With this issue the Journal introduces the first major change in its format in more than nine decades of publication. To be sure, there have been many modifications in typography and details of style during and after the development of the familiar format that has characterized the Journal since the early part of this century, but at no time have substantial changes been instituted.

It may seem like an extreme degree of conservatism to continue for so long a period without substantial changes. However, it was simply a matter of preserving what appeared to be a fully satisfactory style: the Editors were comfortable with it, and as far as we could determine, so were the contributors and the readers. There was little motivation for radical change. As a matter of fact, the new format was not primarily dictated by growing dissatisfaction with the old or by a strongly felt need to “modernize,” but rather by the pressure to provide additional space for the rapidly increasing number of manuscripts submitted to the Journal. Fig. 1 illustrates this problem by showing the record for receipt of manuscripts over the past decade. After maintaining a stable level for the first five years, there has been a steady and precipitous increase in submissions since 1985. The larger page size and double column format will allow the publication of more papers, thus alleviating the pressure resulting from this increase, and at the same time will improve the display of certain types of data.

Changes other than those dictated by page size and double column format have been kept to a minimum. A touch of modernization has been added by having the summary appear at the beginning of each article, where readers are now accustomed to look for it in most publications. The cover retains its conservative flavor; however, the list of editors has been moved from the cover to the first inside page, and a picture of the entrance of Founder’s Hall at The Rockefeller University has been added. An increase in the size of the editorial group, which should enable us to cope more efficiently with the growth of the Journal, is responsible for the first of these modifications. In view of the history of the Journal, the cover picture seems an appropriate decoration that recognizes the origin of the publication. The use of a multicolor design for the cover, with photographs relating to one of the papers in each issue, was considered but rejected as not necessary and as less consistent with the traditional style of the Journal.

The changes in format have required some modifications in the procedures to be followed by contributors, as set forth in the Instructions for Authors, which appears in the first issue of each volume. We have attempted to be as explicit as possible in defining the stages to be taken in the preparation of manuscripts and in describing the review process. Two additions are noteworthy: (1) An explicit statement on the editorial process, emphasizing that all papers are discussed at least twice at weekly meetings of the editorial staff; and (2) a description of a new and improved publication time, which is made possible by a cooperative arrangement between the Editors, The Rockefeller University Press, and the printer. We now plan to publish regular papers within 8–12 weeks of acceptance, and Brief Definitive Reports within 6–8 weeks, if page proofs are returned promptly by the authors.

As the end of the first century of publication of the Journal approaches, it becomes increasingly apparent that there is a need for a coherent account of its origin and subsequent history. The resources that are available to document this are not extensive. Simon Flexner and James T. Flexner deal with origins in their biography of William Henry Welch (1), and George Corner’s history of The Rockefeller Institute touches upon some of the intermediate developments up to 1952 (2). Beyond that, one must rely on the bound volumes of the Journal and a few additional items, notably the correspondence of F. Peyton Rous during his long tenure as Editor (3). The present transition to a new format seems an appropriate time to provide a concise version of the historical developments to date.

The Journal of Experimental Medicine was the first journal in this country devoted to experimental research in the medical sciences, having been founded at The Johns Hopkins University School of Medicine in 1896 as a bimonthly under the editorship of William H. Welch. The growth of laboratory research as an important activity in a group of U.S. medical schools had made it essential to develop new outlets for publication of the growing number of papers in this category. Welch had taken the lead in achieving this and was gratified by receiving financial aid from the University for the new venture. He was a meticulous editor, but unfortunately he seemed unable to delegate any part of the job to an assistant. As a result, he did everything himself without even the aid of a secretary; review of the papers, communication with the authors, checking of bibliographic references, and preparation of manuscripts for the printer. In some cases, he even undertook revision of a paper. As the task of producing issues on a bimonthly basis progressed, he inevitably became bogged down because of interference with his teaching and research activities. Manuscripts began to accumulate in his office and were left unread.

The publication of the Journal became irregular, and no issues appeared from Johns Hopkins after March 1902. Welch could not bring himself to resume the task and began to search for someone who would take it over. An opportunity arose through his involvement as a member of the advisory group for the establishment of The Rockefeller Institute for Med-
ical Research. After negotiations with the new Institute and Johns Hopkins, he succeeded in having ownership transferred to the Institute in October 1904. Even after the official transfer, Welch's mental block on the subject kept him from following through by delivering the long neglected manuscripts that had accumulated in his office. In the end, it was necessary for Simon Flexner, the first Director of the Institute, to go to Baltimore and bring them to New York in a suitcase. Flexner and Eugene L. Opie assumed editorship of the journal and completed Volume 6, dated 1901-1905, with Welch still listed as Editor on the masthead. Thus, the association between The Journal of Experimental Medicine and The Rockefeller Institute had its origin in the very early years of the Institute. Sole responsibility for publication of the Journal has been in its hands since 1906, the year that Founder's Hall, depicted on the new cover, was opened as the first building on the present campus.

