published hitherto and there will still be debate as to whether a given cell is one thing or another.

Differences in terminology have arisen mainly because of differences in interpretation of observations made under a variety of conditions. It is reasonable to expect that as new knowledge is gained, agreement will come naturally as there is better understanding. Terms may then be modified by the normal process of evolutionary selection rather than through arbitrary definition. Emphasis, in short, should be placed on advancing knowledge rather than in too much concern about names.

Since the new terminology is not readily and wholly acceptable, nothing can be gained by its introduction at this time. Haste will but make more difficult the acceptance of terms which time and repeated discussions of all those concerned, including interested individuals in all English-speaking countries, might make possible in the future.

MAXWELL M. WINTROBE, M.D.

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LETTERS TO THE EDITOR

To the Editor:

In the January issue of Blood, a condensation of the first two Reports of the Committee for Clarification of the Nomenclature of Cells and Diseases of the Blood and Blood-Forming organs was published. Since I am not convinced of the soundness with which this unilateral approach has been conducted, I would like to bring certain things to your attention.

Hematology is international in its scope and, as a consequence, its terminology is not the property of any one country. As in other scientific disciplines, the ultimate goal of uniformity in nomenclature is certainly one which is desired by all. It is for this very reason that the constitution of the International Society of Hematology lists one of its purposes—"to attempt to standardize on an international scale hematologic methods and nomenclature."

Such an undertaking would undoubtedly enlist not only the services of clinical pathologists, but also those of embryologists, histologists, physiologists, zoologists, tissue culturists, immunohematologists and others whose work might be influenced by an alteration in hematologic terminology. The approach must be multilateral from the start. Groups serving on this committee should be provided with extremely accurate illustrations of cells under discussion. Furthermore, these illustrations should include the range of variability of cell types.

This is not the first attempt by Americans to alter terminology. As a matter of fact, some of the confusion which is disturbing at the present time is the primary fault of American hematologists. In 1915, Doan, Cunningham and Sabin with very good intentions wrote, "The terminology in hematological literature has become so confused, different investigators using the same designation for wholly different histological entities or the same histological entity being designated by a variety of terms, that it becomes necessary to define the limited sense in which certain names already in the literature will be used in this paper." Then, in the case of erythropoiesis, they disregarded this by using the term megaloblast in a manner quite different from its accepted usage by such leading hematologists of that period as Downey, Ferrata, Maximow and Naegeli. Additional confusion in American hematology was created by Peabody's unequivocal acceptance of Doan, Cunningham and Sabin's theory and by Isaacs and Osgood propounding theories of a similar nature. It is unfortunate that Doan, Cunningham and Sabin advanced
their theory for avian and mammalian erythropoiesis during a period when so much emphasis was being placed on the pathologic physiology of blood forming organs. If one takes time to read British, French, German, Swiss, Italian, Scandinavian and Latin-American contemporary hematologic literature, it soon becomes apparent that Doan et al., Isaacs and Osgood have placed certain phases of American hematology in a very bad light.

For some time, Europeans, Latin-Americans and some Americans have recognized the inadequacy of the theory for red cell genealogy as proposed by Doan et al., Isaacs and Osgood. Apparently, Osgood, too, recognizes that something is amiss and believes it can be rectified by avoiding certain terms like the megaloblast, for example. The importance of this cell type is more clearly understood in Europe today than it has ever been before. In order to illustrate this importance, consider the following from an unpublished manuscript:

