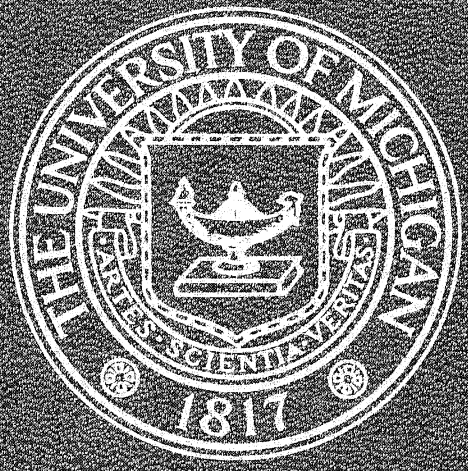
THE UNIVERSITY OF MICHIGAN

Department of Pathology

ANNUAL REPORT



1 July 1990 - 30 June 1991

THE UNIVERSITY OF MICHIGAN

Department Of Pathology

ANNUAL REPORT

1 July 1990 - 30 June 1991

The University of Michigan Department of Pathology Annual Report

This Report was produced by Personal Computer and Network Systems, a division of the Department of Pathology, University of Michigan.

Coordinator:
Mary Anne Tishma

Technical Consultants:
Jim Dignan
Peggy Otto
Tom Peterson

LIST OF FACULTY

LIST OF FACULTY

Name	Rank	Institutional Affiliation
Abell, Murray R.	Professor Emeritus	The University of Michigan
Abrams, Gerald D.	Professor	The University of Michigan
Annesley, Thomas M.	Associate Professor	The University of Michigan
Appelman, Henry, D.	Professor	The University of Michigan
Barnes, Barbara A.	Assistant Professor	The University of Michigan
Barr Jr., Mason+	Professor	The University of Michigan
Beals, Theodore F.	Assistant Professor	Veterans Administration Medical Center
Blaivas, Mila I.	Clinical Assistant Professor	The University of Michigan
Bonadio, Jeffrey	Assistant Professor	The University of Michigan
Capps, Rodney D.	Assistant Professor	The University of Michigan
Chensue, Stephen W.	Assistant Professor	Veterans Administration Medical Center
Courtney, Richard M.*	Assistant Professor	The University of Michigan
D'Amato, Constance J.	Assistant Professor	The University of Michigan
Davenport, Robertson	Assistant Professor	The University of Michigan
de la Iglesia, Felix**	Adjunct Research Scientist	Warner-Lambert;Parke Davis
Dixit, Vishva M.	Assistant Professor	The University of Michigan
Elner, Victor M.++	Assistant Professor	The University of Michigan
England, Barry G.	Associate Professor	The University of Michigan
Fantone, Joseph C.	Associate Professor	The University of Michigan
Flint, Andrew	Associate Professor	The University of Michigan
Frank, Thomas S.	Assistant Professor	The University of Michigan
Friedman, Bruce A.	Professor	The University of Michigan

Name	Rank	Institutional Affiliation
Giacherio, Donald	Assistant Professor	The University of Michigan
Gikas, Paul W.	Professor	The University of Michigan
Glover, Thomas W.+	Assistant Professor	The University of Michigan
Hanks, Carl T.*	Associate Professor	The University of Michigan
Hanson, Curtis A.	Assistant Professor	The University of Michigan
Headington, John T.	Professor	The University of Michigan
Heidelberger, Kathleen P.	Professor	The University of Michigan
Hendrix, Robert C.	Professor Emeritus	The University of Michigan
Hicks, Samuel P.	Professor Emeritus	The University of Michigan
Hinerman, Dorin L.	Professor Emeritus	The University of Michigan
Johnson, Kent J.	Professor	The University of Michigan
Judd, W. John	Professor	The University of Michigan
Keren, David F.	Adjunct Professor	The University of Michigan
Killen, Paul D.	Assistant Professor	The University of Michigan
Kunkel, Steven L.	Associate Professor	The University of Michigan
Lindsten, Tullia	Assistant Research Scientist	The University of Michigan
Lloyd, Ricardo V.	Associate Professor	The University of Michigan
Lowe, John B.	Assistant Professor	The University of Michigan
McClatchey, Kenneth D.	Associate Professor, Associate Chairman, Director, Clinical Laboratories	The University of Michigan
McKeever, Paul E.	Associate Professor	The University of Michigan
Midgley, A. Rees	Professor	The University of Michigan
Miller, Richard A.	Assistant Professor	The University of Michigan
Mitra, Raj S.	Assistant Research Scientist	The University of Michigan

Name	Rank	Institutional Affiliation
Naylor, Bernard	Professor	The University of Michigan
Nickoloff, Brian J.	Associate Professor	The University of Michigan
Nunez, Gabriel	Assistant Professor	The University of Michigan
Oberman, Harold A.	Professor and Associate Director, Clinical Laboratories	The University of Michigan
Phan, Sem H.	Associate Professor	The University of Michigan
Pierson, Carl L.	Assistant Professor	The University of Michigan
Rachmaninoff, Nikolai	Lecturer	The University of Michigan
Regezi, Joseph A.*	Associate Professor	The University of Michigan
Remick, Daniel G.	Assistant Professor	The University of Michigan
Repola, Kenneth L.	Lecturer	The University of Michigan
Ross, Charles W.	Lecturer	The University of Michigan
Rowe, Nathaniel H.*	Professor	The University of Michigan
Schmidt, Robert W.	Professor	The University of Michigan
Schnitzer, Bertram	Professor	The University of Michigan
Selvaggi, Suzanne M.	Assistant Professor	The University of Michigan
Shanberge, Jacob N.	Clinical Professor	William Beaumont Hospital
Sheldon, Susan	Assistant Professor	The University of Michigan
Shope, Thomas C.+	Associate Professor	The University of Michigan
Shu, Suyu+++	Associate Professor	The University of Michigan
Silbart, Lawrence K.	Research Investigator	The University of Michigan
Silverman, Eugene M.	Clinical Associate Professor	The University of Michigan
Smolen, James E.+	Associate Professor	The University of Michigan
Stoolman, Lloyd M.	Assistant Professor	The University of Michigan
Till, Gerd O.	Associate Professor	The University of Michigan

Name	Rank	Institutional Affiliation
Varani, James	Associate Professor	The University of Michigan
Ward, Peter A.	Professor and Chairman	The University of Michigan
Warren, Jeffrey S.	Assistant Professor	The University of Michigan
Weatherbee, Lee	Associate Professor	Veterans Administration Medical Center
Weiss, Bernard	Professor	The University of Michigan
Weiss, Sharon W.	Professor and Director, Anatomic Pathology	The University of Michigan
Wolter, J. Reimer++	Professor	The University of Michigan

* Joint Appointment, Dental School
** Clinical Appointment, Warner-Lambert, Parke Davis
\+ Joint Appointment, Department of Pediatrics and Communicable Diseases
++ Joint Appointment, Department of Opthalmology
+++ Joint Appointment, Department of Surgery

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MISSION STATEMENT

MISSION STATEMENT

The goals of the Department of Pathology are inseparable from goals of the Medical Center: leadership in education, research, and service. In addition, by virtue of its position, the Department is dedicated to serve in a unifying role within the university medical community.

Education. A variety of educational experiences is offered with the objective that persons destined for clinical service may benefit from the scientific literacy gained from exposure to research, and those destined for research careers have a better understanding of disease-related problems. Excellence in teaching is also promoted as an integral part of clinical service; education is what pathologists, as consultants, must do every day.

Research. It is the obligation of a university to contribute to knowledge rather than merely to propagate it. By encouraging research programs we also aim to foster a research mentality among all faculty and trainees, with the objective that they acquire useful habits of analytical thought, become more innovative, and become more likely to devise and to employ state-of-the-art diagnostic developments.

Service. Clinical service, largely diagnostic in nature, is a function that sets the Pathology Department apart from other basic science departments. The Department's objective is to maintain leadership in this field through its emphasis on research, education, innovation, and constant quality assessment, and by so doing to attract the skilled personnel that are the mainstay of this operation.

Unifying role. Because pathology, more than any other discipline, bridges the domains of basic and clinical science, the Department takes advantage of its unique position to encourage interdisciplinary projects and interdepartmental cooperation, thereby assuming a cohesive, collegial, and unifying role within the university medical community.

DEPARTMENTAL OVERVIEW

DEPARTMENTAL OVERVIEW
1990/91

The Department of Pathology continues to be strong and vibrant. The major problems we currently face are related to space constraints effecting both the service and research activities of the Department. The continued consolidation of special limited function laboratories (most recently the Gyn-Endocrine and Pediatric Virology) into the central Pathology Laboratories, together with the yearly growth of clinical diagnostic services has left us space-poor. With expected continued growth of the clinical service functions (due to the inpatient and ambulatory care programs) and plans for physical expansion (Cancer-Geriatric Center, as well as the Taubman Clinics), solutions to the constraint of space for the clinical laboratories will have to be found. The lack of available space for growth of the Department's research programs is also a matter of serious concern. Although much apprehension has developed regarding the impact of implementation of the Resource Based Relative Value Scales, it is possible that this change will not have a substantial adverse impact on our current revenue flow, although this requires very careful watching.

In January, 1991, we were fortunate to recruit from Washington University (St. Louis) Dr. Gabriel Nunez, who has taken charge of the new Molecular Diagnostic Program. This activity involves the application of complex molecular diagnostic techniques to the clinical service arena as well as providing an important foundation for the teaching of residents. This program is supervised by Dr. Nunez, with careful integration into Clinical Pathology (with Dr. Hanson) and Anatomic Pathology (with Dr. Frank), as well as a strong linkage with the Departmentally based Molecular Biology group.

The Anatomic Pathology Division continues to flourish under the leadership of Dr. Sharon Weiss. The establishment of the fellowship program in Surgical Pathology has been an instant success and the positions are filled with outstanding individuals. As a tribute to Dr. Weiss and her colleagues, Ann Arbor has been designated as one of four permanent sites for the Summer Course in Surgical Pathology, sponsored by the United States and Canadian Academy of Pathology Division of the International Academy of Pathology. This reflects the outstanding success of this course that has been held in Ann Arbor during the past two summers.

As of September 1, 1991, the Division of Clinical Pathology ha had the advantage of the leadership of Dr. Curtis Hanson, who replaced Dr. Kenneth D. McClatchey after the latter's eight years of dedicated and effective service. Dr. Hanson has initiated a series of changes in this Division, the result of which will be to strengthen the service and teaching functions of this Division. As indicated above, he also will be assisting in the important development of the Molecular Diagnostic Laboratory. Currently under exploration is the possibility of obtaining external support for academic fellowship training in various sections of Clinical Pathology.

Teaching functions of the Department of Pathology are well served at all levels. The faculty is working carefully to develop a plan for implementing a curricular change in which pathology teaching will probably follow along the lines of an organ system approach during the Second Year of Medical Students, and the introduction of basic concepts of Pathology for First Year Medical Students. The Graduate (Ph.D.) Program in Experimental Pathology now has eight highly qualified students, including one MSTP (M.D./Ph.D.) student. This program has already enriched the teaching environment of the Department and Medical School and will probably continue to act as a magnet because of the orientation of the educational activities towards an understanding of disease-related topics.

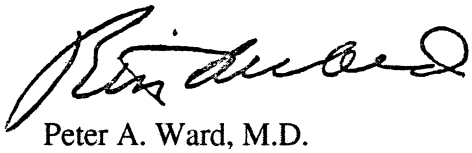
The Research enterprise of the Department continues to flourish as reflected by the research budget (exceeding six million dollars/year), the prolific publications of the faculty and the recognition of many of our faculty members as being international experts in many different areas. The success of the

research activities is also affected in the high number (approximately 32) of postdoctoral fellows in the Department.

In general, the Department of Pathology seems to be doing very well academically. Medical students recruited into our Residency Training Program are of very high caliber and have outstanding credentials. The Department is making an increased effort, through Dr. Fantone who is Residency Program Director, to provide guidance to entering House Officers and help them identify a mentor who can assist the resident in selecting a topic for pursuit of scholarly interests. Attention to this matter will allow our residents to achieve self-distinction long before completion of the Residency Training Program.

Finally, the M-Labs Program is strong and flourishing. Its new Director is Dr. Eugene M. Silverman. During the course of the Winter of 1991/92, we are carefully evaluating the M-Labs Program in order to determine its directions over the next five years and how M-Labs can be more tightly integrated into the academic programs which feature both service and teaching.

Respectfully Submitted,



Peter A. Ward, M.D.
Godfrey D. Stobbe,
Professor of Pathology
Professor and Chairman

INDIVIDUAL FACULTY REPORTS

GERALD D. ABRAMS, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Services - 2 1/2 months (sabbatical leave - six months).
B. Necropsy Service - on call.
C. Pathologist, Cardiac Transplant Team - full time.
D. Consultant for Gastrointestinal Pathology - full time.
E. Consultant for Cardiovascular Pathology - full time.

II. TEACHING ACTIVITIES:

A. Freshman Medical Class:
   1. ICS-500, 501 Sequence Coordinator and Lecturer, "Basic Concepts of Disease" CPC's - 26 contact hours.
B. Sophomore Medical Class:
   1. ICS 600, 601 - CPC's - seven contact hours.
   2. Pathology 600 lectures - seven contact hours.
C. Senior Medical Class:
   1. Pathology Clerkship Mentor.
D. Graduate School/Dental School/College of LS&A:
   1. Pathology 580 (Graduate School), Course Director, Lecturer - 18 contact hours.
   2. Pathology 630 (Dental School), Lecturer - two contact hours.
   3. Environmental and Industrial Health 518 (SPH) - Lecturer 1 1/2 contact hours.
   4. Biology 224 - (LS&A) Lecturer - 1 1/2 contact hours.
E. Hospital Conferences:
   1. Cardiovascular Pathology Conference - monthly.
   2. Internal Medicine CPC - monthly.
   3. Internal Medicine Necropsy Review - monthly.
   4. Gynecologic Pathology, Non-oncologic - monthly.
F. House Officers:
   1. Training in Surgical and Necropsy Pathology.
G. Invited Lectures:
   1. ASCP/CAP Performance Improvement Program Seminar on Gastrointestinal Pathology, October 30, 1989, Washington, D.C.
H. Medical Class of 1992 - Outstanding Lectureship Award.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. University of Michigan Cancer Center, Tissue Procurement Core - NIH 1 - P30 CA 46592.
B. National Collaborative Diagnostic Imaging Trial - NIH 1 - U0l CA 49077.

C. Technetium - 99M Labelled Monoclonal Antibody in Patients With Peripheral Vascular Disease. Centocor C00 50101.

PROJECTS UNDER STUDY:

A. Director - Tissue Procurement Core - U of M Cancer Center.
B. Pathologic-Radiologic Correlation in Pancreatic Neoplasms (with I. Francis).
C. Toxicity of Mitometh (with D.E. Schteingart).
D. Natural History of Myocarditis (multicenter study).
E. Laser Ablation of Accessory Atrioventricular Pathways (with C.D. Schuger, Wayne State University).
F. Reinnervation of Transplanted Human Heart (with M. Schwaiger).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

1. Member, Pathology Doctoral Program Committee.
2. Member, Pathology House Officer Selection Committee.

MEDICAL SCHOOL/HOSPITAL:

1. Member, Historical Center for the Health Sciences Liaison Committee.
2. Member, Hospital Ethics Committee.
3. Member, Inteflex Policy Committee.

REGIONAL AND NATIONAL:

1. President, Gastrointestinal Pathology Society.
2. Editorial Board, "Modern Pathology".
3. Reviewer, "Ophthalmology".
4. Reviewer, "Archives of Pathology and Lab Medicine".
5. Deputy Medical Examiner, Washtenaw County.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Yuzbasiyan-Gurkan, V., Brewer, G.J., Abrams, G.D., Main, B. and Giacherio, D.: Treatment of Wilson's disease with Zinc: V. Changes in serum levels of lipase, amylase, and alkaline phosphatase in patients with Wilson's disease. J. Lab. Clin. Med. 1989;114:520-526.
2. Kluger, M.J., Conn, C.A., Franklin, B., Freter, R. and Abrams, G.D.: Effect of gastrointestinal flora on body temperature of rats and mice. Am. J. Physiol. 1990;258:R552-R557.
3. Bolling, S.F., Putnam, Abrams, G.D., and Deeb, G.M.: Lack of correlation between hemodynamic changes and endomyocardial biopsy findings. Ann. Thor. Surg.. In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Schwaiger, M., Hutchins, G.D., Kalff, V., Rosenspire, K., Haka, M.S., Mallette, S., Deeb, G.M., Abrams, G.D. and Weiland, D.: Evidence for regional reinnervation of the transplanted human heart by positron emission tomography. J. Clin. Invest.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Sulavik, D., Caplan, M. and Abrams, G.: Clinical utility of postmortem cultures. Mod. Path. 1990;3:97A.
2. Abrams, G.D. (Book Review): "Interventional and Surgical Cardiovascular Pathology: Clinical Correlations and Basic Principles", by Schoen F.J. (ed), Am. J. Surg. Path. In Press.
3. Abrams, G.D.: "Pathophysiology: Clinical Concepts of Disease Processes", in, Price, S.A. and Wilson, L.M., (eds), C.V. Mosby, In Press.
   - Chapter 1 - Introduction to General Pathology.
   - Chapter 2 - Heredity, Environment, and Disease.
   - Chapter 3 - Cellular Injury and Death.
   - Chapter 4 - Inflammation and Repair .
   - Chapter 5 - Response of the Body to Immunological Challenge.
   - Chapter 6 - Response of the Body to Infectious Agents.
   - Chapter 7 - Disturbances of Circulation.
   - Chapter 8 - Disturbances of Growth, Cellular Proliferation, and Differentiation.

THOMAS M. ANNESLEY, PH.D.
ASSOCIATE PROFESSOR OF CLINICAL CHEMISTRY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Director, Drug Analysis and Toxicology Laboratory.
B. Section Head, Biochemistry Laboratories.
C. Consultant to Veterans Administration Hospital, Ann Arbor, Michigan.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students:
   1. Lecturer, Pathology 600 Course.
   2. M1 Clerkship, Clinical Chemistry/Toxicology
B. House Officers:
   1. Lecturer, Clinical Pathology Grand Rounds.
   2. Lecturer, Clinical Pathology Didactic Lecture Series.
   3. Daily sign-out and interpretation of Laboratory Results.
C. Graduate Students:
   1. Thesis Committee, Biomedical Engineering.
      Se-Hwan Paek; "An Immunosensor with a Heterobifunctional Enzyme Conjugate as Signal Generator"

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Erythromycin Breath Test as a Predictor of Cyclosporine A Bioavailability. Clinical Research Center NIH M01 RR00042. Co-Investigator.
B. Measurement of Drugs in Saliva. DHHS PHS Phase I Grant. Co-Investigator/Consultant.
C. Multicenter Trial of OG 37-325 in Renal Allograft Recipients. Sandoz Pharmaceutical. Co-investigator.

PROJECTS UNDER STUDY:

A. Microbore Applications to the analysis of drugs.
B. Distribution of cyclosporine and metabolites in blood and tissues.
C. Measurement of therapeutic drugs using alternative fluids beyond serum.
D. Esoteric analysis of drugs by gas chromatography/mass spectrometry.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Drug Analysis an Toxicology Laboratory.
B. M-Labs Technical Group.
C. Pathology Associates.

MEDICAL SCHOOL/HOSPITAL:

A. Standardization of Procedures Committee.

REGIONAL AND NATIONAL:

A. Executive Committee, National Therapeutic Drug Monitoring and Clinical Toxicology Division American Association for Clinical Chemistry.
B. National Awards Committee, American Association for Clinical Chemistry.
C. National Abstracts Committee, American Association for Clinical Chemistry.
D. Experts Panel Committee, American Association for Clinical Chemistry.
E. National Meeting Planning Group, Clinical Ligand Assay Society.
F. Education Committee, Michigan Section, American Association for Clinical Chemistry.
G. College of American Pathologists Chemistry Reference Laboratory.
H. Member, NCAA Drug Testing Team.
I. ETS Advisory Board, Syva Corporation.
J. Member, Academy of Clinical Laboratory Physicians and Scientists.
K. Member, American Association of Pathologists.
L. Member, American Association for Advancement of Science.
M. Member, Clinical Ligand Society.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Clinical Chemistry, Editorial Board.
B. Therapeutic Drug Monitoring, Editorial Board.
C. Biomedical Chromatography, Editorial Board.
D. Therapeutic Drug Monitoring and Clinical Toxicology Newsletter, Editorial Board.

OTHER

A. Clinical Chemistry, Reviewer.
B. Mayo Clinic Proceedings, Reviewer.
C. Journal of Clinical Immunoassay, Reviewer.
D. Journal of International Federation of Clinical Chemistry, Reviewer.
E. Biomedical Chromatography, Reviewer.
F. Therapeutic Drug Monitoring, Reviewer.
G. Drugs and Aging, Reviewer.

INVITED LECTURES/SEMINARS:

1. "Analysis and Clinical Utility of Trace Metals", University of Windsor, Canada, January, 1991.
2. "The Forensic Toxicology Certification Process--Great Opportunity or Excedrin Headache?" Meeting of the American Association for Clinical Chemistry, Detroit, Michigan, February, 1991.

3. "Kinetic Interaction of Microparticles in Solution (KIMS). The On-Line Drugs Abuse Testing System". Roche Analytical Systems National Seminar, Novi, Michigan, June, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Watkins, P.B., Hamilton, J.A., Annesley, T.M., Ellis, C.N. and Voorhees, J.J.: The erythromycin breath test as a predictor of cyclosporine blood levels. Clin. Pharm. Ther. 1990;48:120-129.
2. Bleske, B., Carver, P., Annesley, T. and Morady, F.: The effect of Ciprofloxacin on the pharmacokinetic and ECG parameters of quinidine. J. Clin. Pharmacol. 1990;30:911-915.
3. Vas Binder, E. and Annesley, T.: Liquid chromatographic analysis of mexiletine in serum with alternate application to tocainide, procainamide; and N-acetylprocainamide. Biomedical Chromatogr. 1991;5:19-22.
4. Ellis, C., Fradin, M., Messana, J., Brown, M., Siegel, M., Hartley, H., Rocher, L., Wheeler, S., Hamilton, T., Parish, T., Duell, E., Annesley, T., Cooper, K. and Voorhees, J.: Cyclosporine for plaque-type psoriasis. Results of a multidose, double blind study. New Eng. J. Med. 1991;324:277-284.
5. Bolling, S.F., Lin, H., Annesley, T.M., Boyd, J.A., Gallagher, K. and Levy, R.: Local cyclosporine immunotherapy of cardiac transplants in rats enhances survival. J. Heart Transplant, In Press.
6. Schramm, W., Annesley, T.M., Siegel, G.J., Sackellares, J.C. and Smith, R.H.: Measurement of phenytoin and carbamazepine in an ultrafiltrate of saliva. Ther. Drug Monitor., In Press.

HENRY D. APPELMAN, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. General surgical pathology - 5 1/2 months.
B. Gastrointestinal and hepatic pathology consultation services - full time.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students.
   1. Pathology 600 - nine full class lectures.
   2. Laboratory Instructor, Pathology 600 - one semester.
   3. Pathology 630 (dental) - three full class lectures.
   4. Senior medical student, elective rotation in pathology, supervisor 1 month.

B. House Officers:
   1. Autopsy service tutoring, one week
   2. Surgical pathology diagnosing room instruction for assigned house officer - 5 1/2 months.
   3. Gastrointestinal and hepatic pathology tutoring - full time.
   4. Mentor for two house officers and three fellows in gastrointestinal and liver pathology subspecialty rotations - four months total.
   5. Formal Lectures on GI and Liver Pathology - four hours.

C. Interdepartmental:
   1. Medical Gastrointestinal Pathology Biopsy Conference - 2nd and 4th Wednesday of each month.
   2. G-I Tumor Conference - 4th Tuesday of each month.
   3. Liver Transplant Conference - Every other Thursday.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT: None.

PROJECTS UNDER STUDY:

A. Hepatic histopathologic changes in methotrexate - treated psoriatics, with A. Flint and members of the Gastroenterology Division.
B. Appendiceal epithelial neoplasia.
C. Peptic-associated and Helicobacter-associated gastritis and duodenitis with Grace Elta, Jeffrey Barnett and Tim Nostrant.
D. Interactive Computer Based Diagnostic Program in Colorectal, Appendiceal and Anal Pathology with Bharat Nathwani at USC, plus Intellipath.

E. Thymosin Treatment of Chronic Hepatitis B with Milton Mutchnick (paper accepted for publication, see below).
F. Liver Transplantation for Hepatitis B Disease with Mike Lucey, Keith Henley Bob Merion and Dave Graham.
G. Chronic gasritis in Michigan, with Paul Mazzara.
H. The appendix in ulcerative colits, with John Goldblum (Abstract accepted for presentation as a poster at the annual meeting, American Society of Clinical Pathologists, New Orleans, LA, September 24, 1991).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chairman, Advisory Committee on Appointments, Promotions and Titles.

MEDICAL SCHOOL/HOSPITALS:

A. Member, Cancer Work Group, University Hospital.
B. Member, Tissue and Invasive Procedure Committee, University Hospital.

REGIONAL AND NATIONAL:

A. Reviewer of manucripts for Archives of Pathology and Laboratory Medicine, Cancer, Human Pathology, Gastroenterology, and Am J of Gastroenterology.
B. Chairman, Publications Committee and Member, Executive Committee, Gastrointestinal Pathology Society.
C. Coordinator for Pathology, Randomized Therapeutic Trail in Cancer of the Esophagus, International Organization for Statistical Studies of Diseases of the Esophagus, Paris, France.
D. Visiting Pathologist for Regional Workshops on Pathologic Diagnosis in Inflammatory Bowel Disease, sponsored by the Crohn's and Colitis Foundation of America and the University of Chicago.
E. Member, Education Committee, United Staes-Canadian Academy of Pathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Seminar, "The Biopsied Stomach Need Not Be a Diagnostic Nightmare, Although It Certainly Drives Us Crazy at Times", USCAP Course: Diagnostic Pathology '90, Ann Arbor, Michigan, August, 1990.
2. Lecture, "Surveillance in Ulcerative Colitis", Symposium on Controversies in IBD, October 6, 1990, Quebec City, Quebec, Canada.
3. Short Course, "Inflammatory Conditions of the Esophagus, Stomach and Duodenum", USCAP, Chicago, Illinois, March, 1991, with D. A. Antonioli.
4. Lecture, "The Adenoma-Carcinoma Sequence in the Colon", the Eighth Annual Eisenstein Memorial Lecture, Mercy Hospital, Port Huron, MIchigan, Friday, May 3, 1991.
5. Lecture, "Lymphomas Involving the Gastrointestinal Tract", St. Joseph Mercy Hospital, Pontiac, Michigan, May 15, 1991.
6. Seminar on neoplastic diseases of intestine, American Society of Clinical Pathologists, Minneapolis, Minnesota, June 1991.

7. Lecture, "Gastritis", Grand Rounds, Department of Pathology, University of California at Los Angeles, Los Angeles, California, June 26, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lynch, H.T., Smyrk, T.C., Landspa, S.J., Lynch, P.M., Watson, P., Strayhorn, P.C., Bronson, E.K., Lynch, J.F., Priluck, I.A. and Appelman, H.D.: Phenotypic variation in colorectal adenoma/cancer expression in two families. Cancer 1990;66:909-915.
2. Mutchnick, M.G., Appelman, H.D. et. al.: Thymosin treatment of chronic hepatitis B: A placebo-controlled pilot trial. Accepted for publication in Hepatology, April, 1991.
3. Barnett, J.L., Appelman, H.D. and Moseley, R.H.: A familial form of incomplete septal cirrhosis. Accepted for publication in Gastroenterology.
4. Barnett, J.L., McDonnell, W.M., Appelman, H.D. and Dobbins, W.O.: Familial viceral neuropathy with neuronal intranuclear inclusions: Diagnosis by rectal biopsy. Accepted for publication in Gastroenterology.

BOOKS AND CHAPTERS IN BOOKS:

1. Appelman, H.D.: Barrett's Esophagus: Morphologic Considerations, Chapter 10, in, Orringer, M.B. (ed), Surgery of the Alimentary Tract - The Esophagus, W B Saunders, Philadelphia, 1991.
2. Appelman, H.D.: Mesenchymal Tumors of the GI Tract. Chapter 15, in, Ming, S-C and Goldman, H. (eds), Pathology of the Gastrointestinal Tract, W.B. Saunders, Philadelphia, In Press.
3. Appelman, H.D.: Epithelial Neoplasia of The Appendix. Chapter 9, in, Norris, H.T. (ed), Pathology of The Colon, Small Intestine and Anus, Churchill, Livingstone, New York, 1991.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Graham, D.M., Lucey, M.R., Merion, R.M. and Appelman, H.D.: Hepatitis B reinfection in liver transplant recipients: a model for viral hepatitis in the immunosuppressed host. Modern Pathology 1991;4:92A.
2. Lucey, M.R., Brown, K.A., Merion, R.M., Appelman, H.D. et. al.: The decreasing incidence of acute allograft rejection. Reduced glutathione (GSSH), prostaglandin E1 (PG) or both? Gastroenterology 1991;100:A767.

MASON BARR, JR., M.D.
PROFESSOR OF TERATOLOGY
DEPARTMENT OF PATHOLOGY;
PROFESSOR OF PEDIATRICS
DEPARTMENT OF PEDIATRICS;
PROFESSOR OF OBSTETRICS AND GYNECOLOGY
DEPARTMENT OF OBSTETRICS AND GYNECOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Medical Director, Myelodysplasia Unit: inpatient and outpatient services for children with spina bifida, 300 Clinic Visits.
B. Attending Physician Pediatrics Infant: three months.
C. Pediatric Genetics/Teratology Consultant for Holden and Women's Hospitals - inpatient and outpatient consultations and parent counselling.
D. Teratology Unit (see Research Activities).