From the beginning, Welch was concerned with making the Journal a national publication, not an exclusively Johns Hopkins enterprise. In his introduction to Volume 1, he expressed confidence that the Journal would be truly representative of scientific medicine in the United States and Canada. To this end, he assembled a group of 12 Associate Editors (3 each in the categories of physiology, pathology, pharmacology, and medicine), whose names appeared in Volumes 1-6. The geographical distribution is interesting, 10 in the Northeast corridor from Baltimore to Montreal and 2 in Ann Arbor, and probably accurately reflects the location of the major research-oriented medical centers at that time. It is not clear that these men were called upon for editorial assistance, but most of them contributed papers to the Journal.

The same concerns were felt after the Journal had been moved to Rockefeller, even though an important reason for accepting it had been to provide an outlet for Institute papers. Corner, commenting on this matter in the early 1960s, pointed out that "The proportion of outside contributions was for a long time more than half the total, and in recent years has risen to five sixths" (2, p. 63). This trend has continued with the upsurge of international medical science, and in calendar year 1989, 92% of the 375 papers published were from other institutions, with a total of 29 coming wholly or in part from Rockefeller laboratories. Manuscripts are submitted from most parts of the world, so that the Journal has assumed an increasingly international flavor.

Flexner and Opie edited the Journal together through its initial years at Rockefeller until Opie departed to assume the chair in pathology at Washington University at St. Louis in 1910 (Table 1). During the one year that Flexner was assisted by Benjamin T. Terry, the Journal became a monthly publication, beginning with Volume 13, 1911. Flexner was then the sole editor for the next 10 years. I have not found much information on his editorial style, but it is certain that he did not have Welch's inability to make use of secretarial and editorial assistance. Nevertheless, the burden of editing the Journal together with his duties as Director began to weigh heavily on him, and in 1922 the name of F. Peyton Rous as an additional editor appeared on the masthead, where it remained for 48 years until his death in 1970.

Rous had the longest tenure of any editor and was a major influence in shaping the Journal in its continuing development. It is generally believed that Rous very quickly acquired the role of the sole active editor, and it is true that he was the principal editor and managed the editorial office. However, Flexner continued to review a portion of the submitted manuscripts and had specifically asked to see all of those dealing with poliomyelitis, which he continued to do into the 1940s. When Herbert S. Gasser was added to the editorial group upon succeeding Flexner as Director of The Rockefeller In-

**Figure 1.** Average number of manuscripts submitted per month, 1980-1989.

| Year | No. Mss./month (Average) |
|------|--------------------------|
| 80   | 75                       |
| 81   | 80                       |
| 82   | 85                       |
| 83   | 90                       |
| 84   | 95                       |
| 85   | 100                      |
| 86   | 105                      |
| 87   | 110                      |
| 88   | 115                      |
| 89   | 120                      |

**Table 1.** Editors of The Journal of Experimental Medicine, 1896-1990

| Name                  | Years |
|-----------------------|-------|
| William H. Welch      | 1896-1905 |
| Simon Flexner         | 1904-1946 |
| Eugene L. Opie        | 1904-1910 |
| Benjamin T. Terry     | 1911-1912 |
| F. Peyton Rous        | 1922-1970 |
| Herbert S. Gasser     | 1936-1957 |
| Rene J. Dubos         | 1946-1973 |
| Charles L. Hoagland   | 1946-1965 |
| Vincent P. Dole       | 1953-1965 |
| Frank L. Horsfall, Jr.| 1958-1960 |
| Henry G. Kunkel       | 1960-1983 |
| Maclyn McCarty        | 1963-present |
| Zanvil A. Cohn        | 1973-present |
| James G. Hirsch       | 1973-1980 |
| Richard M. Krause     | 1973-1975 |
| Anthony Cerami        | 1981-present |
| Ralph M. Steinman     | 1988-present |
| Carl F. Nathan        | 1988-present |
stitute, he also participated in the editorial activities, although there were relatively few papers in his area of special interest. During the many years that Rous carried the major burden of reviewing and editing manuscripts submitted to the Journal, he also freely sought assistance from his Rockefeller colleagues in various fields. His Journal correspondence contains letters referring to people such as the following: Avery, Carrel, Landsteiner, Michaelis, Rivers, and Van Slyke. Their reviews, ranging from long analyses to brief verdicts, are filed with the copies of the letters.

