Clinical Immunology Society:

The Early Years 1984-1989

Clinical Immunology Society: The Early Years 1984 - 1989

I. Meet the Founders

Dr. John Fahey and Dr. Noel Rose speak about the early years of CIS.

II. Preparations and Achievements

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Introduction

A separate account provides the background leading to development of the Clinical Immunology Society (Fahey, JL, Clinical Immunology Society: The Early Years 1984-1989, I. Introduction. J. Clinical Immunology. 2011, in press).

CIS Outline

I. **1984 - 1985 – Concept and Consultations**
   1. Academic Immunology - Research Advances Focused on Immune System: Components, Functions, and Regulation
   2. Clinical Disease Specialties and Subspecialties - Involvement of Immunology and Immunologists
   3. Immunological Laboratory Resources Needed for Clinical Research and Care
   4. Procedures and Therapies Requiring Special Expertise Unique to Clinical Immunologists
   5. American Association of Immunology (AAI) and Other Organizations, National Institutes of Health (NIH), Especially National Institute of Allergy and Infectious Diseases (NIAID)
   6. Meetings to Plan a Society and Annual Conference
   7. Decision to Proceed

II. **1986 – Provisional Organization of the Clinical Immunology Society (CIS) and the Initial Annual Conference on Clinical Immunology (ACCI)**
   1. Working Group to develop CIS
   2. CIS Goals
   3. Initial Conference on Clinical Immunology - Preparation and Conduct
   4. Subsequent Annual Conferences on Clinical Immunology

III. **1987 - 1989 – The New Clinical Immunology Society: CIS Organization**
   1. Professional Structure
   2. Administration and Operational Issues
   3. Finances and Fundraising
   4. Use of management companies for the CIS and ACCI
   5. Membership
      a. Overall
      b. Ph.D. Scientists in CIS
      c. Women in CIS
      d. Scientists in Industry
   6. Journals and Educational Activities

IV. **1986 - 1989 –Relationships with Existing Organizations, Conferences, and Certifications**
   1. Immunology - AAI
   2. Clinical Medicine - Subspecialties and Board Certification
      a. Allergy
      b. Organ-Based Medical and Pediatric Subspecialties
      c. Requirements for a New Specialty Field in Medicine
   3. Medical (Clinical) Laboratory Immunology
   4. International - International Union of Immunological Societies (IUIS)

V. **Summary and Opportunities**

Clinical Immunology Society: The Early Years 1984 - 1989

A. 1984-1985 - Concept and Consultations

Preparing for and developing the Clinical Immunology Society (CIS) was somewhat analogous to building and outfitting a ship that would be seaworthy and functional. The first step was to indicate the purpose of the ship and what it would do. The second part was to settle on a general design or pattern and then identify the materials needed for construction of the vessel. (The materials can be assembled into a ship to be launched and then proven to be able to float.) Such a ship would need a power and propulsion system. Finally, a steering and navigation system would be installed to control the ship's direction and see that it followed useful courses that met the intended needs in a timely and effective manner. In the three years leading up to the first meeting of the CIS and in its first year or two of operation, most of the activities noted in the ship sequence were carried out.

The initial concept was that the CIS would, (1) promote research, i.e., facilitate the acquisition of new knowledge and the improvement in the diagnosis and therapy of disease, and (2) foster improved education and training and aid in the translation of research advances into clinical practice. In 1984, and even earlier, consultations began about the concept of the CIS, which would be independent from but also relate effectively to significant existing organizations. Leading immunologists (Table I) were consulted regarding the advantages and disadvantages of a separate society and what it should do to advance both research in and the practice of Clinical Immunology.

Four general areas were considered for involvement in its successful development: (1) Academic Immunology (including industrial laboratories) that were contributing research advances and knowledge of the immune system components, functions, and regulation; (2) Clinical disease specialties and subspecialties, in which training and continuing medical education in the field were needed for the benefit of patients; (3) Medical Laboratory Immunology resources necessary for good clinical practice and clinical research; and (4) Partnership with the NIH, especially NIAID and the AAI and other professional organizations in advancing these efforts.

1. Academic Immunology – Research Advances Focused on Immune System Components, Functions, and Regulation

Much immunological research was done in experimental animals, particularly mice and rabbits. However, the reagents required for comparable measurements in humans needed to be developed, understood, and made more widely available. The process was well underway, but many researchers, especially laboratory scientists, did not have ready access to human material

to study. Many concentrated on animal (especially murine) systems for conducting research on the development and functions of the immune system. Animal models allowed for a greater variety of research studies and for the control of parameters and genetic factors than were possible in the more diverse human population.

Yet, human disease provided striking opportunities for research in Immunology. A prime example is the immune deficiency defects seen particularly in pediatric populations. Also, autoimmune diseases presented many challenges, as did transplantation immunology, in which replacement organs needed to be protected from rejection. In addition, there were opportunities for providing new immune systems by means of bone marrow (lymphoid stem cell) transplantation.

Academic Immunology research broadened substantially when it became more than simply diagnosing and responding to infectious diseases. It began to be concerned with overall problems of homeostasis and immune regulation and replacement and to capitalize more broadly on research opportunities presented in human populations for the treatment of cancer, autoimmune and other diseases.

AIDS presented new challenges for Clinical Immunology research in the 1980s. There was no known animal counterpart. Simian Immunodeficiency Virus (SIV) was only identified later and was not a widely available research tool. Thus, AIDS, with eventual lethal damage to the immune system, also demonstrated that the immune system converted what could have been an acute lethal disease into a long-term disease with ten or more years of survival in some persons without an effective antiviral treatment. This result emphasized the power and value of existing immune responses and the need for better specific immune containment of HIV, the lentivirus that causes AIDS. The challenges for HIV vaccine development were already evident.

Individuals doing laboratory research were consulted to solicit their participation and asked how a Clinical Immunology Society could promote their interest. Providing assistance in making available human samples for research analyses was noted. Also, clinical validation and evaluation of hypotheses and theories developed in in vitro or animal studies needed to be facilitated.