"The megaloblast problem has many ramifications which affect, in varying degrees, the thought in quite a few branches of medical science. Zoologists, who do research in comparative hematology, have pointed out that megaloblasts and the first circulating mammalian embryonic red blood cells should be called ichthyoid, since they resemble the permanent red cells of fish and amphibians. The embryologist is interested in whether or not these cells are present only in the yolk sac during the pre-hapatic period of embryogenesis, or whether they are also found in the embryonic liver, spleen and bone marrow. They would also like to know whether the embryonic and pathologic red blood cells are identical. Some histologists teach that megaloblasts, derived from endothelium of the adult, are present in normal bone marrow and act as normal precursors for definitive erythrocytes; whereas other histologists consider that they belong quite definitely to the realm of pathology. In the latter, many general clinical pathologists maintain that the presence of megaloblasts are pathognomonic for all liver principle deficiency anemias while, on the other hand, some do not consider their presence unusual in any type of anemia. Experimental pathologists and internists have been attempting to produce in laboratory animals a condition which would simulate pernicious anemia of humans and some have purported to have produced a megaloblastic bone marrow. Some physiologists consider that these cells function as the first hemoglobin synthesizing units under normal conditions and the biochemists are confronted with the problem of determining whether or not hemoglobin is identical under all conditions. Pharmacologists, who are interested in the bioassay of antipernicious anemia preparations, would like to know whether or not megaloblasts are the only red cells which will respond in the presence of these substances. Furthermore, they are also concerned with determining what portions of specific molecules of these substances will cause megaloblasts to disappear from the marrow of pernicious anemia patients. They also ponder the question of why all patients with a megaloblastic marrow do not respond to the same specific therapy. Some clinicians are interested in the megaloblast problem because the presence of such cells in a patient's marrow indicates to them a need for the administration of specific therapy which, in most cases, must be maintained at an optimal level throughout the remainder of the patient's life. And, needless to say, the absence of these cells from the sternal marrow of a patient with severe anemia, affords the rationale for an entirely different therapy. Lastly, the hematologist has at least a theoretical interest in many, if not all, of these phases pertaining to the megaloblast problem."

To some it may seem that all of this is so much hogwash and that the difficulty might be solved readily by a change in terminology. Therefore, let us cast aside all hematologic terminology and designate the earliest cell recognizable as a hemoglobin synthesizing unit as 'red cell No. 1.' The next step would be to study this cell under embryonic, fetal, normal adult, pathologic and experimental conditions determining the morphologic features of its nuclear pattern and cytoplasm. If 'red cell No. 1' has the same attributes under all of these conditions, then we are justified in selecting the most appropriate term as a label for all. On the other hand, if 'red cell No. 1' differs under embryonic, normal adult and certain pathologic conditions, we would not be justified in grouping all of these cells together. In addition to this, if there are constant morphologic differences, then cytochemical, physiologic and biologic studies should be made to determine the underlying basis for them. Since there are morphologic and other differences between some of these cells, they should be called 'red cell No. 1 under embryonic conditions,' 'red cell No. 1 under normal adult conditions' and 'red cell No. 1 in liver principle deficiency anemias during relapse.' In the latter instance, it has been appropriate to refer to these cells as megaloblasts because that term—good or bad—was first applied to them by Ehrlich in 1880.
LETTERS TO THE EDITOR

Just for the sake of argument, let us assume that the proposed terminology has been accepted by all. Will it change the megaloblast-normoblast problem? No, it will not! In its place some American clinical hematologists and pathologists will continue to recognize morphologic differences between a pernicious anemia type prorubricyte and a rubriblast and others will not. The problem will remain just as long as some American hematologists either fail to recognize minute but constant differences in nuclear pattern or fail to interpret them properly.

The proposed terminology for red cells might have done better by utilizing good Anglo-Saxon terms like large, medium and small. The proposed terms of rubriblast and prorubricyte are regrettable in that they are hybrid. A Latin-Greek red cell gives rise to a Greek red cell. However, it is consoling to know that megalocytes are not to be avoided and that it is possible for them to come from metarubricytes. The suggested terminology will result in one more complex than existing ones; for example, megaloblasts become "pernicious anemia type prorubricytes." In anatomic nomenclature there is a tendency to avoid cumbersome terms and not create them. Why should, for example, "the pectineal part of the inguinal ligament" be used when "lacunar ligament" is available?

In conclusion, it is generally recognized that problems of nomenclature or classification become less complex when more is learned about the various attributes of the subject in question. Anatomists have more than a casual interest in hematologic nomenclature because they are responsible for teaching embryology and histology to medical students. It would be very unfortunate to teach two terminologies—one for preclinical and the other for clinical courses.

