabbits died in the next 24 to 72 hours from generalized non-specific hemorrhage. This was not related to the previous increase in bleeding time. Bleeding did recur and continue from the cut ear but hemorrhage was much more extensive than this. It is suggested that determination of bleeding time is a marked stress procedure in rabbits.

Bilateral Adrenal Hemorrhage Complicating Dicumarol Therapy for Myocardial Infarction. Chokas, W. V., Dept. Med., The Mountainside Hosp., Montclair, N.J., USA. Amer. J. Med. *24:* 454 (1958).

Suggestive but not conclusive evidence is offered that in the case described death was due to bilateral adrenal hemorrhage, part of a widespread hemorrhagic state complicating dicumarol therapy.

Long-Term Treatment of Angina Pectoris with Dicumarol. Gabrielsen, Z., Myrhe, J. R., Med. Dept. A., Univ. Clinic, Bergen, Norway. Circulation *17:* 348 (1958).

A Critical Evaluation of Anticoagulant Therapy in Peripheral Venous Thrombosis and Pulmonary Embolism. Coon, W. W., Dept. Surg., Univ. of Michigan Med. Coll., Ann Arbor, Mich., USA. Surg. Gynec. Obstet. *106:* 129 (1958).

Intestinal Obstruction Due to Bishydroxycoumarin Poisoning. Pearson, S. C., MacKentie, R. J., Surg. Serv., Seaside Memorial Hosp., Long Beach, Calif., USA. J. Amer. med. Ass. *167:* 455

Case report.

Clinical Experiences with Warfarin (Coumadin) Sodium as an Anticoagulant. Baer, S., Yarrow, M. W., Kravitz, C., Markson, V., Dept. Med., Albert Einstein Med. Center, Philadelphia, Pa., USA. J. Amer. med. Ass. *167:* 704 (1958).

Relation of Hemorrhage and Thrombosis to Prothrombin During Treatment with Cumarin-Type Anticoagulants. Sise, H. S., Lavelle, S. M., Adamis, D., Becker, R., Tufts Med. Service, Boston City Hosp., Boston, Mass., USA. New Engl. J. Med. *259:* 266 (1958).

Cumarin-type anticoagulants reduce the level of prothrombin, proconvertin, Stuart factor and plasma thromboplastin component. Attention is called to the failure of the Quick test to predict hemorrhage and thrombosis in some patients under treatment. It was found that in patients under warfarin the Quick test measures mostly proconvertin and is influenced very little by the levels of other factors. The prothrombin concentrations and Quick times of 84 patients on phenindione over the course of 18 months are recorded and the results discussed. It is then recommended that both Quick time and prothrombin be measured when patients under long term treatment are followed. The management of long-term cases is outlined.

Early Clue to Visceral Carcinoma. Hemorrhage after Intravenously Given Warfarin. Goodman, D. H., Dept. Med., Good Samaritan Hosp., Phoenix, Ariz. J. Amer. med. Ass. *166:* 1037 (1958).

Hyperreaction to warfarin or its congeners, when administered in a therapeutic dose to treat thrombophlebitis, should make one suspect an obscure visceral carcinoma, particularly of the body or tail of the pancreas, or other visceral carcinoma with metastases to the pancreas.

Analysis of Factors Affecting Recurrence of Thromboembolism off and on Anticoagulant Therapy. Carter, S. A., McDevitt, E., Gatje, B. W., Wright, I. S., Vasc. Section., Dept. Med., New York Hosp., New York, N. Y., USA. Amer. J. Med. *25:* 43 (1958).

The present study is a statistical analysis of the results in patients followed up at least 6 months off and 6 months on anticoagulant therapy. Statistical evidence of benefit was obtained. but this was of border-like significance in patients with congestive heart failure, atrial fibrillation, myocardial infarction, and the like. The tendency to thromboembolism increased within the 6 weeks' period following discontinuation of anticoagulant prophylaxis. It seems that still more data on this important subject will be required before definite conclusions can be reached.

Anisindione, a New Anticoagulant with Unusual Properties. Lange, K., Perchuk, E., Mahl, M., Enzinger, J., Mouratoff, G., Amer. Heart J. *55:* 73 (1958).

Anisindione (2-p-anisyl-indandione-1,3) was administered to 52 patients. The effect was immediate and therapeutic prothrombin values were reached within 36 to 72 hours. Dosage: First days 500 mg, 300 mg on the 2nd and 4th day, followed by 250 mg every 3rd day. Prothrombin values remained unusually stable. No side effects were noted except for bleeding tendency in 3 cases. Mephyton rapidly increases prothrombin values.