The Rous style of editing was often extensive, especially on manuscripts that had captured his interest, and his comments reflected his high standards in clarity, precision in exposition, and English usage. Manuscripts that received this attention were sprinkled liberally with pencilled comments and queries in his fine handwriting. I have noted elsewhere that the 1944 paper by Avery, MacLeod, and myself reporting the identification of the pneumococcal transforming substance as DNA was a typical example of this editing style, with numerous comments (4), but no copy exists to serve as an illustration. However, I have since found in my files a 1951 manuscript by Chandler A. Stetson, then in my laboratory, which serves the purpose admirably. The manuscript had been retyped after the extensive editing, and happily the original was retained.

Fig. 2 shows the title sheet of the Stetson manuscript with the suggestions for modification and Rous's initialed acceptance of the paper. The lower portion of the figure includes the title as it appeared in the Journal, showing that the suggestions were all accepted, although Rous would not have insisted on this. The last page of the typescript, including the summary (Fig. 3), gives a picture of the extent to which his comments often appeared in the text. Clearly many of them are directed at achieving clarity and precision, but there is one in typical Rous prose where he admonishes Stetson, "Don't play up your wares too loudly. Let others do it." Rous did not expend this much effort on papers that he did not consider worthwhile. Even if limited to those papers that he considered worthy of publication, it was a demanding editorial chore, and it is my impression that he did much less of this in his later years as editor.

A look through his correspondence for the Journal reveals that he also wrote lengthy letters suggesting ways to modify certain papers. On the other hand, when he felt that the subject matter was more appropriate for another publication, his covering letter would be brief and would make specific recommendations for publishing elsewhere.

After more than 20 years of this activity, Rous began to feel the burden of trying to cope with papers in emerging fields of medical science with which he had little familiarity. As a result, he invited René Dubos to join him as an editor in 1946. At the same time, Rous had also selected another younger colleague, Charles L. Hoagland, who was a rising star in the application of biochemistry and physiology to medical problems. Although his name appears as one of the editors on the first three issues of Volume 84, Hoagland had been in poor health and died tragically soon after his appointment; he was able to serve on the Journal for only a very brief period.

Rous and Dubos worked closely together for the next several years and they initiated the practice of meeting regularly once a week for discussion and review of the current crop of manuscripts. This practice has been continued ever since, and it is well established as an important component of the editorial process. The agenda for this meeting has grown with the growth of the Journal, and today in extended sessions involving the Editors and Assistant Editors, the current manuscripts are presented and decisions concerning such matters as priority, assignment for additional review, and need for revision are made after open discussion. As noted above, each manuscript submitted is discussed at least twice at these meetings. In addition, the weekly sessions provide an opportunity for consideration of other issues relating to the operation of the Journal.

In 1953 Vincent P. Dole was asked to join the editorial group to provide the kind of biochemical expertise that had been visualized earlier with the selection of Hoagland. There then followed a series of additions that were relatively rapid compared with the pace of change in the earlier years. Frank Horsfall became an editor in 1958, but had served only two years before he moved to the Sloan-Kettering Institute. At that point in 1960, Henry Kunkel was added to the editorial group, and I followed in 1963, bringing the total number of active editors to five.

The dominant theme of the papers submitted to the Journal had changed more than once during its first 60 years, and it is difficult to identify the factors that led to these changes. The dominance was not always very great. I have been told, for example, that during the '20s and '30s there were some who jocularly referred to the Journal as the Journal of the Pneumococcus. It is true that the extensive publications from the Avery laboratory had attracted a number of papers on this subject from other groups, but a review of the volumes during this period does not reveal a single issue in which a majority of the papers dealt with the pneumococcus.

The dominance of immunology that emerged in the 1960s is manifestly more real. This is often attributed to the influence of Henry Kunkel, but it is not easy to determine whether this was the only or the major factor involved in this development. Certainly his genius in combining basic and clinical studies and ferreting out fundamental new information from investigation of human immunologic disease had brought him to a role of leadership in medical immunology. Since he published much of his work in the Journal, this may have attracted the work of others even before his editorship. On the other hand, the field of immunology was undergoing a resurgence with a great broadening of its scope, and it seems likely that its representation in the Journal would have increased without any additional stimuli. In any event, the fact that papers on a wide range of immunologic topics form a majority of those submitted to the Journal today is obvious from its content, even though a variety of other areas concerned with physiologic or pathogenetic mechanisms are also well represented.

