NEWS AND VIEWS

American Society of Hematology

During the VI International Congress of Hematology, Boston, Massachusetts, August, 1956, a group of ten American hematologists brought together at the invitation of Mr. Henry M. Stratton, medical publisher, met for the purpose of organizing a society of persons interested in hematology. This meeting was the culmination of many years of thought and discussion. It represented a conviction on the part of certain persons that there was need for a regularly constituted organization through which hematologic knowledge could properly be disseminated to scientists throughout North America. The persons in attendance at the sponsoring luncheon were Drs. Doan, Dameshek, then President of the International Society of Hematology, Berman, Ross, Tocantins, Jacobson, Crosby, Levine, Hill, Jones, and Dr. Henry Stratton, Publisher of the Journal, *Blood*. This group proposed that American hematologists be circularized regarding interest in such a society and that an organizational meeting be called for April, 1957, to precede the annual meeting of the American College of Physicians. Dr. James L. Tullis was asked to assume Chairmanship of a Committee to formulate plans for the gathering.

During the autumn of 1956, a series of letters was, therefore, sent out to all American and Canadian members of the International Society of Hematology as well as to persons with similar training and interests. The response to these letters was strongly supportive for organization of an American Society, and many valuable suggestions were submitted regarding ways in which such a body could bring together the diverse facets of hematology. A program, designed to stimulate discussion on the more provocative issues, was prepared and distributed. An open invitation to all interested parties was then issued through the Journals, *Blood* and the *Annals of Internal Medicine*. A one-day meeting was prepared with a morning session given over to organizational problems and an afternoon session devoted to a brief scientific program restricted to two topics: Bone Marrow Transplantation and Paroxysmal Nocturnal Hemoglobinuria.

Organizational Meeting

The meeting was called to order at 10:00 a.m., Sunday, April 7, 1957, in the Aescalapian Room of the Harvard Club, Boston, Massachusetts. More than 150 persons were in attendance, with representatives from essentially all of the major states, cities, and provinces of the United States and Canada. In addition, a group of 70 telegrams, letters, and other messages arrived from persons who indicated their deep interest in the formation of a Hematology Society but who were unable to attend due to previous commitments. By mid-day, the registrations increased sufficiently to require relocation of the afternoon session in a larger adjoining room. The morning session was opened by Dr. William Dameshek who described the historical background and purposes of the society. The meeting was then turned over to Dr. James L. Tullis. It was pointed out that the group had no charter, rules of order, or legal structure. Any action taken by the group could be advisory only to the Executive and Constitutional Committees which subsequently would be selected. It was urged that all persons in attendance concentrate their attention on the goals to be achieved rather than on the means of accomplishment. An agenda then was presented covering five major areas of interest. These subjects were freely discussed and the following definitive action was taken:

I. Type of Organization

The advantages and disadvantages of various organizational structures were fully discussed. In general, the different proposals fell into three broad groups—a highly restrictive organization with regulatory functions and limited membership, a semirestrictive organization with only moderate limitation of membership, a loose organization with no for-

malized structure. The important points which were raised (pro and con) for the various types were as follows:

In Support of a Restrictive or Semirestrictive Organization

1. A restrictive or semirestrictive organization could help elevate hematologic research and teaching through establishment of standards of training and study.
2. A small, intimate organization would be more flexible than a larger "open" society.
3. Most societies which begin informally end up as highly organized groups.
4. A restrictive or semirestrictive organization could serve as a stimulus to young hematologists through a strong incentive to join.
5. A semirestrictive society could exercise control over the length and quality of an annual scientific program more easily than a loose organization.
6. A semirestrictive society could have subclasses of membership depending on amount, type, and quality of training.

