BOOK REVIEWS

Control of the Peripheral Circulation in Man.

Dr. Whelan, who is professor of human physiology and pharmacology at the University of Adelaide, has written an excellent account of the action of chemical agents on the blood vessels in human limbs. The book is divided into five parts. The first deals with the vasoactive hormones, angiotensin, serotonin, bradykinin, histamine, and acetylcholine. The second part describes the action of certain vasoactive drugs, including reserpine, guanethidine, hexamethonium, alcohol, and the cardiac glycosides. The third part discusses the actions of the adrenergic agents, the fourth presents the role of metabolites in exercise and reactive hyperemia, and the final part deals with the nervous control of the limb vessels.

The author after receiving his medical training at the Queen's University of Belfast developed early his interest in the action of chemical substances on the human circulation while he was working in the department of physiology with Prof. A. D. M. Greenfield in Belfast and Prof. Henry Barcroft at St. Thomas' Hospital in London. He has continued and expanded this interest in collaboration with members of his department in Adelaide, and today is widely recognized for his contributions to the action of hormones, drugs, and adrenergic agents on human blood vessels. These contributions, the outcome of 18 years of study, are described and integrated with the work of others in the present book. The text is clearly and concisely written, and the supporting figures are aptly chosen from the literature available and are well reproduced. The author separates the local action of the chemical agents in question, both on skin and on muscle vessels, from their generalized effects on the cardiovascular system. He delineates what is known from what is hypothesis, thus providing the reader with the available data on mechanisms on which we base our present knowledge of the action of the substances he describes. This knowledge, so well summarized in this book, will be of value to all interested in the pharmacology of the vascular system, either in the clinic or in the laboratory.

JOHN T. SHEPHERD, M.D.

Physiology of Hemostasis and Thrombosis.

The book consists of a collection of papers presented at the 1966 Symposium on Blood at Wayne State University—an annual meeting originated by Dr. Walter H. Seegers 15 years ago. A number of eminent participants were invited to present papers which, for the most part, summarize their contributions to the physiology of hemostasis and thrombosis. With such a distinguished group of participants it is not surprising to find that this book is a major contribution to the literature in this field.

Dr. John W. Reubuck, in a scholarly and concise introduction, has reviewed the major developments in hemostasis since the discovery of the blood platelet by Donne. The subsequent 17 chapters contain a wealth of information about the blood platelet, much less about the coagulation mechanism, and less still about the blood vessel. Dr. Walter Cruz spoke at the meeting, and it is a pity that his untimely death prevented inclusion of his work emphasizing the importance of the blood vessel in hemostasis.

The first aspect of the platelet to be discussed was "viscous metamorphosis," a term which has come to mean so many different things that it has almost lost its usefulness. Lüscher, doubtful that the conversion of platelet fibrinogen to fibrin is the initial step in producing viscous metamorphosis, reported the role of enzymes (including thrombin) and immune complexes in its production. Jackson, on the other hand, expressed the opinion that platelet fibrinogen is important in producing viscous metamorphosis and that it may be essential for normal hemostasis.

One of the most significant discoveries of recent years is the role played by adenosine diphosphate (ADP) in platelet aggregation. Salzman reviewed his experiments leading to the hypothesis that an energy-producing reaction keeps the platelet in its normal "unsticky" state and that ADP inhibits membrane ATPase resulting in platelet stickiness and permitting aggregation to occur. Späet produced data which tend to refute this concept. Other hypotheses for the action of ADP were reviewed in other papers. Haslam stated that ADP plays an essential role in plate-
let aggregation produced by thrombin, collagen, fatty acids, 5-hydroxytryptamine, and adrenalin. Change to spherocytic shape is produced by ADP, and the relation of shape change to aggregation was discussed by Zucker who found certain compounds which could inhibit aggregation by ADP although shape change still occurred. She concluded that spherichy precedes or is unrelated to aggregation. Brambel discussed his observations that divalent cations, particularly strontium, result in the formation of platelet-leukocyte aggregates and showed the effect of various nucleotides in his test system.