2. Clinical Disease Specialties and Subspecialties – Involvement of Immunologists

Clinical specialties and subspecialties already existed, based largely on specific organ systems. Each presented some immunological challenges. Suggestions about how the CIS could foster advances in the recognition and treatment of diseases were solicited. Eventually, interested professionals in 15 clinical specialties had been consulted (Table I). By and large, they welcomed the opportunities for improved contact with advancements in Immunology, for access to research reagents and techniques, and for opportunities to explore new therapies.

In the field of Allergy Medicine, two organizations, the American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology

(ACAAI) had included Immunology in their names but focused mainly on the clinical practice of allergy. They had, however, fostered education and certification programs in their field in the form of a conjoint board (American Board of Allergy and Immunology – ABAI), under both the Medicine and Pediatrics boards. Efforts to relate allergy to the new Immunology were ongoing. (See section D).

Medical specialty meetings usually included some Immunology reports, but most emphasized other areas of the clinical specialties and not the broader reaches of Clinical Immunology, which might be applicable to the problems and treatments associated with disorders of too little or too much immune response. Clinical Immunology training and certification could be conducted as a distinct specialty or linked to an established field such as Rheumatology, Allergy, Oncology, etc. Clearly, it was an area to be resolved, and the CIS could support appropriate developments. There was the hope that having Clinical Immunology meetings would not compete with the specialty meetings but rather promote advances in both directions; for example, Rheumatology experience in immune suppression would be relevant to immune modulation in other clinical areas with too much or inappropriate auto immunity.

3. Immunological Laboratory Resources Needed for Clinical Research

Immunological laboratory resources needed for Clinical Immunology were not well-focused or readily available in hospitals in the 1980s. The available tests were scattered among Hematology, Chemistry, and Microbiology laboratories with fluorescence microscopy in Pathology (or only in research laboratories). In addition, conventional testing was often conducted by individuals not trained in Immunology. There were new procedures to be codified and normal ranges to be defined. Immunologists had developed their own laboratories to make the measurements needed for clinical research. Advancing clinical immunology required methods being developed in research laboratories – but not yet incorporated into the rubric of hospital pathology.

Training in Medical (Clinical) Laboratory Immunology needed to be developed. The status quo was no longer sufficient. In those years, procedures were often done on a small scale. Several test samples and control or reference samples might be evaluated in a typical assay, and immunological assays, for the most part, were not adapted to large-scale, check-list machines. A certification program initiated by the American Board of Allergy and Immunology conducted its first examinations in 1986; however, only M.D. trainees could be certified. The American Board of Medical Laboratory Immunology (ABMLI) sponsored by the American Society for Microbiology (ASM) was available to certify qualified Ph.D. as well as M.D. candidates. Clearly, an effective immunology society could contribute to developments and training in the medical laboratory areas that were essential to quality clinical practice and research in Immunology. Discussions with leading medical immunology laboratory professionals provided assurance that state licensure issues could be accomplished along with recognition and financial compensation for the immunological testing conducted in clinical contexts.

4. Procedures and Therapies Requiring Special Expertise Unique to Clinical Immunologists

These are summarized in an outline prepared in 1986 by Richard O'Reilly (see Table II).

5. American Association of Immunology (AAI) and Other Organizations, National Institutes of Health (NIH), Especially National Institute of Allergy and Infectious Diseases (NIAID)

For some years, the AAI considered how to relate to Clinical Immunology and had developed a working group on Immunopathology. The CIS included Immunopathology within its framework but also had a great interest in immunotherapeutics. AAI was not active in promoting the field beyond having the topics included in its annual meetings; however, it offered assistance and expressed interest in continuing contact. Immunologists working to develop the CIS talked with AAI leadership frequently during this period. (See Section D.)

A crucial agent for development and support in all of biomedical research was the NIH and the NIAID, especially for Immunology. NIAID was concerned that advances in knowledge should be applied to human disease and its prevention and treatment.

Richard Krause, who was the Director of NIAID at that time, and his successor, Anthony Fauci, were strong supporters of Clinical Immunology research. Some funding was available for Clinical Immunology research training programs, for conferences on research advancements, and for other devices to improve and strengthen research in this arena. Robert Goldstein and Bernard Janicki managed these programs in the Allergy and Clinical Immunology Branch within the extramural NIAID.

Other Institutes at NIH also contributed. In the 1980s, the NCI had a larger overall budget than NIAID and had been, for more than a decade, actively supporting immunology research both in-house at the NIH and through grants. Research on immune mechanisms had potential applications to many issues raised in cancer research. Other NIH Institutes also contributed to the support of Clinical Immunology in their particular organ or disease responsibilities. There was good communication at the NIH and cooperation between all the Institutes in this area.

6. Meetings to plan a Society and Annual Conference

More than 50 persons in Clinical and Basic Immunology research and/or active in one of the medical specialties were consulted about the possible value and implications of having a CIS (Table I). Overall, there was substantial support, with many of the consultations occurring at national and international gatherings of immunologists – from those of the AAI, of the American Society for Clinical Investigation (ASCI), and the American Association for Clinical Research, at the council meeting of NIAID, the AIDS research conferences, and the British

Immunology Society meetings in 1984 and 1985. These were places where Clinical Immunology was a focus of research and applications.

On January 23, 1986, I hosted a dinner meeting held at the Chevy Chase Club in Maryland, relatively close to the NIH. The attendees included Noel Rose, Baruch Benacerraf, Tom Waldmann, Allen Kaplan, Henry Metzger (AAI representative) and other immunologists attending an NIAID Council meeting at the NIH. Several emphasized the value of an academic society focused primarily on research, while others envisioned that the CIS would be an opportunity, also, to build clinical (and laboratory) training and practice in the various contexts of Clinical Immunology, particularly new therapeutics.