In Support of an "Open" Organization

1. Restrictive organizations are not in the American tradition.
2. Hematologists come from diverse disciplines: chemistry, physiology, anatomy, medicine, etc. Establishment of admission qualifications would, therefore, be difficult.
3. Individuals who would be eligible for a restrictive society are already members of other restrictive societies. Membership in a Hematology Society should be inclusive rather than exclusive and should provide broad opportunity to assemble, to talk, to listen, and to exchange ideas.
4. Restrictive societies are usually professional rather than scientific (the former type being limited to practising physicians).
5. Some of the best papers often are presented by young persons who might be excluded from the restrictive organization because of insufficient training.
6. A loose organization could be operated with a minimum of administrative overhead and officers.

It was agreed that a wholly unorganized society could serve no useful purpose. Moreover, such a group, The Blood Club, already exists in the United States. A poll of the persons in attendance then was taken as to those favoring a restrictive organization and those favoring an "open" organization. The vote was equally divided. A proposal then was advanced for a middle-of-the-road organization, embodying the best features of both types. The subsequent vote was unanimously favorable.

II. Name of Organization

Discussion in this area was primarily devoted to a title which would embrace both Canada and the United States without inclusion of Central or South America. The point was raised as to whether the name should contain the qualifying phrase, "a Chapter of the International Society of Hematology." Action on this latter point was tabled pending a more thorough study of what relationship, if any, the new Society should bear to the International Organization. The tentative name, "American Society of Hematology," was approved by vote.

III. The Qualifications for Membership

It was agreed that this would be one of the most difficult criteria to establish. The point was raised that membership qualifications usually do not determine whom to admit but rather whom to exclude. A number of persons expressed the hope that continuing activity in hematology would be of more importance for membership than prior training. In this regard, it was voted to recommend at least five years sustained activity in hematology for full membership, with, perhaps, a shorter period for subclasses of membership. A favorable vote also was recorded for recommendation of establishment of such classes. Finally, it was voted that the Interim President be given authority to appoint a specific Membership Committee. This Committee would determine whom to recommend for election. A separate Constitutional Committee would determine what the qualifications for election would be.

The suggestion also was advanced that evidence of "continuing interest" should be reinforced by some type of compulsory attendance at annual meetings. The complexity of defining a "hematologist" was emphasized. A poll of the audience revealed at least six different backgrounds of scientific training: pathology, pediatrics, physiology, anatomy, immunology and internal medicine. The suggestion was made that contemporary science is suffering from "echelon" disease wherein one specialized group of individuals looks askance at another. A plea was made for a broad base of backgrounds with minimal emphasis on prior training qualifications. Then the question of need for a graduate degree was discussed. There was general agreement that it would be best to require an earned doctor's degree (either Ph.D. or M.D.) for full membership. It was suggested that those persons with an earned doctor's degree should also have certain further qualifications but that these should be determined by a Constitutional Committee, subsequently to be appointed. The question next was raised whether or not all current Fellows of the International Society of Hematology would automatically be eligible, and whether all persons in attendance at the morning session similarly would be eligible. After prolonged discussion, it was voted that all current North American Fellows of the International Society of Hematology, all North American Hematologists of similar professional stature, and all persons with an earned doctor's degree present at the organizational session would be eligible for application for membership in the new Society and that future membership qualifications should be determined by the Constitutional Committee.

IV. Time, Location, and Type of Annual Meeting

The advantages and disadvantages of having the American Society of Hematology meet in tandem with the American College of Physicians were discussed. The more important points were:

Favorable: 1. The American College of Physicians peregrinates, thus giving ample opportunity for all sections of the country to be local hosts.

2. It is easier to justify traveling expense for a dual rather than single meeting.

3. The American College of Physicians is a well established organization of high professional competence.

Unfavorable: 1. Only a small percentage of hematologists have an interest in the American College of Physicians.

2. A tandem meeting with the American College of Physicians might, to a great extent, color the nature of the meeting and make it largely clinical, rather than scientific.

3. It might be unwise to align a new society with any single pre-existing organization.

4. Hematology has reached sufficient maturity and magnitude to sponsor a meeting individually without becoming a stepchild of some other society.