Anticoagulant Therapy in Cerebral Vascular Disease — Current Status. Millikan, C. H., Siekert, R. G., Whisnant, J. P., Sec. Neurol., Mayo Clinic, Rochester, Minn., USA. J. Amer. med. Ass. *166:* 587 (1958).

Details are given for the selection of patients with strokes for anticoagulant therapy. Four indications for treatment are suggested. These are: intermittent insufficiency in the vertebral-balisar system, intermittent insufficiency in the carotid system, thrombosis in the vertebral-basilar system with infarction, and actively advancing occlusion of the carotid system. A fifth indication suggested by Wright and McDevitt is multiple thromboembolic episodes. A total of 317 patients in the first 4 of these categories were given anticoagulant treatment, which included the intravenous use of heparin and oral administration of ethyl biscoumacetate and bishydroxycoumarin. The results are discussed and suggest a significant favorable effect of anticoagulant treatment in the 3rd and 4th categories. Although this study does not include sufficient comparative data regarding the other 3 categories, a definite clinical impression exists that anticoagulant therapy also is of benefit in these entities.

Use of Anticoagulants in Treatment of Cerebral Vascular Disease. Ten-Year Experience in Treatment of Thromboembolism. McDevitt, E., Carter, S. A., Gatje, B. W., Foley, W. T., Wright, I. S., Vascular Section, Dept. Med., New York Hosp., Cornell Univ. Med. College, New York, N. Y., USA. J. Amer. med. Ass. *166:* 592 (1958).

This study supports the evidence that continuous anticoagulant therapy can markedly reduce the incidence of thromboembolic episodes due to various primary conditions without high risk of hemorrhagic complications. (100 patients with evidence of cerebral vascular thrombosis or embolism. 2842 patient-months without anticoagulant therapy: 229 thromboembolic episodes: 2291 patient-months with anticoagulant therapy: 20 thromboembolic episodes.

Comparative Clinical Study of Coumadin Sodium and Dicumarol in Patients with Thromboembolic Diseases. Shapiro, M. C., Lisker, R., Lichtman, A. M., Dept. Hematol. Res., Dept. Med., Michael Reese Hosp., Chicago, Ill., USA. Amer. Heart J. *55:* 66 (1958).

The ability of Coumadin Sodium and Dicumarol to maintain a therapeutic hypoprothrombinemic state do not differ. The latency period in the group taking Coumadin Sodium averaged

43.4 hours while in the Dicumarol group it averaged 80.3 hours. Hypersensitivity to the two drugs was not significantly different. The amount and technic of dosage is presented. The ability of vitamin K and related compounds to reverse the action of these drugs was similar. Hemorrhages were seen in 11 patients taking Coumadin Sodium and in 8 taking Dicumarol. Only one death was attributed to anticoagulant therapy (Dicumarol). The mode of action of Coumadin Sodium, as with Dicumarol, seems to reside more in its ability to decrease stable factor activity than in the suppression of prothrombin activity.

Localized Changes in Properties of the Blood and Effects of Anticoagulant Drugs in Experimental Cerebral Infarction. Meyer, J. S., Neurol. Unit, Boston City Hosp., Boston, Mass., USA. New Engl. J. Med. *258:* 151 (1958).

s) Thrombosis (and Thrombelastography)

Untersuchungen zur therapeutischen Beeinflußbarkeit der thromboembolischen Erkrankungen. Kresbach, E., Stepan, K. M., Med. Univ.-Klinik, Graz, Austria. Wien. med. Wschr. *108:* 86 (1958).

Trois ans d'expérience sur la valeur de la thrombélastographie dans les thromboses post-opératoires et dans les thromboses coronariennes. Fischer, R., Dicker, S., Centre Transfusion Sanguine, Genève, Switzerland. Presse méd. *66:* 216 (1958).

Erfahrungen mit Magnosetten zur postoperativen Thrombose- und Embolieprophylaxe. Leonhardt, H., Chir. Abtg., Evang. Krankenhaus, Ibbenbüren, Germany. Münch. med. Wschr. *100:* 347 (1958).

(Magnosetten = magnesium preparation containing magnesium thiosulphate and magnesium citrate).

Verhütung und Behandlung thromboembolischer Komplikationen. Sigg, K., Poliklinik f. Venenerkrankungen, Frauenspital, Basel, Switzerland. Wien. med. Wschr. *108:* 206 (1958).

(Butazolidine).

Laboratory Diagnosis of Venous Thrombosis. Bobek, K., Med. Clinic, Charles Univ., Plzen, CSR. Acta med. scand. *160:* 121 (1958).