A larger planning meeting was organized for May 6, 1986, in conjunction with the American Society for Clinical Investigation (ASCI) Conference held at the Sheraton Washington Hotel in D.C. Those present included Drs. Fahey, Rose, Fathman, Fauci, Waldmann and Janicki; and, Drs. Barton Haynes, Dale McFarlin, Fred Rosen, Warren Strober, Norman Talal, Kirk Osterland, Gary Hunninghake, Lawrence Lichtenstein, Peter Schur, and Allen Kaplan.

- A review of existing organizations indicated that some of the clinical specialty meetings included clinical immunology components, but none brought together a full range of relevant advances in the science and clinical applications of immunology.
- Membership was discussed, and the general desire was to include M.D. immunologists who identified with Clinical Immunology as a major activity as well as clinical investigators in other fields who use immunological interventions or immunological methods to assess treatments of disease. Furthermore, such immunologists should have roles in the development of the organization as well as in the planning of meetings.
- Also, Ph.D. immunologists who work with human disease or in animal systems relevant to human disease should be included in the membership.
- The organization should be separate as a free-standing society, but it should associate as closely as possible with the AAI. Other frameworks were discussed but those present unanimously favored a distinctive organization, not just a division or affiliate of AAI. Although the AAAAI met specific needs of academic and practicing allergists, a separate organization in a much larger modern context of Clinical Immunology was required for many different, but somewhat overlapping groups within this broad field.
- The term that best described this organization was the "Clinical Immunology Society."
- The development of a recognized medical specialty in Clinical Immunology, however, was less certain. Almost all the M.D.s who saw patients had clinical training and certification in a conventional specialty and subspecialty. It was not clear how training and certification in Clinical Immunology could be related to existing specialty fields such as Rheumatology, Oncology, or Dermatology. Their patient referral patterns were well-established. AIDS was less certain. However, the patients of most allergists, oncologists, and others did not want AIDS patients in their waiting rooms in the 1980s, when there was great fear of that disease.
- Hyphenated terms, such as immuno-rheumatologist, were reasonably accurate but cumbersome and generally not used.

7. Decision to Proceed

The general preference by early 1986 was for a research society that would promote clinical and laboratory collaborations, report advances in the field, and foster pathogenesis and therapeutic research. Most physicians indicated a willingness to contribute to the development of a specific identity for Clinical Immunology.

An initial two-day scientific meeting later in 1986 was outlined to include symposia, simultaneous mini-symposia, and posters and poster discussion groups. The time of the year and location were considered. The options were two days before the AAI meeting in spring 1987 or a two to two-and-a-half-day independent meeting in October 1986 in Washington, D.C., or Baltimore. These locations were favored because of the conjunction of many clinical immunologists at the NIH and at academic institutions who could easily attend a meeting relatively close to home and work. The Steering Committee of the working group was charged to carry out this latter arrangement with assistance from the Planning Group.

Clinical Immunology Society: The Early Years 1984 - 1989

B. 1986 - Provisional Organization of the Clinical Immunology Society (CIS) and the Initial Annual Conference on Clinical Immunology (ACCI)

Three general tasks were undertaken. One was to establish a core Working Group to develop the CIS and its operations; the second was a provisional definition of CIS goals; and the third was the planning and conducting of the initial ACCI.

1. Core Working Group to Develop CIS

In moving from planning to an action stage, a core of five persons became the principle organizers of the CIS and its first project – the ACCI. (The ad hoc Steering Committee is listed in Table I.) Others, such as Hugh McDevitt and Tom Waldmann and Robert Goldstein, were frequently consulted.

To be sure that the plans enunciated by the Steering Committee were carried out, an Executive Officer position was established. Susan Kanowith-Klein was appointed to assist with fundraising from commercial and other organizations; with NIAID communications and with the AAI and other interested parties; and maintaining contacts needed for arranging the ACCI. Also, a company headed by Mr. Jack Wyatt was hired to handle the meeting arrangements; he had previously assisted Noel Rose in preparing and conducting scientific meetings.

Consulting on plans continued. Colleagues with a willingness and capacity to contribute were sought out at national and specialty meetings. A broad representation would include those active in major clinical and research fields as well as geographic and institutional diversity. All the persons in Table I were contacted again in 1986.

Pharmaceutical companies with interest in immune diagnostics and therapy were approached by Susan Kanowith-Klein, and many contributed support for the CIS and for the ACCI.

Incorporation of the CIS was important to facilitate the handling of funds for the ACCI and administrative activities, while the bonding of employees was addressed separately. Incorporation was undertaken with the assistance of Arnold Gold of the law firm Pachter, Gold and Schaffer, 5757 Wilshire Boulevard, Los Angeles, California 90036.

Susan Kanowith-Klein had previously obtained information on the incorporation and tax-exemption processes in California, Delaware, and Maryland. She arranged for the papers to be drawn up, and fortunately, this law firm did so *pro bono* to assist medical research. However,

Drs. Fahey and Kanowith-Klein did take the partners to lunch at Jimmy's Restaurant in Beverly Hills. A favorite of the legal set, this upscale bistro, alas, no longer exists.

2. CIS Goals

The proposed goals of the CIS were reviewed at the May 6, 1986, meeting held during the ASCI Conference in Washington, D.C. Both scientific and educational uses were suggested, including:

a. To facilitate the interchange of ideas and information among physicians and other investigators who are concerned with immunological diseases;
b. To promote research on the causes and mechanisms of diseases relating to the immune system and, as a result, to unify concepts of disease pathogenesis;
c. To encourage investigators and clinicians, whether in academic institutions or industry, to share knowledge of immunologically active drugs and other interventions;
d. To foster excellence in research and medical practice;
e. To promote the application of recent advances in biomedical science for the diagnosis and treatment of diseases related to immunity (the immune system).

3. Initial Conference on Clinical Immunology - Preparation and Conduct

Prior recommendations favored having an initial scientific meeting of about two days with a format to include plenary sessions, simultaneous mini-symposia, posters and poster discussion groups, and meet-the-professor exchanges. This plan was adopted. (The scientific program is attached - Table III.)