II. TEACHING ACTIVITIES:

A. Teratology-Obstetrics Conference: weekly case review meeting of Obstetrics, Teratology, Neonatology for planning management of fetuses with prenatally detected malformations.
B. Genetics Clinical Conference - weekly reviews of consultation cases and four times yearly didactic presentations.
C. Pediatrics-Pathology Conference: organize and present CPC-type conferences to the Department of Pediatrics; four per year.
D. Neonatology Pathology Conference: quarterly review and discussion of neonatal deaths.
E. Malformations lecture, Embryology (M-1) Course.
F. Perinatal Pathology Conference: quarterly review and discussion of perinatal deaths (OB-GYN).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT: None.

TERATOLOGY UNIT (DIRECTOR):

A. Detailed postmortem investigations of abortuses, stillborns and selected neonatal deaths for morphologic, pathologic and growth characteristics, correlations with family and prenatal histories, and counselling for future reproductive decisions by the parents.
B. Continuing investigation of normal and abnormal patterns of somatic and visceral growth. Detection of patterns of growth abnormalities associated with specific syndromes, exposures and obstetrical antecedents.
C. Quality control investigations for various prenatal diagnostic methodologies.
D. Teratology Unit Activities: 178 fetal/neonatal examinations (85 from UMMC, 93 referred from 14 outside hospitals)

COLLABORATIVE RESEARCH:

1. Collection and allocation of fetal tissues for research projects in the Departments of Pediatrics, Pathology, Obstetrics, Anatomy, Genetics, and Howard Hughes Institute. Loan of fetal material for research investigations in the Department of Radiology.
2. Collaborative research with Central Laboratory for Embryology at the University of Washington (T.H. Shepard, M.D.) and the Department of Pathology at the University of South Alabama (W.R. Blackburn, M.D.) on standards for normal fetal morphometrics.
3. Research with Wayne State University (M.P. Johnson, M.D.) on fetal growth assessment in aneuploid fetuses.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Departmental - Pathology: none.
B. Departmental - Pediatrics: Editorial Board, Pediatric Rounds; House Officer Selection Committee. Medical Student Clerkship Committee, Ambulatory Care Director Search Committee.
C. Steering Committee for DSCC-funded Cost of Comprehensive Care Study.
D. Standardization and product evaluation committee, vice chair; Infant and Child Care Ethics Committee, co-chair, University Hospital Ethics Committee.

REGIONAL AND NATIONAL:

A. Reviewer for journals: Teratology, Pediatric Pathology.
B. Public Affairs Committee, Teratology Society.
C. Michigan Department of Public Health, Task Force on Provider Approval System.
D. Editorial Board, Birth Defects Encyclopedia.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Workshop: Teratogenic effects of the environment on the fetus, In, Multidimensional Neonatal Care, September 20-21, 1990, Grand Rapids, Michigan.
2. Lecture: A new teratogen (angiotensin converting enzyme inhibitors) OB/GYN-Pediatric Grand Rounds. St. Joseph Mercy Hospital, Ann Arbor, Michigan, September 27, 1990.
3. Lecture: Clinical Teratology. Course on Orthodontics and Pedodontics, University of Michigan Dental School, Ann Arbor, Michigan, October 5, 1990.
4. Seminar: Using growth assessment as part of the teratologic evaluation. University of Wisconsin, Madison, Wisconsin, October 12, 1990.
5. Lecture: A practical approach to teratogenic exposure. In: Congenital Anomalies: New Approaches to Old Problems. Towsley Center, University of Michigan, Ann Arbor, Michigan, November 8-9, 1990.
6. Lecture: Teratology. In, All-Michigan OB/GYN Review Course. Novi, Michigan, April 22, 1991.
7. Lecture: Neural tube defects from a non-neurosurgical perspective. Neurosurgery Grand Rounds. University of Michigan. May 21, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Johnson, M.P., Barr, M., Qureshi, F., Drugan, A. and Evans, M.I.: Symmetrical intrauterine growth retardation is not symmetrical: Organ-specific gravimetric deficits in midtrimester and neonatal trisomy 18. Fetal Therapy 1989;4:110-119 (appeared in 1990).
2. Blane, C.E., Barr, M., DiPietro, M., Sedman, A.B. and Bloom, D.A.: Renal obstructive dysplasia: Ultrasound diagnosis and therapeutic implications. Pediatric Radiology , In Press.
3. Hartshorne, N., Shepart, T. and Barr, M.: Compensatory renal growth in human fetuses with unilateral renal agenesis. Teratology, In Press.
4. Pridjian, G., Nugent, C.E. and Barr, M.: Twin gestation: Influence of placentation on fetal growth. Am. J. Obstet. Gynecol., In Press.
5. Barr, M., Hayashi, R.H., Anderson, H.F., Pridjian, G.C. and Nugent, C.E.: Webster should not affect prenatal diagnosis (Letter) Am. J. Obstet..Gynecol. 1991;164:706-707.

ABSTRACTS, BOOK REVIEWS , PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Review of: The Malformed Fetus and Stillbirth: A Diagnostic Approach by RM Winter et al. Teratology 1990;41:353-354.
2. Review of: Environmental Causes of Human Birth Defects by TVN Persaud. Am. J. Hum. Genet. 1990;47:745.
3. Johnson, M.P., Barr, M. and Evans, M.I.: Third trimester progression of aneuploid-specific aberrant growth patterns of Trisomy 21. Am. Soc. Hum. Genet., Cincinnati, Ohio, October 16-20, 1990.
4. Pridjian, G., Nugent, C.E. and Barr, M.: Twin gestation: Influence of placentation on fetal growth. Soc. Perinat. Obstet., January, 1991.
5. Barr, M. and Pridjian, G.: Growth effects in twins: Clinical implications. Tertology 1991;43:424. Presented to Teratology Society, June 22-27, 1991. Boca Raton, Florida.

JAMES R. BAKER, M.D.
ASOCIATE PROFESSOR
DIRECTOR, TISSUE TYPING LABORATORY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Director, Histocompatibility and Immunogenetics Laboratory.

II. TEACHING ACTIVITIES:

A. Director, Basic Immunology Course for Allergy Fellows-In-Training.
B. Instructor, ICS Course 600-601.
C. Attending General Internal Medicine Service.
D. Instructed Pathology Residents, Renal Fellows and Allergy Fellows in HLA Typing.
E. Supervised Jodi Maastricht (M1), Thomas Ellis (M2) and three undergraduate students in research.
F. Supervisor for Dr. Reina Salazar's (Allergy Fellow) Research Project.
G. Clinical Pathology Grand Rounds x two.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Thyroid Autoantibodies and Antigens, R29-AI30501, NIH-NIAID, May 1, 1990 - April 30, $556,500.
B. The Production of Human Antithyroid Monoclonal Antibodies, The Boots Company Foundation, 1990-1992, $29,585/year.
C. Principal Investigator, UM-MAC: Hybridoma Core, 5 P60 AR 20557, NIH-NIAID. January 1, 1988 - December 31, 1992, $171,413.
D. Principal Investigator, MDRTC: Hybridoma Core, 5-P60 DK20572-14, NIH-NIAID, April 15, 1991 - November 30, 1991, $15.000.

IV. SERVICE ACTIVITIES:

ADMINISTRATIVE ACTIVITIES:

A. Planning Committee, Advances in Internal Medicine, University of Michigan Medical School, 1990-1991.
B. Histocompatibility Committee, Organ Procurement Agency of Michigan.
C. Immunology Subcommittee, Dean's Committee on Curriculum Improvement 1991.

MILITARY SERVICE:

A. Active Duty, US Army Reserve Medical Corps., (in support of Operation Desert Storm) 1991.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Grand Rounds, Department of Medicine, St. Lukes/Roosevelt Medical Center, July 1990.
2. Grand Rounds, Department of Medicine, St. John Hospital, August 1990.
3. Grand Rounds, Department of Pediatrics, Sparrow Hospital, December 1990.
4. Consultant Visit, Allergy Division, Department of Medicine, Walter Reed Army Medical Center, Washington, DC.
5. Allergy Symposium - Basic Immunology, Towsley Center, April 1991.
6. Advances In Internal Medicine - Immunoglobulin Deficiency, Towsley Center, May 1991.
7. Grand Rounds, Department of Medicine, Flint Osteopathic Hospital, May 1991.

SCIENTIFIC ACTIVITIES:

1. Editorial Board, Journal of Clinical Endocrinology and Metabolism.
2. Reviewer, Annals of Internal Medicine.
3. Reviewer, Journal of Clinical Investigation.
4. Reviewer, Endocrinology.
5. Reviewer, Journal of Leukocyte Biology.
6. Reviewer, Autoimmunity.
7. Consultant Director, HLA Laboratory, Walter Reed Army Medical Center, Washington, D.C.
8. Associated Director, Hybridoma Core, University of Michigan Medical School.

WORKSHOPS/PANEL DISCUSSIONS:

1. Current Use of Theophylline, American Academy of Allergy and Immunology, San Francisco, California, March 1991.
2. Drug Allergies, Allergy for the Primary Care Physician, Towsley Center, March, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

1. Ward, F.T., Baker, J.R. Jr., Krishnan, J., Dow, N. and Kjobech, C.H.: Hairy cell leukemia in two siblings. A human leukocyte antigen-linked disease? Cancer 1990;65:319-321.
2. Weiss, R.B., Donehower, R.C., Wiernik, P.H., Ohnuma, T., Gralla, R.J., Trump, D.L., Baker, J.R., Jr, Van Echo, D.A., Von Hoff, D.D. and Leyland-Jones, B.: Hypersensitivity reactions from taxol. J Clin Oncol. 1990;8:1263-8.
3. Humphrey, M., Mosca, J., Baker, J.R., Jr., Drabick, J.J., Carr, F.E., Burke, D.S., Wartofsky, L., Djuh, Y-Y. and Burman KD. Absence of retroviral sequences in Graves' disease. Lancet 1991;337:17-18.
4. Baker, J.R., Jr., Miller, F.W., Steinberg, A.D. and Burman, K.D.: Thyroid stimulating and thyrotrophin binding-inhibitory immunoglobulin activity in patients with systemic lupus erythematosus having thyroid function abnormalities. Thyroid, In Press, 1991.

5. Hansen, K.A.,.Opsahl, M.D., Nieman, L.K., Baker, J.R., Jr and Klein, T.A.: Natural killer cell activity from pregnant subjects is modulated by RU 486. Amer J of Obstetrics & Gynecology, In Press, 1991.

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN NON PEER REVIEWED:

1. Baker, J.R., Jr and Leigh T. Immunopathogenesis of HIV infection. Dermatology Clinics of North America, 1990, In Press.

BOOK CHAPTERS:

1. Baker, J.R., Jr.: Immunogenetics, the HLA system and endocrine disease, chapter XXIII, in. Becker. L, (ed), The Principles and Practice of Endocrinology and Metabolism, J.B. Lippincott & Co., 1990.
2. Baker, J.R., Jr: Endocrine immune disorders, Chapter IX, in, Stites, D.P. and Terr, A. (eds), Textbook of Clinical Immunology, Lange Medical Books, 1990

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Peele, M., Carr, F.E., Baker, J.R., Jr., Wartofsky, L. and Burman, K.D.: Thyrotropin gene expression in human lymphocytes. Clin. Res 1990;38:296A.
2. Humphrey, M., Mosca, J., Baker, J.R., Jr., Drabick, J., Carr, F.E., Burke, D., Wartofsky, L. and Burman, K.D.: The search for retroviral DNA sequences in genomic DNA sequences isolated from patients with Graves' disease. Clin Res 1990;38:383A.
3. Arscott, P., Rosen, E., Koenig, R.J., Kaplan, M.M., Ellis, R., Kerouac, B., Thompson, N. and Baker, J.R., Jr.: Immunoreactivity to Yersinia Enterocolitica antigens in patients with autoimmune thyroid disease. Clinical Res 1991;38:376A.
4. Maastricht, J., Koenig, R.J. Kaplan, M.M., Thompson, N. and Baker, J.R., Jr.: Localization of an epitope in thyroid peroxidase (TPO) recognized by Hashimoto's patients (HP) autoantibodies. Presented, Annual Meeting of The Endocrine Society, June 1991, Washington, D.C.

ARTICLES SUBMITTED FOR PUBLICATION TO PEER REVIEWED JOURNALS:

1. Sack, J., Zilberstein, D., Geinski, P., Baker, J.R., Jr., Wartofsky, L. and Burman, K.D.: Thyrotropin binding sites in Yersinia Enterocolitica. Submitted 1991.
2. Burman, K.D., Lukes, Y.G., Wartofsky, L. and Baker, J.R., Jr.: Iodiotypic anti-iodiotype immune complexes in Graves disease. Submitted 1991.
3. Baker, J.R., Jr., Dow, N., Toro, L., Clark, L. and Wright, D.C.: Identification of HIV-antigen positive lymphocytes using flow cytometry. Submitted 1991.
4. Salazar, R.O., Arscott, P., Klapper, D., Burge, H.B., Solomon, W.R. and Baker, J.R., Jr.: Detection and quantitation of airborne ragweed pollen using an immunoblotting technique. Submitted, 1991.
5. Cai, W.-Y., Lukes, Y.D., Burch, H.B., Djuh, Y.-Y., Carr, F., Wartofsky, L., Rhooms, P, D'Avis, J., Baker, J.R., Jr. and Burman, K.D.: Analysis of human TSH receptor hene and RNA transcripts in patients with thyroid disorders. Submitted 1991.
6. Schaudies, R.P., Djuh, Y.-Y., La Rocca, R.V., Wartofsky, L., Rhooms, P., Carr, F., Nicholson, D., D'Avis, J., Baker, J.R., Jr, and Burman. K.D.: Epidermal growth gactor receptor gene in normal and pathologic tissue in patients with autoimmune thyroid disease, cancer and multinodular goiter: Correlation of unique genetic hybridization pattern with cellular responsiveness. Submitted 1991.

7. McClain, J.B. COL, MC, Bharati, J., Baker, J.R., Jr and Cross, A., COL MC: Alternative pathway complement activity to E. coli K1 and 25922 contrasted to Leptospira interrogans and Leptospira biflexa. Submitted 1991.
8. Wortsman, J., McConnachie, P., Baker, J.R., Jr. and Mallette, L.E.: T lymphocyte activation in adult onset idiopathic hypoparathyroidism. Submitted 1991.
9. Peele, M.E., Carr, F.E., Baker, J.R., Jr., Wartofsky, L. and Burman, K.D.: TSH beta subunit gene expression in human lymphocytes. Submitted 1991.
10. Hansen, K.A., Opsahl, M.S., Baker, J.R., Jr., Bennett, W.A. and Cowan, B.D.: Hydatidiform mole extract stimulates natural killer cell activity *in vitro*. Submitted 1991.
11. Wilson, J.M., Grossman, M., Gupta, S., Chowdhury, N.R., Baker, J.R., Jr. and Chowdhury, J,R.: *Ex vivo* gene therapy in LDL receptor deficient rabbits leads to permanent improvement of hypercholesterolemia. Submitted 1991.

BARBARA A. BARNES, MT(ASCP) SBB
ASSISTANT PROFESSOR OF MEDICAL TECHNOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Coordinate quality assurance activities in Blood Bank Laboratory.
B. Coordinate training of Blood Bank Laboratory Staff.

II. TEACHING ACTIVITIES:

A. House Officers.
   1. Introductory Blood Bank Seminar Series for Pathology House Officers.
   2. Coordinator, Blood Bank/Coagulation Rotation for Pediatric Hematology Fellows.
B. Blood Bank Technical Staff.
   1. Coordinator, Continuing Education Weekly Conferences in Blood Banking.
   2. Coordinator, Orientation Treaining for New Employees in Blood Banking.

III. RESEARCH ACTIVITIES:

A. Project Under Study.
   The role of premedication and leukocyte poor blood components in multiply transfused pediatric oncology patients.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Blood Bank Communication Committee.
B. Conducted individual courses of instruction for each new employee of the hospital Blood Bank.
C. Drafted and implemented a weekly schedule of in-service education for Blood Bank staff.
D. Coordinated Blood Bank/Coagulation experience for each Pediatric Hematology Fellow.
E. Designed and implemented Blood Bank orientation sessions for students and residents from other departments.

REGIONAL AND NATIONAL:

A. Inspector for the Inspection and Accreditation Program of the American Association of Blood Banks.

V. OTHER RELEVANT ACTIVITIES:

WORKSHOP:

1. "Training and Education Concepts", Effective Training Workshop, Current Topics in Blood Banking, Towsley Center, Ann Arbor, Michigan, June 5, 1991.

VI. PUBLICATIONS

POSTER:

1. Singer, D.A. and Barnes, B.A.: Reducing nonindicated routine pretransfusion prophylactic medication through physician education. International Society for Blood Transfusion and American Association of Blood Banks, Los Angeles, California, November 10-15, 1991.

THEODORE F. BEALS, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1989 - 30 JUNE 1990

I. CLINICAL ACTIVITIES:

A. Diagnostic Electron Microscopy, Veterans Affairs Medical Center.
B. Director of Electron Microscopy Center of Excellence.
B. Cytopathology, Veterans Affairs Medical Center.
C. Coordinator of Decentralized Hospital Computer Program in Laboratory Service, Veterans Affairs Medical Center.
D. Fine Needle Aspiration, Veterans Affairs Medical Center.
E. Surgical/Autopsy Pathology, Veterans Affairs Medical Center.
F. Tumor Board, Veterans Affairs Medical Center.
G. Deputy Washtenaw County Medical Examiner.
H. Consultant: Diagnostic Electron Microscopy, Allen Park, VAMC and Danville, VAMC.

II. TEACHING ACTIVITIES:

A. Pathology House Officer monthly elective: Diagnostic Electron Microscopy, 10 months.
B. Diagnostic Electron Microscopy Case Conference, bi-weekly.
C. Pathology House Officers, fine needle aspiration technique and interpretation.
D. Pathology 600 Lab Section.
E. M4 elective in Pathology, Diagnostic EM and Cytopathology.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Pathologist for: Veterans Administration Cooperative Study #268. A New Strategy to Preserve the Larynx in the Treatment of Advanced Laryngeal Cancer.(G. Wolf, Principal Investigator).
B. Marijuana-Bronchoscopy Project (Fligiel/Gong/Tashkin), NIH.
C. A Prospective, Controlled, Randomized and Double-Blind Multi-Center Clinical Evaluation of Monoclonal Antibody 17.13.C1.10 for its Capability to Detect Head and Neck Squamous cell carcinoma in Primary Site Malignancies and Lymph Nodes.(Co-Investigators: Baker,Beals,Carey,Krause, McClatchey,Wolf).
D. Crescentic Nephritis -Core B- NIH Program Project, Consultant (Wiggins, Johnson)

PROJECTS UNDER STUDY:

A. Clinical Relevance of Ultrastructural Characteristics of Small Cell Carcinoma (with R. Green).
B. Role of Plastic Embedded Cell-Blocks and Electron Microscopy in Fine Needle Aspiration.

C. Morphometric Analysis of Cells and Tissue using the Scanning Light Microscope.
D. Surface Markers for Antigen Localization in Scanning and Transmission Electron Microscopy.(with S. Chensue and with D. Remick).
E. Growth of Cells on Microcarriers (with J. Varani).
F. Endothelial Cell Damage Caused by Oxidants (with D. Hinshaw).
G. Changes in Alveolar Macrophages in Monkeys smoking Marijuana (with S. Fligiel).
H. DNA Cytomorphometry of Laryngeal Squamous Carcinoma (with G. Wolf and J. Truelson).
I. Differentiation of Isolated Renal Tubular Cells in Culture (with D. Humes).
J. Ultrastructural Changes in Fuchs' Heterochromic Cyclitis (with B. Cohan).
K. Gap Junction Changes in Uterine Smooth Muscle in Women with Dysfunctional Labor (with Laudin).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Electron Microscopy Committee.
B. Resident Selection Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Surgical Case Review Committee, Veterans Affairs Medical Center.
B. Electron Microscopy Committee, chair, Veterans Affairs Medical Center.
C. Medical Records Review Committee, Veterans Affairs Medical Center.
D. Information Resources Management Oversite Committee Veterans Affairs Center.
E. Medical School Admissions Committee.
F. Executive Admissions Committee, Medical School.

REGIONAL AND NATIONAL:

A. Association of Veterans Affairs Pathologists
Secretary-Treasurer.
B. Veterans Affairs Central Office Electron Microscopy Review Group.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Pulmonary Neoplasm: Diagnostic Problems and Ultrastructural Characteristics (Department of Internal Medicine, Pulmonary Conference).
2. Electron Microscopy as an Aid to Diagnostic Cytopathology. Henry Ford Medical Center

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1 Rockerbie, N., Solomon, A.R., Woo, T.Y., Beals,T.F. and Ellis, C.N.: Malignant dermal cylindroma analogue tumors of parotid gland. Am. J. Dermatopathol. 1989:11;353-359.

2. Gilsdorf, J.R., Wilson, K. and Beals,T.F.: Bacterial colonization of intravenous catheter materials in vitro and in vivo. Surg. 1989L106;37-44.

BOOKS AND CHAPTERS IN BOOKS:

1. Wolber, R.A. and Beals, T.F.: Streptavidin-gold labeling for ultrastructural in situ nucleic acid hybridization, Chapter 19, in, Hayat, M.A. (ed), Principles, Methods and Applications Volume 2 Colloidal Gold , Academic Press, Inc., New York., pp. 379-396, 1989.
2. Wolf, G.T., Beals, T.F., Carey, T.E., Hudson, J.L., Buiting, N., Bradford, C.R. and Peterson, K.A.: Cytophotometric analysis of DNA content of human head and neck carcinoma cell lines, in, Fee, W.E., Goepfert, H., Johns, M.D, Strong, E.W. and Ward, P.H. (eds), Head and Neck Cancer, B.C. Decker, Inc., Toronto, pp 102-108, 1990.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Cohan, B.E., Beals, T.F., Chensue, S.W., Miles, J. and Stuth, S.: Fuchs' heterochromic cyclitis: SEM of aqueous cytology and iris anterior border layer. Assoc. Res. Vision and Opthol., Sarasoto, Florida, 1990. Invest. Ophthalmol. Vis. Sci. 1990:41;444.
2. Wolf, G., Truelson, J., Beals, T. and Fisher, S.: Nuclear area (NA) and adjusted DNA index (aDI): A new correlate of prognosis in squamous carcinoma of the larynx. AACR, 1990.
3. Fligiel, S.E.G., Beals, T.F. and Tashkin, D.P.: Pulmonary pathology in cocaine smokers. Am. Rev. Respir. Dis. 1990;141:A780.
4. Wolf, G., Truelson, J., Beals, T. and Fisher, S.: Nuclear area (NA) and adjusted DNA index (aDI): A new correlate of prognosis in squamous carcinoma of the larynx. AACR , 1990.

MILA BLAIVAS, M.D., PH.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. M-LABS AP/CP coverage at Lapeer Community Hospital, Albion Community Hospital, Thorn Hospital, and The University of Michigan Hospital.
B. Four months of Neuropathology Service.
C. Six rotations in Autopsy Service.
D. Muscle and nerve biopsies referred by other hospitals in and out of state throughout the year.
E. Consultations on brain biopsies and rheumatology cases.

II. TEACHING ACTIVITIES:

A. Taught residents, fellows and staff in Neurology, Rheumatology and Pediatrics and medical students on muscle and nerve biopsies.
B. Taught pathology residents how to perform and read out autopsies.
C. Lectured on muscle, nerve and brain pathology to residents in Pathology and Neurology
D. Monthly conference on muscle and nerve cases with Neurology and Rheumatology departments.
E. Biweekly and later, monthly muscle, nerve and brain cases review with pathology residents.
F. Weekly conference with Neuromuscular staff.
G. Bimonthly conference with Neuroradiology and Pediatric Neurology.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Histology and histochemistry of orbicularis muscle, normal, aging, diseased.
B. Embiology and pathology of soft palate muscles of human and mice.
C. Pelvic floor muscles.
D. Masseter and other facial muscles, normal and diseased.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Supervision of the muscle histochemistry.
B. Continuing improvement of interdepartmental coordination of muscle and nerve biopsy service.

MEDICAL SCHOOL:

A. Member of the Admission Committee.

REGIONAL AND NATIONAL:

A. Visits to Lapeer Community Hospital and Albion Community Hospital.
B. Director of the Knollwood Clinic Laboratory, Lapeer.
C. Member, American Association of Neuropathologists, IAP, AAN and AMA.

V. OTHER RELEVANT ACTIVITIES:

A. Attended IAP and American Association of Neuropathologists meeting and presented posters.
B. Took and passed Neuropathology Boards of American Board of Pathology.

INVITED LECTURES/SEMINARS:

1. None.

VI. PUBLICATIONS:

1. Oxenkrug, G.F., Anderson, G.F., Dragovic, L., Blaivas, M. and Riederer, P.: Circadian rhythms of human pineal melatonin, related indoles and beta adrenoreceptors: Postmortem evaluation. J. Pineal Research 1990;9:1-11.
2. Selwa, J.F., Feldman, E.L. and Blaivas, M.: Mononeuropathy multiplex in tryptophan-associated eosinophilia-myalgia syndrome. Neurology 1990;40:1632-1633.
3. Nelson, C.C. and Blaivas, M.: Histologic and histochemical characteristics of the orbicularis oculi muscle in children. Investigative Ophthalmology and Visual Science 1991;32:646-654.
4. Feldman, E.L., Bromberg, M.B., Blaivas, M. and Junck, L: Acute pandysautonomic neuropathy. Neurology 1991;42:746-748.

ARTICLES SUBMITTED:

1. Drury, I., Blaivas, M., Aboy-Khalil, B.W. and Beydoun, A.: Biopsy results in a kindred with Lafora disease. Submitted to Neurology.
2. Nelson, C.C. and Blaivas, M.: Histology and histochemistry of protractor muscles in Blepharospasm with and without Botulinum treatment. To Modern Pathology.

ABSTRACTS, BOOK REVIEWS PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Nelson, C.C. and Blaivas, M.: Histologic and histochemical characteristics of eyebrow and eyelid muscles. American Association of Neuropathologists Meeting, June, 1991.
2. Nelson, C.C. and Blaivas, M.: Histochemistry of protractor muscles in blepharospasm. ARVO Meeting, May, 1991.
3. Blaivas, M. and Nelson, C.C.: Ultrastructure of normal and aging human orbicularis oculi muscle. American Association of Neuropathologists Meeting, June 19-23, 1991.
4. Simmons, Z., Blaivas, M., Bromberg, M.B. and Feldman, E.L.: Polyneuropathy association with IGA monoclonal gammopathy. To be presented at the AAEM meeting in September 27-28, 1991.

CHAPTER IN BOOKS

1. McKeever, P.E., Sima, A.A.F. and Blaivas, M.: Neoplasms of the sellar region, Chapter 13, in, Lloyd, R.V. (ed), Surgical Pathology of the Pituitary Gland, MPP Series, W.B. Saunders, Company. To be published.

JEFFREY BONADIO, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Inherited Connective Tissue Disease Diagnostic Service (Biochemical Analysis of Skin Biopsy Material).
B. Attending Staff, University of Michigan Autopsy Service.

II. TEACHING ACTIVITIES:

A. Graduate Student:
   a. Thesis Co-Chairman with Steven Goldstein: Ms. Monique Mansoura (Bioengineering).
   b. Thesis Co-Chairman with Steven Goldstein: Mr. John Germiller (MSTP).
   c. Thesis Co-chairman with Steven Goldstein: Mr. Karl Jepsen (Bioengineering).
   d. Thesis committee: Ms. Patricia Sherman (Human Genetics).
   e. Thesis committee: Ms. Elizabeth Allen (Human Genetics).
   f. Thesis committee: Ms. Linda Kallikan (Cellular and Molecular Biology).
B. Supervision of four postdoctoral fellows: (David Bole, Ph.D., Loretta R. O'Donnell, M.D., Thomas Lawton, M.D. and Marcy Wong, Ph.D.).
C. Mentor, Summer Medical Research Program, University of Michigan, 1990 Summer Student, Haining Shao.
D. Courses:
   1. Lecturer, Pathology 600.
   2. Lecturer, Pathology 580.
   3. Lecturer, Biochemistry 501.
   4. Course Co-Director, Pathology 581.
   5. Mentor, Pathology 650.
E. Continuing Medical Education:
   1. General Surgery Seminar Series, Department of Surgery, University of Michigan, 1990.
   2. Rheumatology Seminar Series, Department of Medicine, University of Michigan, 1990.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Molecular Basis of Osteogenesis Imperfecta Type II, NIH-DK, AR38473-04 (50% effort), $44,520.00/year direct costs, ($194,771.00/5 years).
B. Principal Investigator, "Transgenic Mouse Model of Osteogenesis Imperfecta Type I", NIAMSD, NIH, AR40679 (25% effort), $162,679.00/year direct costs $462,843.00/3 years 1991-1993.

PROJECTS UNDER STUDY:

A. Molecular pathogenesis of osteogenesis imperfecta.
B. Regulation of osteoblast gene expression.
C. Structure/function relationships in connective tissue.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

A. Member, Planning Committee, University of Michigan Skeletal Dysplasia Clinic.
B. Member, Preclinical Advisory Program, University of Michigan Medical School.
C. Biomechanics Core Steering Committee, University of Michigan Multipurpose Arthritis and Musculoskeletal Diseases Center.

DEPARTMENTAL:

A. Oversight Committee, Graduate Program, Department of Pathology, University of Michigan.

V. OTHER RELEVANT ACTIVITIES:

A. Assistant Investigator, Howard Hughes Medical Institute.
B. Ad-hoc Reviewer
   1. American Journal of Human Genetics.
   2. The Journal of Clinical Investigation.
   3. The Journal of Biological Chemistry.
   4. The March of Dimes Grants Program.
   5. Genomics.
C. Consultant Editor: European Journal of Experimental Musculoskeletal Research.
D. Member
   1. Multipurpose Arthritis Center.
   2. Michigan Cancer Center.
   3. Program in Bioengineering.
   4. Rheumatology Fellowship Training Grant, University of Michigan Multipurpose Arthritis and Musculoskeletal Diseases Center.