A number of electron-microscope studies of platelet ultrastructure were presented. White included unusually fine electron-micrographs which he has interpreted in a dynamic way relating structural chemistry to many aspects of the physiology of platelet function. His evidence suggests that platelet factor 3 activity is associated with the platelet granules. Marcus, on the other hand, interpreted platelet factor 3 activity in terms of the platelet membrane which provides a catalytic lipoprotein surface for intrinsic prothrombin activator formation. He reviewed his separation of platelet components (granules, membranes, and cell sap) using sucrose density gradient ultracentrifugation. Further data about platelet factor 3 were presented by Barnhart who has localized this factor in the megakaryocyte by immunofluorescent antibody techniques. She suggested that this activity arises in the promegakaryocytes and is therefore intrinsic to platelets rather than being adsorbed onto them. Rodman's electron-microscope studies showed that the ultrastructural changes after recalcification of platelet-rich plasma proceed to thrombocytorrhexis and can occur in plasma from patients with no fibrinogen. Membrane dissolution, however, is greatly delayed in fibrinogenenemic plasma and the platelet thrombus undergoes dissolution into unaggregated "serum platelets."

A number of contributors presented their comprehensive views on hemostasis. The well-controlled animal experiments of Jaques are familiar to all who are interested in this subject. He emphasized that the coagulation mechanism, the blood vessel, and the blood platelet are involved in hemostasis and that in order to produce spontaneous hemorrhage in animals, one must produce a defect in two of the three areas. His studies suggest that a fibrin clot forms in the late stages of hemostasis. In contrast, Dr. Shirley Johnson found electron-microscopic evidence of fibrin formation 15 seconds after transection of guinea pig mesentery. She reviewed, also, the endothelial supporting function of platelets and emphasized the importance of ADP release from hemolyzed red cells in producing platelet aggregation. Spaet, on the other hand, pointed out that platelets themselves may be the source of ADP in the hemostatic process, and in his excellent article he reviewed his ideas about the hemostatic process expressing his opinion that blood coagulation plays a secondary role to the formation of the platelet plug.

In the final chapter of the book, Mustard outlined his studies on platelet collagen reaction, release of ADP, and stabilization of the hemostatic plug by fibrin. He also pointed out, like Jaques, that the combined interference with both the formation of the hemostatic plug and the coagulation process produces a profound effect on hemostasis.

In an earlier chapter, Stormorken presented a good concise review of von Willebrand's disease and an account of his own studies. He stated that platelet aggregation is normal in von Willebrand's disease and that platelet adhesiveness, although slightly decreased, is perhaps not significantly decreased. He found that platelet adhesiveness is not affected by plasma transfusions. The contents of ATP and ADP were increased in von Willebrand's platelets, but the ratio was normal in contrast to the studies of others. The possibility that abnormalities of platelet aggregation in this disease may be due to a decreased release of ADP from red cells was discussed, and Stormorken found that release of ATP and ADP from red cells was normal. He considered it premature to exclude the possibility of a capillary abnormality in the present state of knowledge. Von Willebrand's disease affects so many areas of hemostasis that it is a fitting subject for such a symposium, and it seems most likely that the elucidation of the basic abnormality will contribute significantly to our knowledge of the physiology of hemostasis.

The book is an informative account of many of the major advances in hemostasis in recent years, and Drs. Seegers and Johnson are to be congratulated on formulating such an excellent program and on having the foresight to arrange for its publication. The material will be of interest to clinical pathologists, hematologists, and investigators interested in the hemorrhagic diseases and thromboembolism. In his paper, Spaet said, "one need only consider the relatively well preserved hemostatic integrity maintained by certain patients with severe clotting disorders or platelet deficiencies for a certain anxiety to develop concerning the present state of knowledge." It is obvious that many investigators have similar anxieties and are working diligently to assuage them. Perhaps in 3 or 4 years' time another symposium will attest to the fact that some of these tensions have been relieved.

E. J. Walter Bowie, B.M., B.Ch.