NEWS AND VIEWS

The following letter has been received from Roger C. Crafts, Ph.D., Department of Anatomy, Boston University School of Medicine, Boston:

To the Editor:

In the March 1947 issue of *Blood*, Doctors E. S. Jones, K. B. McCall, C. A. Elvehjem, and P. F. Clark published a paper entitled "The effect of diet on the hemoglobin, erythrocyte, and leukocyte content of the blood of the rhesus monkey (Macaca Mulatta)." I would like to offer a few comments on the findings concerning the neutrophil-lymphocyte ratio only.

These authors reported that the neutrophil-lymphocyte ratio could be reversed from $\frac{30}{60}$ to $\frac{60}{30}$ with vitamin B or whole liver factor deficiencies (see fig. 2) and that a "normal" ratio of about $\frac{30}{60}$ could be produced with a diet "adequately supplemented with all the vitamins and a supply of whole liver substance." Are these changes actually due to diet?

In a paper published in *Endocrinology* in 1941,[1] the data obtained from a 3 month study of 3 normal adult female rhesus monkeys were published. These monkeys exhibited initial total white cell counts of 15.0, 26.5, and 34.6 thousand cells per cu. mm. Each of these monkeys showed a predominance of lymphocytes when differential counts were made, i.e., 67.5, 67.0, and 92.0 per cent respectively. Because of the range in the total white cell counts and the unexpected predominance of lymphocytes, these animals were further studied to determine the actual normal count. Two of the monkeys showed a gradual decrease in total white counts to between 10–15 thousand cells and remained at that level. The third monkey, a particularly fierce animal, showed a decrease from 34.6 to 25.0 thousand cells in 60 days. Because the animal showed no signs of becoming tame, further work on this animal was given up as hopeless. During the 3 month training period the neutrophil-lymphocyte ratio of the first 2 monkeys reversed to a ratio typical of the human. In other works, the neutrophil-lymphocyte ratio reversed with no treatment whatsoever. This reverse is exactly the same as reported by Jones, et al. as due to dietary deficiencies.

As both F. P. Rous[2] and B. F. Davis and A. S. Carlson[3] reported a tremendous pouring of lymphocytes into the blood stream as a result of excitement and muscular exercise, the high white counts and the high lymphocyte level in these monkeys were attributed to the resistance these animals exhibited when being handled. The reverse of the neutrophil-lymphocyte ratio and the decrease in total white cell count mentioned above seemingly were due to the training of the animal to the routine of blood removal during a period of 3 months.

Is this reverse of the neutrophil-lymphocyte ratio due to inadequate diet or to the monkey becoming accustomed to being handled? The diet of the two monkeys mentioned above, to my knowledge, was not changed during the 3 months of observation. Jones, et al, mentioned in their discussion that many of their monkeys, due to excitement, exhibited a high total white cell count when first handled, but do not mention this excitement as a cause for the large number of circulating lymphocytes. These authors also tabulate the blood picture of 12 monkeys from a zoo. Four of these monkeys show the neutrophils predominating while 8 show the lymphocytes in great numbers. If these animals had the same diet, why the discrepancy?

I do not state that Doctors Jones, McCall, Elvehjem, and Clark are in error. I simply raise the question as to the actual cause of the neutrophil-lymphocyte reverse during an experiment on the rhesus monkey

[1] R. C. Crafts: The effect of endocrines on the formed elements of the blood. Part 2: The effect of estrogens on the dog and monkey. Endocrinology *29:* 606, 1941.

[2] J. Exper. Med. *10:* 537, 1908.

[3] Am. J. Physiol. *25:* 173, 1909.

and to what the normal differential white cell count of the resting monkey actually is. This is an interesting and important problem and the evaluation of further hematologic work on the monkey would seem to depend on a solution of it.