INVITED LECTURES/SEMINARS:

1. Workshop on Childhood Osteopenia, American Society of Bone and Mineral Research Annual Meeting, Atlanta Georgia, 1990.
2. IV International Conference on Osteogenesis Imperfecta (Session Chair), Pavia, Italy, 1990.
3. Department of Biochemistry Seminar Series, University of Michigan, 1991.
4. Seminar Series, Department of Genetics, M.D. Anderson Hospital, University of Texas, Houston, Texas, 1991.
5. 17th Annual Conference on Craniofacial Biology, University of Michigan, Ann Arbor, Michigan, 1991.
6. Workshop on Osteobiology, Bari, Italy, 1991.
7. Gordon Research Conference, Structural Macromolecules, 1991.
8. European Society for Pediatric Research Annual Meeting, Plenary Session on Inherited Connective Tissue Disease, Zurich, Switzerland, 1991.
9. Seminar Series, Instituto Nazionale per la Ricerca sul Cancro, Genoa, Italy, 1991.

10. NIH Workshop on Transgenic Models of Human Disease, NIH, Bethesda, Maryland, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Beckwith, J.B., Kiviat, N.B. and Bonadio, J.F.: Nephrogenic rests, nephroblastomatosis, and the pathogenesis of Wilms' Tumor. Pediatr Pathol 1990;10:1-36.
2. Majmudar, G., Bole, D., Goldstein, S.A. and Bonadio, J.F.: Bone cell culture in a three-dimensional polymer bead stabilizes the differentiated phenotype and provides evidence that osteoblastic cells synthesize type III collagen and fibronectin. J. Bone and Min. Res., In Press.
3. Biesecker, L.G., Erickson, R.P., Glover, T.W. and Bonadio, J.F. Molecular and cytologic studies of Ehlers-Danlos syndrome type VIII. Am. J. Hum. Genet., in press.

BOOKS/CHAPTERS IN BOOKS:

1. Bonadio, J. and Goldstein, S.A.: The inherited disorders of the vascular wall, in, Roberts, R. (ed), Molecular Biology of the Cardiovascular System, Blackwell Scientific Publications, Cambridge, Massachusetts, In Press.
2. Bonadio, J. and Goldstein, S.A.: Osteogenesis imperfecta: An inherited connective tissue disease of bone, in Carlson, D.S. and Goldstein, S.A., eds, Bone Biodynamics in Orthodontic and Orthopedic Treatment, Craniofacial Growth Series, Vol. 27, Center for Human Growth and Development, The University of Michigan, Ann Arbor, Michigan, In Press.

ABSTRACTS:

1. Jepsen, K., Mansoura, M.K, Bonadio, J.F. and Goldstein, S.A.: Adaptational response of cortical bone to defective type I collagen synthesis. Orthopedic Research Society, Anaheim, California, 1991.
2. Bole, D.G., Smiley, E and Bonadio, J.F.: Expression of human collagen a1(I) chains in COS-7 cells. FASEB, Atlanta, Georgia, 1991.
3. Smiley, E., Bole, D. and Bonadio, J.F.: CNBr peptide maps accurately and reproducibly localize osteogenesis imperfecta mutations in type I collagen. FASEB, Atlanta, Georgia, 1991.
4. Bonadio, J.F., Smiley, E., Bole D., Greenfield, N.J. and Montelione, G.: Structure function relationships in collagen subdomains. FASEB, Atlanta, Georgia, 1991.
5. Jepsen, K., Kuhn, J., Goldstein, S.A., Mansoura, M.K. and Bonadio, J.F.: A geometrical adaptation effectively compensates skeletal fragility in heterozygous Mov13 mice. FASEB, Atlanta, Georgia, 1991.
6. Jepsen, K., Kuhn, J., Goldstein, S.A., Mansoura, M.K. and Bonadio, J.F.: A geometrical adaptation effectively compensates skeletal fragility in heterozygous Mov13 mice. Molecular Basis of Bone Cell Physiology: Transcellular Signaling, St. Louis, Missouri, 1991.
7. Majmudar, G., Bole, D., Goldstein, S.A. and Bonadio, J.F.: Bone cell culture in a three dimensional polymer bead stabilizes the differentiated phenotype and provides evidence that osteoblastic cells synthesize type III collagen and fibronectin. Molecular Basis of Bone Cell Physiology: Transcellular Signaling, St. Louis, Missouri, 1991.
8. O'Donnell, L.R., Majmudar, G. and Bonadio, J.F.: Temporal and spatial distribution of mRNA for transforming growth factor-b types 1,2,3, and 4 in embryonic chick bone. Workshop on Osteobiology, Brindisi, Italy, 1991.
9. Wong, M., Lawton, T., Pasternak, A., Jepsen, K., Goetinck, P., Kuhn, J.L., Goldstein, S.A., and Bonadio, J.F.: Aggrecan is expressed in membranous bone of the chick embryo: molecular genetic and biomechanical studies of wild-type and nanomelia embryos. Workshop on Osteobiology, Brindisi, Italy, 1991.

10. Jepsen, K., Kuhn, J.L., Goldstein, S.A., Mansoura, M.K. and Bonadio, J.F.: A geometrical adaptation effectively compensates skeletal fragility in heterozygous Mov13 mice. Workshop on Osteobiology, Brindisi, Italy, 1991.
11. Majmudar, G., Bole, D., Goldstein, S.A. and Bonadio, J.F.: Bone cell culture in a three-dimensional polymer bead stabilizes the differentiated phenotype and provides evidence that osteoblastic cells synthesize type III collagen and fibronectin. Workshop on Osteobiology, Brindisi, Italy, 1991.
12. Bonadio, J.F., Goldstein, S.A., Kuhn, J.L., Jepsen, K. and Mansoura, M.: Osteogenesis imperfecta: Fragile molecules make brittle bones. European Society for Pediatric Research Annual Meeting, Zurich, Switzerland, 1991.
13. Bonadio, J.F., Goldstein, S.A., Kuhn, J.L., Jepsen, K.A. and Mansoura, M.: Osteogenesis imperfecta type I in Mov13 transgenic mice. NIH Workshop: Transgenic Animal Models in Biomedical Research, 1991.

STEPHEN W. CHENSUE, M.D., PH.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Director, Clinical Laboratories, Veterans Affairs Medical Center, responsibilities include, new equipment and methodology evaluation, review and consultation regarding quality management programs, personnel evaluation, peronnel counseling and greivance procedures.
B. Hematology/Coagulation, daily evaluation of pathologist referred blood smears and interpretation of special coagulation studies (12 months/yr), Veterans Affairs Medical Center.
C. Surgical/Frozen Section Diagnosis, 2 days/week (12 months/yr), Veterans Affairs Medical Center
D. Autopsy Service, rotational basis, on call 18 weeks/yr.
E. Special Chemistry/Immunology, daily interpretation of protein electrophoreses, isoenzyme studies, and problem ligand studies Veterans Affairs Medical Center (12 months/yr).
F. Blood Bank, consults and investigations, full time as needed, Veterans Affairs Medical Center.

II. TEACHING ACTIVITIES:

A. Sophomore medical students, Pathology 600 laboratory course, (1 semester, 30 contact hours).
B. Graduation course, Pathology 580, 1 contact hour.
C. Pathology house officers, Surgical Pathology/Autopsy supervision and instruction, 2 days/week (12 months/yr).
D. Technologists and technicians, ongoing inservice instruction on clinical laboratory topics.
E. Physicians, educational lectures regarding aspects of clinical pathology (1-2 lectures/yr).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Cytokine Cascades in Granuloma Formation", VAMC Merit Review ($55,000 annual) 1990-1993.
B. Consultant on NIH-HL-R01-31237, "Macrophage Function in Pulmonary Inflammation", Dr. S. Kunkel, Principal Investigator.

PROJECTS UNDER STUDY:

A. Role of cytokines in Schistosoma mansoni egg-induced granulomatous inflammation.

B. Immunolocalization of interleukin 1 and tumor necrosis factor mouse and human inflammatory lesions.
C. Regulation and orchestration of cytokine production during granulomatous inflammation.
D. In situ hybridization to demonstrate local cytokine induction and synthesis of monokine mRNA in cultured cells and tissue sections.
E. In vivo analysis of cytokine cascades in experimental endotoxemia.
F. Analysis of neutrophil and monocyte chemoattractants by immunolocalization in cultured cells and tissue sections.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member of graduate student thesis committees.

MEDICAL SCHOOL/HOSPITAL:

A. Blood Utilization Review Committee, Veterans Administration Medical Center, Chairman.
B. Research and Development Committee, Veterans Administration Medical Center, voting member.
C. Ambulatory Care Committee, Veterans Administration Medical Center, voting member.
D. Hospital Quality Assurance Investigations, ad hoc committees.
E. Personnel employment and evaluation
F. Editor, "VALABS Interface Laboratory News", Laboratory Newsletter.

REGIONAL AND NATIONAL:

A. Editorial Review:
American Journal of Pathology.
Journal of Immunology, Associate Editor.
Clinical Immunology and Immunopathology.
American Journal of Respiratory Cell and Molecular Biology.
Agents and Actions.
B. Inspector, College of American Pathologists.
C. Reviewer and on site inspection for Merit Review Board.
D. Reviewer for NIH SCOR proposals regarding pulmonary disease.

V. OTHER RELEVANT ACTIVITIES:

A. Case presentations at GI and Hematology Conferences.
B. Case presentations at Morbidity and Mortality Conferences.
C. Tissue evaluation for clinical researchers
D. Invited lecture, Tri-County Clinical Microbiology Association.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Standiford, T.J., Strieter, R.M., Chensue, S.W., Westwick, J., Kasahara, K. and Kunkel, S.L.: Interleukin 4 inhibits the expression of interleukin 8 from stimulated human monocytes. J. Immunol. 1990;145:1435.
2. Kunkel, S.L., Strieter, R.M., Chensue, S.W. and Remick, D.G.: The role of TNF in diverse pathologic processes. Biotherapy 1991;3:145.
3. Chensue, S.W., Terebuh, P.D., Remick, D.G., Scales, W.E. and Kunkel, S.L.: In vivo biologic and immunohistochemical analysis of interleukin-1 alpha, beta and tumor necrosis factor, during experimental endotoxemia: Kinetics, Kupffer cell expression and glucocorticoid effects. Am. J. Pathol. 1991;138-395.
4. Rolf, M.W., Kunkel, S.L., Standiford, T.I., Chensue, S.W., Allen, R.M., Evanoff, H.L., Phan, S.H. and Strieter, R.M.: Pulmonary fibroblast expression of interleukin 8: A model for alveolar macrophage-derived cytokine networking. Am. J. Respir. Cell Mol. Biol. 1991, In Press.
5. Kasahara, K., Strieter, R.M., Chensue, S.W., Standiford, T.J. and Kunkel, S.L.: Mononuclear cell adherence induces neutrophil chemotactic factor/interleukin 8 gene expression. J. Leuk. Biol. 1991, In Press.
6. Lin, H., Chensue, S.W., Strieter, R.M., Remick, D.G., Gallager, K.P., Bolling, S.F. and Kunkel, S.L.: Anti-tumor necrosis factor antibody prolongs allograft survival in the rat. Transplant. Proc. 1991, In Press.

SUBMITTED ARTICLES

1. Chensue, S.W., Terebuh, P.D., Evanoff, H.L., Kunkel, S.L. and Higashi, G.I.: Role of interleukin-4 and gamma interferon in *schistosoma mansoni* egg-induced hypersensitivity granuloma formation: Orchestration, relative contribution and relationship to macrophage function. J. Immunol.
2. Terebuh, P.D., Otterness, I.G., Strieter, R.M., Lincoln, P., Danforth, J., Kunkel, S.L. and Chensue, S.W.: Biologic and immunohistochemical analysis of interleukin 6 expression in vivo: Constitutive and induced expression in murine polymorphonuclear and mononuclear phagocytes. Am. J. Pathol.

BOOKS AND CHAPTERS IN BOOKS:

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Terebuh, P., Otterness, I., Kunkel, S. and Chensue, S.W.: Cellular distribution of IL-6 expression in normal and endotoxin challenged mice. Fed. Proc. 1991;5:A1009.
2. Chensue, S.W., Terebuh, P., Evanoff, H. and Kunkel, S.L.: Anti-interleukin 4 but not anti-interferon antibodies suppress schistosome egg hypersensitivity-type granuloma formation. Fed. Proc. 1991;5:A1491.
3. Spengler, R.N., Chensue, S.W., Giacherio, D.A. and Kunkel, S.L.: Endogenous norepinephrine regulates tumor necrosis factor production from macrophages in culture. Red. Proc. 1991;5:A4994.
4. Rolfe, M., Kunkel, S., Strandiford, T., Allen, R., Chensue, S., Evanoff, H. and Strieter, R.: Human pulmonary fibroblasts express interleukin 8: A model of cellular communication. Fed. Proc. 1991;5:A6205.
5. Lin, H., Chensue, S.W., Strieter, R.M., Bolling, S.F. and Kunkel, S.L.: Anti-tumor necrosis factor antibody prolongs heart allograft survival in the rat. Fed. Proc. 1991;5:A7256.

6. Moore, S., Strieter, R., Standiford, T., Chensue, S.W.and Kunkel, S.L.: Constitutive expression of IL-1 receptor antagonist by alveolar macrophages. Fed. Proc. 1991;5:A8179.
7. Olson, A., Ayass and Chensue, S.W.: Expression of tumor necrosis factor and IL-1 beta in ulcerative colitis. American Gastroenterology Association and American Association for the Study of Liver Diseases 1991 Meeting, New Orleans, Louisiana.
8. Koch, A.E., Kunkel, S.L., Chensue, S.W., Hains, G.K. and Strieter, R.M.: Constitutive expression of interleukin-1 and interleukin-1 receptor antagonist protein by human rheumatoid synovial tissue macrophages. American College of Rheumatology Meeting 1991.

CONSTANCE J. D'AMATO, B.S.
ASSISTANT PROFESSOR OF NEUROBIOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Work daily with house officers and staff in Pathology and other departments in the gross and microscopic examination of brains from autopsies at University Hospital.
B. Attend and instruct house officers in the removal and gross examination of brains from nearly all autopsies at University Hospital.
C. Work with Neuropathology Staff on autopsy brain material sent for consultative study from University-associated hospitals, other hospitals, and institutions.
D. Plan and conduct weekly Brain Cutting Conference for house officers, students and staff, for gross diagnosis and demonstrations of diagnostic methods, and teaching.
E. Plan and present gross and microscopic Neuropathology Conference on alternate months for the Neurology Department, and participate occasionally in their Grand Rounds.
F. Continuous review of quality control of diagnostic techniques, autopsy and surgical neuropathology, and search for improved and new methods.

II. TEACHING ACTIVITIES:

A. Neural and Behavioral Sciences 600 (NBS 600), Neuropathology for second year medical students, 5 hours of lectures and 12 hours of brain cutting sessions. Sequence coordinator for NBS 600, Neuropathology; responsible for implementing general plan of course, selection of much of the teaching material, coordination and integration of the lectures of the course with other instructors, lecturing, and conducting the brain cutting sessions.
B. Neuropathology for Pathology house officers. This exercise is integrated with Clinical Activities A, B, and D.
C. Neuropathology 858. Intensive laboratory-lecture course for house officers and fellows, in Pathology and in the several clinical services concerned with the nervous system, and medical students, graduate students, and faculty; implement general plan of course and lecturing. Annual, 18 hours. One credit hour elective.
D. Neuropathology teaching for house officers and fellows from the several clinical services concerned with the nervous system, and medical students who take an elective rotation in Neuropathology.
E. Teach laboratory techniques and basic neuroanatomy and neuropathology to our laboratory technologists.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None

PROJECTS UNDER STUDY:

A. With S.P. Hicks in collaboration with colleagues:
   1. Experimental work concerned in the role of fetal rat brain phagocytes in repair after radiation injury, and the association of thrombospondin with the development of astrocytic gliosis after surgical brain injury in adult rats.

B. The pathologic examination of human autopsy brains from patients with clinical diagnosis of Alzheimer's, Huntington's, Pick's and other dementing diseases is being done in collaboration with Drs. A.B. Young and J.B. Penney, Michigan Alzheimer Disease Research Center, who are examining the brains biochemically.

C. Growth, spread and antigenicity of ENU-induced gliomas in rats, in collaboration with Paul E. McKeever, M.D., Ph.D. and Terry Hood, M.D..

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Anatomic Pathology Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Director of the Neural and Behavioral Sciences Program.
B. Basic Science Phase Committee.
C. Basic Science Academic Review Board.
D. Neural and Behavioral Sciences Curriculum Committee.
E. Neural and Behavioral Sciences Examinations Committee.
F. Sequence Coordinator for Neural and Behavioral Sciences 600 (Neuropathology).
G. Admissions Committee, U of M Medical School.
H. Executive Committee of the Admissions Committee.
I. Admissions Committee Counselor

REGIONAL AND NATIONAL:

A. American Association of Neuropathologist.
B. American Academy of Neurology.
C. Society for Neuroscience.
D. Michigan Chapter: Society for Neuroscience.
E. Teratology Society.
F. Neurobehavioral Teratology Society.
G. Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Committee

V. OTHER RELEVANT ACTIVITIES:

A. Presentation: Alzheimer's Disease and other dementias, at Eastern Michigan University, March 1991.

B. Member: Dementia Subcommittee of the Chronic Disease Advisory Committee (State of Michigan)

C. Member: Executive Committee of the Postmortem Examination Work group of the Dementia Subcommittee (State of Michigan).

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Brunberg, J.A., DiPietro, M., Venes, J.L., Dauser, R., Muraszko, K.M., Berkey, J., D'Amato, C.J., Rubin, J.M.: Intramedullary lesions in pediatric spinal cord: Correlation of MRI. Intraoperative Sonography, Operative Findings, and Tissue Histology. Accepted for publication June 1991 in Radiology.
2. Foster, N.L., Gilman, S., Berent, S., Sima, A.A.F., D'Amato, C.J., Koeppe, R.A. and Hicks, S.P.: Progressive subcortical gliosis and progressive supranuclear palsy can have similar clinical and pet abnormalities. Revised and resubmitted to J. of Neurol., Neurosurg, Psychiatry.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. D'Amato, C.J., O'Shea, K.S. and Hicks, S.L.: Lack of Neuritic Outgrowth in Hydrocephalic Mutant Rat Embryo Neurons (Abstract and Poster), Society for Neuroscience Abstracts, 16:314, 1990.
2. D'Amato, C.J., Sima, A.F., Foster, N.L., Dickson, D.W. and S.P. Hicks: Cerebral Lewy bodies with progressive supranuclear palsy (Abstract and Poster), J. Neuropathol. & Exper. Neurol. 1991;50:308.
3. Fratkin, J.D., Jones, M.L., D'Amato, C.J., Foster, N.L., Remick, D., Dragovic, L., Garcia, J.H., Ho, K.L., Huang, T.E., Sima, A. and Lowell, K.L.: J. Michigan Dementia Postmortem Examination Program: Neuropathological Efforts Towards Morphological Standardization of Dementia Diagnoses (Abstract and Poster). Neuropath. Exper. Neurol. 1991;50:300.

ROBERTSON D. DAVENPORT, M. D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Associate Medical Director, Blood Bank and Transfusion Service, University of Michigan Hospitals.
B. Cytopathology, consultation and staff coverage.
C. Staff coverage of Necropsy Service.
D. Deputy Medical Examiner, Washtenaw County.

II. TEACHING ACTIVITIES:

A. Introductory course in Blood Banking/Transfusion Medicine for Pathology House Officers.
B. Daily teaching rounds for Pathology House Officers assigned to the Blood Bank.
C. Continuing education presentations for Blood Bank technologists.
D. Clinical Pathology Grand Rounds: Blood Product Related Sepsis, May 10, 1990.
E. Clinical Pathology Grand Rounds: Pathophysiology of Hemolytic Transfusion Reactions, June 21, 1990.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY

A. Cytokine production in hemolytic transfusion reactions.
B. Interleukin-8 production by monocytes in response to Fc receptor stimulation.
C. Lymphocyte engraftment following blood transfusion.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL

A. Transfusion Committee, Interim Chair.

V. OTHER RELEVANT ACTIVITIES:

A. Reviewer, Chest.
B. Reviewer, Transfusion.
C. Reviewer, American Journal of Clinical Pathology.

INVITED LECTURES AND SEMINARS:

1. Appropriate Use of Plasma. Workshop: Transfusion Therapy, Guidelines for Practice. American Association of Blood Banks, Los Angeles, California, November 10-11, 1990.

2. Component Therapy in Coagulopathies. Workshop: Current Topics in Blood Banking, Ann Arbor, Michigan, June 5, 1990.

3. Impact of the Proposed 25 Day Outdate for Red Blood Cells on the Hospital Transfusion Service. Blood Products Advisory Committee of the Food And Drug Administration. Washington, D.C., May 9, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Davenport, R.D., Strieter, R.M., Standiford, T.J. AND Kunkel, S.L.: Interleukin-8 production in red cell incompatibility. Blood. 1990;76:2439-2442.

2. Davenport, R.D., Register, L.J., Schnitzer, B. and McKeever, P.E.: Non-Hodgkin's lymphoma of the brain following Hodgkin's disease: An immunohistochemical study. Cancer. 1991;67:440-443.

3. Davenport, R.D., Streiter, R.M. and Kunkel, S.L.: Red cell ABO incompatibility and production of tumor necrosis factor-alpha. Br. J. Haematol. (in press).

ABSTRACTS:

1. Davenport, R.D. and McCoy-Pardington, D.: Prophylactic transfusion before liver biopsy. Book of Abstracts, International Society of Blood Transfusion/American Association of Blood Banks Joint Congress, Los Angeles, 1990, p.40.

2. Davenport, R.D., Strieter, R.M. and Kunkel, S,.L.: Tumor necrosis factor production in hemolytic transfusion reactions. Book of Abstracts, International Society of Blood Transfusion/American Association of Blood Banks Joint Congress, Los Angeles, 1990, p.72.

3. Judd, W.J., Steiner, E.A., Abruzzo, L., Davenport, R.D., Oberman, H.A., Pehta, J. and Nance, S.: Anti-i causing acute hemolysis following a negative immediate-spin crossmatch. Book of Abstracts, International Society of Blood Transfusion/American Association of Blood Banks Joint Congress, Los Angeles, 1990, p.188.

4. Adams, P.T., Davenport, R.D., Ginsburg, D. and Roth,. M.S.: Detection of circulating donor white blood cells (WBCs) in patients receiving multiple transfusions. American Society of Hematology, Boston, 1990.

FELIX A. DE LA IGLESIA, M.D.
ADJUNCT RESEARCH SCIENTIST
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Instructor and Course Coordinator: "Advanced Topics in Toxicology: Toxicologic Pathology".
      b. Instructor: "Fundamentals in Electron Microscopy".
      c. Student Raining and Doctoral Committees.
      d. Joint Student Training in Pharmacology and Toxicology with Florida A&M School of Pharmacy.
      e. Direct a Postdoctoral Research Fellowship Program in Immunotoxicology, Gastrointestinal Inflammatory Disease, Molecular and Cellular Toxicology, Endocrine Toxicity, Molecular Biology of Cell Proliferation, Cardiac Toxicity, and Hepatotoxicity.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. All research activities are conducted with intramural support from Parke-Davis, including a co-sponsored program with the Medical Research Council of Canada.
B. Collaborates with K. Johnson in developing morphometric models for the evaluation of renal fibrotic changes.
C. Consultation with Dr. Ward and colleagues regarding application of morphometric techniques to lung research studies.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. None.

MEDICAL SCHOOL/HOSPITAL:

A. None.

REGIONAL AND NATIONAL:

A. Member, Steering Committee of External Advisors, Wayne State University Institute of Chemical Toxicology.
B. Society of Toxicology Liaison Member to the Society of Toxicologic Pathologists.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Editorial Board, Drug Metabolism Reviews.
B. Editorial Board, Toxicology.
C. Editorial Board, Toxicologic Pathology.

INVITED LECTURES/SEMINARS:

1. Chairman, Symposium on "Toxicologic Pathology of Peroxisome Proliferation", Annual Meeting of the American College of Toxicology, Orlando, Florida, October, 1990.
2. Invited Lecturer, "Perspectives in Peroxisome Proliferation", American College of Toxicology, Orlando, Florida, October, 1990.
3. Invited Lecturer: "Career Opportunities in Drug Toxicology Research", College of Pharmacy and Pharmaceutical Sciences, Florida A&M University, Tallahassee, Florida, April, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Bleavins, M.R., de la Iglesia, F.A., Munson, A.E., McCay, J.A., Stern, M.L., Fuchs, B.A. and White, K.L.: Effects of CI-949, a novel antiallergy agent, on immune function of male Fischer 344 rats. J. Pharm. Exp. Ther. 1991;257:316-322.
2. Bleavins, M.R. de la Iglesia, F.A., Munson, A.E., McCay, J.A., Fouant, M.M. and White, K.L.: Effects of CI-949, a novel antiallergy agent, on host resistance in mice. Fund. Appl. Toxicol., In Press, 1991.
3. McGuire, E.J., Lucas, J.A., Gray, R.H. and de la Iglesia, F.A.: Peroxisome induction potential and lipid-regulating activity in rats: Quantitative microscopy and chemical structure-activity relationships. Amer. J. Path., In Press, 1991.
4. Watkins, J.R., Kim, S.N., Anderson, J.A., Rothwell, C.E. and de la Iglesia, F.A.: Long-term studies in rats and dogs with the antiarrhythmic agent Pirmenol Hydrochloride. Drug Invest., In Press, 1991.

ARTICLES SUBMITTED FOR PUBLICATION:

1. de la Iglesia, F.A., Gray, R.,H. and McGuire, E.J.: Subcellular organelle biogenesis and dynamics in peroxisome proliferation. J. Am. Coll. Toxicol., Submitted, 1991.
2. McGuire, E.J., Gray, R.H. and de la Iglesia, F.A.: Chemical structure-activity relationships of peroxisome proliferation and lipid regulation in rats. J. A. Coll. Toxicol., Submitted, 1991.
3. Watkins, J.R., McGuire, E.J., Goldenthal, E. and de la Iglesia, F.A.: Calcium valproate-induced uterine adenocarcinomas in Wistar rats. Toxicology., Submitted, 1991.
4. Dethloff, L. and de la Iglesia, F.A.: Cholecystokinin antagonists. A toxicologic perspective. Drug Metab. Rev., Submitted, 1991.

5. Bleavins, M.R., Brott, D.A., Alvey, J.D. and de la Iglesia, F.A.: Lymphocyte subpopulation characterization in Cynomolgus monkeys. Clin. Immunol. Immunopathol., Submitted, 1991.
6. Rothwell, C.E., McGuire, E.J., Margin, R.A. and de la Iglesia, F.A.: Chronic toxicity and carcinogenisity studies with the β-adrenoceptor antagonist levobunolol. Fund. Appl. Tox., Submitted, 1991.

BOOKS/CHAPTERS IN BOOKS:

1. Feuer, G and de la Iglesia, F.A.: Molecular biochemistry of human disease, Volume III, CRC Press, Boca Raton, Florida. pp. 1-415, 1990.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. de la Iglesia, F.A., Gray, R.H. and McGuire, E.J.: Subcellular organelle dynamics and species differences in chemically induced peroxisome biogenesis in rat liver. J. Am. Coll. Toxicol. Proc. Ann. Mtg. Am Coll. Tox. p.51, 1990.
2. McGuire, E.J., Gray, R.H. and de la Iglesia, F.A.: Peroxisome induction potential and lipid regulation in rats: Quantitative microscopy and chemical structure activity relationships. J. Am. Coll. Toxicol. Proc. Ann. Mtg. Am. Coll. Tox., p.51,1990.
3. McGuire, E.J., Lucas, J.A., Gray, R.H. and de la Iglesia, F.A.: Subcellular organelle dynamics during chemically-induced peroxisome biogenesis in rat liver. FASEB Journal. 1990;4:A570.
4. McGuire, E.J., Anderson, J.A., Gough, A.W. and de la Iglesia, F.A.: Carcinogenicity studies in rodents with the angiotensin converting enzyme (ACE) inhibitor Quinapril hydrochloride. The Toxicologist 1990;10:49.

VISHVA M. DIXIT, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES: None.

II. TEACHING ACTIVITIES:

A. Supervised the following undergraduate students: Kara Reynolds.
B. Supervised the following graduate students: Carol Laherty, Tony Opipari, Ron Katz, Muneesh Tewari.
C. Supervised the following post doctoral fellows: Larry Holzman, Vidya Sarma, Rachel Yabkowitz, Theresa Bacon-Baguely, Valarie Castle.
D. Graduate School Pathology Course. Lectures on Extracellular Matrix.
E. Cell and Molecular Biology course to clinical fellows.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

1. NIH-R01-39037-01 - "Structure and Regulation of Human Platelet Thrombospondin", Period 07/01/87 - 06/30/92, Budget - $105,621, Principal Investigator, 35% effort.
2. #89-217 - American Heart Association Established Investigatorship Award - "Structure and Function of Thrombospondin", Period 07/01/89-06/31/94, Budget $35,000 annually, Principal Investigator.
3. DK39255-03 - "Mechanisms of Glomerular and Tubular Injury", Period 09/01/87-07/31/92, Budget - $44,156, Co-Investigator, 10% effort, Roger C. Wiggins, Program Director.
4. American Heart Association - Grant-in-Aid - "Thrombospondin Heparin Binding Domain and Platelet Function", Period 07/01/90-06/30/93, $35,000 per year, Principal Investigator, 10% effort.
5. ACS-CD-466 - "Novel Thrombospondin Receptors on Squamous Carcinoma Cells", Period 07/01/90 - 06/30/92, Budget - $136,000, Principal Investigator, 10% effort.
6. NIH-HL45351-01 - "Cytokine Modulation of Endothelial Gene Expression", Response to RFA entitled "Developmental Biology of the Vessel Wall", Period 07/01/90 - 04/30/93, Budget $194,745, Principal Investigator, 15% effort.
7. NIH-CA51888 - "Novel Thrombospondin Receptors on Squamous Carcinoma Cells", Period 02/01/91 - 01/31/94, Budget $97,454, Principal Investigator, 20% effort.