Oliver P. Jones
Professor of Anatomy,
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Dr. Wintrobe's Editorial and Dr. Jones' letter were referred to Dr. E. E. Osgood, who replied as follows:

To the Editor:

Both Doctor Wintrobe and Doctor Jones admit a state of confusion in definitions and terminology has existed in the field of hematology. Their criticisms, which are not clearly answered in the reports of the Committee, condense to the following four statements:

1. Next year we will know more; therefore we should wait.
   Answer: This has been and will always be true. If we were to wait until all is known or until 100 per cent agreement is reached, nothing would ever be done.

2. They and some others criticize the term, "progranulocyte," the terms selected for the erythrocytic series and the qualifying adjective phrase, "pernicious anemia type."
   Answer: It is admitted that "promyelocyte" would be more consistent with other terms selected for cells of the granulocytic series. However, the Committee recommended the term, "progranulocyte," because the definition accompanying it excludes cells containing neutrophilic, eosinophilic or basophilic granules. The term, "promyelocyte," has been used for cells variously defined as containing 10 per cent, 30 per cent or 50 per cent of their full quota of such granules, and these are lines of division between stages of differentiation which two observers cannot exactly duplicate.

   The definitions and terms in current use for the erythrocytic series were fully discussed at each of three meetings and the recommended terms resulting were agreed on as being the best solution to an admittedly difficult problem. The question is not, "Is this solution ideal?", but is rather, "Can anyone suggest a better solution?". General agreement on one definition and one term for each cell stage is more important than the particular term selected. These were the terms and definitions recommended. Agreement is more easily reached around a conference table, so it seems most unfortunate that neither Dr. Jones nor Dr. Wintrobe found it possible to attend any of the Committee meetings to which they were invited. Dr. Hal Downey, whom Doctor Jones mentions in his letter, was present at the meetings and fully concurs in the recommendations. The 30 members of the Committee who have approved the recommendations of the second report include competent men in most of the fields mentioned in Doctor Jones' letter. During some of the meetings, atlases of hematology as well as blood and marrow smears...
and microscopes were available to all discussants, so that morphologic differences and similarities could be visually evaluated during the process of reaching agreement for recommended terms and definitions.

Both letters imply that use of these terms binds one to a particular theory. One of the most fundamental principles guiding Committee decisions and emphasized in the reports has been to avoid any attempt to settle around a conference table anything which could be settled only by investigation. If anyone wishes to teach his students that a polychromatic erythrocyte is less differentiated than a normochromatic rubricyte, he can express that opinion clearly in this recommended terminology.

One of the major weaknesses of other terminologies has been that they failed to distinguish between stages of differentiation and the disappearance of ribonucleoprotein with simultaneous appearance of hemoglobin in the cytoplasm. With the recommended terms, both can be clearly indicated. Dr. Wintrobe pleads for more consistency in the terms for the granulocytic series, but would retain the suffix, -blast, in the erythrocytic series for a cell with a pyknotic, partially extruded or partially autolyzed nucleus which does not fit the criteria for any other blast stage. One needs to ask but one question regarding the term, "pernicious anemia type," versus "megaloblastic." Even if "megaloblastic" had only one definition, would it not be clearer to the student of medicine studying it for the first time to learn about "pernicious anemia type" granulocytes and "pernicious anemia type" marrow picture than about a "megaloblastic" marrow picture? Certainly one could not speak of "megaloblastic granulocytes," yet the morphologic changes are just as striking as those in the erythrocytic series.

3. A special atlas is necessary.

Answer: If the definitions are carefully read—and these definitions are just as important as the terms—it will be seen that the criteria for differentiation of the stages are clearly illustrated in every atlas of hematology that has ever been published. The Committee clearly recognizes that all subdivision is arbitrary and that an infinite number of subdivisions would be possible. They selected that number of subdivisions which in their experience was clinically and diagnostically useful, and tried to phrase definitions that would put the same cell in the same category when seen by different observers, but made provision for as much further subdivision through the use of modifying adjectives as might be needed for any investigative purpose.

4. The recommendations should be international before they are published.

Answer: The problem seems sufficiently difficult to settle in one language at a time. It is the sincere hope of the Committee that other language groups will form similar committees and that they will give serious consideration to the advisability of selecting the same definitions at least, and to achieving a comparable nomenclature.