Roger C. Crafts

Dr. C.A. Elvehjem, Department of Biochemistry, University of Wisconsin, Madison, replies as follows:

To the Editor:

We have read the preceding letter by Dr. Roger C. Crafts with much interest and agree that studies on the actual causes of the observed changes in the neutrophil-lymphocyte ratio in the blood of monkeys is an interesting and important hematologic problem. The possible relationship of endocrines to the production of formed elements of the blood should be given consideration. However, we believe that our studies have been controlled sufficiently to demonstrate that diet does have a specific effect on the neutrophil-lymphocyte ratio in the blood of monkeys.

We have used a large number of animals rather than 2 or 3 as indicated in Dr. Crafts' letter and have carried the animals over sufficient periods of time to eliminate the possible effect of handling. He states that the neutrophil-lymphocyte ratio was reversed in two of his animals with no treatment whatsoever. He does not give the diet used and if his diet were incomplete, such a reversal would be exactly what one would expect when the animals were kept on the diet for several months. We know from experience that different monkeys develop a deficiency in varying periods of time and this would explain why 4 of the animals which we kept at the zoo showed a reversal while 8 of the monkeys did not. The diet which the animals received at the zoo probably did not supply adequate amounts of the monkey anti-anemia factor and during the period at the zoo 4 of the animals developed a deficiency.

The best evidence for the nutritional effect is based on the fact that specific reversals have been obtained in a large number of animals and these reversals have been corrected upon administration of liver and milk. The early observations have been reported by J. M. Cooperman, H. A. Waisman, K. B. McCall, and C. A. Elvehjem[4] and specific effects of milk have been described by J. M. Cooperman, W. R. Ruegamer and C. A. Elvehjem.[5] Therefore, under controlled conditions a syndrome has been produced on 2 different diets and corrected by the addition of 2 different food materials. I doubt that better evidence can be presented for the nutritional effect although it is entirely possible that the mechanism of the nutritional effect may be related to the endocrines.

C. A. Elvehjem, M.D.

The following letter is from Dr. Edwin E. Osgood, University of Oregon Medical School, Portland, to Dr. A. S. Giordano, Secretary-Treasurer, American Society of Clinical Pathologists, 531 North Main Street, South Bend, Indiana:

Dear Doctor Giordano:

The purpose of this letter is to offer suggestions aimed toward clarifying the present confusion in the terms used for the cells and diseases of the blood and blood-forming organs. This confusion is so great at present that it is difficult to interpret a differential cell count on blood or bone marrow from one laboratory or even from different technicians of the same laboratory without personally visiting the laboratory and learning of the criteria of cell identification and disease classification in use there.

Not only have many different names been used for the same cell and disease, but the same names have been used for entirely different cells and diseases. As an example, one cell of the granulocyte series (cell No. 76 in Osgood and Ashworth's Atlas) if observed in different laboratories would be called a neutrophil

[4] J. Nutrition *30:* 45, 1945.

[5] Proc. Soc. Exp. Biol. & Med. *62:* 101, 1946.

staff cell, neutrophil rod cell, neutrophil stabkernige, neutrophil band cell, neutrophil stab cell, nonsegmented neutrophil, nonfilamented neutrophil, neutrophil class I, neutrophil juvenile, neutrophil metamyelocyte, polymorphonuclear neutrophil, or neutrophil rhabdocyte, while the terms metamyelocyte (metagranulocyte) and polymorphonuclear as used elsewhere would not even include this cell. As an example of the confusion in the terminology of disease, the same patient with leukemia might be classified in different clinics as having subacute leukopenic myelogenous leukemia, acute aleukemic myeloid leukemia, stem cell leukemia, myeloblastic leukemia, subacute aleukemic myelocytic leukemia, acute myelosis, acute leukemia, subacute subleukemic granulocytic leukemia, or misclassified as acute lymphoid, lymphogenous or lymphocytic leukemia. The confusion is not in the cell or disease. All or nearly all the different observers would have a clear idea of the proper place of the cell and probable course of the disease. While most of the terms are probably correctly interpreted by hematologists who are familiar with the publications of the person using the term and who may have visited his laboratory or clinic and seen his particular criteria of cell identification and disease classification, the average general practitioner, clinical pathologist, or even internist cannot be expected to have this degree of familiarity with the criteria used elsewhere and often is unfamiliar with the criteria used in the various laboratories and clinics even in his own city. The basis for the confusion appears to be that terminology has gradually developed with each author suggesting his own terms and many failing to clearly illustrate and describe sharp lines of demarcation that are easily recognized by others.