PENDING GRANTS:

1. NIH-1-R01-HL47857-01 - "Heparin and Aortic Smooth Muscle Cell Proliferation", Response to RFA NIH-91-HL-02-H "Mechanisms of Restenosis After Coronary Angioplasty", Period 09/01/91 - 08/31/96, Budget $150,476, Principal Investigator, 20% effort.

PROJECTS UNDER STUDY:

A. Structure/function relationships in thrombospondin.
B. Mechanisms of action of tumor necrosis factor.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interview prospective graduate students for a) Molecular and Cell Biology Program, and b) Medical Scientist Training Program.
B. Taught a graduate school course on Extracellular Matrix.
C. Taught a pathology resident course on molecular biology.
D. Participated in graduate school pathology program.

MEDICAL SCHOOL/HOSPITAL:

A. Review BMRC grants.
B. Taught in Cell and Molecular Biology course for fellows.
C. Committee on Cell and Molecular Biology.

REGIONAL AND NATIONAL:

A. Reviewer for the following journals: Journal of Biological Chemistry, Journal of Clinical Investigation.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Invited Speaker, The International Conference on Biological Treatment of Melanoma and Other Cancers, New Castle, Australia, 1990.
2. Invited Speaker, Cor Therapeutics, Inc., S. San Francisco, California, 1990.
3. Invited Speaker, NIEHS, Research Triangle Park, North Carolina, 1991.
4. Invited Speaker, FASEB, Atlanta, Georgia, 1991.
5. Invited Speaker, Wahsington University Medical Center, Respiratory and Critical Care Division, St. Louis, Missouri, 1991.
6. Invited Speaker, Mesangial Cells and Extracellular Matrix, International Society of Nephrology, Kloster Banz, Germany, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Dixit, V.M., Green, S., Sarma, V., Holzman, L., Wolf, F.W., O'Rourke, K., Ward, P.A., Prochownik, E.V. and Marks, R.M.: Tumor necrosis factor-α induction of novel genes in human endothelial cells including a macrophage specific chemotaxin. J. Biol. Chem. 1990;265:2973-2978.

2. Barker, J.N.W.N., Sarma, V., Mitra, R.S., Dixit, V.M. and Nickoloff, B.J.: Marked synergism between TNF-α and IFN-γ in regulation of keratinocyte-derived adhesion molecules and chemotactic factors. J. Clin. Invest. 1990;85:605-608.
3. Wolf, F.W. and Dixit, V.M.: Structure of the thrombospondin gene provides evidence for exon shuffling. Genomics 1990;6(4):685-691.
4. O'Shea, K.S., Rheinheimer, J.S.T. and Dixit, V.M.: Deposition and role of thrombospondin in the histogenesis of the cerebellar cortex. J. Cell. Biol. 1990;110(4):1275-1284.
5. Long, M.W. and Dixit, V.M.: Thrombospondin functions as a cytoadhesion molecule for human hematopoietic progenitor cells. Blood 1990;75(12):2311-2318.
6. Opipari, A.W., Boguski, M.S. and Dixit, V.M.: The A20 cDNA induced by tumor necrosis factor-α encodes a novel type of zinc finger protein. J. Biol. Chem., 1990;265:14705-14708.
7. Holzman, L.B., Marks, R.M. and Dixit, V.M.: A novel immediate-early response gene of endothelium is induced by cytokines and encodes a secreted protein. Mol. Cell. Biol. 1990;10:5830-5838.
8. O'Shea, K.S., Liu, L.-H.J., Kinnunen, L.H. and Dixit, V.M.: Role of the extracellular matrix protein thrombospondin in the early development of the mouse embryo. J. Cell Biol. 1990;111:2713-2723.
9. Schuger, L., Dixit, V.M., Carey, T.E. and Varani, J.: Modulation of squamous carcinoma cell growth, morphology, adhesiveness and extracellular matrix production by interferon-γ and tumor necrosis factor-α. Pathobiol. 1990;58:279-286.
10. Nickoloff, B.J., Karabin, G.D., Barker, J.N.W.N., Griffiths, C.E.M., Sarma, V., Mitra, R.S., Elder, J.T., Kunkel, S.L. and Dixit, V.M.: Cellular localization of interleukin-8 and its inducer-tumor necrosis factor-alpha in psoriasis. Am. J. Pathol. 1991;138(1):129-140.
11. Barker, J.N.W.N., Mitra, R.S., Griffiths, C.E.M., Dixit, V.M. and Nickoloff, B.J.: Keratinocytes as initiators of Inflammation. Lancet 1991;337:211-214.
12. Barker, J.N.W.N., Jones, M.L., Swenson, C.L., Sarma, V., Mitra, R.S., Ward, P.A., Johnson, K.J., Fantone, J.C., Dixit, V.M. and Nickoloff, B.J.: Monocyte chemotaxis and activating factor production by keratinocytes in response to IFN-γ. J. Immunol. 1991;146(4):1192-1197.
13. Tripathi, B.J., Tripathi, R.C., Yang, C., Millard, C.B. and Dixit, V.M.: Synthesis of a thrombospondin-like cytoadhesion molecule by cells of the trabecular meshwork. Invest. Ophthalmol. Vis. Sci. 1991;32:181-188.
14. Yabkowitz, R. and Dixit, V.M.: Human carcinoma cells express receptors for distinct domains of thrombospondin. Cancer Res. 1991;51:1645-1650.
15. Suchard, S.J., Burton, M.J., Dixit, V.M. and Boxer, L.A.: Human neutrophil adherence to thrombospondin occurs through a CD11/CD18-independent mechanism. J. Immunol. 1991;146:3945-3952.
16. Castle, V.P., Varani, J., Fligiel, S., Prochownik, E.V. amd Dixit, V.M.: Antisense-mediated reduction in thrombospondin reverses the malignant phenotype of a human squamous carcinoma. J. Clin. Invest. 1991;87:1883-1888.
17. O'Shea, K.S., Liu, L-H.J. and Dixit, V.M.: Thrombospondin promotes neuron attachment and neurite outgrowth. Neuron 1991;7:231-237.
18. Yabkowitz, R. and Dixit, V.M.: Human carcinoma cells bind thrombospondin through a 80/105 kD receptor. Cancer Res. 1991;51:3648-3656.
19. Suchard, S.J., Boxer, L.A. and Dixit, V.M.: Human neutrophils express two distinct thrombospondin receptors. J. Immunol. 1991;147:651-659.
20. Bornstein, P., O'Rourke, K., Wikstrom, K., Wolf, F.W., Katz, R., Li, P. and Dixit, V.M.: A second, expressed thrombospondin gene (THBS2) exists in the mouse genome. J. Biol. Chem. 1991;266:12821-12824.
21. Wolf, F.W., Marks, R.M., Sarma, V., Byers, M.G., Katz, R.W., Shows, T.B. and Dixit, V.M.: Characterization of a novel tumor necrosis factor-α induced endothelial primary response gene. J. Biol. Chem., In Press.
22. Laherty, C.D., O'Rourke, K., Wolf, F.W., Katz, R., Seldin, M.F. amd Dixit, V.M.: Characterization of mouse thrombospondin 2 sequence and expression during cell growth and development. J. Biol. Chem., In Press.

ARTICLES SUBMITTED FOR PUBLICATION

1. Johnson, K.J., Dixit, V.M. and Varani, J.: Role of thrombospondin in the acute inflammatory response. Am. J. Pathol., Submitted.
2. Sarma, V., Wolf, F.W., Marks, R.M., Byers, M.G., Shows,T.B. and Dixit, V.M.: Characterization from endothelium of a novel primary response gene induced by tumor necrosis factor-α. J. Biol. Chem., Submitted.

BARRY G. ENGLAND
ASSOCIATE PROFESSOR OF REPRODUCTIVE BIOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Director, Ligand Assay Laboratory.

II. TEACHING ACTIVITIES:

A. Instructor for Pathology House Officers Laboratory Rotation.
B. Instructor for Nuclear Medicine Residents Laboratory Rotation.
C. Thesis Committee Member for Hamed Benghuzzi, University of Dayton.
D. Postdoctural Mentor for Hamed Benghuzzi, Ph.D.
E. Participant, Clinical Pathology Grand Rounds.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. USPHS (NIDDKD) 2P60AM20572-10: Michigan Diabetes Research and Training Center; Director Ligand Assay Core Facility, 129,322/yr., 1987-1992.
B. USPHS (NICHD) 5T32HD07048-13: Training Program in Reproductive Endocrinology, Co-Investigator, 193,082/yr, 1975-1990.
C. Protocol to evaluate the transdermal delivery of estradiol-17B in postmenopausal women. Sponsor: Ciba-Geigy Corp.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Director, Central Ligand Assay Laboratory.

MEDICAL SCHOOL/HOSPITAL:

A. Director, Ligand Assay Core Laboratory, Diabetes Research and Training Center.
B. Co-Director, Standards and Reagents Core Facility, Reproductive Sciences Program.
C. Member, Selection Committee, Reproductive Sciences Program.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Vinik, A.I., Gonin, J., England, B.E., Jackson, T., McLoed, M.K. and Cho, K: Plasma substance P in Neuroendocrine tumors and idiopathic flushing: The value of pentagastrin stimulation tests and the effects of somatostatin analogue. J. Clin. Endocrinol. & Metabolism. 1990;70:1702-1709.
2. Benghuzzi, H.A., Bajpai, P.K., and England, B.E.: Delivery of testosterone and dihydrotestosterone by ALCAP ceramic implants in rats. J. Invest. Surg. 1990;3:197-215.
3. Grenman, S.E., Worscham, M.J., Van Dyke, D.L., England, B.E., McClatchey, K.D., Babu, V.R., Roberts, J.A., Maenpaa, J. and Carey, T.E.: Establishment and characterization of UM-EC-2, a tamoxifen sensitive estrogen receptor negative human endometrial carcinoma cell line. Gynecol. Oncol. 1990;37:188-199.
4. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Long-term delivery of testosterone by ALCAP ceramics in rats. J. Appl. Biomaterials 1990;I;233-240.
5. Song, J., Jin, L., Chandler, W.F., England, B.G., Smart, J.B., Landefeld, T.D. and Lloyd, R.V: Gonadotropin-releasing hormone regulates gonadotrophin B-subunit and chromogranin-B messenger ribonucleic acids in cultured chromogranin-A-positive pituitary adenomas. J. Clin. Endocrinol. & Metabolism 1990;71;622-630.
6. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: The Effects of Long-term Sustained Delivery of DHT by Polylactic Acid Impregnated and Noncoated Biodegradable Ceramic Devices in Male Rats. Journal of Bioactive and Compatible Polymers (In Press).

BOOKS AND CHAPTERS IN BOOKS:

1. Benghuzzi, H.A., Bajpai, P.K and England, B.G.: Suppression of spermatogenesis by means of continuous delivery of danazol in combination with dihydrotestosterone from ALCAP drug delivery devices, in, Frenger, P. (ed.), The 27th Annual Meeting of the Rocky Mountain Bioengineering Symposium, April 6-7, 1990, Denver, Colorado, pp.141-149.
2. Benghuzzi, H.A., Bajpai, P.K., and England, B.G.: Regulation of spermatogenesis by means of sustained delivery of testosterone from biodegradable ceramic implants, in, Rau, G. (ed.), The Ninth Southern Biomedical Engineering Conference, November 17-18, 1990, Miami, Florida, In Press, 1990.
3. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Tricalcium phosphate amino acid capsules as a drug delivery system for steroid hormones, in, Carlson, D. (ed.), Proceedings of the 28th Annual Meeting of the Rocky Mountain Bioengineering Symposium, Rochester, Minnesota, Biomedical Sciences Instrumentation (ISA), Vol. 27, pp.198-203,1991.
4. England, B.G., Benghuzzi, H.A., Possley, R.M. and Bajpai, P.K.: The effect of various testosterone concentrations released from ceramic delivery system on the circulating hormone levels of adult castrated rams, in, Carlson, D. (ed.), Proceedings of the 28th Annual Meeting of the Rocky Mountain Bioengineering Symposium, Rochester, Minnesota, Biomedical Sciences Instrumentation (ISA), Vol. 27, pp. 190-195,1991.
5. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: In vivo delivery of estradiol from ceramic drug delivery devices, in, Carlson, D. (ed.), Proceedings of the 28th Annual Meeting of the Rocky Mountain Bioengineering Symposium, Rochester, Minnesota, Biomedical Sciences Instrumentation (ISA), Vol.27,pp.181-187,1991.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Flinn, M.V. and England, B.G.: Daily variations in stress in a rural Caribbean village as measured by radioimmunoassay of salivary cortisol. Sixtieth Annual Meeting of the American Association of Physical Anthropologists. April 2-6, 1991. Milwaukee, Wisconsin.
2. England, B.G., Benghuzzi, H.A., Possley, R.M. and Bajpai, P.K.: The effect of varius testosterone concentration released from ceramic delivery system on the circulating hormone levels of adult castrated rams. Proceedings of the 28th Annual Meeting of the Rocky Mountain Bioengineering Symposium, Rochester, Minnesota, April 12-13, 1991.
3. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Tricclium phosphate amino acid capsules as a drug delivery system for steroid hormones. Proceedings of the 28th Annual Meeting of the Rocky Mountain Bioengineering Symposium, Rochester, Minnesota, April 12-13, 1991.
4. Benghuzzi, H.A., England, B.G., and Bajpai, P.K: In vivo delivery of estradiol from ceramic drug delivery devices. Proceedings of the 28th Annual Meeting of the Rocky Mountain Bioengineering Symposium, Rochester, Minnesota, April 12-13, 1991.
5. Benhuzzi, H.A., England, B.G. and Bajpai, P.K.: Inhibition and recovery of spermatogenesis by sustained delivery of dihydrotestosterone released from ceramic implants in rodents. FASEB J. 1991:5;259.
6. England, B.G., Benghuzzi, H.A., Possley, R.M. and Bajpai, P.K.: Sustained delivery of testosterone by means of ceramic delivery system in adult castrated rams. FASEB J. 1991:5;260.
7. Benghuzzi, H.A., Giffin, B.F., Bajpai, P.K. and England, B.G.: Successful antidote of multiple lethal injections with sustained delivery of difluoromethylonithine by means of tricalcium phosphate drug delivery devices. The 17th Annual Meeting of the Society for Biomaterials, May 1-5, 1991, Scottsdale, Arizona. 1991:XIV;153.
8. Benghuzzi, H.A., Bajpai, P.K and England, B.G.: The effects of density of the ceramic delivery devices on sustained release of androgens in castrated rats. The 17th Annual Meeting of the Society for Biomaterials. May 1-5, 1991, Scottsdale, Arizona. 1991:XAV;159.
9. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Suppression of spermatogenesis by means of continuous delivery of danazol plus testosterone from ceramic delivery devices. 73rd Annual Meeting of the Endocrine Society, June 19-22, Washington, D.C., 1990.
10. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Effects of sustained delivery of androgens by ceramic implants in rats: Morphology of various tissues. Scanning Electron Microscopy International: Cells and Materials, May 4-9, Bethesda, Maryland, 1990.

JOSEPH C. FANTONE, M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Autopsy Service.

II. TEACHING ACTIVITIES:

A. Director, Resident Training Program.
B. Graduate Program Committee (Chairman).
C. Course Director - Pathology 600.
D. Laboratory Instructor - Pathology 600.
E. Coordinator - Senior Medical Student Clerkships.
F. Sequence Coordinator and Lecturer - Sophomore Medical Students (ICS-600) Immunopathology.
G. Associate Director - Sophomore Medical Student ICS Course (600/601).
H. Coordinator, Department of Pathology Summer Clinical/Research Program for Minority Medical Students.
I. Pulmonary Pathology Conference (monthly to Pulmonary Division - Internal Medicine).
J. Lecturer - Microbiology and Immunology 624.
K. Preceptor, Microbiology 620, Problem-Based Learning Tutorial.
L. Lecturer - Pathology 580.
M. Preceptor, Pathology 650
N. Preceptor - Undergraduate and Medical Student Research (6).
O. Graduate Student Ph.D. Thesis Committee (3).
P. Preceptor for one Postdoctoral Fellow.

III. RESEARCH ACTIVITIES:

A. Mechanisms of phagocytic cell-mediated tissue injury.
B. Signal transduction pathways of phagocytic cells.

SPONSORED SUPPORT:

A. Principal Investigator: Mechanisms of Myocardial Ischemia/Reperfusion Injury (NIH-R01-HL44085).
B. Principal Investigator: Myocardial Ischemia and Reperfusion Injury, (American Heart Association Grant-in-Aid).
C. Principal Investigator: Phagocytic Cell and Glomerular Injury. Section IV of Renal Center Grant (NIH-P50-DK39255).
D. Co-Investigator: Mechanisms and Genetic Regulation of Pulmonary Fibrosis. (S.H. Phan; Principal Investigator) (NIH-5-R01-HL-28737).
E. Co-Investigator: Pharmacologic Studies on the Ischemic Heart (B. Lucchesi, Principal Investigator) (NIH-R01-HL-19782).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chairman's Advisory Committee.
B. Coordinator - Educational Activities.
C. Department ACAPT Committee.
D. Human Resource Commmittee.
E. Research Space Advisory Committee.
F. Department Computer Committee.
G. Department Photography Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Medical Student Advisor (3rd and 4th year).
B. ICS - Executive Committee.
C. Basic Science Phase Committee.
D. Clinical Phase Committee.
E. Medical Student Basic Science Academic Review Board.
F. Medical Student Clinical Phase Academic Review Board.
G. Medical School Admissions Committee.
H. Medical School Retreat on Medical Education.

REGIONAL AND NATIONAL:

A. NIH Site Visit, SCOR: Atherosclerosis. Louisiana State University, New Orleans, Louisiana, 1990.
B. NIH Study Section: Pathology Á, 1990.
C. Reviewer, Searle's Pharmaceutical Company Research Grants, Chicago, Illinois, 1991.
D. NIH Site Visit: Program Project: Physical Properties and Biologic Functions of Lipids, Hormel Institute, Austin, Minnesota, 1991.
F. Reviewer, Veteran's Administration Research Grants.
G. United States of America Federal Grand Jury, U.S. District Court, Detroit, Michigan, 1990.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Editorial Board, Infection and Immunity.
B. Editorial Board, Laboratory Investigation.
C. Reviewer, of Clinicl Investigation.
D. Reviewer, Immunology.
E. Reviewer, Science
F. Reviewer, American Journal of Pathology.
G. Reviewer, Laboratory Investigation.
H. Reviewer, Journal of Biological Chemistry.
I. Reviewer, American Review of Respiratory Disease.
J. Reviewer, Journal of Leukocyte Biology.
K. Reviewer, Circulation Research.
L. Reviewer, Biochemical Pharmacology.
M. Reviewer, American Journal of Physiology.

N. Reviewer, Circulation.
O. Reviewer, Infection and Immununity.

INVITED LECTURES AND SEMINARS:

1. Invited Speaker, British Association of Lung Research, Edinburgh, Scotland, 1990.
2. Co-Chairperson, Symposium on Leukocyte Stimulation: Receptors for Agonists. American Association of Pathologists, FASEB Meeting, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Crockett-Torabi, E. and Fantone, J.C.: Soluble and insoluble immune complexes activate human neutrophil NADPH oxidase by distinct Fcγ receptor-specific mechanisms. J. Immunol. 1990;145:3026-3032.
2. Brieland, J. and Fantone, J.C.: Ferrous iron generation from transferrin by human neutrophil-derived superoxide anion: Effect of pH and iron saturation. Arch. Biochem. Biophys. 1991;284:78-83.
3. Barker, J.N.W.N., Jones, M.L., Swenson, C.L., Sarma, V., Mitra, R.S., Ward, P.A., Johnson, K.J., Fantone, J.C., Dixit, V.M. and Nickoloff, B.J.: Monocyte chemotaxis and activating factor (MCAF) production by keratinocytes in response to interferon-gamma. J. Immunol. 1991;146:1192-1197.
4. Werns, S.W., Grum, C.M., Ventura, A., Hahn, R.A., Ho, P.P.L., Towner, R.D., Fantone, J.C., Schork, M.A. and Lucchesi, B.R.: Xanthine oxidase inhibition does not limit canine infarct size. Circulation. 1991;83:995-1005.
5. Barker, J.N.W.N., Jones, M.L., Mitra, R.S., Crockett-Torabi, E., Fantone, J.C., Kunkel, S.L., Warren, J.S., Dixit, V.M. and Nickoloff, B.J.: Modulation of keratinocyte-derived interleukin-8 which is chemotactic for neutrophils and T-lymphocytes. Am .J. Pathol., In Press.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Cunningham, M.R., Mu, D-x., Driscoll, E.M., Moon, S.D., Schwaiger, M., Fantone, J.C. and Nedelman, M.A.: Indium-anti-myosin and thallium distribution in myocardial tissues - eight weeks postinfarction. FASEB J. 1991;5:A1046.
2. Brieland, J. and Fantone, J.C.: Release of transferrin-derived iron by rat pulmonary artery endothelial cells: Lack of evidence of a plasma membrane diferric transferrin reductase. FASEB J. 1991;5:A1614.

ANDREW FLINT, M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Rotations, July (2/4), August (1/4), September (4/4), December (2/4). Autopsy Rotation, August (1/4). Sabbatical Leave, January-June.
B. Thoracic Tumor Review Board (Weekly).

II. TEACHING ACTIVITIES:

A. Pathology 600 Lectures:
   1. Pulmonary Pathology I - February, 1991.
   2. Pulmonary Pathology II - February, 1991.
   3. Pulmonary Pathology III - February, 1991.
   4. Pulmonary Pathology IV - February, 1991.

B. Pathology 630:
   1. Respiratory Disease I - October, 1990.
   2. Respiratory Disease II - November, 1990.

C. Residency Training:
   1. Diseases of the Chest I - November, 1991.
   2. Diseases of the Chest II - November, 1991.
   3. Diseases of the Chest III - November, 1991.

D. Other educational activities:
   1. M4 student elective mentor, September, 1990.
   2. Pulmonary Pathology - Radiology Conference, Department of Radiology, September, 1990.
   3. Pulmonary Pathology - Radiology Conference, Department of Radiology, November, 1990.
   4. Pulmonary Pathology - Radiology Conference, Department of Radiology, May, 1991.
   5. Career Choices and Perspectives, Office of Student Affairs Seminar, November, 1990.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Pathology Consultant, Morphologic Studies of Diffuse Interstitial Lung Diseases, A Multi-Institution Project, Reuben M. Cherniak, M.D., National Jewish Hospital, Program Director.
B. Monoclonal Antibodies to Bladder Tumor Antigens, H. Barton Grossman, M.D. (Principal Investigator), Andrew Flint, M.D. (Co-Investigator).
C. Pathology Consultant, Prospective Investigation of Pulmonary Embolism Diagnosis, John G. Weg, M.D., Principal Investigator.

D. Occupational and Immunologic Lung Diseases Scor Grant, Galen B. Toews, M.D., (Principal Investigator).

PROJECTS UNDER STUDY:

A. Methotrexate-induced Hepatic Disease: An Analysis of Sequential Liver Biopsy Samples.
B. DNA Analysis of Renal Cell Carcinoma: Entrophy of DNA Histograms.
C. Evaluation of a Novel Monoclonal Antibody (DD 23): Correlation of Antigen Expresion with DNA Contene of Transitional Cell Neoplasms.
D. Interstitial Lung Disease: Influence of Biopsy Site on Diagnosis.
E. The Morphologic Manifestations of Metastatic Renal Cell Cacinoma to the Lung.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interviewed House Officer Candidates (September, 1990-December, 1990).
B. House Officer Recruitment Brochure Revision and Publication.
C. Coordinator, Senior Staff Service Rotations.
D. Director, Surgical Pathology Fellowship Program.
E. Residency Selection Committee.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

1. Reviewer, American Review Respiratory Disease.
2. Reviewer, Archives of Pathology and Laboratory Medicine.

INVITED LECTURES/SEMINARS:

1. Guest Pathologist, Tri-State Thoracic Society, Orange Beach, Alabama, January, 1991.

VI. PUBLICATIONS:

1. Flint, A. and Lloyd, R.V.: Pulmonary metastases of colonic carcinoma: Distinction from pulmonary adenocarcinoma. Arch. Pathol. Lab. Med., In Press.
2. Flint, A., Davenport, R.D. and Lloyd, R.V.: The tall cell variant of papillary carcinoma of the thyroid gland. Arch. Pathol. Lab. Med. 1991;115:169-171.
3. Cherniak, R.M., Colby, T.V., Flint, A., et al: Quantitative assessment of lung pathology in idiopathic pulmonary fibrosis. Amer. Rev. Resp. Drs., In Press.
4. Liebert, M., Wedemeyer, G., Chang, J.H.C., Stein, J.A., McKeever, P.E., Carey, T.E., Flint, A., Steplewski, Z., Buchsbaum, D.J., Wahl, R.L. and Grossman, H.B.: Comparison of antigen expression on normal urothelial cells in tissue sections and tissue culture. J. Urol. 1990;144:1288-1292.
5. Flint, A. and Lloyd, R.V.: Colonic carcinoma metastatic to lung: Cytologic manifestations and distinction from primary pulmonary adenocarcinoma. Acta Cytol., In Press.
6. Hegg, C.A., Flint, A. and Singh, G.: Papillary adenoma of the Lung. Amer J Clin Pathol., In Press.

SUBMITTED PUBLICATIONS:

1. Flint, A., Grossman, H.B. and Liebert, M.: DNA content of renal cell carcinoma: Entrophy of DNA histograms and correlation with prognostic parameters. J. Urol.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Hegg, C.A., Flint, A., Fantone, J.C. and Singh, G.: Papillary adenoma of the lung. Am. J. Clin. Pathol. 1990;94:501.
2. Flint, A. and Lloyd, R.V.: Pulmonary metastases of colonic carcinoma: Distinction from primary pulmonary adenocarcinoma. Mod. Pathol. 1991;4:115A.

THOMAS FRANK, M.D.
ASSISTANT PROFESSOR OF CLINICAL CHEMISTRY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Surgical Pathology - 1,935 cases.
B. Necropsy Service - one week.
C. Consultations on surgical gynecologic pathology from other hospitals and medical centers.
D. Weekly interdisciplinary Gynecologic Oncology Tumor Board Review.

II. TEACHING ACTIVITIES:

A. Pathology 600 Lectures:
   1. Neoplasia I, January 1990.
   2. Neoplasia II, January 1990.
   3. Neoplasia III, January 1990.
   4. Neoplasia IV, January 1990.
   5. Gynecology III, March 1990.
   6. Gynecology IV, March 1990.
B. Introduction to Clinical Sciences 601 Course.
C. Preceptor for medical student research project (Biomedical Research Program): Loss of heterozygosity of p53 in adenocarcinoma of the endometrium (Brad Slywka, B.A.).
D. Lecturer, two Anatomic Pathology Didactic Conferences.
E. Monthly Pathology-Gynecology teaching conference for house officers in OB-GYN.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Horace H. Rackham Faculty Grant from the University of Michigan ($6,429 5/91 - 4/93): molecular analysis of clonality.
B. Phoenix Memorial Research Grant from the University of Michigan ($4,811 4/91 - 6/92): molecular analysis of clonality.

PROJECTS UNDER STUDY:

A. Loss of heterozygosity of p53 gene in epithelial malignancies of ovary and endometrium (with James A. Roberts, M.D., Dept. of Obstetrics and Gynecology).
B. Retrospective analysis of somatic and tumor-associated alterations of p53 gene in familial breast carcinoma (with Barbara L. Weber, M.D. and Francis S. Collins, M.D., Ph.D, Dept. of Internal Medicine).
C. Diagnosis of histologically occult cytomegalovirus infection in immunocompromised patients using the polymerase chain reaction.

D. Diagnosis of mycobacterial infection in paraffin-embedded tissues using the polymerase chain reaction.
E. Mutations and gene loss of p53 locus in hepatocellular carcinoma.
F. Pathologic-radiologic correlation of Paget's disease of the breast, with D.M. Ikeda, M.D.; results submitted to Sciencitic Assembly of the Radiologic Society of North America.
G. Morphologic assessment of renal injury during vascular surgery, with L.G.D'Alecy, M.D.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Surgical Pathology representative to the Departmental Quality Assurance/Quality Control Committee.
B. Co-director, Clinical Molecular Diagnostics Laboratory (preserved tissue analysis development).

REGIONAL AND NATIONAL:

A. Member, American Association for the Advancement of Science.
B. Member, United States & Canadian Academy of Pathology (US-CAP).
C. Member, A. James French Society.
D. Member, American Society of Clinical Pathologists.