No general agreement could be reached on these diverse points. As a compromise, it was voted to recommend that the forthcoming 1958 meeting of the Society be held on April 26 and 27, at Atlantic City, New Jersey, preceding the American College of Physicians, and that no long term commitment be made pending discussion at committee level.

The other major points concerned whether or not the American Society should meet annually, except for the years in which the International Society meets in North America, or whether the American Society should meet annually irrespective of any other meetings here or abroad. Poignant feelings were expressed in both regards, but no action was taken. It was voted that the Scientific Program in 1958 should comprise the better part of two full days.

V. Appointment of Standing Committees and Election of Officers

Constitutional Committee.—The following persons were nominated from the floor for membership in a Constitutional Committee: Dr. Lawrence Berman (Detroit), Dr. William Dameshek (Boston), Dr. Israel Davidsohn (Chicago), Dr. Thomas Hale Ham (Cleveland), and Dr. Louis Lowenstein (Montreal). A vote that the nominations be closed then was recorded, and the clerk was instructed to cast one ballot in unanimous election of this group.

Membership Committee.—It was voted to delegate to the officers and to the Constitu-

tional Committee the appointment of a Membership Committee to work closely with the Committee on Organization and Constitution.

Election of Officers.—The Chair advanced the proposal that a Nominating Committee be appointed for submission of a panel of officers to be returned during the afternoon session. It was pointed out from the floor that this would be an anomalous parliamentary procedure. Permanent officers properly could not be elected prior to establishment of a constitution and bylaws. It was then moved, seconded and voted that the present Chairman be appointed Interim President with authority to appoint such other temporary officers as would be necessary to conduct the Society's business during the next year, and that a Nominating Committee be appointed from the membership of the Constitutional Committee or founders' group to bring in a slate of permanent officers for consideration at the time of the next annual meeting. There being no further business, on motion duly made and seconded, the meeting was adjourned at 12:30 p.m.—*J.L.T.*

Program—First Organizational Meeting of the American Society of Hematology, Boston, Massachusetts, April 7, 1957

Scientific Sessions

1. Preservation and Transplantation of Human Marrow. 1. Culture of Human Marrow. Contraindications to its Use in Transplantation. *Lawrence Berman.* Wayne State University, Detroit, Michigan.

Dr. Berman presented photomicrographs of cultured human cells developed from several sources including bone marrow of patients with and without cancer, ascitic and pleural carcinomatous and lymphomatous fluid, solid tumors and, more recently, peripheral blood. It was noted that the cells lost their identity with culturing and often developed a morphologic appearance of malignant cells, including pleomorphism and nucleoli, whether or not they originally arose from normal or malignant cells. Chromosome counts on these cultured cells revealed marked heteroploidy, and some studies with ascitic tumor cells show that the antigenicity of the cells decreases inversely as heteroploidy of the chromosomes increases, rendering them more readily transplantable.

As a result of his studies, Dr. Berman posed a number of questions. Do normal human cells become malignant when grown in vitro? Do morphogenic potentialities develop in vitro which are not possible in vivo, and, if so, what are the controlling forces in vivo? Since cultured cells do not appear to become malignant, Dr. Berman feels that such material should never be transplanted and that a biologic method for testing the degree of malignancy of cultured cells may be helpful.

2. Trials in Preservation and Transplantation of Marrow. *Robert Schwartz and L. M. Tocantins.* Jefferson Medical College of Philadelphia, Philadelphia, Pennsylvania. (Paper presented by Dr. Tocantins.)

Dr. Tocantins presented the experiences of his group with procurement and preservation of human bone marrow. They originally attempted to obtain marrow from fetuses but abandoned this source because the number of nucleated cells obtained was too small and the legal restrictions presented too great an obstacle.

More recently, they have obtained adult marrow from three sources: (1) adult donors, (2) ribs removed in the course of operations, and (3) postmortem. Their main source has been operative rib marrow, twenty-four ribs having been obtained to date. These are cut aseptically with rongeurs in 1 and 2 cm. pieces and then leached for one-half hour in phosphate buffer containing sequestrene. The average yield from each rib is approximately two billion nucleated cells. Viability of these cells has been checked by culturing aliquots.