The usefulness of clot retraction time, the silicone tube coagulation time and the platelet adhesiveness for the diagnosis of venous thrombosis has been investigated. For the recognition of the active stage of venous thrombosis the platelet-adhesive-index proved to be most reliable. The clot retraction time and the silicone tube coagulation time have only supporting value.

Die Blutgerinnung bei der venösen Stase. Sartori, C. H., Univ.-Augenklinik, Hamburg, Germany. Münch. med. Wschr. *100:* 481 (1958).

Observations are reported concerning the effect of long bedrest on circulation rate and coagulation tendency in veins of the lower extremities. It was found that after 8 days in bed venous circulation becomes markedly decreased, coagulation, however, increased. After a discussion of the cause of increased coagulation the author reports upon experiments to diminish this thrombogenetic tendency. It is concluded that the regular administration of vitamin B_1 — containing horse-chestnut extract inhibits venous stasis and its effect on blood coagulation.

Thrombosis of the Internal Carotid Artery. Clarke, E., Harris, P., Postgraduate Med. School, London W 12, England. Lancet *1:* 1085 (1958).

Thrombélastographie. Szirmai, E., Gaertner, H., 3ième Clinique Maladies Int., Académie de Méd. Cracovie, Poland. Haematologica Cravoviensia *2:* 209 (1958).

Butazolidin als Antithromboticum. Bobek, K., Cepelak, V., Med. Univ.-Klinik, Pilsen. Gynaecologia (Basel) *145:* 434 (1958).

On the Lysis of Thrombi Experimentally Produced Within Veins. Kwaan, H. C., Lo, R., McFadzean, A. J. S., Univ. Dept. Med., Queen Mary Hosp., Hongkong. Brit. J. Haematol. *4:* 51 (1958).

A thrombus produced in the marginal vein of the rabbit's ear by the injection of thrombin has been found invariably to lyse. Experiments designed to investigate this phenomenon are described and the results indicate that platelets by virtue of their content of serotonin are responsible for initiating the mechanism which results in the lysis of the thrombus. It is shown that fibrinolytic activity develops within the marginal vein of the rabbit's ear as the result of the stimulation of cholinergic effectors within the vein wall. Serotonin and adrenaline are shown to stimulate the effectors and augment the rate of lysis of a thrombus. A thrombus does not lyse if it is produced following surgical operation or the administration of corticotrophin. The feeding of cholesterol results in an inhibition of lysis of a thrombus which is distinct from that exerted by corticotrophin.

Acute Thrombosis of the Renal Vein in an Adult. Naeraas, N., Ugeskr. Laeg. *120:* 186 (1958).

Häufigkeit und Verlauf thrombotischer und embolischer Erkrankungen nach gynäkologischen Operationen. Lasagni, F., Univ.-Frauenklinik, Basel, Switzerland. Gynaecologia (Basel) *145:* 295 (1958).

Zum Problem der Thromboembolie-Prophylaxe. Morger, R., Bezirkspital, Laufenberg (AG), Switzerland. Praxis *47:* 549 (1958).

The author discusses the possibilities of prophylactic therapy in thromboembolism and reports two years' experience with the combined preparation PH 203 (panthesin + hydergin). The advantage of this therapy as compared to anticoagulation is mentioned in particular the absence of bleedings, and the resulting omission of laboratory control.

Statistik der Thromboembolie in Gynäkologie und Geburtshilfe. Stamm, H., Hertig, H., Univ.-Frauenklinik, Basel, Switzerland. Zbl. Gynäk. *80:* 628 (1958).

Aortic Thrombosis. Starer, F., Sutton, D., Radiological Dept., St. Mary's Hosp., London W 2, England. Brit. med. J. 5082: 1255 (1958).

Current Status of the Problem of Thrombosis, Barker, N. W., Mayo Found. Graduate School, Univ. of Minnesota, Rochester, Minn., USA. Circulation *17:* 487 (1958).

The pathogenesis of intravascular thrombosis involves 1 or a combination of 3 factors: an endothelial lesion, a disturbance of blood flow, and hypercoagulability of blood. The fate of fresh thrombi is probably dependent on the fibrinolytic activity of the plasma. While some tests for coagulation factors have given some positive results among patients with various types of thrombosis, no test has consistently demonstrated its value in predicting a thrombosing tendency. Carefully administered anticoagulant therapy has been effective in the prevention of thrombosis in many patients. Treatment of acute thrombosis by injections of fibrinolysin is still in the experimental stage. Recent advances in surgical technic have led to successful restoration of continuity of some of the large arteries previously occluded by thrombosis.