V. OTHER RELEVANT ACTIVITIES:

A. Gynecologic Oncology Group study section (Pathology).
B. Member of the University of Michigan Cancer Center.
C. Member of the University of Michigan Kughn Clinical Research Center.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Frank, T.S., Bhat, N., Noumoff, J.S. and Yeh, I.: Residual trophoblast as a source of highly atypical cells in the postpartum cervicovaginal smear. Acta Cytologica 1991;35:105-108.
2. Shinkwin, M.A., Lenkinski, R.E., Zlatkin, M.B., Frank, T.S., Holland, G.A., Schmidt, R.G., Kressel, H.Y. and Daly, J.M.: Assessment of soft tisue tumors using integrated magnetic resonance imaging and ^{31}P-spectroscopy. Cancer 1991;67:1849-1858.
3. Helvie, M.A., Hessler, C., Frank, T,S. and Ikeda, D.M.: Atypical hyperplasia of the breast: Mammographic appearance and histologic correlation. Radiology 1991;179:759-764.
4. Pelkey, T.J., Frank, R.S., Frank, T.S., Stanley, J., Zelenock, GB. and D'Alecy, L.G.: Minimal physiologic temperature variations during renal ischemia alter functional and morphologic outcome. J Vasc Surgery, Accepted, August, 1991.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Wilson, M.D., DelBuono. E.A. and Frank, T.S.: A simplified method for the detection of cytomegalovirus by polymerase chain reaction from histologic sections of small biopsies.
2. Frank, T.S., Reed, J.C. and Brooks, J.J.: Absence of c-*sis* and transforming growth factor-beta mRNA expression in malignant fibrous histiocytoma.

3. Frank, R.S., Frank, T.S., Zelenock, G.B. and D'Alecy, L.G.: Intermittent reperfusion reduces functional and morphologic damage following renal ischemia.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Ikeda, D.M., Helvie, M.A., Frank, T.S., Anderson, I., Linnell, F. and Chapel, K.: Paget's disease of the nipple: Radiologic/pathologic correlation. 77th Scientific Assembly of the Radiologic Society of North America, 1991.
2. Frank, T.S.: Book review, Pathology of the Mediastinum, Am. J. Surg Pathol. 1991;15:204.

BRUCE A. FRIEDMAN, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Director, Pathology Data Systems.
B. Director, Phlebotomy Services and Central Distribution.
C. Staff supervision of the Autopsy Service.

II. TEACHING ACTIVITIES:

A. Co-Director of a laboratory section for Pathology 600.

MEDICAL SCHOOL/HOSPITALS:

A. Program Director of the Ninth Annual Clinical Laboratory Computer Symposium at the Towsley Center for Continuing Medical Education, June 13-15, 1990. The Symposium attracted 210 registrants from 30 states and Canada plus 28 system vendors/laboratory consultants.

III. WORK IN PROGRESS:

A. Friedman, B.A.: Information management aphorisms for the laboratory professional. (Submitted to MLO).
B. Friedman, B.A. and Mitchell, W.: Integrating information from decentralized laboratory testing sites. (Solicited article in preparation for the "Patterns" supplement to the AJCP).
C. Mitchell, W. and Friedman, B.A.: Information systems in hospitals: technical, political, and transaction costs explanations for departmental success and interdepartmental failure.
D. Mitchell, W. and Friedman, B.A.: An evolutionary typology of vendors of laboratory information systems with special reference to clinical laboratory information systems (To be submitted to Clinical Laboratory Management Review).

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Quality Assurance Committee.
B. Editor, Pathology Electronic News (PEN).

HOSPITAL COMMITTEES:

A. ITN (Information Technology and Networking) Steering Committee.

UNIVERSITY OF MICHIGAN:

A. Executive Committee, Center for Statistical Consultation and Research (CSCAR), 1991-1994.

REGIONAL AND NATIONAL:

A. Council on Medical Informatics of the American Society of Clinical Pathologists.
B. Chairman of the Executive Council, Cerner User's Group.
C. Editorial Advisory Board, Clinical Laboratory Management Review.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1.. Strategic Uses of the Laboratory Information System. A lecture presented to a joint meeting of the Pittsburgh Society of Pathologists and the Western Pennsylvania Chapter of the Clinical Laboratory Managers Association, Pittsburgh, Pennsylvania, September 27, 1990.
2. The Role of the Director of the Laboratory Information System. A lecture presented at a symposium entitled "The Information Management Executive" sponsored by HIMMS, CHIM, and the University of Michigan Department of Health Services Management and Policy, October 31, 1990, Ann Arbor, Michigan.
3. An Organizational Model for Medical Informatics for the 1990s. A lecture presented at the Medical Services Evaluation Seminar series of the Health Information Technology Center, Medical College of Wisconsin, Milwaukee, Wisconsin, December 10, 1990.
4. Clinical Information Systems: Centralized vs. Decentralized. One of two speakers participating in a workshop of the same name presented at the Spring Meeting of the College of American Pathologists, Nashville, Tennessee, March 2, 1991.
5. The Role of the Director of the Laboratory Information System. A lecture presented at a symposium entitled "The Information Management Executive" sponsored by HIMMS, CHIM, and the University of Michigan Department of Health Services Management and Policy, March 28, 1991, Ann Arbor, Michigan.
6. The Politics of Managing the Information Product of Pathology. A lecture delivered at the Spring Meeting of the Michigan Society of Pathologists, St. Clair, Michigan, May 18, 1991.
7. Centralization Versus Decentralization of Hospital Information Systems: Quality and Efficiency Considerations. Managing an LIS: An Operational and Strategic Approach. A lecture and workshop presented to the Ninth Annual Laboratory Information System Symposium, Ann Arbor, Michigan, June 13, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Friedman, B.A. and Mitchell, W.: Horizontal and vertical integration in hospital laboratories and the laboratory information system. Clin. Lab. Med. 1990;10:627-641.
2. Friedman, B.A.: Informatics as a separate section within a Department of Pathology. Amer. J. Clin. Pathol. 1990;94:S2-S6.
3. Friedman, B.A. and Mitchell, W.: Organization innovation and the laboratory information system. Clin. Lab. Man. Rev. 1990;4:345-351.
4. Friedman, B.A. and Mitchell, W.: Competition and control in clinical laboratories: An information technology perspective. Clin. Lab. Sci. 1991;4:30-32.

5. Friedman, B.A.and Mitchell, W.: Using the laboratory information system to achieve strategic advantage over the competitors of hospital-based clinical laboratories. Clin. Lab. Med. 1991;11:187-202.
6. Friedman, B.A. and Mitchell, W.: An analysis of the relationship between a department of pathology and the vendor of its laboratory information system. Am. J. Clin. Pathol., Accepted for Publication.
7. Friedman, B.A. and Mitchell, W.: An exploration of the interface between information technology and quality: Implications for the professional role of pathologists. Clin. Lab. Man. Rev., Accepted for Publication.

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN NON-REFEREED JOURNALS:

1. Friedman, B.A.: Using the laboratory information system as a strategic tool. Computers in Healthcare 1990;September:38+.

DONALD A. GIACHERIO, PH.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Director, General Chemistry Laboratory.
B. Daily sign-out and interpretation of electrophoresis results.
C. Direct operation of blood gas-electrolyte analyzers in operating rooms of Main and Mott Hospitals.
D. Direct work group for the establishment of a quality assurance program for bedside blood glucose testing.
E. Planning group for establishment of STAT labs at alternative sites in University Hospitals.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Medical School:
   1. Developed case presentation on acute myocardial infarction for Path 600 Laboratory.
B. Pathology House Officers:
   1. Lecturer, Clinical Pathology Rounds (two lectures).
   2. Coordinator, Pathology House Officer rotation through General Chemistry Lab.
   3. Review daily sign-out and interpretation of electrophoresis results.
   4. Review of selected topics in Clinical Chemistry.
C. Medical Technologists:
   1. Program Director, Continuing Education Series for Medical Technologists.

III. RESEARCH ACTIVITIES:

A. Evaluation and standardization of an assay for Lipoprotein (a).
B. Evaluation of a kinetic microparticle assay for drugs of abuse in urine.
C. Evaluation of instruments for the measurement of blood glucose at the patients bedside.
D. CRC Protocol: Oxalate dynamics and removal in endstage primary hyperoxaluria (with J. Turcotte, et al).
E. CRC Protocol: Hourly variation in serum potassium and magnesium concentrations in patients with congestive heart failure (with J. Nicklas).
F. IDMH Study. Changes in serum lipids, apolipoproteins, and lipoprotein (a) in hypercholesterolemic patients following dietary therapy (with C. Orringer).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Quality Assurance Committee.

B. M-Labs Technical Operations Group.
C. Coordinator, Chemistry Lab Supervisors Meetings.
D. Biochemistry Section Directors Group.
E. Coordinator, Clinical Chemistry In-Service Education Program.

MEDICAL SCHOOL/HOSPITAL:

A. Pathology representative to the "Standardization and Product Evaluation Committee".
B. Chair, Task Force on Standardization of Blood Glucose Testing.

REGIONAL AND NATIONAL:

A. Coordinator, College of American Pathologists Clinical Chemistry Standards Assay Laboratory.
B. Education Committee, Michigan Section, AACC.
C. Program Committee Chairman, Michigan Section, AACC.
D. Lipids and Lipoproteins Subgroup, AACC.
E. AACC Student Poster Presentation Judges Group

V. INVITED LECTURES:

1. "Accuracy of Cholesterol Determinations", Southeast Michigan/Toledo Lipid Club, Livonia, Michigan. February, 1991.
2. "Critical Care Testing: What, How, Where, and by Whom?", Michigan Section AACC Meeting, Lansing, Michigan, May, 1991.
3. "Evaluation of the Roche OnLine Drugs of Abuse Testing Reagent System", Roche Diagnostic Systems Customer Symposia, Novi, Michigan, June, 1991.

VI. PUBLICATIONS:

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Giacherio, D. and Matz, K.: Evaluation of an enzyme immunoassay kit for the determination of lipoprotein (a). Clin. Chem. 1990;36:955.
2. Giacherio, D. and Pyzik-Shuler, R.: Evaluation of the Abbott IMx CK-MB Immunoassay: Comparison with the Roche Isomune MB assay. Clin. Chem. 1990;36:1132.
3. Spengler, R.N., Chensue, S.W., Giacherio, D.A. and Kunkel, S.L.: Endogenous Norepinephrine (NE) Regulates Tumor Necrosis Factor (TNF) Production from Macrophages (MO) in Culture. FASEB J. 1990;5:A1214.
4. Bleske, B.E., Justice, J., Giacherio, D.A., Bajwa, H., Schreiber, S.F., Stemmer, K., Das, S.K. and Nicklas, J.M.: Marked Variability in Hourly Potassium Levels in Congestive Heart Failure Patients Treated with High Dose Diuretics and in Normal Controls. American College of Cardiology Annual Scientific Session, 1991.

PAUL W. GIKAS, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Surgical Pathology - Room I and Room II, 17 weeks.
B. Diagnostic electron microscopy - share nephropathology work with Dr. K. Johnson.
C. Consultation service for Uropathology.
D. Conduct monthly conference in Urologic Pathology with Urology Section.
E. Participate in weekly Renal Biopsy Conference for Nephrology Section with Dr. K. Johnson.
F. Frozen Section "on call" Rotation.
G. Consultant, Veterans Administration Hospital.

II. TEACHING ACTIVITIES:

A. Lectures to sophomore Pathology 600 students:
   1. Death certification and forensic pathology.
   2. Pathogenesis of highway injuries.
   3. Renal neoplasms and renal allograft rejection.
   4. Diseases of prostate and external genitalia.
   5. Testicular disease.
B. Lab instructor for Pathology 600.
C. Lecture on Urologic Pathology and Pathogenesis of Highway Injury to Dental Pathology 630 students.
D. Monitor for M-4 clerks during Elective Pathology Rotation, August 20-September 14.
E. Pathology Resident Teaching.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Collaborate with Urology Staff and Radiology Staff on projects.
B. Radiological Diagnostic Oncology Group Prostate Study correlating imaging techniques with morphologic findings. This specific project is funded by the National Cancer Institute and is a cooperative study with three other institutions.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Member, Advisory Committee on Appointments, Promotion and Tenure.

MEDICAL SCHOOL/HOSPITAL:

A. Assistant Dean for Medical School Admissions.
B. Hospital Claims Control Committee.

UNIVERSITY:

A. None.

REGIONAL AND NATIONAL:

A. National Collegiate Athletic Association (NCAA) Drug Testing Appeals Committee.
B. NCAA Special Planning Committee for Drug Testing.
C. NCAA Drug Testing Crew Chief.
D. NCAA Committee on Competitive Safeguards and Medical Aspects of Sports.
E. NCAA, NFL, U.S. Olympic Committee, American Association Clinical Chemists and College of American Pathologists Committee on Sports Drug Testing Laboratory Accreditation.
F. Deputy Medical Examiner, County of Washtenaw.
G. Board of Directors, Public Citizen, Inc. (Ralph Nader, Initial Chairman and Founder).

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Lecture, "Epidemiology & Pathological Diagnosis of Prostate Cancer" at Prostate Cancer Seminar, Blanchard Valley Hospital, Findlay, Ohio, May 4, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS

1. Quint, L.E., Van Erp, J.S., Bland, P.H., Del Buono, E.A., Mandell, S.H., Grossman, H.B. and Gikas, P.W.: Prostate cancer: Correlation of MR images with tissue optical density at pathologic examination. Radiology 1991;179:837-842.
2. Quint, L.E., Van Erp, J.S., Bland, P.H., Mandell, S.H., Del Buono, E.A., Grossman, H.B., Glazer, G.M. and Gikas, P.W.: Carcinoma of the prostate: MR images obtained with body coils do not accurately reflect tumor volume. AJR 1991;156:511-516.

BOOK REVIEW

1. Gikas, P.W.: Tumors and Tumor-like Conditions of the Kidneys and Ureters, Eble, J.N. (ed.), Contemporary Issues in Surgical Pathology Series. American Journal of Surgical Pathology, In Press.

ABSTRACT

None.

CARL T. HANKS, D.D.S.
PROFESSOR OF DENTISTRY
DEPARTMENT OF ORAL PATHOLOGY
ASSOCIATE PROFESSOR OF ORAL PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES: None.

II. TEACHING ACTIVITIES:

A. D.D.S. Level:
   a. Oral Pathology 694.10 Hours (Lecture).

B. Graduate Level Advisement:
   a. John Wataha - Ph.D. Program (Biomaterials) - three years.
   b. Celeste Swamidoss - MSD Program (Oral Pathology) - 18 months.
   c. Rod Parsell - Undergraduate Research - three years.
   d. Fawzi El Shefei - MSD Program (Biomaterials) - nine months.
   e. John C. Fat - MSD Program (Endodontics) - 15 months.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. National Institute of Dental Research, No. 1-P50-DE09296-01, "Specialized Materials Science Research Center, "(R. G. Craig, Director; C.T. Hanks, Co-director and P.I. of one of four sections), 9/29/89-9/28/94.

IV. ADMINISTRATIVE ACTIVITIES:

SCHOOL OF DENTISTRY AND DEPARTMENT OF ORAL PATHOLOGY:

A. Admissions Committee, School of Dentistry, 1985-1991.
B. Nominations and Elections Committee, School of Dentistry, 1987-1990.
C. Hazardous Waste Committee, School of Dentistry, 1987-1990 (Chairman).
D. Table Clinics Committee (1989-1991).
E. Search Committees for faculty for Department of Prosthodontics, 1990-1991.
F. Director of Research, School of Dentistry 1989-1991.
G. Vice-Chairman, Department of Oral Medicine, Pathology and Surgery, School of Dentistry, 1991.
H. Organizer of Specialized Materials Center Fall Conference, 1990 -1991.
I. Biomedical Research Council, University of Michigan School of Medicine 1990-1993.
J. Research Advisory Committee, Department of Surgery, 1990-.
K. Research Dean's Committee (OVPR U/M), 1989-1991.
L. Medical Affairs Advirosy Committee to Vice Provost Zuidema, 1989-1991.

REGIONAL AND NATIONAL:

A. President of Pulp Biology Group, International Association for Dental Research, 1989-1990.
B. ADA Subcommittee on Biological Evaluation of Dental Materials (Committee Member), 1987-1992.
C. U.S. Technical Advisory Group for International Standards Organization Tissue Culture Group 194: Biological Evaluation of Medical and Dental Materials and Devices (Nominated Member), 1989-1992.
D. Organizing Committee for Pulp Biology conference on "Pathobiology of the Dentin/Pulp Complex," May, 1991.

V. OTHER RELEVANT ACTIVITIES:

A. Consultant: W. R. Grace Co.
B. Consultant: Kerr Manufacturing Co.
C. Consultant: Paladin Medical (Baxter).
D. Special Study Sections, NIDR, 1988-1991.

PROFESSIONAL ORGANIZATIONS:

A. International Association for Dental Research.
B. American Academy of Oral Pathology.
C. American Association for the Advancement of Science.
D. Omicron Kappa Upsilon.
E. Tissue Culture Association (National).
F. Michigan Biomedical Materials and Prosthetic Group.
G. New York Academy of Sciences.
H. Sigma Xi.

EDITORIAL REVIEW BOARDS:

A. Journal of Dental Research.
B. Journal of the American Dental Association.
C. Journal of Periodontal Research.

INVITED LECTURES/SEMINARS:

1. Invited lecture, "In Vitro Testing of Dental Pulp Toxicity", Philadelphia section of the AADR as a part of a one-day symposium in the Summer of 1990.
2. Lecture, "Cyto-Toxicity and Adhesion as Measures of Responses by Eukaryotic Cells and Bacteria to Materials", Fall Conference of Specialized Materials Center in October, 1990.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hanks, C.T., Syed, S.A., Craig, R.G., Hartrick, J.M. and Van Dyke, T.E. Modeling bacterial damage to pulpa cells *in vitro*. J. Endodontics 1991;17:21-25.
2. Craig, R.G. and Hanks, C.T. Cytotoxicity of experimental casting alloys evaluated by cell culture tests. J. Dent. Res. 1990;69:1539-1542.

3. Rathbun, M.A., Craig, R.G., Hanks, C.T. and Filisko, F.E. Cytotoxicity of a Bis-GMA dental composite before and after leaching in organic solvents. J. Biomed. Mater. Res. 1991;25:443-457.

ARTICLES IN PRESS OR ACCEPTED BY PEER-REVIEWED JOURNALS:

1. Wataha, J.C., Hanks, C.T. and Craig, R.G. The *in vitro* effects of metal cations in eukaryotic cell metabolism, J. Biomed. Mater. Res., Accepted for publication.

ARTICLES SUBMITTED TO PEER-REVIEWED JOURNALS:

1. Wataha, J.C., Craig, R.G. and Hanks, C.T. The release of elements of dental casting alloys into cell culture medium, Submitted to J. Dent. Res.
2. Wataha, J.C., Craig, R.G. and Hanks, C.T.: Precision and new methods for testing in vitro alloy toxicity, Submitted to Dental Materials.
3. Nassiri, M.R., Hanks, C.T., Cameron, M.J., Strawn, S.E. and Craig, R.G.: Application of flow cytometry for determining the biocompatibility of urethane dimethacrylate, Submitted to Cytometry.
4. Hanks, C.T., Strawn, S.E., Wataha, J.C. and Craig, R.G.: Cytotoxic effects of composite resin components on cultured mammalian fibroblasts, Submitted to J. Dent. Res..

ABSTRACTS:

1. Wataha, J.C., Craig, R.G. and Hanks, C.T.: Precision of new methods for testing in vitro alloy toxicity. J. Dent. Res. 1991;70:361.
2. Nassiri, M.R., Cameron, M.J., Strawn, S., Wataha, J.C., Hanks, C.T. and Craig, R.C.: Metal ion affects the cell cycle progression. J. Dent. Res. 1991;70:361.
3. Hanks, C.T., Parsell, R.R., Strawn, S.E., and Wataha, J.C.: Cytotoxicity of dentin bonding agents with monolayer and dentin diffusion. J. Dent. Res. 1991;70:384.
4. Strawn, S.E., Nassiri, M.R., Hanks, C.T., Cameron, M.J., Wataha, J.C. and Craig, R.G.: Bis-GMA and UDMA effects on cell metabolism and cell cycle. J. Dent. Res. 1991;70:384.
5. El-Shafei, F.A., Nassiri, M.R., Hanks, C.T. and Craig, R.G.: Cytotoxic evaluation of heat-treated composite resin inlay by flow cytometry. J. Dent. Res. 1991;70:396.
6. Dahlgren, J.A., Syed, S.A. and Hanks, C.T.: In vitro adhesion of oral bacteria to three biomaterials. Abstract at 1991 Annual Meeting of the American Society of Microbiologists.

CURTIS A. HANSON, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Clinical Flow Cytometry Laboratory.
B. Clinical Hematology Laboratory.
C. Diagnostic Surgical Pathology, Hematopathology.
D. Consultant for Hematopathology cases.
E. Clinical Molecular Diagnostics Laboratory.

II. TEACHING ACTIVITIES:

A. Medical Students and Graduate Students:
   1. Three lectures, Hematopathology - Pathology 600 course.
   2. Laboratory Instructor (2 sessions), Hematopathology - Pathology 600 course.
   3. M4 Clerkship, Hematology portion of Clinical Pathology Rotation.
   4. Dental students, One Lecture on Hematologic Disorders.
   5. Preliminary planning for M4 elective in Laboratory Medicine.

B. House Officers:
   1. Sign-out of bone marrow biopsies and aspirates.
   2. Review of blood smears and body fluids in Hematology Laboratory.
   3. Review of Flow Cytometry results and correlation with hematologic diagnosis.
   4. Molecular Diagnostics Rotation

C. Hematopathology teaching:
   1. Hematopathology Lectures/Weekly.
   2. Hematopathology unknown conferences/biweekly.

D. Clinical Pathology Grand Rounds (two lectures).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT: None

PROJECTS UNDER STUDY:

A. Acute Biphenotypic Leukemias.
B. Immunophenotyping in Chronic Lymphoproliferative Disorders.
C. CD2-Positive Acute Myeloid Leukemia.
D. CD7 Expression in Acute Leukemias.
E. Cytogenetic Abnormalities in Myeloproliferative and Myelodysplastic Syndromes.
F. Automated Blood Differential Counts.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Clinical Flow Cytometry Laboratory
B. Associate Director, Clinical Hematology Laboratory
C. Leukemia Conference, biweekly
D. Chairman's Advisory Committee
E. Director, Hematopathology Fellowship Program
F. Residency Advisory Committee

REGIONAL AND NATIONAL:

A. Associate Editor of Pathology Patterns (American Journal of Clinical Pathology, Supplement).
B. Editorial Board, American Journal of Clinical Pathology
C. Council for New Scientific Technology in Clinical Pathology, American Society of Clinical Pathologists.
D. Reviewer of articles for Blood, American Journal of Pathology, American Journal of Clinical Pathology, Laboratory Medicine and Clinical Immunology and Immunopathology.
E. Review of Southwest Oncology Group (SWOG) leukemia cases

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, "Applications of Molecular Pathology to Diagnostic Pathology", Ontario Association of Pathologists, Windsor, Ontario, October 12, 1990.
2. Invited Lecturer, "Chromosomal Translocations in Human Tumors: From Cellular Biology to the Bedside", Molecular Biology Symposium, American Society of Clinical Pathologists (ASCP), October 23, 1990.
3. Lecturer, "Flow Cytometry and Southern Blotting in the Diagnosis of Leukemia and Lymphoma", Course presented at the American Society of Clinical Pathologists (ASCP), October 24, 1990.
4. Invited Lecturer, "S100-Positive Chronic Lymphoproliferative Disorder", University of Wisconsin, Madison, Wisconsin, March 18, 1991.
5. Invited Lecturer, "Acute Biphenotypic Leukemia", Department of Pediatrics, University of Michigan, June 12, 1991.
6. Director, Clinical Applications of Flow Cytometry in Diagnostic Pathology, American Society of Clinical Pathologists, June 26-29, 1991.
7. Lecturer, "Flow Cytometric Detection of Anti-Platelet and Anti-Neutrophil Antibodies", at Clinical Applications of Flow Cytometry in Diagnostic Pathology, American Society of Clinical Pathologists, June 29, 1991.
8. Lecturer, "Quality Control and Assurance in Flow Cytometry", at Clinical Applications of Flow Cytometry in Diagnostic Pathology, American Society of Clinical Pathologists, June 29, 1991.
9. Lecturer, "Economics of Flow Cytometry, at Clinical Applications of Flow Cytometry in Diagnostic Pathology", American Society of Clinical Pathologists, June 29, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hanson, C.A., Holbrook, E.A., Sheldon, S., Schnitzer, B. and Roth, M.S.: Detection of Philadelphia chromosome-positive cells from glass slide smears using thepolymerase chain reaction. Am. J. Pathol. 1990;137:1-6.
2. Ho, V.C., Baadsgaard, O., Elder, J.T., Hansen, E., Hanson, C., Wantzin, G. and Cooper, K.D.: Genotypic analysis of T-cell clones derived from cutaneous T-cell lymphoma lesions demonstrates selective growth of tumor infiltrating lymphocytes. J. Invest. Derm. 1990;95:4-8.
3. Patton, D.F., Wilcowski, C., Hanson, C.A., Shapiro, R., Frizzera, G., Gajl-Peczalska, K.J. and Filipovich, A.H.: EBV determined clonality in post transplant lymphoma. Transplantation 1990;49:1080-1084.
4. Fishel, R.S., Farnen, J.P., Hanson, C.A., Silver, S.M. and Emerson, S.G.: Acute lymphoblastic leukemia with eosinophilia. Medicine 1990;69(4):232-243.
5. Ross, C.W., Stoolman, L.M., Schnitzer, B., Schlegelmilch, J.A. and Hanson, C.A.: Immunophenotypic aberrancy in adult acute lymphoblastic leukemia. Am. J. Clin. Pathol. 1990;94:590-599.
6. Hanson, C.A. and Ross, C.W.: The molecular genetics of the immunoglobulin and T-cell receptors: applications in diagnostic hematopathology. Adv. Pathol. 1990;3:33-74.
7. Hanson, C.A., Stoolman, L.M., Gribbon, T.E., Schlegelmilch, J.A., Schnitzer, B. and Mitchell, B.S.: CD11c (Leu-M5) expression in B-cell chronic lymphoproliferative disorders: Recognition of a spectrum of clinical disorders distinct from hairy cell leukemia. Blood 1990;76:2360-2367.
8. Hanson, C.A., Levine, E.G., Frizzera, G. and Peterson, B.A.: True histiocytic lymphoma: A review of clinical and pathologic findings. Semin. Oncol. 1991;18:39-49.
9. Gupta, D.K, Cooper, K.D., Ellis, C.N., Nickoloff, B.J. and Hanson, C.A.: Papulonodular lymphocytic infiltrates of the skin developing in association with cyclosporine A therapy. J. Am. Acad. Dermatol. 1990;23:1137-1141.
10. Ross, C.W., Schnitzer, B., Weston, B. and Hanson, C.A.: Chronic-active Epstein-Barr virus infection and viral-associated hemophagocytic syndrome. Arch. Pathol. Lab. Med. 1991;115:470-474.
11. Grossman, D.M., Hanson, C.A. and Schnitzer, B.: Simultaneous lymphocyte predominant Hodgkin's diseaes and large cell lymphoma. Am. J. Surg. Pathol., In Press.
12. Reardon, D.A., Roskos, R. and Hanson, C.A.: Viral-associated hemophagocytic syndrome in bone marrow transplantation. Am. J. Ped. Hem. Onc., In Press.
13. Hanson, C.A., Chan, L.S. and Cooper, K.D.: Concurrent eosinophilic fascitis and cutaneous T-cell lymphoma. Arch. Dermatol., In Press.
14. Kueck, B.D., Parkin, J., Peterson, L.C., Hanson, C.A. and Smith, R.E.: Eosinophilic leukemia - A myeloproliferative disorder distinct from the hypereosinophilic syndrome. Hematol. Pathol., In Press.
15. Hanson, C.A., Ross, C.W. and Schnitzer, B.: Anti-CD34 immunoperoxidase staining in paraffin sections of acute leukemia: Comparison with flow cytometric immunophenotyping. Human Pathol., In Press.
16. Hanson, C.A., Bockenstedt, P.L., Schnitzer, B., Fox, D.A., Kueck, B. and Braun, D.K.: S100-positive, T-cell chronic lymphoproliferative disease: Possible association with human herpes virus-6. Blood, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Hanson, C.A., Swanson, P.E., Gajl-Peczalska, K.J., Jaszcz, W., Frizzera, G. and Wick, M.R.: Immunohistochemical analysis of "true histiocytic" lymphoma in paraffin sections.
2. Hanson, C.A.: Antibody Diversity.

3. Baddoura, F.K., Hanson, C.A. and Chan, W.C.: Plasmacytoid T-zone lymphoma in myelofibrosis with myeloid metaplasia.
4. Abruzzo, L.V., Thornton, A.J., Hanson, C.A., Evanoff, H., Westwick, J., Emerson, S. and Kunkel, S.L.: Chemotactic cytokine gene expression in human bone marrow stromal cells.
5. Ross, C.W., Hanson, C.A. and Schnitzer, B: CD30 (Ki-1)-positive large cell lymphoma mimicking gastrointestinal carcinoma.
6. Nowell, P.C., Kant, J.A., Finan, J.B., Cassileth, P. and Hanson, C.A.: Marrow fibrosis associated with a Philadelphia chromosome.

BOOKS AND CHAPTERS IN BOOKS:

1. Hanson, C.A.: The acute leukemias and myelodysplastic syndromes, in, McClatchey, K.D. (ed.), Clinical Laboratory Medicine, Williams & Wilkins, Baltimore, Maryland, In Preparation.
2. Hanson, C.A. and Ross, C.W.: Clinical applications of molecular biology: Hematopoietic disorders, in, McClatchey, K.D. (ed.), Clinical Laboratory Medicine, Williams & Wilkins, Baltimore, Maryland, In Progress.