The ambitiously designated First Annual Conference on Clinical Immunology (ACCI) was held October 10-12, 1986, at the Hyatt Regency Hotel, Baltimore. It began at 7:00 p.m. on a Friday evening and concluded by noon on Sunday. Five plenary sessions included the first account by Robert Peter Gale of U.S. assistance in Bone Marrow Transplantation for victims of the Nuclear Catastrophe at Chernobyl in the U.S.S.R. Other plenary sessions addressed "Soluble Factors Regulating the Immune Response," "Immunogenetics," "Molecular Pathogenesis of Human Leukemia," and "AIDS Viruses and Immunopathogenesis of AIDS." There were more than 50 abstracts and two groups of four concurrent workshops with each containing six-to-eight contributions.

The proposal for development of the CIS was outlined by John Fahey on the opening evening of the ACCI so that there would be good opportunities during the following day-and-a-half for discussions and suggestions. More than 300 immunologists attended and urged that such a society should continue to develop. Support was provided by eight companies, three foundations, the AAI, and NIAID.

Evaluations collected at the end of the ACCI meeting indicated that there had been good scientific coverage in the day-and-a-half, which also allowed for contacts and discussions. Areas

suggested for further development were Immunology of Infectious Diseases, Diseases involving the Gastrointestinal Tract, Pulmonology, and Dermatology.

In conversation, a pediatric immunologist noted that he hoped the CIS Conference would be an established event for those studying primary immune deficiency diseases, since these immunologists had no place with organ-based specialists or allergists.

Arrangements were made at Johns Hopkins for CME credits for qualified attendees.

There were no honoraria, but speaker expenses were reimbursed. Jack Wyatt had done a good job of preparing for the ACCI.

The premise was established that a separate (from the AAI) Clinical Immunology conference could be significant and attract medical scientists and educators. It also verified that the nascent CIS did have the capacity to organize and conduct a significant scientific meeting.

4. Subsequent Annual Conferences on Clinical Immunology

The CIS planners in 1986 not only had to prepare for that ACCI, but also had to encourage 1986 attendees to plan to attend the second ACCI already scheduled for November 30-31 and December 1, 1987, at the Sheraton Hotel in Washington, D.C.

Subsequent ACCIs:

Second - Washington, D.C., October 30 - November 1, 1987
President: John L. Fahey

Third - San Francisco, CA, November 4-6, 1988
President: Thomas Waldmann

Fourth - Arlington, VA (Washington, D.C.) November 3-5, 1989
President: Hugh McDevitt

Attendance at these conferences ranged between 350 and 450. The programs were structurally similar to the preceding ones, and about 100 abstracts were submitted to each conference. Topics for poster and workshop presentations in 1987 are outlined in Table IV. Many had been included in the 1986 program.

Therapeutic emphasis was on Immunopharmacology, clinical trials, and laboratory evaluation in clinical trials. Also included were lymphokines, immune-suppressive agents, biologicals such as monoclonal antibodies, organ transplantation, bone marrow transplantation, disease diagnosis, epidemiology, and immunogenetics

A few clinical practitioners were attracted to the ACCI meetings. The suggestion of having *State-of-the-Art Reviews* for them to be held on a Saturday morning in conjunction with future ACCI was discussed. Such programs were conducted in several later years but did not attract large numbers of practitioners.

Clinical Immunology Society: The Early Years 1984 - 1989

C. 1987 - 1989: The New Clinical Immunology Society: CIS Organization

1. Professional Structure

Originally, there were four elected officers – President, President-Elect, Secretary-Treasurer, and Councilor–Elect. The latter would succeed to become President-Elect and eventually President. The President would have another year as a Past-President on the premise that each President would want to develop some area of particular interest and would need more than a year to get it established. Also, the lead-in time would educate the future Presidents about ongoing issues and possibilities for new developments in the CIS. Subsequently, elected Councilors were identified to be two, three, four, and five years from becoming President. In theory, this setup should encourage new initiatives and provide time for their achievement. Appointed Councilors were identified and included on the Board to represent important fields in Clinical Immunology not already represented. Also, the Secretary-Treasurer had a four-year term, which could be renewed one time. Later, when the CIS secured a journal, the Editor became a member of the Council.

CIS committees were established in the first year and were functioning in 1988:

a. Planning and Finance Committee was headed by the President (T. Waldmann) and President-Elect (H. McDevitt) in conjunction with six other members of the Council
b. Organizational Liaison - J.L. Fahey
c. Programs for the ACCI - Richard Lynch, T. Waldmann
d. Clinical Practice and Education - A. Kaplan, R. Goldstein
e. Clinical Laboratory Immunology - K. Osterland, Dan Stites
f. Scientists in Industry – J. Farrar and Nolan Sigal
g. Publication - Peter Lipsky
h. Membership Committee and Nomination Committee - Mary Ellen Conley, John Sullivan

Additional contributors to the program and to Topic Subcommittees included Warren Strober – Mucosal Immunology; Malcolm Mitchell – Lymphokines; Thomas Lawley – Immunodermatology; James Folds – Medical (Clinical) Laboratory Immunology; and, Vicki Kelley – Autoimmunity.

The principal features of individual committees were drafted by Susan Kanowith-Klein in consultation with the principle members in each. The purposes of the committees were detailed and agreed to by the Executive Committee. Specific actions, activities, and organizational responsibilities were indicated for each committee or workgroup.

Comments:

The Physician-in-Practice Committee basically did not function because most of the participants in the CIS were academically oriented. Physicians in practice had already established professional relationships, with educational and support systems needed in their current circumstances. Thus, the CIS did not identify needs that could be met by that committee as it was constituted.

2. Administration and Operational Issues

The CIS conducted its activities in 1987 from offices at UCLA and at The Johns Hopkins University. In Los Angeles, John Fahey and Susan Kanowith-Klein were working on the CIS's definition and development as well as on the interrelationship with other societies. S. Kanowith-Klein was the principal agent raising funds from industry and foundations. Financial records and membership roles were focused in the office of Noel Rose at The Johns Hopkins School of Public Health in Baltimore. The ACCI meeting management was continued by Jack Wyatt in 1987 and 1988.