An attempt was made by the writer to solve the problem by publishing in the "Atlas of Hematology" by Osgood and Ashworth tables of cell nomenclature and identification and illustrations of both typical, atypical and borderline cells of each series with the criteria of identification and differentiation from other cells beside them, giving clear-cut criteria for the borderline cells and tables of criteria for differentiation of diseases of the blood and blood-forming organs. Some of these tables and criteria were also published in Osgood's "Textbook of Laboratory Diagnosis," third edition. This attempt has been a failure as indicated by the infrequent use of these terms outside of the Northwest and the fact that these terms have not been adopted by any major publication or clinical group. When the attempt was made, it was made with the one objective of clarifying a confused subject. The writer holds no brief for the terms he suggested but does feel that the time is ripe for clarification by a competent committee.

I suggest that a committee be appointed to meet during the week before the meeting of the American Society of Clinical Pathologists in Chicago, October 28–30, 1947, to make recommendations to that body as to the preferred name and the criteria of differentiation for the cells and diseases of the blood and blood-forming organs. It is suggested that the membership of the committee include representatives from the group of clinical hematologists known as the Hematology Club, the International Society of Hematology, the American Society of Clinical Pathologists, interested groups in Canada and Great Britain, and at least one member or consultant who is a lexicographer well versed in Latin and Greek. Recommendations should include specific criteria for distinction between borderline cells and diseases and include a corresponding classification for both the Romanovsky and supravital techniques. Later or in conjunction with this meeting, a similar committee could meet for each country or group of countries constituting one language group to determine the comparable preferred names in that language.

I would further suggest that, as a guide for this committee and to provide the committee with the opinions of all interested persons, a copy of this letter be published in the correspondence section of the *Journal of the American Medical Association*, the *Journal of Laboratory and Clinical Medicine*, *Blood*, *The Journal of Hematology*, and the *American Journal of Clinical Pathology*, and that in the latter two journals there be included tear-out pages or folded inserts similar to that illustrated below for recording the usage and preference of all interested persons. This data should give the committee a clear conception of the degree of present confusion and also of the preferences of those who are actually using the terms. The recommendations of the committee could then be presented to the American Society of Clinical Pathologists at its fall meeting for acceptance or rejection and an approved plan could be presented to the other interested groups at their next meetings. They would still stand merely as recommendations, there being nothing compulsory about the use of the suggested terms, but they might serve as a guide to editors, authors and clinicians and directors of clinical laboratories and in time might become generally accepted terms, which would greatly simplify the task of reading hematologic literature with understanding and full comprehension of the meaning of the author and lead to greater accuracy in the interpretation of day to day laboratory reports.

The major objection which might be raised is that standardization tends to halt progress. That is

true, and it is certain that the terms should be revised by committee action every 5 or 10 years and that new terms may need to be added and old ones deleted from time to time. It is equally certain that not all persons will at first accept the recommendations of the committee, but it seems worthwhile to see if there is not now a sufficient area of agreement to permit a real clarification in the criteria for cell identification and disease classification in the field of hematology as has been done by the American Heart Association for cardiovascular disease and the American Rheumatism Association for arthritis. Then the disease terminology recommended could be incorporated in the next edition of the Standard Classified Nomenclature of Disease.

Copies of this letter are being sent to Stanley P. Reimann, President of the American Society of Clinical Pathologists, Joseph M. Hill of the International Society of Hematology, William Dameshek, Editor of *Blood, The Journal of Hematology*, and a representative member of the informal Hematology Club formed at the last meeting of the American Society of Clinical Investigation, Morris Fishbein, Editor of the A. M. A. publications, S. E. Gould, Editor of the *American Journal of Clinical Pathology*, Carl Moore, Editor of the *Journal of Laboratory and Clinical Medicine*, H. E. MacDermot, Editor of the *Canadian Medical Association Journal*, and T. F. Fox, Editor of *Lancet*.