There is no doubt that Kunkel's guidance during his 24 years as editor had much to do with the direction that the publication took during that period. He was devoted to the
STUDIES ON THE MECHANISM OF THE ARTHUS PHENOMENON

(Certain Relationships Between the Mechanisms Involved in the Production of the Arthus Phenomenon and the Schwartzman Phenomenon.)

SIMILARITIES IN THE MECHANISMS DETERMINING THE ARTHUS AND SCHWARTZMAN PHENOMENA

BY CHANDLER A. STETSON, JR., M.D.

(From the Hospital of The Rockefeller Institute for Medical Research)

PLATE 26

(Received for publication, June 4, 1951)

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Figure 2. (Upper part) Title sheet of manuscript with editorial notes of Peyton Rous. (Lower part) Title of published paper, illustrating response to editing.
The demonstration of the close similarity between the vascular injury of the Shwartzman phenomenon and the Arthus phenomenon may be of considerable significance. The fact that a wide variety of antigens are capable of producing the Arthus phenomenon and that numerous bacteria and bacterial products are active in eliciting the Shwartzman phenomenon suggests that the tissue reaction demonstrated above may be of importance in the pathogenesis of certain infectious diseases and in the development of various phenomena associated with the "immune" or "hypersensitive" state.

SUMMARY

The intradermal injection of antigen in sensitized animals causes a systemic reaction involving alterations in leucocytes and platelets, and results in cellular thrombosis of capillaries and veins in the injected skin areas. The vulnerability of these vessels to leucocyte-platelet thrombosis appears to be conditioned by the abnormal metabolic environment which develops in the injected skin areas. This form of vascular damage is similar to that previously observed in the case of the Shwartzman phenomenon, and the results of various metabolic, hematologic and histologic studies indicate that the mechanisms involved in the production of both phenomena are closely related.
maintenance of its high standards and to the introduction of new features, such as the Brief Definitive Report, that would increase its usefulness to the readership.

One of the effects of the changing content of the Journal was that Dole found progressively fewer papers for review in his area of expertise, and as a result he chose to step down as an Editor in 1965. Dubos also noted that not only were there fewer papers of immediate interest to him, but also that the research reported had become more and more dependent on new technology and terminology with which he was unfamiliar. When he chose to retire as an Editor in 1973, his colleagues James G. Hirsch and Zanvil A. Cohn, joined the editorial group, bringing with them a cell biological approach to the study of immunology and disease pathogenesis that had already been introduced into the Journal through their publications. Richard M. Krause, who also became an Editor at that time, left in 1975 when he became Director of the National Institute for Allergy and Infectious Diseases. Anthony Cerami, on becoming an Editor in 1981, added expertise in several areas of medical biochemistry, including that of the emerging field of the cytokines. Hirsch resigned in 1980 when he became President of the Josiah Macy, Jr. Foundation.

One effect of the expansion of biomedical science in the post-war period, and the introduction of new research tools and technical approaches, was the increased need for specialized expertise in the review of many manuscripts. In 1963, at the time that I became an editor, the decision was made to invite a group of Advisory Editors to serve with us. This quickly improved our ability to deal effectively with the diversity of specialties required for thorough review. The panel of Advisory Editors has increased gradually over the years, and the current changes will include further additions to the panel. We feel privileged to have been able to obtain the cooperation of so distinguished a group of Advisory Editors. Their contribution has gone well beyond that of scientific expertise, since they have brought a high standard of fairness and speed to the review of manuscripts and have strongly supported our desire to see that the work published is of the highest caliber.

As time went on and the load of manuscripts grew, it was apparent to the Editors that they also needed assistance with the day-to-day activities necessary for the timely completion of the editorial process. Accordingly, in 1978 we recruited some of our younger colleagues to serve with us as Assistant Editors. This was an immediate success, and the added group has continued to play an important role on a regular basis. Two of the early Assistant Editors, Ralph Steinman and Carl Nathan, have recently joined Zanvil Cohn, Anthony Cerami, and me as Editors, bringing our number again to five. The currently active group of Assistant Editors, Alan Aderem, Ellen Pure, and Helen Vlassara, carries a substantial share of the reviewing responsibilities.

This brief historical review is obviously focused on the editorial process. Little has been said about the activities involved at the production and publishing levels once the review and acceptance of manuscripts have been completed. These important areas obviously have a history of their own in connection with the publication of the Journal, but this will have to be related at another time.

The Journal of Experimental Medicine, nearing the end of its first century of publication, is initiating a series of changes that are designed to carry it forward into its second century. We hope that they will meet with the approval of our readers and our contributors.

Maclyn McCarty, M.D.
For the Editors

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