Acute Mesenteric Venous Thrombosis Simulating Acute Pancreatitis. Gray, E. B., Amador, E., Peter Bent Brigham Hosp., Boston, Mass., USA. J. Amer. med. Ass. *167:* 1734 (1958).

Case report. The value of peritoneal fluid analysis.

Thrombophlebitis of Superficial Abdominal Veins. Houston, A. N., Roy, W. A., Faust, R. A., Dept. Surg., Louisiana State Univ. Med. School, New Orleans, La., USA. J. Amer. med. Ass. *166:* 2158 (1958).

An unsusual complication of inferior vena cava ligation. Case report.

Further Observations Concerning the Prognosis of Myocardial Infarction Due to Coronary Thrombosis. White, P. D., Bland, E. F., Levine, A. A., 264 Beacon Street, Boston, Mass., USA. Ann. intern. Med. *48:* 39 (1958).

Main Branch Pulmonary Artery Thrombosis with Pulmonary Abscess Formation: Case Report. Doust, B. C., Rathe, J. W., Dept. int. Med., The Akron Clinic, Akron 3, Ohio, USA. Ann. intern. Med. *48:* 170 (1958).

Acute and Chronic Thrombosis of the Mesenteric Arteries Associated with Malabsorption: A Report of Two Cases Successfully Treated by Thromboendarterectomy. Shaw, R. S., Maynard, E. P., Depts. Surg. and Med., Massachusetts General Hosp., Boston, Mass., USA. New Engl. J. Med. *258:* 874 (1958).

Chronic Aortoiliac Thrombosis. A Review of Sixty-Five Cases. Beckwith, R., Huffman, E. R., Eiseman, B., Blount, S. G., Dept. Med. and Surg., Univ. of Colorado Med. School, Denver, Col., USA. New Engl. J. Med. *258:* 721 (1958).

Internal Carotid Artery Thrombosis. Roberts, B., Harrison Dept. Surg. Research, Univ. Pennsylvania Med. School, Philadelphia, Pa., USA. Arch. Surg. (Chicago) *76:* 483 (1958).

Thrombophlebitis — A Sign of an Unrecognized Neoplasm. Gelfand, M. L., Goodkin, L., Dept. Med., N. Y. Univ. Postgraduate Med. School, New York, USA. Angiology *9:* 15 (1958).

Use of Trypsin in the Treatment of Experimental Coronary Thrombosis. Conrad, C. R., Geis, A. F., Research Dept. Millard Fillmore Hosp., Buffalo, N. Y., USA. Circulation Research *6:* 352 (1958).

The Clinical and Surgical Aspects of Chronic Pulmonary Artery Thrombosis. Schein, C. J., Rifkin, H., Hurwitt, E. S., Lebendiger, A., Montefiore Hosp., New York, N. Y., USA. Arch. intern. Med. *101:* 592 (1958).

Pulmonary Arteriosclerosis and Thromboembolism in Chronic Pulmonary Emphysema. Kernen, J. A., Dept Path., Indiana Univ. Med. Center, Indianapolis, Ind., USA. Arch. Path. (Chicago) *65:* 471 (1958).

Thrombelastography. Toledo, F. B., Milanes-Lopez, B., Peripheral Vasc. Disease Clinic, Lila Hidalgo Hosp., Baltimore, O., Angiology *9:* 88 (1958).

Buchbesprechungen / Book Reviews / Livres nouveaux

Metabolism of Lipids. British Medical Bulletin 14, 3 (1958).

In einem Heft von 81 Seiten werden 12 Artikel über den Stoffwechsel der Lipide veröffentlicht.

Zunächst wird die Synthese, sodann die Resorption der Fettsäuren und des Cholesterins geschildert. Frazer widmet der Pathogenese der Sprue ein interessantes Kapitel, und macht darin auf die Bedeutung des Folsäuremangels für die Fettresorption aufmerksam. Die hormonale Steuerung des Lipoidstoffwechsels wird in 2 Arbeiten eingehend diskutiert. Die aktuelle und praktisch sehr wichtige Frage nach den Beziehungen zwischen Koronaraffektion und Lipoidstoffwechsel wird eingehend und von verschiedenen Autoren, insbesondere von B. Bronte-Stewart, bearbeitet. Die Hypothese des Mangels essentieller Fettsäuren als Ursache der Atheromatose wird abgelehnt, die Bedeutung der gesättigten Fettsäuren dagegen betont. Den Beziehungen zwischen Fettgehalt des Blutes und Gerinnung wird ein besonderes Kapitel gewidmet.

Das Heft gibt eine ausgezeichnete Übersicht über den derzeitigen Stand des Fettstoffwechsels und seiner praktischen Anwendungen.

F. Koller, Zürich