Issues that were addressed in 1988 included the purposes of various working groups and committees that had been identified in the earlier plans for the CIS. By-Laws were proposed and legal advice obtained. Colleagues who had participated in the development or leadership of comparable professional societies contributed on the basis of their experiences.

The By-Laws were modified advantageously. One of the interesting features had to do with an original clause relating to "expulsion" from membership. It was suggested that this term be changed to "removal of membership," although the possible reasons for such actions were not detailed in the By-Laws intentionally.

To facilitate development of the CIS, S. Kanowith-Klein's role evolved to concentrate on operational development relating to the Council, including the Senior Officers, and to fundraising with approaches to potential funding sources. A key post of hers was to see that important questions were addressed by the Council and officers regarding the organizational and operational issues of the CIS in light of its goals. She worked with the specific committees, and her responsibilities were to make sure that their charges were identified and addressed, that officers understood their roles, and that those decisions were made and the results carried out. She knew the CIS’s operation and thinking, so she was in a good position to represent it in efforts to obtain funding from commercial and philanthropic sources. S. Kanowith-Klein prepared the initial brochures describing the CIS (Table V).

3. Finances and Fundraising

The budget in 1986, including the cost of the initial ACCI, came to about $50,000. In 1987, $70,000 was raised from commercial sources to supplement grant awards and expenditures

totaled $67,000. There was a carry forward of funds from 1986 of $14,525, and at the end of 1987, $17,739. The 1988 budget totaled $75,000, including ACCI expenses.

The dues in 1987 were $50 per year, which was raised in 1988 to $60.

4. Use of Management companies for the CIS and the ACCI

Initially, the membership listing was retained in the office of Noel Rose at Johns Hopkins. The organization and the management of the ACCI were carried out by Jack Wyatt in 1986, 1987, and 1988. In 1988, organizations were solicited that might take on CIS management as well as conference activities. The responses were from the Slack Company, the Federation of Societies for Experimental Biology (FASEB), and Jack Wyatt. Eventually, the decision was made to ask Slack with its wider capabilities to start with CIS management and ACCI meeting organization in 1989.

The CIS was eager to involve as many academically-oriented clinical immunologists as possible. A wide range of clinical fields were identified (Table IV). Individuals working in those fields were invited to join the CIS and take a role in the ACCI and other activities.

5. Membership

a. Overall
   The initial membership group based on the attendance at the 1986 meeting was about 300, which increased to approximately 450 by 1989.

   Several membership categories were recognized. Initially, most regular members were established scientists in immunology research with M.D. and/or Ph.D. degrees (and based at academic institutions). The clinical disciplines were mainly Internal Medicine or Pediatrics and a wide array of subspecialties. Associate members were individuals with M.D., Ph.D., or equivalent academic or professional degrees engaged in the practice of Clinical Immunology or with a demonstrated interest in the field.

   Trainee members were enrollees in predoctoral or postdoctoral training programs relevant to Clinical Immunology but not yet qualified to be a Regular or Associate member. Early on, provisions were made for fellowship awards to allow trainees who had submitted abstracts for poster presentations to be funded to attend the ACCI.
b. Ph.D. Scientists in the CIS
   It might have seemed that the "Clinical" title meant a restriction or major emphasis on clinical care responsibilities, which was not the case. "Clinical" conveyed a primary focus on immunology and related disease of human systems but was not exclusive. Studies of autoimmunity or cancer that were conducted in animals were often highly relevant to human situations and frequently reported at ACCI meetings. Some of the most active members had Ph.D. qualifications.

   All CIS meetings had many presentations based on collaborations by clinical and laboratory

investigators. Biostatistical Ph.D.s contributed to clinical studies, but not many became active CIS members.

c. Women in the CIS
Women with expertise and experience were involved in CIS from the beginning but they were much outnumbered by men. Relatively few women had graduated from medical schools in the 1950s and 1960s and had time to develop careers in biomedical sciences. In ensuing years, women have had increasing roles in the CIS.

Women scientists who did take active roles in CIS in the early years included Rebecca Buckley, chair of the AAI Clinical Immunology Committee and advisor to the CIS as an academic pediatrician. Mary Ellen Conley was already a leader in pediatric immunology with emphasis on primary immune deficiencies. Vicki Rubin Kelley was a major contributor to autoimmune disease studies. Janis Giorgi was widely known for her contributions to HIV/AIDS immune pathology. Charlotte Cunningham-Rundles focused on immune deficiency and reconstitution. Like Mary Ellen Conley, she later became a president of the CIS.

d. Scientists in Industry
Immunologists working in the pharmaceutical industry or in biomedical start-up or other companies were welcomed into the CIS. Many worked on novel therapeutic or diagnostic areas of great relevance to Clinical Immunology research and practice. Their membership was expected to be a major contributor with two-way traffic. On the one hand, the CIS could meet their needs for knowing when and where various types of clinical research was occurring, with the potential for collaborations as well as applications to clinical research and practice. On the other hand, such members provided critiques and constructive suggestions based on their experience in a different environment. Some had resources not available in most academic settings.

Pharmaceutical support for the CIS and its meetings and educational programs was welcome. Individual scientists from these companies participated in activities on the basis of their interests and professional qualifications.

6. Journals and Educational Activities

Early on, the CIS considered but deferred initiation of a societal journal. The *AAI Journal of Immunology* had a Clinical Immunology section, which the CIS co-sponsored for several years. The AAAAI had the *Journal of Allergy and Clinical Immunology*. These journals, however, did not meet the needs of the CIS, and it was judged that the interests of clinical immunologists were not being well-served by the AAI and AAAAI publications. Independently, *Journal of Clinical Immunology* was developed by Sudhir Gupta.