The other points raised in the two letters are clearly answered in the text matter of the reports of the Committee. The Committee reports were circulated before publication to all Committee members, whether or not they were in actual attendance at meetings. These published reports represent the combined efforts of a number of persons, with the approval of the majority of the members of the Committee; they are not the recommendations of any one individual.

The "terms to be avoided" are not synonymous in most instances with the "term to be used." They are merely terms that have been used by some for the cells included under the terms recommended and defined in the reports. The Committee reports are recommendations only, and provision has been made to review and revise terminology periodically. It is not to be expected that they will receive 100 per cent acceptance in areas where scientific freedom exists. A statistical analysis of the response to the recommended nomenclature which has been received by Committee members and the American Society of Clinical Pathologists has not yet been made, but it will be brought into presentable form and the result will be made public in a future Committee report.

In conclusion, it is felt that to debate the values of any nomenclature in the scientific press can result only in the amassing of a large body of print and a loss of considerable time. The interested reader of these letters should be referred to the published reports of the Committee, for therein are included all of the purposes and guiding principles. If the recommended nomenclature has merit, it will be used; if it lacks merit, it will atrophy from disuse. The present indications—obtained from verbal comments and letters—are that the recommended terms and definitions are being widely adopted.

As stated in the Committee reports, the primary purpose of this Committee has at all times been to clarify hematologic terms for the benefit of the medical profession as a whole and future students of medi-
cine and related sciences, rather than for the relatively small proportion of the present medical profession which devotes most of its time to hematology.

For the Committee for Clarification of the Nomenclature of Cells and Diseases of the Blood and Blood-Forming Organs

Edwin E. Osgood, M.D., Chairman
Roy R. Kracke, M.D., Dean, The Medical College of Alabama
F. J. Hack, M.D., Mayo Clinic

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A subsequent letter received from Dr. Jones indicates that he was unable to attend two of the last meetings, and that he does not agree on all points with the report. The following letter on the subject was received from Dr. Frank H. Bethell.

To the Editor

The statements of the chairman of the Committee on Classification of Nomenclature of Cells and Diseases of the Blood and Blood-Forming Organs made in answer to the criticisms of Doctors Jones and Wintrobe have my whole-hearted endorsement. I believe that the publication of these letters will serve a useful purpose if it leads to a broader understanding of the objectives and achievements of the Committee. As Dr. Wintrobe says, the opposition to the recommendations of the Committee has been expressed for the most part in informal conversations. My participation in some of these discussions has convinced me that the discussants, with few exceptions, have not been well-informed on the content of the Committee’s reports. I should like to urge that every interested person, before he takes a position in this controversy, read carefully the published reports of the Committee with particular attention to the definitions.

Frank H. Bethell, M.D.
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Further Comment on Nomenclature Discussion

From the vantage point of the Editorial chair, there seems to be a good deal of merit in both points of view regarding the proposed revision and systematization of hematologic nomenclature. Although faint echoes are heard in this discussion of the frequently polemic articles which were seen in Folia Haematologica years ago, it can be stated that the proposed system of nomenclature, as worked out by a serious group of well-intentioned observers, is not only in the interests of simplicity, but slanted frankly for the students and the younger generation of physicians. Although some of us may dislike to have terms changed or systematized, many of
the younger men in the field have evidently taken to the newer terms without too much difficulty, even to the seemingly outlandish ones of "rubrocytes" and the like. Certainly, consistency is always something to be applauded so why not use for leukemia the terms myelocytic, lymphocytic, and monocytic rather than myelogenous, lymphatic and monocytic? It is admittedly easy to slip into this particular consistency but on the other hand, one finds it hard to take to one's bosom the "rubriblast" or to understand the actual need for its use. Therefore, it is good to note Dr. Osgood's statement that the proposed system of nomenclature is by no means rigid and that by a process of selection the fundamentally correct and the simple terms will be retained and the wrong and the difficult ones will atrophy from disuse. The members of the Committee are to be congratulated for the vast amount of time and patience they have spent around the conference table. They are doubtless correct in having obtained the impression that some of their critics might have been less critical had they spent some time with them in discussing their problems. In any event, there can be little doubt that out of all this great effort, at least some good will ensue to the innocent bystander in hematologic nomenclature.

William Dameshek, M.D.