Very truly yours,
Edwin E. Osgood, M.D.

Condensed example of blank to be used for the information of the committee appointed to make recommendations as to nomenclature of cells and diseases of blood and blood-forming organs.

If you are in charge of a clinical laboratory or an internist interested in clinical hematology, you are requested to fill out, sign, and mail before October 1, 1947, the blanks below to A. S. Giordano, Secretary-Treasurer, American Society of Clinical Pathologists, 531 North Main Street, South Bend, Indiana.

The numbers refer to the cells in Osgood-Ashworth, "Atlas of Hematology," but if you prefer, numbers of cells in any other standard atlas or journal may be substituted if the reference is given and blanks are provided for inclusion of other cell types.

Cell No.*	Name now used	Name preferred if generally agreed upon
1. ———		
2. ———		
3. ———		
4. ———		
5. ———		
. ———		
. ———		
. ———		
316. ———		

* Use these numbers if cells referred to are those illustrated in Osgood and Ashworth "Atlas of Hematology." Insert number in blank if other reference is used and give reference.

For Diseases

Underline name now used and circle name preferred in following list. Note blank for adding name not listed.

(Example)

1. Hemolytic anemia of newborn; erythroblastosis fetalis; icterus gravis neonatrum; hydrops fetalis; congenital anemia; erythroleukoblastosis; _____

2.

3.

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Attach any comments on separate sheet. If you do not refer to published illustrations and description, be sure to include exact criteria of differentiation from other cells or diseases with which it might be confused.

Under the sponsorship of Dr. Alexander S. Wiener of Brooklyn, New York, a meeting was held in Atlantic City on June 8, 1947 for the purpose of forming an American Society for the Study of the Blood. About 25 physicians attended. After much discussion it was decided by those present to support an informal Hematology Club (*Blood*, *2:* 404, 1947) to meet just prior to the annual May meetings of the Society for Clinical Investigation and the Association of American Physicians. It was felt that this Hematology Club which was sponsored by internists with relatively broad interests, was to be preferred to an organization comprising a rather narrow group of specialists having transfusions and blood groups as their chief interest. It was conceivable that from the former group might evolve at some later date a full-fledged national organization. It was also the consensus that full support should be given to the newly formed International Society of Hematology, which had much to offer in fostering international relationships and which would hold biennial meetings in different countries. Motions by Dr. Wiener to form, (1) a new American Society for the Study of the Blood, and (2) an American Society for the Study of Blood Groups and Transfusions were defeated.

Joseph M. Hill, director of the William Buchanan Blood Center, Baylor University, Dallas, Texas, and professor of clinical pathology at Southwestern Medical College, received the first Marchman Award for notable research in medicine at the annual dinner of the Dallas Southern Clinical Society, January 21. Dr. Hill won the award for his recent investigations of the Rh factor.

Dr. Cecil J. Watson of Minneapolis has been elected recorder of The Association of American Physicians at their 60th annual meeting in Atlantic City on May 7th.

The Swiss Hematologic Society was founded on November 17, 1946. Professor Alder of Aarau was elected the first president. The Society was founded as one of the subsections of the Swiss Society for Internal Medicine.

As we wish the 1947 Index of *Blood* to include the Special Rh Issue (immediately following the present issue), the Index will appear in February 1948 instead of the current issue, as previously planned.

Errata

The following information has been received from Dr. Solomon Estren. On page 92, volume II, Blood (January 1947) in the article, "Congenital hypoplastic anemia associated with multiple developmental defects (Fanconi syndrome)," by Estren, Suess, and Dameshek, the second paragraph on the page concludes with the statement: "Death here also occurred three years later." This should have read: "This patient is living and well seven years after the operation (personal communication, Dr. J. V. Dacie[5])."

A communication from Dr. J. H. Whitlock (The use of photo-electric turbidometry in the determination of red cell counts, hematocrits, and hemoglobin. Blood *2:* 463, September 1947) states that he has the D.V.M. and M.S., but not the Ph.D. as used erroneously after his name on the title page of the article.