Initially, CIS communication needs were met by a twice-yearly CIS Newsletter and Information Update prepared by Susan Kanowith-Klein (Table V). Included were reports of meetings and workshops, new developments, and a news-and-views column from 1988 - 1992. Co-sponsorship of several journals were explored including the *Clinical Spectrum*, and later, *The Immunologist* with the IUIS.

Peter Lipsky's goal in 1990 was to provide timely scientific information as quickly and comprehensively as possible. There were many questions, however, relating to financing and whether it would be free or sold to members or others. Arrangements were made for the monthly publication, *Clinical Immunology and Immunopathology*, to be available at reduced rates from the Academic Press. Also, the *Journal of Clinical Immunology*, published every two months, was offered at reduced rates to CIS members. Another proposal was to have information from ACCI symposia and workshops published in a hardcover volume called *Immunology and Allergy Clinics of North America*, which was then being published by Saunders. This did not materialize and the publication ceased.

In his 1997 presidential message, Raif Geha indicated that there were four areas in which the CIS demonstrated great strength: Immunodeficiency, HIV/AIDS, Medical Laboratory Immunology, and Immunotherapeutics. He suggested that they could be the main themes of a CIS-sponsored journal but, of course, not the only areas to be covered. Subsequently, the CIS Publications Committee established *Clinical Immunology* as a transfer from the *Journal of Clinical Immunology and Immunopathology* edited by Noel Rose. This CIS publication flourished under the editorial leadership of Andrew Saxon and George Tsokos.

Clinical Immunology Society: The Early Years 1984 - 1989

D. 1986 - 1989 – Relationships with Existing Organizations, Conferences, and Certifications

In parallel, with the development of the CIS and ACCI in 1984-1989, many additional important issues and relationships required attention. These are discussed here.

1. Immunology - AAI

The AAI, which had been in existence for 50 years, was focused on basic immunological sciences and was the major representative of the field in the U.S. In 1976, the AAI had established a Committee on Clinical Immunology and Immunopathology; however, the AAI defined itself as a "scholarly society" and would not itself engage in certification but would be available to advise such certification boards in Immunology. We understand that they offered to contribute to such boards under the American Academy of Microbiology, the American Board of Pathology, and the American Board of Allergy and Immunology, if requested.

In the years 1984-1986 preceding the initial ACCI, J.L. Fahey, N. Rose, and H. McDevitt had many discussions with AAI Council members regarding the plans being developed for an Annual Conference of Clinical Immunology and the formation of a society to represent clinical immunology research and the clinical application of immunological advances. We emphasized that research would be fostered and reported on clinical issues, e.g., immune deficiencies, autoimmunity, hypersensitivity, the immunology of cancer, diabetes and endocrine diseases, and AIDS as a way of bringing together those working with patients and the immunology of human diseases.

A constant on the AAI side was Henry Metzger, executive secretary of the AAI. Henry was an early colleague of mine (JLF) at the NIH and had been a neighbor in Chevy Chase, Maryland. I felt that he would have preferred that the CIS be a part of the AAI or be definitely affiliated with AAI. He did not want to see a splintering (or a perception of splintering) of the field of Immunology research. However, he acknowledged the special additional features of clinical research and practice. Ultimately, Dr. Metzger was helpful in the launching of the CIS and ACCI and essential in maintaining full communication and cooperation between the AAI and CIS.

The AAI agreed to co-sponsor and publicize the original ACCI meetings of the CIS in 1986. In subsequent years, the AAI Council suggested that the CIS be recognized as an autonomous society formally affiliated with the AAI. The affiliation would involve the exchange of Council and Board members of each organization for the purpose of coordination and communication. The AAI Council also suggested on several occasions that the CIS arrange for its meetings to be

held in conjunction with the AAI. Other concerned scientists advised, however, that the identity of the CIS would be compromised by the dominance of the large, long-established AAI and the significance of CIS would not be well-appreciated. There was no acrimony. There may have been some concern about the CIS drawing off funding from pharmaceutical sources that was already going to the AAI, but this potential problem did not develop. Communication continued but was less formal than an affiliation might have required.

In the first years, CIS meetings were held in November or other fall months, since the AAI meetings were normally held in the spring. It was felt that holding CIS meetings within a month or two of the AAI's would reduce attendance at the CIS meetings. Max Cooper, who was a CIS Councilor, was president of the AAI in 1988, which facilitated communication in both directions and an understanding of the institutional similarities and differences.

The *Society for Biological Therapy* was developed as a separate organization about the same time as the CIS. Its organizers and functions were focused almost entirely upon immune-based therapies for a range of neoplastic diseases. The CIS continued to evolve with a broader array of activities that also included cancer diagnosis and treatment but did not develop a partnership with the Society for Biological Therapy.

2. Clinical Medicine - Subspecialties and Board Certification

A survey of organizations developing activities in this area was undertaken, and their leadership was contacted. In the 1980s, the American Boards of Internal Medicine (ABIM) and of Pediatrics (ABP) began to explore the recognition of subspecialty certification for physicians concentrating on the immunological aspects of specific organ system diseases. In the field of Allergy, the ABIM and ABP formed a conjoint board - the American Board of Allergy and Immunology (the ABAI).

a. Allergy:
   The AAAAI was the principal association representing the allergy practitioners and had a well-developed funding and clinical base. It included both pediatric and medical allergists. While the scientific base was not very broad or deep, it was an established, recognized society which advocated training programs.

   At one time, there was a joint meeting of the annual conference of the AAI, the CIS, and the AAAAI – an effort to bring together the major immunological societies. This meeting served to indicate the much broader array of immunological research and applications within the CIS domain and the more restricted focus of the AAAAI. This last organization, however, had hugely greater funding than the CIS.
b. Requirement for Establishing a New Specialty Field in Medicine:
   Contact was established with the American Board of Internal Medicine regarding the ground rules and procedures for establishing an Immunology subspecialty within the Boards of Internal Medicine. Other new clinical areas were also applying for subspecialty status such as Sports Medicine and Genetics. Moreover, the successful development 20 years earlier of Clinical Oncology was a positive model for Clinical Immunology.