ABSTRACTS, BOOK REVEIWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Hanson, C.A.: Multilobular variant of hairy cell leukemia: Case of the Quarter, Society for Hematopathology.
2. Hanson, C.A.: Book Review on, "Lymphoid Malignancy: Immunocytology and cytogenetics", Hanoaka, M., Kadin, M.E., Mikata, A., Watanabe, S. (eds.), Am J Surg Pathol., In Press.
3. Hanson, C.A.: Book Review on, "Diagnostic Flow Cytometry", Coon, J.S. and Ronald S. Weinstein, R.S. (eds.), Lab. Med., In Press.
4. Sheldon, S., Farnen, J., Emerson, S.G., Ross, C.W. and Hanson, C.A.: Chromosomal and growth factor abnormalities in leukemia: Utility of granulocyte macrophage-colony stimulating factor in cytogenetic analysis of chronic myeloproliferative disorders and acute myeloid leukemia, presented at American Association of Cancer Research, October, 1990. Cancer Res., 1990, In Press.
5. Hanson, C.A., Reardon, D.A., Roskos, R., Sheldon, S., Holbrook, E.A. and Roth, M.S.: The detection of leukemia-specific mRNA transcripts from archival glass slide smears in Philadelphia-Chromosome (Ph')-positive, Pediatric leukemia patients, presented at the American Society of Hematology, Boston, Massachusetts, December, 1990. Blood.
6. Abruzzo, L.V., Thornton, A.J., Hanson, C.A., et.al.: Chemotactic cytokine gene expression in human bone marrow stromal cells, presented at the American Society of Hematology, Boston, Massachusetts, December, 1990, Blood.
7. Bikkina, S., Carey, J., Sawdyk, M.A. and Hanson, C.A.: A case of a B-Cell follicular NH lymphoma in remission with occurence of a second, diffuse non-Hodgkin's lymphoma of T-cell lineage documented by immunoglobulin and TCR beta gene rearrangement, presented at the American Society of Hematology, Boston, Massachusetts, December, 1990, Blood.
8. Braun, D.K. and Hanson, C.A.: Association of human Herpesvirus 6 with S100 + chronic lymphoproliferative disease. Clin Res 1990;38:847A.
9. Hanson, C.A., Ross, C.W. and Schnitzer, B.: CD34 immunoperoxidase (IP) staining in bone marrow paraffin sections: Correlation with flow cytometric (FC) studies. Lab. Invest. 1991;64:73A.
10. Hanson, C.A., Abaza, M., Ross, C.W., Sheldon, S., Schnitzer, B. and Stoolman, L.: Acute biphenotypic leukemia (ABL): Immunophenotyping (IPH), morphology, and cytogenetics. Lab. Invest. 1991;64:73A.
11. Ross, C.W., Schlegelmilch, J., Grogan, T., Schnitzer, B. and Hanson, C.A.: Detection of Epstein-Barr virus (EBV) genome in Ki-1 (CD30)-positive, large cell anaplastic lymphomas (LCAL) using the polymerase chain reaction (PCR). Lab. Invest. 1991;64:83A.

12. Ross, C.W., Hanson, C.A., Appelman, H. and Schnitzer, B.: Ki-1 (CD30)-positive, anaplastic large cell lymphoma (ALCL) mimicking gastrointestinal carcinoma. Lab. Invest. 1991;64:40A.

JOHN T. HEADINGTON, M.D.
PROFESSOR OF PATHOLOGY AND DERMATOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Dermatopathology, private consultations.
B. Dermatopathology, M-Labs.
C. Dermatopathology, UMH.
D. Dermatopathology, tutorials.
E. Autopsy Service (January).

II. TEACHING ACTIVITIES:

A. Medical Students: (second year):
   1. Dermatopathology lectures.
   2. Second year Pathology Laboratory.
B. Pathology and Dermatology House Officers:
   1. Dermatopathology.
C. Dermatology House Officers:
   1. Clinical Dermatology.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Immunologic responses in the dermis in tryptophan-related sclerosis.
B. Unclassified malignant cutaneous neoplasms of neural crest origin.
C. The histology of the alopecia of secondary syphilis.
D. Textbook: The Pathology of the Hair Follicle.
E. Genetic Changes in Melanoma (with J. Trent)

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Pigmented Lesion Clinic.

MEDICAL SCHOOL/HOSPITAL:

A. Director, Dermatopathology Unit.

REGIONAL AND NATIONAL:

A. Editorial Board, Archives of Dermatology. American Board of Pathology.

B. Chairman, Task Force on Dermatopathology, The American Academy of Dermatology.
C. Test Committees For Dermatopathology. (American Boards of Pathology and Dermatology).
D. Member, Council on Clinical and Laboratory Services, American Academy of Dermatology.
E. Board of Directors, National Alopecia Areata Foundation.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. XVIII International Congress, The International Academy of Pathology. Buenos Aires, Argentina, September, 1990.
2. Ohio Valley Dermatology Society, Greenbrier, West Virginia, October 1990.
3. National Institute of Health. Alopecia areata workshop. Washington, D.C.,October, 1990.
4. Visiting Professor, The University of Minnesota. Minneapolis, Minnesota, November, 1990.
5. American College of Osteopathic Pathologists, Los Vegas, Nevada, November, 1990.
6. American Society of Dermatopathology, Atlanta, Georgia, November, 1990.
7. Canadian Reference Center, Skin Tumor Panel. Ottawa, Ontario, February, 1991.
8. Visiting Professor, The University of Iowa, Iowa City, Iowa, February, 1991.
9. The American Dermatologic Association, Laguna Niguel, California, February, 1991.
10. The University of South Florida, Tampa, April, 1991.
11. Florida West Coast Society of Pathologists, Tampa, Florida, April, 1991.
12. Visiting Professor, The University of Oklahoma, Oklahoma City, Oklahoma, May, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wahl, R.L., Liebert, M., Headington, J.T., et al: Lymphoscintigraphy in melanoma: Initial evaluation of a monoclonal antibody cocktail. Cancer Res. 1990;50:941S-948S.
3. Headington, J.T.: Histologic changes in forearm skin after application of topical tretinoin. J.A.A.D, In Press.
4. Bulengo-Ramsby, S.M. and Headington, J.T.: Pseudopelade of brocq in a child. J.A.A.D 1990;23:944-945.
5. Burns, M.K. and Headington, J.T.: Palisaded myofibroblastoma simulating indolent lymphadenopathic Kaposi's sarcoma. J.A.A.D., In Press.

KATHLEEN P. HEIDELBERGER, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Pediatric Surgical and Placental Pathology, daily, twelve months.
B. Pediatric Necropsies, daily, twelve months.
C. Pediatric Consultation Cases, daily, twelve months.
D. Adult Necropsy Service, 0.5 months.
E. Continued to organize and maintain the Michigan Cardiac Registry, twelve months.
F. Continued to direct and interpret the Lung Morphometric Program, twelve months.
G. Teratology Unit, histology, as necessary, approximately 40 cases per year.
H. Children's Cancer Study Group, coordinate all pathological material and data necessary for all children registered in national tumor protocols. (Collaborating investigator, NCI #2-U10-CA-02971-33, CCSG, R. Hutchinson, M.D., P.I.)

II. TEACHING ACTIVITIES:

A. M2: Pathology 600, three whole class lectures on Pediatric Pathology.
B. M4: Pediatric Surgical Pathology, twelve months, while they were on their pathology electives.
C. Supervised M4s on Pathology elective, one rotation (four weeks).
D. House Officers in Pathology, daily reading of pediatric surgicals, twelve months.
E. House Officers in Pathology, gross and microscopic supervision of most pediatric necropsies, twelve months and adult cases 0.5 months plus on-call weekends.
F. Surgical Pathology Conference, one hour/week, twelve months.
G. Lectures on Pediatric Necropsy Pathology in Core Curriculum Series for House Officers in Pathology.
H. Gross Necropsy Conference, one hour/week, twelve months.
I. Supervised Pediatric Hematology Fellows (three) for AP elective period.
J. Conferences:
    1. Pediatric Cardiology Death Conference, monthly, all year.
    2. Pediatric Tumor Conference, twice monthly, all year.
    3. Pediatrics CPC/General Death Conference, quarterly.
    4. Pediatric Liver-GI Conference, approximately twice a month.

III. RESEARCH ACTIVITIES:

A. Multiphased, ongoing study with pediatric cardiologists and thoracic surgeons of effects of various congenital heart defects on the pulmonary vasculature.
B. Studies of regional variations in lung structure.
C. Compiling data base of morphometric characteristics of normal lungs at various ages.

PROJECTS UNDER STUDY:

A. Ongoing review of the effects of pulmonary artery banding on the lung biopsy findings in young children with complete atrioventricular septal defect with pediatric cardiologists.
B. Continued long term study of aneurysm formation of repaired coarctation with pediatric cardiologists (see articles submitted).
C. Study of correlation, if any, of ECHO study of heart transplant patients with the histologic findings on simultaneous heart biopsy (see articles submitted).
D. Review of neoplasms in post transplant patients with the pediatric cardiologists.
E. Study of the differential development of renal tubules and glomeruli in twin fetuses and newborns with Mason Barr, M.D.
F. Study of the effect of ACE inhibitors on renal tubular maldevelopment with Mason Barr, M.D.
G. Correlation of x-rays, operative findings and histologic features of osteoblastoma and osteoid osteoma of the spine with orthopedic surgeons (see abstracts).
H. Review of the predictie valve of pre-ECMO lung biopsy in determining recovery of pulmonary function with ECMO surgeons, pediatric pulmonologist and Dr. Andrew Flint.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Departmental ACAPT.
B. Interviewing fellowship candidates for Surgical Pathology.

MEDICAL SCHOOL/HOSPITAL:

A. Executive Committee for Mott/Women's/Holden/Psychiatric Hospitals.
B. Executive Committee of the Medical School, 1987-1990 (until August 31).
C. Interviewing Pediatric Cardiology Fellowship Candidates.
D. Dean's External Review Committee for Department of Physical Medicine and Rehabilitation.

REGIONAL AND NATIONAL:

A. Member, American Board of Pathology Test Committee for Pediatric Pathology.

V. OTHER RELEVANT ACTIVITIES:

A. Certified, by examination of the American Board of Pathology, for Special Qualification in Pediatric Pathology. November, 1990.
B. Recipient of the Mother Mary Catherine McGrann Alumni Achievement Award of College Misericordia, Dallas, Penn., June, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Evans, D., Baugh, R., Gilsdorf, J., Heidelberger, K.P. and Niparko, J.K.: Lymphangiomatosis of skull manifesting with recurrent meningitis and cerebrospinal fluid otorrhea. Otolaryngology-Head and Neck Surgery. 1990;103:642-646.
2. Keim, D.,Ragsdale, C., Heidelberger, K.P. and Sullivan, D.: Hepatic fibrosis with use of methotexate for juvenile rheumatoid arthritis: A case report. J Rheumatol. 1990;17:846-848.
3. Delius, R.E., Zwischenberger, J.B., Cilley R., Behrendt, D.M., Bove, E.L., Deeb, G.M., Crowley, D., Heidelberger, K.P. and Bartlett, R.H.: Prolonged extracorporeal life support of pediatric and adolescent cardiac transplant patients. Ann. Thor. Surg. 1990;50:791-795.
4. Grossman, D.M, Long, J., Heidelberger, K.P. and Lloyd, R.V.: Expression of tyrosine hydroxylase protein and chromogranin A protein and messenger RNA in paraffin-embedded sections of neuroendocrine neoplasms. Endocrine Pathology, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Minich, L., Beekman, R.H., Rocchini, A.P., Bove, E.L. and Heidelberger, K.P.: Surgical repair is safe and effective after unsuccessful angioplasty of native coarctation. J. Am Coll. Cardiol., Submitted.
2. Bogaards, M.A., Snider, A.R., Crowley, D.C., Meliones, J.N. and Heidelberger, K.P.: Echocardiographic indexes of cardiac allograft rejection in transplant recipients. J. Am. Soc. Echocardiography, Submitted.

ABSTRACTS:

1. Bogaards, M.A., Snider, A.R., Crowley, D.C., Meliones, J.N. and Heidelberger, K.P.: Echocardiographic indexes of cardiac allograft rejection in transplant recipients. Presented at the American Heart Association Annual Meeting. Poster Session, Nov, 1990, Circulation: 1990;82, 53:403.
2. Raskas, D.S., Graziano, G.P., Herzenberg, J.E., Heidelberger, K.P. and Hensinger, R.N.: Osteoid osteoma and osteoblastoma of the spine in children. Submitted.

SAMUEL P. HICKS. M.D.
PROFESSOR EMERITUS OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
July 1, 1990 - June 1, 1991

I. CLINICAL ACTIVITIES

A. With C.J. D'Amato prepare microscopic descriptions of most UM autopsy brains and those sent here for consultation. In UM cases, house officers compare them with their findings and incorporate them into final autopsy reports. In consultations they become part of the final report together with gross findings. Occasional neurosurgical pathology diagnoses.

II. TEACHING ACTIVITIES

A. Review some of these autopsy brains with Pathology, and other house officers spending time in Pathology, and with students and staff as needed.
B. Neural and Behavioral Sciences 600 for second year medical students: 2 hours.
C. Neuropathology 858 for house officers in Pathology, Neurology, Neurosurgery and other departments, and graduate students. 18 hours including 2 lectures.

III RESEARCH ACTIVITIES

With C.J. D'Amato in three areas in collaboration with colleagues:

A. Thrombospondin in astrocyte reactions. Thrombospondin (TSP), a glycoprotein of extracellular matricies, has been known to be associated with migrating cells and neurite growth in the developing nervous system and is found in the surfaces of mature astrocytes. Our interest has been in what the relation might be between TSP and the hypertrophy and multiplication of astrocytes (gliosis) that follows destructive injuries of the central nervous system. We reported earlier that TSP increases in astrocytes near a surgical incision in the mature rat cerebral cortex during the third week after the injury when the hypertrophic growth is most active. Further studies are in progress to see whether increased TSP persists in the astrocytes which remain hypertrophied indefinitely. The matter is of interest because gliosis, which may have originated early in the course of evolution as part of the process of regeneration of injured nerve cell axons, has become a liability by forming an impenetrable barrier of fibers preventing the regeneration. Might excessive TSP be to blame for the hypertrophy? (O'Shea, D'Amato, Dixit, Hicks).
B. Functions of fetal rat brain phagocytes. We reported earlier that the phagocytes produced superoxide anion and phagocytosed disintegrating premature neural cells killed by radiation, but paradoxically those regions in which phagocytes appeared showed the greatest regenerative capacity, malformation occurring in regions where phagocytes were absent. Since phagocytes (macrophages) play an important role in regeneration of adult injured peripheral nerves but not injured CNS axons, we wish to determine whether the fetal CNS is exceptional, its phagocytes possibly promoting all aspects of fetal regeneration. (Varani, Fleigiel, D'Amato, O'Shea, Hicks and others).
C. Pathologic studies of the autopsy brains of people with various forms of dementia and related nervous diseases in collaboration with members of the Department of Neurology and others.

IV PUBLICATIONS

1. D'Amato, C.J., O'Shea, K.S. and Hicks, S.P.: Lack of neurite outgrowth in hydrocephalic mutant rat embryo neurons. Soc. Neuroscience Abstracts 1990;16:314.
2. D'Amato, C.J., Sima, A.A.F., Foster, N.L., Dickson, D.W. and Hicks, S.P.: Cerebral Lewy bodies with supranuclear palsy. Abstract and Poster. J. Neuropath. Exper. Neurol. 1991;50:308.
3. Foster, N.L., Gilman, S., Berent, S., Sima, A.A.F., D'Amato, C.J., Koeppe R.A. and Hicks, S.P., Progressive subcortical gliosis and progressive supranuclear palsy can have similar clinical and pet abnormalities. J. Neur., Neurosurg., Psychiatry, Submitted, June, 1991.

ABSTRACTS

1. D'Amato, C.J., O'Shea, K.S. and Hicks, S.P.: Lack of neurite outgrowth in hydrocephalic mutant rat embryo neurons. Society for Neuroscience Annual Meeting, St. Louis, November, 1990. (Submitted for Poster Presentation.)

KENT J. JOHNSON, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Immunopathological evaluation of skin and renal biopsies.
B. Director, Electron Microscopy Service.
C. Renal pathology.
D. Autopsy coverage.

II. TEACHING ACTIVITIES:

A. Lecturer Genitourinary Pathology - Second year pathology course.
B. Lectures on Renal Pathology - Nephrology Fellows.
C. Lectures on Renal and Skin Immunopathology - Pathology Residents.
D. Lectures on Genitourinary Pathology - Dental Pathology Course.

III. RESEARCH ACTIVTIES:

SPONSORED SUPPORT:

A. "Oxidants and Protease Interaction in Acute Lung Injury". National Institutes of Health. Principal Investigator. $834,625 for five years.
B. "Oxidants and Glomerular Injury", Project V, Renal Center Grant. National Institutes of Health. Principal Investigator, $246,585 for five years.
C. "Mechanisms of Glomerular and Tubular Injury", Core B, Renal Center Grant. National Institutes of Health, Principal Investigator, $147,795.
D. "Inflammatory Cells and Lung Injury", Core C, National Institutes of Health, Principal Investigator, $291,025.
E. "Crescentic Nephritis Program Project", Core B, Principal Investigator, National Institutes of Health, $204,490.

PENDING SUPPORT:

A. "Pathogenesis of Cyclosporin A Arteriopathy", with J. Varani, Pathology and J. Messana, Nephrology. Sandoz Research Institute, Principal Investigator.
B. "Adhesion Molecules and Cytokines in Glomerulonephritis", with J. Varani. National Institutes of Health, Principal Investigator.
C. "Aging, Anesthesia and Influenzia Infection", with Paul Knight, Anesthesia and Dan Remick, Pathology. National Institutes of Health, Co-Investigator.
D. "DNA Methylation and SLE", with Bruce Richardson, Rheumatology. National Institutes of Health, Co-Investigator.
E. "Amino Acids and Cell Injury", with Joel Weinberg, Nephrology and James Varani, Pathology. National Institutes of Health, Co-Investigator.

PROJECTS UNDER STUDY:

A. Pathogenesis of IgG and IgA Immune Complex Lung Injury.
   1. Role of oxygen radicals.
   2. Role of proteases.
   3. Role of terminal components of the complement system.
B. Oxidant and protease interaction in inflammation.
C. Pathogenesis of aspiration pneumonitis.
D. Pathogenesis of viral pneumonitis.
E. Pathogenesis of pancreatitis and pancreatitis Induced ARDS.
F. Adhesion molecules and cytokines in inflammation.
G. Cyclosporine induced nephrotoxicity.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Immunopathology Fellowship Program.
B. Renal Pathology Conference - Biweekly.
C. Space Utilization Committee.
D. Stobbe Funds Committee.
E. Chariman's Advisory Committee.

REGIONAL AND NATIONAL:

A. Associate Editor - Laboratory Investigation
B. Reviewer for the following journals:
   1. American Journal of Pathology
   2. American Review of Respiratory Diseases
C. Consultant/Grant reviewer for the Veteran's Administration.

V. INVITED LECTURES AND SEMINARS:

1. Management of patients with lupus nephritis. Continuing Medical Education Conference. University of Michigan.
2. Retionic Acid and Inflammation (with James Varani). Symposium on Retinoids. Geneva, Switzerland.
3.. Visiting Professor, Sandoz Pharmaceuticals and the University of Basle, Basle, Switzerland.
4.. New Concepts in Glomerulonephritis. St. John's Hospital, Lecture Series, Detroit, MI.

VI. OTHER RELEVANT ACTIVITIES:

A. Consultant on Dermatology and Nephrology training grants.

VII. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Guice, K.S., Oldham, K.T., Caty, M.G., Johnson, K.J. and Ward, P.A.: Neutrophil-dependent oxygen-radical mediated lung injury associated with acute pancreatitis. Ann. Surg. 1990;210:740-747.
2. Penna, A.M., Johnson, K.J., Camilleri, J.M. and Knight, P.R.: Alterations in influenza A, virus specific immune injury in mice anesthetized with halothine or ketamine. Intervirology. 1990;31:188-196.
3. Gannon, D.E., He, X., Ward, P.A., Varani, J. and Johnson, K.J.: Time-dependent inhibition of oxygen radical induced lung injury. Inflammation 1990;14:509-522.
4. Warren, J.S., Johnson, K.J. and Ward, P.A.: PAF and immune complex injury. J. Lipid Mediators 1990;2:5229-5237.
5. Warren, J.S., Yabroff, K.R., Mandel, D.M., Johnson, K.J. and Ward, P.A.: Role of O_2^- in neutrophil recruitment into sites of dermal and pulmonary vasculitis. Free Rad. Biol. Med. 1990;8:163-172.
6. Guice, K.S., Oldham, K.T., Johnson, K.J. and Ward, P.A.: Mechanisms of capillary endothelial cell injury in acute pancreatitis. Ann. Surg. 1990;210:740-747.
7. Warren, J.S., Johnson, K.J. and Ward, P.A.: PAF and immune complex induced injury. J. Lipid Mediators 1990;2:S229-237.
8. Barker, J.N.W.N., Jones, M.L., Swenson, C.L., Sarma, V., Mitra, R.S., Ward, P.A., Johnson, K.J., Fantone, J.C., Dixit, V.M. and Nickoloff, B.J.: Monocyte chemotaxis and activating factor production by keratinocytes in response to IFN-g. J. of Immunol. 1991;146:1192-1197.
9. Schmeling, D.J., Oldham, K.T., Guice, K.S., Kunkel, R.G. and Johnson, K.J.: Experimental obliterative cholangitis. A model for the study of biliary atresia. Ann. Surg. 1991;213:350-355.
10. Varani, J., Stoolman, L., Wang, T., Schuger, L., Flippen, C., Dame, M., Dixit, V.M., Johnson, K.J., Todd, R.F., Ryan, U.S. Ward, P.A.: Thrombospondin production and thrombospondin mediated adhesion on U937 cells. Exp. Cell Res. 1991;195:177-182.

ARTICLES ACCEPTED FOR PUBLICATION:

1. Ward, P.A. and Johnson, K.J.: Lung inflammatory mechanisms. J. Human Path., In Press.
2. Ward, P.A., Warren, J.S., Remick, D., Varani, J., Gannon, D. and Johnson, K.J.: Cytokines and oxygen radical mediated tissue injury, in, Shoemaker, W.C. (ed.), New Horizons III, Critical Care Medicine, In Press.
3. Ward, P.A., Johnson, K.J. and Till, G.O.: Mechanisms of lung injury. Prax. Klin. Pneumonol., In Press.
4. Varani, J., Ginsburg, I., Johnson, K.J. Gibbs, D.F., Weinberg, J.M. and Ward, P.A.: Amino acids and metal ions protect endothelial cells from lethal injury. FASEB J., In Press.
5. Varani, J., Gibbs, D.F., Johnson, K.J., Weinberg, J.M., Ryan, U.S., Ginsburg, I. and Ward, P.A.: Hydrogen peroxide-induced cell and tissue injury: protective effects of MN^{2+}. Inflammation, In Press.
6. Varani, J., Jones, J., Dame, M.K., Sulavik, C., Gibbs, D.F. and Johnson, K.J.: Effects of all-trans retionic acid on neutrophil-mediated endothelail cell injury and immune complex injury in rats. Am. J. Pathol., In Press.
7. Weinberg, J.M., Varani, J., Johnson, K.J., Rosser, N.F., Dame M.K., Davis, J.A. and Venkatachelam, M.S.: Protection of human umbilical vein endothelial cells of glycine and structurally similar amino acids against calcium and hydrogen peroxide-induced lethal cell injury. Am. J. Pathol., In Press.
8. Weinberg, J.M., Venkatachalam, M.A., Roeser, N.F., Davis, J.A., Varani, J. and Johnson, K.J.: Amino acid protection of cultured kidney tubule cells against calcium ionophore-induced lethal cell injury. Lab. Invest., In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Tait, A.R., Davidson, B.A., Johnson, K.J., Remick, D.G. and Knight, P.R.: Halothine alters the cellular immune response to influenza virus infection in mice. Submitted for publication.
2. Tait, A.R., Davidson, B.A., Johnson, K.J., Remick, D.G. and Knight, P.R.: Production of tumor necrosis factor following influenza infection in mice: The effect of Halothine Anesthesia. Submitted for publication.
3. Knight, P.R., Druskovich, G., Tait, A.R. and Johnson, K.J.: Investigation into the pathogenesis of acid pulmonary injury. Submitted for publication.
4. Ward, P.A., Till, G.O., Kunkel, R.G. and Johnson, K.J.: Protection against neutrophil-mediated lung injury by platelet depletion. Submitted for publication.
5. Ginsburg I., Schuger L., Gibbs, F., Johnson, K.J., Ryan, U.S., Ward, P.A. and Varani, J.: Endothelial cell killing by polymorphonuclear leukocytes: Independent and synergistic roles for oxygen radicals and proteases. Am. J. Pathol., submitted.
6. Chan, L.S., Hammerberg, C., Soong, H.K., Johnson, K.J. and Cooper, K.D.: Cicatricial pemphigoid: Its clinical spectrum and its distinction from bullous pemphigoid. Submitted.
7. Varani, J., Jones, J., Gibbs, D.F., Sulavik, C., Dame M. and Johnson, K.J.: In vitro and in vivo modulation of the acute inflammatory response by all-trans retinoid acid. Submitted for publication.
8. Quddus, J., Johnson, K.J., Gavalchin, J., Amento, E., Crisp, C. and Richardson, B.: Mature T cells treated with a DNA methylation inhibitor induce a lupus-like disease in syngeneic mice. Submitted for publication.
9. Johnson, K.J., Dixit, V.M. and Varani, J.: Role of thrombospondin in the acute inflammatory response. Submitted for publication.
10. Johnson, K.J., Sulavik, C. and Rehan, A.: Role of oxygen radicals in autologous anti-GBM nephritis. Submitted for publication.
11. Mulligan, M.S., Johnson, K.J., Smith, C.W., Anderson, D.C. and Ward, P.A.: Requirements for CD18 and TNFa in Nephrotoxic Nephritis. J. Clin. Invest. Submitted for publication.
12. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: PAF, cytokines, toxic oxygen products and cell injury. Submitted for publication.
13. Huber, A.R., Johnson, K.J. and Varani, J.: Monocyte diapedesis through an in vitro vessel wall construct: Inhibition with monoclonal antibodies to thrombospondin. Submitted for publication.

BOOKS AND CHAPTERS IN BOOKS

1. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: Cytokines, toxic oxygen products and cell injury. Molecular Aspects of Medicine, In Press.
2. Ward, P.A., Till, G.O. and Johnson, K.J.: Oxygen-derived free radicals and inflammation, in, Leadbetter, W.B., Buchwalter, J.A. and Gordon, S.L. (eds.), Sports Induced Inflammation, Amer. Soc. Ortho. Surgeons. 1990;315-324.
3. Ward, P.A., Johnson, K.J. and Till, G.O.: Animal models of oxidant lung injury, in, Proceedings of Stressa Symposium, in Zambon, Italy, In Press.
4. Ward, P.A., Warren, J.S., Till, G.O., Varani, J. and Johnson, K.J.: Free radicals in lung disease, Rice-Evans, C. (ed), Free Radicals, Diseased States and Anti-Radical Interventions, Proceeding of the special colloquium, Richelieu Press, London, England, 1989;57-77.
5. Ward, P.A., Warren, J.S., Till, G.O., Varani, J. and Johnson, K.J.: Modification of disease by preventing free radical formation: A new concept in pharmacologic intervention, in, Hershko, C. (ed.), Iron Chelating Therapy, Bailliere Tindall Limited, Harcourt Brace Jovanovich, Publishers, London, England, In Press.
6. Johnson, K.J.: Inflammatory mediators in glomerulonephritis, in, Churg, J. and Sinniah, R., (eds.), Classification and Atlas of Infectious Diseases of Kidney, WHO Vol. IV, Amer. Soc. Clin. Pathol., 1988.