Dr. Tocantins then showed photomicrographs of marrow cells preserved by glycerol freezing and maintained at −70 C. There were some morphologic changes, yet mouse marrow cells preserved in this manner were capable of protecting mice against lethal radiation. The opinion was expressed that future stockpiling of marrow will necessarily require the glycerol technic to maintain viability.

3. Experiences with Effects of Animal Marrow Transplantation. *J. K. Weston.* Parke, Davis & Co., Detroit, Michigan.

Dr. Weston presented a very brief review of extensive animal marrow transplantation experiments with particular emphasis on rat experiments. As a result of studies in which marrow aplasia was produced by the administration of 20 mg. Myleran/Kg. to rats, a bioassay method was developed and standardized, making it possible to test the effect of noncellular elements in bone marrow recovery. Marrow aplasia so produced is maximum at the end of one week, and this has been studied by total cell counts, DNA synthesis, differential count of smears, and histologic sections of marrow. Radiation was also used to produce aplasia and resulted in more rapid reduction of cellular elements, presumably because of its greater effect on lymphocytes which are prominent in rat marrow.

Dr. Weston's group found that bone marrow administered intravenously within five days following Myleran resulted in lowered mortality figures, the marrow recovery rate being greatest about the eleventh day. Of 128 rats not treated with bone marrow transplantation, 90 per cent died. Over 150 rats given 125 million nucleated cells intravenously within the first five days after Myleran resulted in only 5 per cent mortality.

Preliminary results of similar experiments using Rhesus monkeys were briefly reviewed but were not sufficiently crystallized to permit definite conclusions.

4. Homotransplantation After "Immunoparalysis." *R. Wayne Rundles and Jay P. Sanford.* Duke University, Durham, North Carolina. (Paper presented by Dr. Sanford.)

Dr. Sanford expressed the opinion that plasma cells are most important in maintaining integrity of the immune mechanism, and that in order for a transplant to "take," plasma cells must be destroyed. Accordingly, they attempted to "paralyze" the immune mechanism in three patients prior to bone marrow transplantation by the use of combinations of alkylating agents, antipurines, and steroids. In each case, bone marrow was obtained from close relatives utilizing general anesthesia and multiple trephines of the sternum and posterior ilium. Each "transplant" consisted of an average of one billion nucleated cells administered intravenously.

The first patient had aplastic anemia and was treated with nitrogen mustard prior to marrow administration. The second patient had acute granulocytic leukemia and was treated with 6-mercaptopurine, amethopterin, nitrogen mustard, and steroids prior to marrow administration. This patient was given a second "transplant" following a course of urethane and thio-TEPA. The third patient had acute monoblastic leukemia and was prepared for marrow transplantation by the administration of nitrogen mustard. Ashby counts in the second case failed to reveal the presence of red cells from the donated marrow, and the other two patients expired before such counts could be followed. In no case was there evidence of pulmonary emboli, and plasma cells remained in the marrow in all cases. Dr. Sanford concluded that nitrogen mustard in usual therapeutic doses is not sufficient to paralyze the immune mechanism.

5. General Review of Problems in Marrow Preservation. *Joseph Ferrebee,* Children's Hospital, Boston, Massachusetts and *Donell Thomas,* Imogene Bassett Hospital, Cooperstown, New York.

Dr. Ferrebee spoke very briefly of the efforts to freeze marrow cells. He found that although many of the nucleated cells appeared damaged after freezing and thawing, rat marrow cells so treated were capable of protecting rats following lethal radiation. He concluded, therefore, that these cells are viable in spite of their appearance.

Dr. Thomas added that they have been testing viability of nucleated cells obtained from post mortem material by studying DNA synthesis, since this should be closely related to cell proliferation. They have done two sterile post mortems and found DNA synthesis by marrow cells to be normal if obtained within six hours after death.