There was a need to document examples of patient flow and training opportunities as well as special facilities including procedures and laboratory resources that would be better available in the context of this new specialty. Pediatric immunodeficiency disorders were a prime example. Recent laboratory and therapeutic advances could be documented (Table II).

c. Organ-Based Medical and Pediatric Subspecialties:
Boards of various subspecialties such as Rheumatology and Dermatology included some immunological components. However, neither was primarily focused in this area. Discussions with the National Boards about setting up a separate Clinical Immunology training and examination system were slowed, in part, by the broadening of existing subspecialties to include Immunology and partly because the clinical training in special fields of Medicine required a patient flow, such as autoimmune diseases seen in Rheumatology, multiple sclerosis in Neurology, viral diseases seen in Infectious Diseases, or neoplasia in Oncology. In fact, many Departments of Medicine and of Pediatrics added Immunology to existing Divisions; e.g., the Division of Rheumatology and Immunology and the Division of Clinical Immunology and Allergy. However, efforts to establish totally independent Divisions of Clinical Immunology did not fit well with the established patient flows and administrative relationships. Special procedures like transplantation immunology were created in both medical and surgical contexts. Bone marrow transplantation was a vibrant specialty of Immunology which required special knowledge and was administratively located in the Divisions that developed the needed competence.

3. Medical (Clinical) Laboratory Immunology

Clinical Laboratory Immunology was an important element in the CIS. Laboratory measurements were essential for disease characterization and therapeutic evaluations in all the clinical areas of Immunology. Medical (Clinical) Laboratory Immunology needed to be recognized as a specialty or subspecialty in Laboratory Medicine. Training programs and certification procedures needed to be established.

Immunological assessments in hospitals and other clinical settings in the early 1980s were cobbled together from Hematology (white-blood-cell counts and differentials for lymphocyte, neutrophil, monocyte percentage and numbers), Chemistry (albumin/globulin levels or ratios, rarely gamma globulin levels by electrophoresis), and Microbiology (diagnostic tests for specific organism detection but rarely quantification or characterization of antibody levels or vaccine effectiveness).

The American Board of Dermatology explored a Special Qualification in Dermatological Immunology/Diagnostic and Laboratory Immunology. The American Board of Pathology outlined a Special Qualification Certificate in Immunopathology that could be obtained by additional training for M.D.s already certified in Anatomic Pathology or in Clinical Pathology. Furthermore, the conjoint American Board of Allergy and Immunology, which had its own

clinical certification procedures, also offered a Special (additional) Qualification in Diagnostic Laboratory Immunology for M.D.s with training in current laboratory methods relevant to Clinical Immunology.

All of the above programs were just being developed, and their quality, content, consistency, and value from practical standpoints still remained to be established. All required standard and appropriate prior medical training and certification. Thus, all Ph.D.s and those without the specific specialty clinical training and certification were excluded.

An Accredited Postdoctoral Residency Program and the American Board of Medical Laboratory Immunology (ABMLI) were established by the American Academy of Microbiology in the mid-1980s. They were patterned on the well-established training program of the American Board of Medical Microbiology. Didactic instruction, laboratory bench experiences, and clinical laboratory management phases conducted at two or more institutions to be sure training experiences in all major areas of Medical Laboratory Immunology were covered. Trainees would be expected to:

a. Develop and manage a Medical Immunology Laboratory and provide diagnostic service that would support clinical diagnoses, therapeutic evaluations and epidemiological investigations;
b. Develop and communicate reliable interpretations of immunological data and other relevant information for use in the management and treatment of patients and in solving epidemiological problems;
c. Plan and conduct effective training programs in Medical Laboratory Immunology for technical and professional personnel;
d. Design and conduct immunological research to solve medical and public health problems.

A Medical Laboratory Immunology training program had been developed along these lines at UCLA with the cooperation of the Departments of Medicine, Pediatrics, Pathology, Surgery (Tissue Typing Laboratory), and Microbiology, Immunology, and Molecular Genetics, to provide essential training for Ph.D. and M.D. scientists for careers in science and medicine.

In fact, there were two categories of Immunology laboratory needs. One was for Medical Laboratory Immunology to conduct widely usable immune measurements with all the requirements for quality control, standardization, and definition of normal ranges (with information about the significance of out-of-range values) for various populations – infant and adult – and other quality-control features necessary in all medical laboratory fields.

The second was the need for laboratory research conducted in conjunction with clinical research, which addresses questions about parameters that might (or might not) have direct clinical applications. Laboratories that could develop new procedures or modify old ones were mainly in clinical research groups. By-and-large, hospital service laboratories would institute well-developed assays, but few were contributing new immunologic methodologies. The whole

field of lymphocyte sub-typing, with different functions, different stages of maturation, etc., stimulated the expansion of flow cytometry for diagnostic and preparative procedures. The roles of cytokines, chemokines, and receptor identification and functions was becoming clearer and were ripe for definition in the contexts of Clinical Immunology practice. Certainly, a lot more could be done in the development of laboratory procedures with major clinical importance. How was this essential field to be recognized, organized, set up for training, and rewarded for contributions to Clinical Immunology?

A challenge for the CIS was to help develop better Medical (Clinical) Laboratory Immunology training programs and foster recognition for this field. CIS members could be encouraged to get certification in these settings so as to strengthen the practice of Medical (Clinical) Laboratory Immunology in the United States. Training mostly was done in hospital-based Departments of Pathology or Laboratory Medicine, within the old disciplines of Microbiology, Chemistry, and Histology/Cytology, which were skimpy in Immunology. The CIS faced the challenge of helping achieve some recognition for the distinctiveness of Laboratory Immunology assessments for both diagnoses and the evaluation of therapies. This effort involved dealing with the already established training systems as well as with certification contexts at the national and, especially, state levels, where laboratory components of medical practice were required to have official approval. The United States government had a similar but separate system for Veteran and other federal medical facilities. The ABMLI certification was recognized in this Federal context.