7. Warren, J.S., Johnson, K.J. and Ward, P.A.: Phagocytes and reactive oxygen substances as mediators of acute lung injury, in, Hyers, T. (ed.), Diffuse Alveolar Damage and Respiratory Failure, Futura Press, New York, In Press.
8 Till, G.O., Johnson, K.J. and Ward, P.A.: Oxygen free radicals in inflammation, in, Messmer, K. and Hammersen, F. (eds.), Prog. Appl. Microcirc., Vol. 9, Karger, Basel, In Press.
9. Ward, P.A., Johnson, K.J. and Till, G.O.: Leukocyte oxygen radicals and acute lung injury, in, Proceedings of a Symposium on "Acute Lung Injury", PSG Publishing Co., Littleton, Massachusetts, In Press.
10. Ward, P.A., Johnson, K.J. and Till, G.O.: Tissue injury as a consequence of oxygen radicals produced by phagocytic cells, in, Proceedings of a Symposium by the Comparative Respiratory Society, Anaheim, California, 1986, In Press.
11. Ward, P.A., Johnson, K.J. and Sulavik, M.D.: Lung injury produced by oxygen derived free radicals from leukocytes, in, Mechanisms of Lung Injury Symposium, given at the Graduate Hospital, Philadelphia, Pennsylvania, 1986, In Press.
12. Warren, J.S., Ward, P.A. and Johnson, K.J.: Immune complex injury, in, Cantor, J.D. (ed.), CRC Handbook of Animal Models of Pulmonary Disease, CRC Press, Baco Raton, Florida, 1987, In Press.
13. Warren, J.S., Ward, P.A. and Johnson, K.J.: The inflammatory response, Chapter 8, in, W.J. Williams (ed), Hematology, 4th Edition, 1991.
14. Warren, J.S., Ward, P.A. and Johnson, K.J.: ,Oxygen radicals as 'Mediators of inflammation', Volume 6, in, Henson, P.M. (ed.), The Handbook of Inflammation, Vol.6, Elsevier Biomedical Division, Amsterdam, The Netherlands, In Press.
15. Warren, J.S., Ward, P.A. and Johnson, K.J.: The respiratory burst and mechanisms of oxygen radical mediated tissue injury, in, Sbarra, A.J. and Strauss, R.P. (eds.), The Respiratory Burst and its Physiological Significance in Medicine, Plenum Press, New York, New York, In Press.
16. Warren, J.S., Johnson, K.J. and Ward, P.A.: Consequences of oxidant injury, in, Crystal, R.G. and West, T.B. (eds.), The Lung: Scientific Foundations, In Press.
17. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: PAF, cytokines toxic oxygen products and cell injury, in, Molecular Aspects of Medicine, Proceedings of the VIIth Annual Inflammation Meeting, Birmingham, U.K., Pergammon Press, In Press.
18. Ward, P.A., Till, G.O., Gannon, D.E., Varani, J.A. and Johnson, K.J.: The role of iron in injury of endothelial cells in vitro and in vivo, in, Simic, M.D., Taylor, K.A., Ward, J.F. and Sonntag, C.C. (eds), Oxygen-Radicals in Biology and Medicine, 4-ICOR Conference, Plenum Press, New York, pp. 969-974, 1989.
19. Ward, P.A., Warren, J.S. and Johnson, K.J.: Oxygen radicals, inflammation and tissue injury, in, Pryor, W. and Godber, S.L. (eds), Free Radical Biology and Medicine, In Press.
20. Warren, J.S., Johnson, K.J. and Ward, P.A.: 7.5.2 Immunoglobulin and complement mediated immune injury, in, Crystal, R.G., West, J.B., Barnes, P.J., Cherniack, N.S. and Weibel, E.R. (eds), The Lung: Scientific Foundations, Raven Press, New York, pp. 1939-1946. 1991.
21. Warren, J.S., Ward, P.A. and Johnson, K.J.: Oxygen radicals as "mediators of inflammation", Volume 6, in, Henson, P. (ed), The Handbook of Inflammation, Elsevier Biomedical Division, Amsterdam, The Netherlands, In Press.
22. Ward, P.A., Warren, J.S., Johnson, K.J. and Varani, J.: Inflammation, oxygen radicals and tissue injury, in, Oxidative Damage and Repair: Clinical, Biological and Medical Aspects, In Press.
23. Johnson, K.J., Varani, J. and Smolen, J.E.: Neutrophil activation and function in health and disease, in, Granulocyte Responses to Cytokines: Basic and Clinical Research, R.G. Coffey (ed.), Marcel Dekker, Inc., New York, In Press.
24. Johnson, K.J., Chensue, S.W., Kunkel, S.L. and Ward, P.A.: Immunopathology in essential pathology, in, Rubin, E. and Farber, J.L. (eds.), J.B. Lippincott, Inc., Philadelphia, 1991.
25. Wiggins, R.S., McCune, J. and Johnson, K.J.: Lupus nephritis: When to be aggressive, in, Michigan Postgraduate Review, 1990;7(3)84-87.
26. Varani, J. and Johnson, K.J.: Modulation of endothelial cell injury by all-trans retinoic acid: Role of the anti-inflammatory effects of RA, in, Jesaitis, A. (ed.), Molecular Basis of Oxidative Damage by Leukocytes, CRC Press, In Press.

27. Warren, J.S., Johnson, K.J. abd Ward, P.A.: Consequences of oxidant injury, in, Crystal, R.G., West, J.B., Bames, P.J., Cherniack, N.S.,and Weibel, E.R. (eds.), The Lung: Scientific Foundations, Raven Press, New York, pp.1829-1838. 1991.

ABSTRACTS, PRELIMINARY COMMUNICATIONS, PANEL DISCUSSIONS

1. Druskovich, G.M., Kyff, J., Johnson, K.J. and Knight, P.R.: The role of leukocytes and hydroxyl radicals in mediation of acute acid aspiration injury. Midwest Anest. Res. Conf. 1990.
2. Chan, L.S., Hammerberg, C.H., Soong, H.K., Cantu, C., Johnson, K.J. and Cooper, K.D.: The spectrum of cicatricial pemphigoid. Soc. Invest. Derm. 1990;94(4)513.
3 Swenson, C.L., Chapo, J.A., Grande, J.P., Lovett, D.J., Ward, P.A., Johnson, K.J. and Killen, P.D.: Tumor necrosis factor (TNFa) induces expression of macrophage chemotactic and activating factor (MCAF) by human mesangial cells (HMC). ASN 1990.
4. Tait, A.R., Davidson, B.A., Johnson, K.J., Remick, D. and Knight, P.R.: Halothine alters the virus - specific immune response to influenza infection in mice. Amer. Soc. Anest. (A340) 1990.
5. Messana, J.M., Leichtman, A.B., Johnson, K.J., Gartside, M., Ellis, C.N., Voorhees, J.J. and Swartz, R.D.: Glomerular filtration rate (GFR) and renal histology in cyclosporine (CSA) treated psoriasis patients. Amer. Soc. Nephrol. 1990.
6. Johnson, K.J., Sulavik, C., Gibbs, D.and Varani, J.: In vivo suppression of immune complex injury by all-trans retinoic acid. FASEB J. 1991;5:5207.
7. Varani, J., Ginsburg, I., Johnson, K.J., Gibbs, D.F., Weinberg, J.M. and Ward, P.A.: Amino acids and metal ions protect endothelial cells from lethel injury. FASEB J. 1991;5:3008.
8. Sulavik, C. and Johnson, K.J.: The role of oxygen radicals in autologous anti-GBM glomerulonephritis. FASEB J. 1991;5:5299.
9. Johnson, K.J., Jones, J., Dame, M., Gibbs, D.F. and Varani, J.: In vitro and in vivo modulation of the acute inflammatory response of all-trans retinoic acid. J. Cell Biochem. 1991;150:220.
10. Varani, J., Gibbs, D.F., Mukhopadhyay, P.S., Sulavik, C., Johnson, K.J., Weinberg, J.M., Ginsburg, I. and Ward, P.A.: Hydrogen peroxide-induced cell and tissue injury; protective effects of manganese. J. Cell Biochem. 1991;150:223.
11. Gilardy, A.K., Johnson, K.J., Brammer, D.W., Spilman, S.C. and Dysko: Immune complex vasculitis and glomerulonephritis with secondary ulcerative dermatitis in aged C57B1/6 mice. AALAS, 1991.
12. Coleman, B.S., Rutler, T., Tait, A.R., Johnson, K.J. and Knight, P.R.: The effect of duration of anesthetic exposure on pulmonary acid injury. ASA, 1991.
13. Knight, P.R., Tait, A.R., Druskovich, G. and Johnson, K.J.: Pathogenesis of pulmonary acid injury. ASA, 1991.
14. Knight, P.R., Tait, A.R., Davidson, B., Remick, D. and Johnson, K.J.: Pulmonary production of tumor necrosis factor during halothine anesthesia in mice. ASA, 1991.
15. Mulligan, M.S., Johnson, K.J., Smith, C.W., Anderson, D.C. and Ward, P.A.: Requirements for CD18 and TNFa in nephrotoxic nephritis. ASN, 1991.

W. JOHN JUDD, F.I.M.L.S., M.I.BIOL.
PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENT REPORT
1 JULY, 1990 - 30 JUNE, 1991

I. CLINICAL ACTIVITIES:

A. Director, Blood Bank Reference Laboratory.
B. Consultant, Veteran's Administration Medical Center, Ann Arbor.

II. TEACHING ACTIVITIES:

A. Directed weekly 1990-91 Clinical Pathology Grand Rounds.
B. Coordinated weekly 1990-91 Anatomical Pathology Conferences.
C. Coordinated Core-Lecture Series in Blood Banking for 1st-year Pathology House Officers.
D. Attended and participated in weekly Clinical Pathology Case Study Conferences.
E. Presentations at Clinical Pathology Grand Rounds:
   1. Resolution of ABO Typing Problems
   2. Biochemistry/Genetics of ABH, Se, Le, P and I systems
   3. Rare blood typed.
F. Trained Pathology and Pediatric Hematology Residents in Immunohematology.
G. Provided instruction to Pathology Residents during their Blood Bank Rotation.
H. Director, Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
   1. Planned and Coordinated the June, 1991 Blood Bank Symposium and Preconvention Workshops.
   2. Presented Workshop entitled: Shake, Bake and Agglutinate.
   3. Presented talk entitled: Pretransfusion Testing: What Else Can Go?

III. RESEARCH ACTIVITIES:

A. Judd, W.J., Steiner, E.A., Oberman, H.A. and Nance, S.: Should the 37 C reading be eliminated from antibody screening? Transfusion, In preparation.
B. Judd, W.J. and Steiner, E.A.: Hemolytic anti-M: A second example, In preparation.
C. Judd, W.J., Steiner, E.A. and Davenport, R.D.: Genetic basis for weak expression of B in a group A Korean family, with F. Yamomoto and S. Hakomori, University of Washington.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Blood Bank Daily Rounds.
B. Weekly Blood Bank Communication Meetings.
C. Monthly Clinical Pathology Faculty Meetings.

REGIONAL/NATIONAL:

A. Michigan Association of Blood Banks:
   1. Chairman, Specialist in Blood Banking Program.
   2. Annual Meeting Program Committee.
   3. Spring Workshop Committee.

B. American Association of Blood Banks: Board of Directors, North Central District Representative.

C. Reviewer of articles submitted for publication in Transfusion.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES:

1. Shake, Bake and Agglutinate - What to Use and When. Michigan Association of Blood Banks Annual Meeting. Troy, Michigan, September, 1990.
2 Testing, Testing, Testing - What to Use and When. Rhode Island Blood Bank Society Annual Meeting, Providence, Rhode Island, September 1990.
3. Shake, Bake and Agglutinate - What to Use and When, Ortho Diagnostics, Raritan, New Jersey, September, 1990.
4. Shake, Bake and Agglutinate - What to Use and When, Michigan Association of Blood Banks Travelling Seminar, Houghton, Michigan, September, 1990.
5. Shake, Bake and Agglutinate - Prenatal Testing. Michigan Association of Blood Banks Travelling Seminar, Houghton, Michigan, September, 1990.
6. Shake, Bake and Agglutinate - What to Use and When. Michigan Association of Blood Banks Travelling Seminar, Gaylord, Michigan, September, 1990.
7. Shake, Bake and Agglutinate - Antibody Identification. Michigan Association of Blood Banks Travelling Seminar, Houghton, Michigan, September, 1990.
8. Current Rends in Blood Banking. Physician's Continuing Education Program. Central Michigan Community Hospital, Mount Pleasant, Michigan, October, 1990.
9. Shake, Bake and Agglutinate - What to Use and When. Port Huron General Hospital, Port Huron, Michigan, April, 1991.
10. Shake, Bake and Agglutinate - What to Use and When. Indiana Association of Blood Banks Annual Meeting. Indianapolis, Indiana, May, 1991.
11. Pretransfusion testing: challenges for the 90's, Annual Meeting, Michigan Society for Medical Technology, Novi, Michigan, May, 1991.

WORKSHOPS/PANEL DISCUSSIONS:

1. Respondent, Food and Drug Administration's Workshop: Blood Bank Reagent Standards. Bethesda, Maryland, November, 1990.
2 Investigation and management of immune hemolysis: autoantibodies and drugs. Joint Congress of the International Society of Blood Transfusion and the American Association of Blood Banks, Los Angeles, California, November, 1990.
3 Pretransfusion Testing for the 90's. Joint Congress of the International Society of Blood Transfusion and the American Association of Blood Banks, Los Angeles, California, November, 1990.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Judd, W.J.: Are there better ways than the crosmatch to detect ABO incompatibility? Transfusion 1991;31:192-4.
2. Nugent, C.E., Gelinas, J.R., Judd, W.J. and Steiner EA.: Anti-Yt^a does not cause hemolytic disease of the newborn. Obstetr and Gynecol., In Press.
3. Judd, W.J. and Butch, S.H.: When is blood transfused relative to its date of expiration? Transfusion 1991;31:464-5.

CHAPTERS IN BOOKS:

1. Judd, W.J.: Pretransfusion testing, in, McClatchey, K,D, (ed.), Clinical Laboratory Medicine, Williams and Wilkins, Co., Baltimore, Maryland.

ABSTRACTS/LETTERS:

1. Knafl, P., Horan, M., Judd, W.J. and Oberman, H.A.: Is autologous blood over-utilized? Proceedings of the 1990 Joint Congress of the International Society of Blood Transfusion and the American Association of Blood Banks. Arlington: American Association of Blood Banks. 1990:42.
2. Judd, W.J., Steiner, E.A., Abruzzo, L.V., Davenport, R.D. and Oberman,, H.A.: Acute intravascular hemolysis due to anti-i. Proceedings of the 1990 Joint Congress of the International Society of Blood Transfusion and the American Association of Blood Banks. Arlington: American Association of Blood Banks. 1990:188.
3. Judd, W.J. and Steiner, E.A.: Adsorption of anti Cr^a by human platelet concentrates. Transfusion 1991;31:286.
4. Judd, W.J. and Steiner, E.A.: Multiple hemolytic transfusion reactions due to anti-Do^a. Transfusion 1991;31:477-8.
.5 McCoy-Pardington, D., Judd, W.J. and Oberman, H.A.: Blood utilization durig extracorporeal membrane oxygenation. Transfusion 1991;31:477.

PAUL D. KILLEN, M.D.,PH.D.
ASSISTANT PROFESSOR AND
ASSISTANT RESEARCH SCIENTIST
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Autopsy Pathology.
B. Diagnostic Renal Biopsy Service.

II. TEACHING ACTIVITIES:

A. Pathology 631 - Pathology Laboratory for Dental Student. Approximately 60 contact hours.
B. Pathology 580 - 2 contact hours.
C. Gross Pathology Conference.
D. Renal Pathology Conference.
E. Renal Pathology for Nephrology Fellows (20 contact hours.
F. Post Doctoral Fellows (three).
G. Graduate Students (four).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIH-P01-HL31963, Principal Investigator, Project VI "Molecular Biology of Alveolar Wall Injury", (40% Effort) $87,140/year, 3/1/89 - 2/28/94.
B. NIH-DC39225 Principal Investigator, Project XI "Monokine-Mediated Matrix Biosynthesis by Mesangial Cells", (10% Effort) $39,110/year, 8/1/88-7/30/93.
C. NIH-RO1. Principal Investigator, "Collagen IV Gene Transcription in cpk/cpk Mice", (25% Effort) $143,000/first year, 9/30/91-9/29/96.
D. NIH-RO1-DK37448, Co-Investigator, "Cellular Function of the Juxtaglomerular Complex", (5% Effort), $913,156 total, 07/01/91-06/30/96 .
E. American Heart Association of Michigan, Principal Investigator, "Mesangial Cell Expression of Collagen IV Genes", (5%) $24,500/year, $49,000/2 years, 07/01/89-06/30/91.
F. American Heart Association-Grant-in-Aid, Principal Investigator, "Collagen IV Gene Regulation During Renal Development", $25,500, 07/01/91-06/30/92 .
G. MDRTC Pilot/Feasibility, Principal Investigator, "Collagen IV Metabolism by Human Retinal Pigment Epithelial Cellls in Vitro"

PENDING SUPPORT:

PROJECTS UNDER STUDY:

A. Basement membrane gene expression by alveolar wall cells.

B. Regulation of collagen IV gene expression during development.
C. Regulation of basement membrane gene expression by glomerular cells in culture.
D. Localization of nephron segment-specific genes by PCR.
E. Role of aldose reductase in diabetic complications.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Post-doctoral candidate recruitment, Immunopathology Training Grant.

MEDICAL SCHOOL/HOSPITAL:

A. Faculty recruitment - Department of Pathology.
B. Faculty recruitment - Department of Internal Medicine.

REGIONAL AND NATIONAL:

A. Planning Committee, Genetic Basis of Renal Disease. NIDDK, NIH.
B. Ad hoc reviewer, Division of Extramural Activities, NIDDK, NIH.
C. Ad hoc Reviewer, Juvenile Diabetes Foundation.
D. Reviewer, Laboratory Investigation, American Journal of Pathology, Journal of Clinical Investigation. Journal of Cell Biology, Journal of Biological Chemistry, Journal of American Soc. of Nephrology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Structure, Function and Pathobiology of Laminin", XI International Congress of Nephrology, Tokyo, July, 1990.
2. "Basement Membrane Biosynthesis in the Kidney", XI International Congress of Nephrology, Tokyo, July, 1990.
3. "Regulation of Collagen IV Expression", University of Erlanger, Germany, October, 1990.
4. "Mesangial Sclerosis - Pathogenesis of Matrix Alterations", University of Heidelberg, Germany, October 1990.
5. "Developmental Expression of Collagen IV Genes", Senior Registrars in Nephrology Annual Meeting. Windemere, United Kingdom, October, 1990.
6. "Regulation of Collagen IV Transcription", Forefronts in Nephrology, Banz, Germany, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Weiser, M.M., Sykes, D.E. and Killen, P.D.: Rat intestinal basement membrane synthesis epithelial versus nonepithelial contributions. Lab. invest. 1990;62:325-330.
2. Merritt, S., Killen, P., Phan, S., Downer, G. and Wiggins, R.C.: Intraglomerular inflammation is associated with extraglomerular collagen synthetic activity early in a crescentic model of anti-GBM disease in the rabbit. Evidence from measurement of alpha 1(IV) collagen and beta-actin mRNA from glomeruli and renal cortex. Lab. Invest. 1990;63:762-769.

3. Wolf, G., Killen, P.D. and Neilson, E.G.: Cyclosporin a stimulates transcription and procollagen secretion in tubulointerstitial fibroblasts and proximal tubular cells. J Am. Soc. of Nephrol. 1990;1:918-922.
4. Trivedi, B.K., Briggs, J.P. and Killen, P.D.: Application of polymerase chain reaction techniques to study of rabbit renin gene expression. Kid. Internatl. 1990;39:1-5.
5. Killen, P.D.: Sclerosis: A Glomerular Response to injury. Semin. Nephrol. 1990;11:354-360.
6. Wolf, G., Killen, P.D. and Neilson, E.G.: Intracellular signalling of transcription and secretion of type IV collagen after angiotensin II-induced cellular hypertrophy in cultured proximal tubular cells. Cell regulation, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Schuger, L., Killen, P.D., Skubitz, A.P.N., Fin-Chang, J. and Varani, J.: Expression of laminin A and B chains in the epithelium and mesenchyme during murine lung development. 1991, Submitted.
2. Grande, J.P., Owens, C.A., Yu, G.H., Killen, P.D. and Ward, P.A.: Adenine nucleotide binding to human mesangial cells 1991, Submitted.

BOOKS/CHAPTERS IN BOOKS:

1. Killen, P.D., Ebihara,I., Laurie,G.W., Yamada,Y., Martin,G.R. and Brown, K.S.: Abnormal expression of basement membrane genes in murine congenital polycystic kidney disease, in, Carone, F.A., and Dobbie, J.W. (eds.), Advances in Polycystic Kidney Disease, Baxter Healthcare Corporation, Deerfield, Illinois, 1990, pp. 23-25.
2. Killen, P.D., DeMeester, C.A., Long, R.A., O'Brien, E. and Grande, J.P.: Regulation of collagen IV expression. in nephrology, Vol II, Michinobu Hatano, ed. Springer-Verlag Press, Tokyo, 1991, 1156-1162.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Henry, D.N., Greene, D.A., Del Monte, M.A. and Killen, P.D.: Assessment of aldose and aldehyde reductase mRNA in cultured human retinal pigment epithelial cells by polymerase chain reaction amplification of cDNA. Presented 50th Scientific Meeting American Diabetes Association, 1990.
2. Briggs, J.P., Trivedi, B., Schnermann, J. and Killen, P.D.: Detection of β-actin and Renin mRNA in microdissected renal vessels and renal tubules by PCR amplification of cDNA. Presented XI International Congress of Nephrology, 1990.
3. Killen, P.D., DeMeester, C.A., Long, R. and O'Brien, E.: Identification of sequences which enhance and repress collagen IV gene transcription. Presented XI International Congress of Nephrology, 1990.
4. Briggs, J.P., Trivedi, B., Todd, K.M., Chen, M., Schnermann, J., Lorenz, J.N., Weiprecht and H., Killen, P.D.: Application of polymerase chain reaction to study of renin gene expression in single rabbit juxtaglomerular apparatus (JGA). Accepted 44th Annual Scientific Meeting American Council for High Blood Pressure Research.
5. Briggs, J.P., Trivedi, B., Todd, K.M., Chen, M., Schnermann, J., Lorenz, J.N., Weiprecht, H. and Killen, P.D.: Application of polymerase chain reaction to study of renin gene expression in single rabbit juxtaglomerular apparatus (JGA). Submitted 21st Kongreb der Gesellschaft fur Nephrologie.
6. Briggs, J.P., Trivedi, B., Schnermann, J. and Killen, P.D.: Detection of b-actin and renin mRNA in microdissected renal vessels and renal tubules by PCR amplification of cDNA. XIth International Congress of Nephrology, page 31A, 1990.

7. Killen, P.D., DeMeester, C.A., Long, R. and O'Brien, E.: Identification of sequences which enhance and repress collagen IV gene transcription. XIth International Congress of Nephrology, page 69A, 1990.
8. Wiggins, R.C., Merritt, S., Phan, S.H. and Killen, P.D.: Extraglomerular collagen mRNA associated with intraglomerular inflammation in anti-GBM disease in the rabbit. XIth International Congress of Nephrology, page 42A, 1990.
9. Rother, K., Jahn, B., Schonermark, M., Berger, B., Killen, P. and Hansch, G.M.: The terminal complement components C5b-9 stimulate the collagen type IV, synthesis in human glomerular epithelial cells (GEC). FASEB J. 1990;4(4):A892.
10. Henry, D.N., Greene, D.A., Del Monte, M.A. and Killen, P.D.: Assessment of aldose and aldehyde reductase mRNA in cultured human retinal pigment epithelial cells by polymerase chain reaction amplification of cDNA. Am. Diabetes Assoc., 1990.
11. Briggs, J.P., Weihprecht, H. and Killen, P.D.: Application of polymerase chain reaction to study of renin gene expression in single rabbit juxtaglomerular apparatus (JGA). Kongreb der Gesellschaft fur Nephrologie Badgastein, Submitted, 1990.
12. Briggs, J.P., Todd, K.M., Weihprecht, H., Lorenz, J., Killen, P. and Schnermann, J.: PCR quantification of mineralocorticoid and glucocorticoid receptor mRNA from isolated nephron segments. Am. Soc. Nephrology, Submitted, 1990.
13. Kuncio, G.S., Killen, P.G. and Neilson, E.G.: Modulated expression of the a1(IV) collagen gene in murine renal tubular cells cultured with fibrosis-relevant cytokines. Am. Society of Nephrology, Submitted, 1990.
14. Chen, M., Killen, P.D., Schnermann, J. and Briggs, J.P.: Furosemide produces rapid stimulation of renin mRNA in rat kidney. Am. Society of Nephrology, Submitted, 1990.
15. Todd, K.J., Killen, P., Schnermann, J. and Briggs, J.P.: Differential regulation of glucocorticoid receptor and mineralocorticoid receptor mRNA in rat kidneys. Am. Soc. Nephrology, Submitted, 1990.
16. Briggs, J.P., Trivedi, B., Todd, K., Chen, M., Schnermann, J., Lorenz, J.N., Weihprecht, H. and Killen, P.D.: Application of polymerase chain reaction to study of renin gene expression in single rabbit juxtaglomerular apparatus (JGA). American Heart Association, Submitted, 1990.
17. Scott, M.J., Reza, M.M., Killen, P. and Simon, R.H.: Type IV collagen gene expression in rat pulmonary alveolar epithelial cells. American Thoracic Society, Submitted, 1990.
18. Jones, M.L., Grande, J.P., Killen, P.D., Yoshimura, T., Ward, P.A. and Warren, J.S.: Regulation of monocyte chemoattractant protein (MCP-1) mRNA expression in rat mesangial cells. FASEB J., Submitted, 1990.
19. Owens, C.A., Grande, J.P., Yu, G.H., Killen, P.D. and Ward, P.A.: Adenine nucleotide binding to cultured human mesangial cells. FASEB J., Submitted, 1990.
20. Grande, J.P. and Killen, P.D.: TGF-β induces collagen IV expression in cultured human mesangial cells. FASEB J., Submitted, 1990.
21. Chen, M., Schnermann, J., Killen, P.D. and Briggs, J.P.: Assessment of reninin mRNA in isolated JG cells by competitive PCR. Council for High Blood Pressure Research; 45th Annual Fall Conference and Scientific Sessions, Chicago, Illinois, 1991.
22. Wiggins, R.C., Goyal, M., Merritt, S.E. and Killen, P.D.: Localization of α2(I) collagen mRNA by in situ hybridization to the periarterial and periglomerular regions in anti-GBM crescentic nephritis in the rabbit. American Society of Nephrology, Submitted, 1991.
23. Hansch, G.M., Wagner, C., Stoeck, M., Killen, P.D. and Rother, K.: TGF-β_1 induces collagen IV expression in cultured human glomerular mesangial cell. American Society of Nephrology, Submitted, 1991.
24. Chen, M., Schnermann, J., Killen, P.D. and Briggs, J.P.: Assessment of rennin mRNA in isolated JC cells by competitive PCR. American Heart Association, Submitted, 1991.
25. Chen, M., Schnermann, J., Killen, P.D. and Briggs, J.P.: Cyclic amp-mediated regulation of renin mRNA in cultured juxtaglomerular cells. American Society of Nephrology, Submitted, 1991.

26. Todd-Turla, K.M., Briggs, J.P., Smart, A., Killen, P. and Schnermann, J.: Distribution of mineralocorticoid and glucocorticoid receptor mRNA along the rat kidney nephron. American Society of Nephrology, Submitted, 1991.

STEVEN L. KUNKEL, PH.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES: None.

II. TEACHING ACTIVITIES:

A. Inflammation/Immunopathology Series ICS-600.
B. Pathology 581.
C. Pathology 650.
D. Pathology 850.
E. Course co-director "Cellular and Molecular Basis of Disease" (with Dr. Jeffrey Bonadio)
F. Epidemiology 570.
G. Member, Pathology Graduate Program Committee
H. Member, Molecular Pathogenesis Training Grant (Microbiology).
I. Member, Immunopathology Training Grant (Pathology).
J. Member, Operating Committee, Systems and Intergrative Biology Training Grant (Physiology).
K. Teaching/Research Seminars in various departments.
L. Supervised the following postdoctoral fellows, residents, and graduate students: Drs. Kim Brown, Amanda Thornton, Lynn Abruzzo, Mark Rolfe, Robert Schmouder, Ted Standiford, Charles Dibb, Andy Metinko, Kieta Kasahara and John Ham, and Susan Moore and Rob Smith.
M. Undergraduate students: Mark Milia, Andy Gilbert, Paul Holman, Rick Dwyer, and Dan Scharbaum.
N. Doctoral Committee Member/Oral Presentation Committee for the following graduate students: Susan Moore, Ron Allen, Cindy Hoorn, Paul Bohjanen and Oswald D'Auvergne.
O. Mentor for Dr. Alisa F. Koch, Northwestern University Medical School; sabbatical leave.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIH - Macrophage/Monocyte Signals in Lung Granuloma Formation; HL-R01-35276; Principal Investigator.
B. NIH - Monokine Gene Expression/Regulation in Lung Injury; HL-R01-31237; Principal Investigator.
C. NIH - Inflammatory Cells and Lung Injury; Program Project HL-31963; Principal Investigator for Section II and Core II.
D. NIH - Crescentic Nephritis; Program Project P01-DK38149; Principal Investigator - Section II.
E. NIH - Fibroblast Heterogeneity in Pulmonary Fibrosis; HL-39925; Co-investigator.
F. Tobacco Research Institute - Principal Investigator.

PROJECTS UNDER STUDY:

A. Regulation of macrophage signals that dictate immune responsiveness.
   1. Tumor necrosis factor production.
   2. Chemotactic cytokines.
   3. Endogenous regulators of cytokine expression.
B. Role of macrophages - lymphocyte interactions in the initiation, maintenance, and resolution of chronic immune response.
C. Regulation of macrophage gene expression.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Operating Committee Graduate Program.
B. Space Utilization and Research committee.
C. Committee on Master Planning.
D. Interview Candidates for Residency Program/Graduate Program.

MEDICAL SCHOOL/HOSPITAL:

A. Member, University Senate Assembly.
B. Committee on Medical Student Research.
C. Medical School Admission Interview Committee.
D. Medical School Admissions Executive Committee.
E. Medical Scientist Training Program Interview Committee.
F. Biomedical Research Council Committee.
G. Member, Michigan Cancer Center.