They have given bone marrow to six patients, all with terminal malignancy. Four had large doses of nitrogen mustard and TEM, and two had total body radiation. In one case

that received total body radiation, there was evidence, by Ashby count, of circulating red cells from the donated marrow cells.

Designated Discussion

William McFarland. New England Center Hospital, Boston, Massachusetts.

Dr. McFarland reviewed briefly the reasons for renewed interest in marrow transplantation in recent years. The various problems as pointed out in the several papers were mentioned, including: (1) procurement of marrow, (2) preservation, (3) the possibility of altering the immune mechanism of the recipient, and (4) the possibility of altering the antigenicity of the cells to be transplanted. Experience with five patients that were administered fresh marrow from healthy donors was mentioned.

Hugh M. Pyle. Protein Foundation, Boston, Massachusetts.

Dr. Pyle reviewed briefly the experiences of Protein Foundation in preserving marrow cells with glycerol and storage at −80 C. These cells appear normal morphologically on thawing, and 20 per cent of them are stained normally with neutral red, indicating viability.

Paroxysmal Nocturnal Hemoglobinuria. *Carl F. Hinz, William Crosby, Andre Eyquem, Henry Isliker, Robert C. Hartmann, Scott Swisher, Frank Gardner, Thomas Hale Ham.*

In the program on paroxysmal nocturnal hemoglobinuria (PNH) Hinz discussed the requirement for the properdin system for the hemolysis of PNH erythrocytes in vitro. The properdin system exists in normal human serum and includes the serum protein properdin, magnesium, and the four components of complement. Serum lacking any of these constituents fails to hemolyze PNH erythrocytes. Addition of purified properdin to a properdin deficient serum restores the hemolytic property of that serum. Properdin is not required for the activity of immune hemolytic systems but is essential for the hemolysis by normal human serum of tannic-acid-treated-human red cells. An antibody to properdin has been prepared in the rabbit, one which specifically inactivates properdin and completely inhibits PNH hemolysis, although it has no effect on immune hemolytic systems. Isliker reported that he and Martin of Frankfort have confirmed the requirement for properdin in PNH lysis and have observed that the stroma of PNH erythrocytes removes properdin from serum at 37 C., whereas normal stroma does not. Stroma from normal red cells hemolysed with digitonin behaves as does PNH stroma. Isliker proposes that red cells contain high molecular weight polysaccharide constituents which may interact with properdin, but only when they are in an exposed position on the cell as may be the case with PNH or digitonin treated cells.

Crosby reported on the effect on PNH hemolysis in vitro of clinical dextrans which consist of polysaccharides of molecular weight that are not large and do not combine with properdin. Clinical dextrans from a variety of manufacturers inhibit PNH hemolysis when added to whole PNH blood during clotting or to normal serum before PNH cells are added. This effect is overcome if magnesium is added to the system. Crosby is using this approach in an attempt to separate the PNH hemolytic reaction into several phases.

Gardner has observed that the infusion of large amounts of clinical dextran into one patient with PNH was followed by variable periods of freedom from hemoglobinuria. The dextran produced a bleeding tendency on prolonged use. He emphasized the difficulty in interpretation of clinical results because of the marked spontaneous variation in PNH.

Ham reviewed data from Hinz, Weisman, and Hurley indicating that there is correlation between severity of the clinical process, shortened red cell survival, and the portion of cells subject to hemolysis in vitro. However, it was not possible to relate changes in susceptibility of red cells to hemolysis in vitro or the hemolytic activity of serum to the occurrence of hemolytic crisis or remission in the patient.

Swisher reported on work done by Altman, Tabechian, and Young indicating that the carbohydrate metabolism of PNH cells differs from that of other cell types studied. There is slow phosphate uptake which is accelerated by flouride, slow release of phosphate by the cells, and slow flux of P^{32} into 2-3 diphosphoglyceraldehyde. It is not known whether this represents a basic metabolic abnormality of the cell or is a result of the hemolytic process.