To address the field of Medical Laboratory Immunology, the CIS began to consider developing training programs, certification procedures, and the provision of workshops, courses, conferences, publications, and other means of both broadening the availability of quality immunological laboratory testing and introducing and validating new procedures.

There was a need to get past the restrictive term – Diagnostic Laboratory. Yes, diagnosis was one function of immunological procedures. However, with the introduction of a wide range of therapeutic interventions, the assessments of immune-based therapies became crucial. Clinical parameters were often imprecise and delayed in appearance. An intervention with or without benefit can often be detected much more rapidly by a laboratory measurement than by waiting for a clinical upturn (or downturn). Laboratory measurements are probably not greatly subject to the placebo effect.

In subsequent years, CD4 T cell levels of 200/mm^3 or lower in HIV-seropositive patients were acceptable indications for the institution of prophylactic antibiotics, and later, for the institution of anti-retroviral therapy as well as for the non-clinical definition of AIDS.

4. International - International Union of Immunological Societies (IUIS)

a. While the CIS primarily functioned from its inception as a North American-based institution, it had interest in and contacts with comparable or related programs and individuals in other nations. Many ad hoc contacts already existed between CIS

members and colleagues in other countries. International and WHO programs with immunological content were developing, especially in relation to HIV/AIDS. Many CIS members were active participants in such international activities.

Separately, the CIS had the opportunity to contribute to education, training and applications of clinical immunology in international contexts through active participation in programs of the International Union of Immunological Societies (IUIS).

b. The International Union of Immunological Societies (IUIS) was founded in 1970 by John Humphrey (Chief, Department of Immunology at the National Institute for Medical Research, Mill Hill, London, England) and Bernard Cinader of Canada and a world-wide network of immunological colleagues. The first IUIS meeting was held in Washington, D.C. (1971), and has continued subsequently at three-year intervals. The general purpose was to facilitate the advancement of immunological research and to share the new knowledge with all countries. The IUIS was also intended to bring people from all countries together in spite of international tensions and political and economic differences.

   Many members of the CIS in the 1980s were actively involved in international efforts because so much of the world's HIV/AIDS research was being done in and with the United States.

IUIS officially recognized only one society in each country, and the AAI was the United States representative. However, the AAI offered to recognize the CIS as the clinical arm of its activities, thus allowing the CIS to become a significant partner with the IUIS.

In parallel with the CIS development and the first ACCI in 1986 was a Conference on Clinical Immunology held in Toronto, Canada, on July 5-6, 1986, that was sponsored by the IUIS. The organizer was W. Pruzanski. It was a new departure for the IUIS, which had previously considered Immunology as one big bag! This conference emphasized the fact that immunologists in other countries (other than the U.S.) also regarded Clinical Immunology as important and as a stand-alone topic.

As the CIS developed, it concentrated its association with the IUIS through membership and active participation in the IUIS Clinical Immunology Committee. Both John Fahey and Noel Rose helped to develop international conferences on Clinical Immunology in association with the IUIS international meetings, usually in the day or two preceding the general International Immunology Conference.

Jacob Natvig and other presidents of the IUIS were attentive to the needs in many countries for clinical applications of immunological research. Dr. Natvig proposed that the IUIS and the CIS join in the publication, the Immunologist, in the 1990s. This publication was tried for about three years but was discontinued due to low circulation and a broad focus that failed to convey research nuances in specific research areas.

International linkages provided continuing information exchange on the development of clinical immunology training and certification procedures in other countries. Discussions involved Ron Thompson and Helen Chapel from Great Britain and Vivian Wells and John Bradley of Australia. Latin American immunologists such as Roberto Kretschmer and Jose R. Villarreal of Mexico and Nicolas E. Bianco and Irma Machado of Venezuela were especially active. They and their national colleagues fostered Clinical Immunology training and certification procedures in their home countries.

Clinical Immunology Society: The Early Years 1984 - 1989

E. Summary and Opportunities

1. Over a period of six years (1984-1989), as many as possible of the clinicians dealing with diseases having significant immunologic components as well as the immunologists active in laboratory research on the human immune systems in the United States and Canada were consulted and invited to participate in the development of a Clinical Immunology Society and an Annual Conference on Clinical Immunology.
2. Immunology was emphasized as an important component in most fields of clinical medicine. The Medical (Clinical) Immunology Laboratory was an essential part of this enterprise.
3. The Clinical Immunology Society (CIS) was created to foster research and education on disease recognition, pathogenesis and especially on therapy.
4. A core structure was established to plan meetings and advance the goals of the CIS.
5. A system of shared leadership was planned to involve a progression of elected officers to facilitate growth and utilize the talents of many individuals.
6. The existence of many medical contexts for clinical applications of Immunology was recognized as well as opportunities for individual leadership in specific areas.
7. An Annual Conference on Clinical Immunology was initiated in 1986 and conducted annually in the following years.
8. Interested immunologists in other countries were included in planning discussions and the annual conferences sponsored by the CIS. Linkage was established with the International Union of Immunological Societies
9. The issues important to the validity and vitality of the CIS were developing concurrently with the other professional demands on the time and creativity of the CIS Leadership. All of the participants also had their own research agendas, teaching responsibilities and, in some cases, clinical duties to conduct while helping to found the CIS.

There were many unfinished issues:

- Recognition of Clinical Immunology as a specialized area of clinical practice based on: (1) a defined organ system; and, (2) a comprehensive basic science area; (3) the growth of immune-based therapies; and, (4) unique medical laboratory methodologies needed to support clinical immunology research and practice.
- Creation of clinical training programs to foster high standards in the clinical applications of immunology.
- Development of Medical (Clinical) Laboratory Immunology training and practice as an essential component and partner in Clinical Immunology practice and research.

- Continued negotiation of mutually advantageous associations with already existing clinical specialty societies, recognizing the multifaceted nature of disease in man and the importance of immunology in many areas.

Clearly a start had been made. There were enormous opportunities for innovation, for growth, and contributions professionally and personally – at the interface of Immunology and Medicine.