Hartman reported four new patients with PNH. Two occurred in Negroes. Two patients had leg ulcers. Three of the four patients had decreased platelet counts, but no platelet utilization could be demonstrated during PNH lysis.

Guest Editors

The following individuals gave of their time and knowledge in helping our editorial staff in the reviewing of certain papers during the past year, and the Editor takes this opportunity of publicly thanking them for this important service.

Edward Adelson, Washington, D.C.
Benjamin Alexander, Boston, Mass.
Fred H. Allen, Boston, Mass.

Mario Baldini, Boston, Mass.
Joseph Beard, Durham, N. C.
Marion Beard, Louisville, Ky.
Marcel Bessis, Paris, France
Ernest Beutler, Chicago, Ill.
Joseph H. Burchenal, New York, N. Y.

Amoz Chernoff, Durham, N. C.
Byron Clark, Boston, Mass.
Charles C. Congdon, Oak Ridge, Tenn.
Lloyd F. Craver, New York, N. Y.
Eugene P. Cronkite, Brookhaven, N. Y.

Israel Davidsohn, Chicago, Ill.
Louis K. Diamond, Boston, Mass.
Thomas Dougherty, Salt Lake City, Utah

Allen J. Erslev, Boston, Mass.

Stuart Finch, New Haven, Conn.
H. Hugh Fudenberg, Boston, Mass.

Robert Goldstein, Boston, Mass.
Albert S. Gordon, New York, N. Y.
Tibor J. Greenwalt, Milwaukee, Wis.
Ludwik Gross, New York, N. Y.
George Guest, Cincinnati, O.
F. W. Gunz, Christ Church, New Zealand

Leonard Hamilton, New York, N. Y.
Malcolm Hargraves, Rochester, Minn.
William Harrington, St. Louis, Mo.
J. W. Harris, Cleveland, O.

James H. Jandl, Boston, Mass.
Wally Jensen, Pittsburgh, Pa.
George B. Jerzy Glass, New York, N. Y.
A. Richardson Jones, Boston, Mass.
F. L. J. Jordan, Utrecht, Holland
Aaron M. Josephson, Chicago, Ill.

Henry G. Kunkel, New York, N. Y.

Miguel Layrisse, Caracas, Venezuela
Hermann Lehmann, London, England
Irving M. London, New York, N. Y.
Louis Lowenstein, Montreal, Canada

William McFarland, Boston, Mass.
W. J. Mitus, Boston, Mass.
William C. Moloney, Boston, Mass.

Saul Nitzberg, Boston, Mass.

Edwin E. Osgood, Portland, Ore.
R. R. Overman, Memphis, Tenn.

Jack Pensky, Cleveland, O.

Henry Rappaport, Chicago, Ill.
John Rebuck, Detroit
Seymour Reichlin, St. Louis, Mo.
Edward H. Reisner, Jr., New York, N. Y.
Robert L. Rosen, Boston, Mass.
Alexander Z. Ružić, Belgrade, Jugoslavia

Robert F. Schilling, Madison, Wis.
Rudi Schmid, Bethesda, Md.
Walter H. Seegers, Detroit, Mich.
Jacob Shanberge, Boston, Mass.
Sol Sherry, St. Louis, Mo.
Steven O. Schwartz, Chicago, Ill.
William B. Schwartz, Boston, Mass.
Richard T. Silver, New York, N. Y.
Carl Smith, New York, N. Y.
Theodore H. Spaet, New York, N. Y.

James L. Tullis, Boston, Mass.

Arthur C. Upton, Oak Ridge, Tenn.

Bert Vallee, Boston, Mass.

Richard Wagner, Boston, Mass.
Louis R. Wasserman, New York, N. Y.
Alexander Wiener, Brooklyn, N. Y.
Irwin M. Weinstein, Los Angeles, Calif.