REGIONAL AND NATIONAL:

A. Associate Editor, Journal of Immunology.
B. Section Editor, Journal of Immunology.
C. Associate Editor, American Journal of Respiratory Cell and Molecular Biology.
D. Associate Editor, Pathobiology.
E. Editorial Board Rapid Communications/Mediators of Inflammation.
F. Program Advisory Committee, Third International Workshop on Cytokines.
G. Member, American Association of Pathology Program Committee.
H. Reviewer for the following journals: American Journal of Pathology, American Review of Respiratory Disease, Circulation, Clinical Immunology and Immunopathology, Infection and Immunity, Journal of Rheumatology, Laboratory Investigation, Science, Journal Immunology, American Journal of Respiratory Cell and Molecular Biology.
I. Grant Reviewer, United States Department of Agriculture.
J. Grant Reviewer, The Arthritis Society.
K. Grant Reviewer, Veterans' Administration.
L. Grant Reviewer, The Scleroderma Foundation.
M. Session Chair, FASEB, Regulation of Cytokine and Cytokine Receptor Gene Expression.
N. Long Range Planning Committee, American Association of Pathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Visiting Professor, Department of Medicine, Division of Pulmonary Medicine, Mayo Clinic, Rochester, Minnesota, September, 1990.
2. Invited Speaker, Biogen, Cambridge, Massachusetts, October, 1990.
3. Visiting Professor, Department of Microbiology/Immunology, University of Kansas Medical School, Kansas City, Kansas, November, 1990.
4. Invited Speaker, Seventh International Center for Alterations to Animal Testing Symposium, Baltimore, Maryland, Nov, 1990.
5. Invited Speaker, Athena Neuroscience, San Francisco, November, 1990.
6. Invited Speaker, Univ. Hannover Medical School, Hannover, Germany, December, 1990.
7. Invited Faculty Lecturer, German Society of Pharmacology, Hannover, Germany, December, 1990
8. Visiting Professor, Department of Microbiology and Infectious Diseases, University of Calgary, Calgary, Alberta, December, 1990.
9. Invited Speaker, Department of Microbiology/Immunology, Wayne State University, Detroit, Michigan, January, 1991.
10. Invited Speaker, Department of Surgery and Critical Care, University of Massachusetts, Worchester, Massachusetts, January, 1991.
11. Invited Speaker, Division of Hematology Oncology "Blood Club", University of Minneapolis, Minnesota, February, 1991.
12. Invited Speaker, 2nd International Congress on the Immune Consequence of Trauma, Shock and Sepsis, Munich, Germany, March, 1991.
13. Invited Speaker, Department of Microbiology/Immunology, University of Oklahoma Health Science Center, Oklahoma City, Oklahoma, March, 1991.
14. Invited Speaker, Symposium on Cytokines that Promote Inflammation, FASEB, Atlanta, Geogia, April, 1991.
15. Invited Speaker, American Red Cross, Washington D.C., May 1991.
16. Invited Speaker, Symposium on New Frontiers in Endotoxin Biology, ATS, Anaheim, California, May, 1991.
17. Invited Speaker, 17th International Congress on Chemotherapy, Berlin, Germany, June, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Spengler, R.N., Allen, R.M., Remick, D.G., Strieter, R.M. and Kunkel, S.L.: Stimulation of the alpha-adrenergic receptor augments the production of macrophage-derived tumor necrosis factor. J. Immunol. 1990;145:1430-1434.
2. Standiford, T.J., Strieter, R.M., Chensue, S.W., Westwick, J., Kasahara, K. and Kunkel, S.L.: Interleukin 4 inhibits the expression of interleukin 8 from stimulated human monocytes. J. Immunol. 1990;145:1435-1439.
3. Standiford, T.J., Strieter, R.M., Kasahara, K. and Kunkel, S.L.: Disparate regulation of IL-8 gene expression from blood monocytes, endothelial cells, and fibroblasts by IL-4. Biochem. Biophys. Res. Comm. 1990;171:531-536.
4. Kunkel, S.L. and Strieter, R.M.: Cytokine Networks in Lung Inflammation. Hospital Practice. 1990;25:63-76.
5. Strieter, R.M., Lynch, J.P., Basha, M.A., Standiford, T.J., Kasahara, K. and Kunkel, S.L.: Host response in mediating sepsis and ARDS. Seminars in Resp. Infect. 1990;5:233-247.

6. Long, N.C., Otterness, I., Kunkel, S., Vander, A.J. and Kluger, M.J.: Roles of interleukin 1β and tumor necrosis factor in lipopolysaccharide fever in rats. Am. J. Physiol. 1990;259:R724-R728.
7. Deforge, L.E., Nguyen D.T., Kunkel, S.L. and Remick, D.G.: Regulation of the pathophysiology of tumor necrosis factor. J. Lab. Clin. Med. 1990;116:429-438.
8. Standiford, T.J., Kunkel, S.L., Bash, M.A., Chensue, S.W., Lynch, J.P., Toews, G.B. and Strieter, R.M.: Interleukin-8 expression by pulmonary epithelial cells: A model for cytokine networks in the lung. J. Clin. Invest. 1990;86:1945-1953.
9. Strieter, R.M., Kasahara, K., Allen, R., Showell, H.J., Standiford, T.J. and Kunkel, S.L.: Human neutrophils exhibit disparate chemotactic factor gene expression. Biochem. Biophys. Res. Comm. 1990;173:725-730.
10. Davenport, R.D., Strieter, R.M., Standiford, T.J. and Kunkel, S.L.: Interleukin-8 production in red cell incompatibility. Blood. 1990;76:2439-2442.
11. Nickoloff, B.J., Karabin, G.D., Barker, J.N.W.N., Griffiths, C.E.M., Sarma, V., Mitra, R.A., Elder, J.J., Kunkel, S.L. and Dixit, V.M.: Cellular localization of interleukin-8 and its inducer, tumor necrosis factor-alpha in psoriasis. Am. J. Pathol. 1991;138:129-140.
12. DeMarco, D., Kunkel, S.L., Strieter, R.M., Basha, M. and Zurier, R.B.: Interleukin-1 induced gene expression of neutrophil activating protein (interleukin-8) and monocyte chemotactic peptide in human synovial cells. Biochem. Biophys. Res. Comm. 1991;174:411-416.
13. Chensue, S.W., Terebuh, P.D., Remick, D.G., Scales, W.E. and Kunkel, S.L.: In vivo biologic and immunohistochemical analysis of interleukin-1 alpha, beta and tumor necrosis factor during experimental endotoxemia. Am. J. Pathol. 1991;138:395-402.
14. Wharram, B.L., Fitting, K., Kunkel, S., Remick, D.G., Merritt, S.E. and Wiggins, R.C.: Tissue factor expression in endothelial cell/monocyte cocultures stimulated by lipopolysaccharide and/or aggregated IgG. J. Immunol. 1991;146:1437-1445.
15. Kunkel, S.L., Standiford, T., Kasahara, K., and Strieter, R.M.: Interleukin-8 (IL-8): The major chemotactic factor in the lung. Exp. Lung Res. 1991;17:17-23.
16. Kunkel, S.L., Strieter, R.M., Chensue, S.W., Campbell, D.A. and Remick, D.G.: The role of TNF in diverse pathologic processes. Biotherapy 1991;3:135-141.
17. Kunkel, S.L., Standiford, T., Chensue, S.W., Kasahara, K. and Strieter, R.M.: Cellular and molecular mechanisms of cytokine networking. Agents and Action 1991;32S:205-219.
18. Liebert, M., Wedemeyer, G., Abruzzo, L.V., Kunkel, S.L., Hammerberg, C., Cooper, K.D. and Grossman, H.B.: Stimulated urothelial cells produce cytokines and express and activated cell surface antigenic phenotype. Seminars in Urology. 1991;9:124-130.
19. Standiford, T.J., Kunkel, S.L., Phan, S.H., Rollins, B.J. and Strieter, R.M.: Alveolar macrophage-derived cytokines induce monocyte chemoattractant protein-1 expression from human pulmonary type II-like epithelial cells. J. Biol. Chem. 1991;266:9912-9918.
20. Kasahara, K., Strieter, R.M., Chensue, S.W., Standiford, T.J. and Kunkel, S.L.: Mononuclear cell adherence induces neutrophil chemotactic factor/interleukin-8 gene expression. J. Leuk. Biol. 1991;50:287-295.

BOOKS AND CHAPTERS IN BOOKS:

1. Kunkel, S.L., Standiford, T., Metinko, A. and Strieter, R.M.: Endothelial cell-derived novel chemotactic cytokines, in, Lenfant, P. (ed.), Lung Vascular Injury: Molecular and Cellular Response, Marcel Dekker.
2. Kunkel, S.L., Chensue, S.W., Standiford, T.J. and Strieter, R.M.: Cellular and molecular mechanisms that regulate the production of interleukin-8: The potential role of chemotactic cytokines in ARDS and multiple organ failure, in, Faist, E. (ed.), Second International Congress on the Immune Condsequence of Trauma, Shock, and Sepsis-Mechanisms and Therapeutic Approaches, Springer Verlag, Berlin.
3. Strieter, R.M., Standiford, T.J., Rolfe, M.W. and Kunkel, S.L.: Interleukin-8, in, Lemfanst and Kelly J. (eds.), Lung Biology in Health and Disease, Marcel Dekker, Inc.

4. Kunkel, S.L., Standiford, T. and Strieter, R.M.: Cytokine-dependent interleukin-8 expression and its role in cell communication, in, Schlag, G., Redl, H., Siegel, J.H. and Traber,D.L.Shock (eds.), Sepsis and Organ Failure, Springer-Verlag, 1991, pp. 279-293.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Remick, D.G., Negussie, Y., Deforge, L.E., Kunkel, S.L., Eyon, A. and Griffin, G.E.: Cytokine production during the jarisch-herxheimer reaction (JH-R). FASEB, 1991.
2. Terebuh, P., Otterness, I., Kunkel, S. and Chensue, S.: Cellular distribution of IL-6 expression in normal and endotoxin challenged mice. FASEB, 1991.
3. Chensue, S., Terebuh, P., Evanoff, H., Higashi, G. and Kunkel, S.: Anti-interleukin 4 but not anti-interferon antibodies suppress schistosome egg hypersensitivity-type granuloma formation. FASEB, 1991.
4. Phan, S.H., McGarry, B.M., Kunkel, S.L. and Ryan, U.S.: Modulation of endothelial cell transforming growth factor-β production by interleukin-1β and tumor necrosis factor-α. FASEB, 1991.
5. Moore, S., Strieter, R., Standiford, T., Chensue, S. and Kunkel, S.: Constitutive gene expression of IL-1 receptor antagonist by alveolar macrophages. FASEB, 1991.
6. Strieter, R., Kasahara, K., Allen, R., Standiford, T. and Kunkel, S.: Human neutrophil gene expression of interleukin-8 by LPS, TNF-α, and IL-1β. FASEB, 1991.
7. Danforth, J., Elner, S., Scales, W., Kunkel, S., Strieter, R. and Elner, V.: Interleukin-6 (IL-6) gene expression and secretion by cytokine-stimulated human retinal pigment epithelial cells. FASEB, 1991.
8. Kasahara, K., Kunkel, S., Standiford, T. and Strieter, R.: Adherence is synergistic with LPS, IL-1, and TNF stimulation of human mononuclear phagocyte-derived interleukin-8. FASEB, 1991.
9. Metinko, A., Kunkel, S., Standiford, T. and Strieter, R.: Monocyte expression of interleukin-8 in response to oxidant stress. FASEB, 1991.
10. Allen, R., Kunkel, S., Rollins, B., Standiford, T., Rolfe, W. and Strieter, R.: Stimulation of human mononuclear phagocytes by monocyte chemotactic peptide (MCP-1). FASEB, 1991.
11. Rolfe, M., Kunkel, S., Standiford, T., Allen, R, Chensue, S., Evanoff, H. and Strieter, R.: Human pulmonary fibroblasts express interleukin 8: A model of cellular communication. FASEB, 1991.
12. Kunkel, S.L., Standiford, T. and Strieter, R.M.: Cellular and molecular regulation of cytokine network: Induction and regulation of distal cytokines. 17th International Congress on Chemotherapy.
13. Standiford, T., Kunkel, S., Kasahara, K., Rolfe, M. and Strieter, R.: Regulation of interleukin 8 expression from human monocytes and alveolar macrophages by PGE_2 and dexamethasone. FASEB, 1991.
14. Dibb, C., Strieter, R. and Kunkel, S.: Peripheral blood and bone marrow mononuclear cell production of IL-8. FASEB, 1991.
15. Schmouder, R., Strieter, R., Wiggins, R. and Kunkel, S.: Regulation of IL-8 gene expression in human renal epithelial cells. FASEB, 1991.
16. Lin, H., Chensue, S.W., Strieter, R.M., Bolling, S.F. and Kunkel, S.L.: Antitumor necrosis factor antibody prolongs heart allograft survival in the rat. FASEB, Atlanta, Georgia, April, 1991.
17. Metinko, A.P., Kunkel, S.L., Standiford, T.J. and Strieter, R.M.: Anoxia-hypoxia: A model of ischemia-reperfusion for interleukin-8 expression by monocytes. American Thoracic Society, Anaheim, California, May, 1991.
18. Rolfe, M.W., Kunkel, S.L., Standiford, T.J., Allen, R., Evanoff, H. and Strieter, R.M.: Interleukin-8 expression by human pulmonary fibroblasts: A model of cellular communication. American Thoracic Society, Anaheim, California, May, 1991.

19. Standiford, T.J., Kunkel, S.L., Rolfe, M.W., Kasahara, K. and Strieter, R.M.: IL-4 differentially regulates the expression of TNF, IL-1β, and IL-8 from human peripheral blood monocytes and alveolar macrophages. American Thoracic Society, Anaheim, California, May, 1991.
20. Lynch, J.P. III, Standiford, T.J., Kunkel, S.L., Rolfe, M.W. and Strieter, R.M.: Interleukin-8 gene expression is augmented in idiopathic pulmonary fibrosis and correlates with neutrophilic alveolitis. American Thoracic Society, Anaheim, California, May, 1991.
21. Kasahara, K., Kunkel, S.L., Standiford, T.J. and Strieter, R.M.: Adherence-induced mononuclear phagocytic cell-derived interleukin-8 gene expression. American Thoracic Society, Anaheim, California, May, 1991.
22. Allen, R., Kunkel, S.L., Rollins, B.J., Standiford, T.J., Rolfe, M.W. and Strieter, R.M.: Monocyte chemotactic/activating peptide (MCP-1)-induced interleukin-8 by human mononuclear phagocytes. American Thoracic Society, Anaheim, California, May, 1991.
23. Basha, M.A., Kunkel, S.L., Rowens, B., Popovich, J., Jr. and Strieter, R.M.: Interleukin-8 expression in HIV-dependent PCP associated neutrophilic alveolitis. American Thoracic Society, Anaheim, California, May, 1991.
24. Elner, S.G., Elner, V.M., Pavilack, M.A., Todd, R.F. III, Kunkel, S.L., Strieter, R.M. and Huber, A.R.: Intercellular adhesion molecule-1 (ICAM-1) mediates leukocytes binding to human RPE cells. ARVO, Sarasota, Florida, May, 1991.
25. Elner, V.M., Strieter, R.M., Pavilack, M.A., Elner, S.G., Remick, D.G. and Kunkel, S.L.: Interleukin-8 (IL-8) gene expression and secretion by whole human corneas. ARVO, Sarasota, Florida, May, 1991.
26. Koch, A.E., Kunkel, S.L., Burrows, J.C., Evanoff, H.L., Haines, G.K., Pope, R.M. and Strieter, R.M.: The synovium and synovial fluid as a source of interleukin-8. AFCR national convention, Seattle, Washington, May, 1991.

TULLIA LINDSTEN, M.D., PH.D.
ASSISTANT RESEARCH SCIENTIST
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES: None.

II. TEACHING ACTIVITIES: None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Tullia Lindsten, "Lymphokine-specific RNA binding proteins, NIH CA54521 (50%). $70,717/year ($350,000/five years). 4/15/91 - 03/31/96.

IV. ADMINISTRATIVE ACTIVITIES:

None.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

None.

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, "Lymphokine-specific RNA binding proteins", Hematology/Oncology Division Seminar, June 25, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ledbetter, J.A., Imboden, J.B., Schieven, G.L., Grosmaire, L.S., Rabinovitch, P.S., Lindsten, T., Thompson, C.B. and June, C.H.: CD28 ligation in T cell activation: Evidence for two signal transduction pathways. Blood 1990;75:1531-1539.
2. Bhat, N.K., Thompson, C.B., Lindsten, T., June, C.H., Fujiwara, S., Koizumi, S., Fisher, R.J. and Papas, T.S.: Reciprocal expression ets-1 and ets-2 genes during T-cell activation: A novel regulatory role for the proto-oncogene ets-1. Proc. Natl. Acad. Sci. USA 1990;87:3723-3727.

3. Ho, I.-C., Bhat, N.K., Gottschalk, L.R., Lindsten, T., Thompson, D.B., Papas, T.S. and Leiden, J.M.: Sequence-specific binding of human ets-1 to the T cell receptor a gene enhancer. Science 1990;250:814-818.
4. Bohjanen, P.R., Petryniak, B., June, C.H., Thompson, C.B. and Lindsten, T.: An inducible cytoplasmic factor (AU-B) binds selectively to AUUUA-multimers in the 3' untranslated region of lymphokine mRNA. Mol. Cell Biol. 1991;11:3288-3295.
5. Standiford, T.J., Lindsten, T., Thompson, C.B., Strieter, R.M. and Kunkel, S.L.: Interleukin 4 differentially regulates tumor necrosis factor-alpha gene expression by human T lymphocytes and monocytes. Pathobiology 1991, In Press.

RICARDO V. LLOYD, M.D., PH.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES

A. Surgical pathology - 12 weeks.
B. Autopsy Pathology - 1 week
C. Consultant for endocrine lesions.
D. Consultant to Veterans Administration Medical Center, Ann Arbor, Michigan.
E. Consultant for immunochemistry cases.

II. TEACHING ACTIVITIES:

A. Lectures to sophomore medical students - Pathology 600
B. Pathology 600 Laboratory - 1 semester.
C. Fourth Year medical student rotation in Pathology - 1 month.
D. Lecture to dental students - Pathology 630.
E. Lectures to pathology house officers.
F. Immunoperoxidase Rounds - twice monthly.
G. Supervision of four postdoctoral fellows in research laboratory (Dr. L. Jin, Dr. E. Kulig, Dr. K. Zhang, Dr. T. Maeda).
H. Honors Elective Course for undergraduate students (Annie Chang)- 1 semester.
I. Laboratory Session for Graduate Students in Pathology 650 Course - Immunochemistry and In situ hybridization.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Regulation of Rat Pituitary Hyperplasia and Neoplasia. NIH Grant 1R23 CA 37238, 3/84 - 2/87 and NIH CA 37238, 5/87 - 4/92 (Competing Renewal Score of 1.27 (4 percentile), 12/1991-11/1996, (PI - R. Lloyd), $1,243,059.
B. Studies of Normal and Neoplastic Human Pituitary Tissues. NIH Grant CA 42951, 7/86 - 6/90 and 7/90 - 6/95 (PI - R. Lloyd), $1,065,133

PROJECTS UNDER STUDY:

A. Regulation of pituitary growth and differentiation in humans, rats and mice.
B. Applications of immunochemical and molecular biological techniques to diagnostic pathology.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director of Immunoperoxidase Service.
B. Coordinator of Anatomic Pathology Journal Club.
C. Pathology Graduate Training Program Committee.
D. Space Utilization Committee.
E. Committee to Update Surgical Pathology Cutting Manual

MEDICAL SCHOOL/HOSPITAL:

A. Endocrine Surgery Conference.
B. Pituitary Study Group.
C. Pathology presentations at General Endocrine Conference.
D. Search Committee for Medical School Dean.

REGIONAL AND NATIONAL:

A. Editorial Board - American Journal of Pathology.
B. Editorial Board - Endocrine Pathology.
C. Editorial Board - American Journal of Surgical Pathology.
D. Editorial Board - Modern Pathology.
E. Reviewer of articles for Laboratory Investigation, Journal of the American Medical Association, Journal of Histochemistry and Cytochemistry, the American Journal of Medical Sciences, New England Journal of Medicine, Journal of Clinical Endocrine Metabolism, and others.
F. Review Committee for US Academy of Pathology Abstracts.
G. College of Pathologist - Cell Markers Committee.
H. Pathology B Study Section, National Cancer Institute, Member 1987 - June 1991.
I. NIH - Reviewer Reserve (NRR, July 1991 - June 1995).

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURE AND SEMINARS

1. Invited Speaker. International Pituitary Pathology Club. Various Lectures and Presentations. Lyon, France. September 15-21, 1990.
2. Invited Speaker. University of Minnesota. Minneapolis, Minnesota. "In Situ Hybridization in Pathology". October 24, 1990.
3. ASCP Course. Chicago, Illinois. Immunohistology techniques and interpretation. August, 1990.
4. Invited Symposium Speaker. 5th European Workshop on Pituitary Adenomas. "Chromogranin Regulation in the Pituitary". Venice, Italy. March 17-20, 1991.
5. Invited Speaker. University of Wisconsin, Madison, Wisconsin. "In Situ Hybridization" and "Regulation of Tumor Development in Human and Rodent Pituitaries". April 3rd and 4th, 1991.
6. Invited Speaker. Workshop on Modern Diagnostic Techniques in Pathology. Caracas, Venezuela. April 10-13, 1991.
7. Invited Speaker. Memphis Society of Pathologist--Spring Dinner Meeting and Scientific Session. May 17, 1991.
8. The Merlin L. Trumbull Lectureship in Pathology--Endocrine Pathology. May 18, 1991. Baptist Memorial Hospital. Memphis, Tennessee.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Lloyd, R.V., Jin, L., Fields, K.: Detection of chromogranins A and B in endocrine tissues with radioactive and biotinylated oligonucleotide probes. Am J Surg Pathol 1990;14:35-43.
2. Lloyd, R.V., Long, J., Song, J., Kovacs, K., Horvath, G.: Effects of propylthiouracil on growth hormone and prolactin messenger ribonucleic acid in the rat pituitary. An *in situ* hybridization histochemical analysis. Lab Invest. 1990;62:347-354.
3. Song, J., Jin, L., England, B., Smart, J., Lloyd, R.V.: Gonadotropin releasing hormone regulates gonadotropin subunit and chromogranin B mRNAs in cultured chromogranin A positive pituitary adenomas. J. Clin Endocrinol Metab 1990; 71:622-630.
4. Jin, L., Song, J., Lloyd, R.V.: Hybridization studies of cultured human pituitary PRL and GH producing adenomas cells. Effects of thyrotropin-releasing hormone somatostatin and phorbol ester. Endocr Pathol 1990;1:25-36.
5. Vinik, A.I., Lloyd, R.V., Cho, K. The use of somatostatin analogue in gastroenteropancreatic tumors other than carcinoid. Metabolism 1990; 39 (Suppl 2):156-162..
6. Horvath, E., Lloyd, R.V., Kovacs, K., Losinski, N.E.: PTU-induced hypothyroidism results in reversible transdifferentiation of somatotrophs into thyroidectomy cells. A Morphologic study of the rat pituitary including immunoelectron microscopy. Lab Invest 1990; 63:511-520.
7. Lloyd, R.V., Jin, L., Horvath, E., Kovacs, K.: Analysis of endocrine active and clinically silent corticotropic pituitary adenomas analyzed by *in situ* hybridization. Am J Pathol 1990; 137:479-488.
8. Lloyd R.V.: Ultrastructure of spontaneous and transplanted tumors in laboratory animals. J Electron Micro Tech (In Press), 1991.
9. Lloyd, R.V., Jin, L., Song, J.: Ultrastructural localization of chromogranin and prolactin mRNAs with colloidal gold in cultured human pituitary tumor cells. Lab Invest 1990; 63:413-419.
10. Flint, A., Davenport, R.D., Lloyd R.V.: The tall cell variant of papillary carcinoma of the thyroid gland. Comparison with the common form of papillary carcinoma by DNA and morphometric analysis. Arch Pathol Lab Med 1991; 115:169-171.
11. Lloyd, R.V., Jin, L., Fields, K., Kulig, E.: Regulation of prolactin gene expression in DMBA-estrogen induced transplantable rat pituitary tumor. Am J Pathol 1990; 135:1525-1537.
12. Lloyd, R.V., Jin, L., Fields, K., Kulig, E. Regulation of estrogen receptor mRNA in normal and neoplastic rat pituitary tissues. Endocr Pathol 1991; 2:74-82.
13. Graham, D.M., Jin, L., Lloyd, R.V.: Detection of estrogen receptor in paraffin-embedded sections of breast carcinoma by immunohistochemistry and *in situ* hybridization. Am J Surg Pathol 1991; 15:475-485.
14. Kovacs K., Stefaneanu L., Horvath E., Lloyd R.V., Lancronjan I, Buchfelder M, Fahlbusch R: Effect of dopamine agonist medication on prolactin-producing pituitary adenomas. A morphologic study including immunocytochemistry, electron microscopy and *in situ* hybridization. Virch Arch A Pathol Anat 1991; 418:439-446.
15. Jin, L., Hemperly, J.J., Lloyd, R.V.: Expression of neural cell adhesion molecules (N-CAM) in normal and neoplastic human neuroendocrine tissues. Am J Pathol 1991; 138:961-969.
16. Kulig, E., Landefeld, T.D., Lloyd, R.V.: Estrogen regulates prolactin gene methylation in transplantable rat pituitary tumors. Am J Pathol (In Press).
17. Flint, A., Lloyd, R.V.: Pulmonary metastases of colonic carcinoma. Distinction from pulmonary adenocarcinoma. Arch Pathol Lab Med (In Press).
18. Lloyd, R.V., Jin, L., Chandler, W.F.: In situ hybridization in the study of pituitary tissues. Pathol Res Pract (In Press).
19. Lloyd, R.V., Jin, L., Fields, K, Kulig, E.: Effects of estrogens on pituitary cell and pituitary tumor growth. Pathol Res Pract (In Press).

20. Stefaneaunu, L., Kovacs, K., Horvath, E., Lloyd, R.V.: In situ hybridization study of proopiomelanocortin (POMC) gene expression in human pituitary corticotrophs and their adenomas. Virch Arch Pathol (In Press).
21. Eusebi, V., Damiari, S., Riva, C., Lloyd, R.V., Capella, C.: Calcitonin free oat-cell carcinoma of the thyroid gland. Virch Arch A Pathol Anat 1990; 417:267-271.
22 Grossman, D., Jin, L., Heidelberger, K.P., Lloyd, R.V.: Expression of chromogranin A protein and messenger RNA and tyrosine hydroxylase protein in paraffin-embedded sections of neuroendocrine neoplasms. Endocrine Pathol (In Press).
23. Lloyd, R.V., Jin, L., Fields, K., Chandler, W.F., Horvath, E., Stefaneanu, L, Kovacs, K.: Analysis of pituitary hormones and chromogranin A mRNAs in null cell adenomas, oncocytomas and gonadotroph adenomas by in situ hybridization. Am J Pathol (In Press).

ARTICLES SUBMITTED FOR PUBLICATION

1. Lloyd, R.V., Hawkins, K., Jin, L., Fields, K., Kulig, E.: Chromogranin A and B and secretogranin II in the pituitary and adrenal medulla. (Submitted to Lab Invest).
2. Kendall, S.K., Sauders, T.L., Jin, L., Lloyd, R.V., Glode, L.M., Nett, T.M., Nilson, J.H., Camper, S.A.: Targeted ablation of pituitary gonadotrophs in transgenic mice. (Submitted to Mol Endocrinol).
3. Flint, A., Lloyd, R.V.: Colonic carcinoma metastatic to lung: cytologic manifestation and distinction from primary pulmonary adenocarcinoma. (Submitted).
4. Wang, X., Tafra, L., Berezmiak, R., Lloyd, R.V., Muraike, L., Dafoe, D.C.: Co-transplanted fetal liver (FL) benefits fetal pancreas (FP) isografts. (Submitted to Transplantation).
5. Jin, L., Kulig, E., Fields, K., Camper, S.A., Lloyd, R.V.: Regulation of PRL and Pit-1/GHF-1 expression in normal and neoplastic rat pituitary cells by bFGF and estrogen. (Submitted).
6. Lloyd, R.V., Jin, L., Kulig, E., Fields, K., Camper, S.A., Frohman, L.A.: Pituitary hyperplasia and neoplastic development in mice with the GHRH transgene. (Submitted).

BOOKS/CHAPTERS IN BOOKS

1. Lloyd, R.V.: Tumors of the pituitary, In Stinson, S.F., Schuller, H.M. and K, G. (Eds), Atlas of Tumor Pathology of the Fischer Rat, CRC Press, Boca Raton, Florida 1989. Chapter 13, 1990, pp. 265-289.
2. Lloyd, R.V.: Immunohistochemical localization of chromogranin in polypeptide hormone producing cells and tumors in J. Lechago and T. Kameya (eds.), Endocrine Pathology Update. Field and Wood Publishers, PA. 1990.
3. Lloyd, R.V.: Tumors of the pituitary gland in V. Turusov and U. Mohr (eds.). Pathology of Tumors in Laboratory Animals. International Agency for Research on Cancer. World Health Organization, IARC Scientific Publ 99 Lyon France, 1990, pp. 499-538.
4. Lloyd, R.V.: Morphologic Methods, In Kovacs and Asa S. (eds) Functional Endocrine Pathology. Blackwell Scientific Publishers, Boston, MA 1991, pp. 94-103.
5. Chandler, W.F., Lloyd, R.V.: Surgical Endocrinology--Pituitary. In: Greenfield, L.J., Mulholland, M.W., Oldham, K.T., Zelenock, G.B. (eds.) Surgery Scientific Principles and Practice. J. B. Lipincott Co. 1992 (In Press).
6. McKeever, P., Lloyd, R.V.: Pituitary adenomas and selected intracranial tumor. In: Garcia, J.H., Escabona-Zapata, J., Sandback, V., Cervas-Nararra, J. (eds). Diagnostic Neuropathology, Vol IV. Field and Wood Medical Publisher Inc., 1992 (In Press).
7. Lloyd, R.V.: Embryology and anatomy of the pituitary gland. In: Lloyd, R.V. (ed). Surgical Pathology of the Pituitary Gland. W. B. Saunders, Chapter 1, 1992 (In Press).
8. Lloyd, R.V.: Cytology and Function of the Pituitary Gland. In: Lloyd, R.V. (ed). Surgical Pathology of the Pituitary Gland. W. B. Saunders, Chapter 2, 1992 (In Press).
9. Lloyd, R.V.: Practical Approaches to the diagnosis of pituitary lesions. In: Lloyd, R.V. (ed). Surgical Pathology of the Pituitary Gland. W. B. Saunders, Chapter 3, 1992 (In Press).

10. Lloyd, R.V.: Frozen sections in the diagnosis of pituitary lesions. In: Lloyd, R.V. (ed). Surgical Pathology of the Pituitary Gland. W. B. Saunders, Chapter 4, 1992 (In Press).
11. Lloyd, R.V.: Non-neoplastic pituitary lesions including hyperplasia. In: Lloyd, R.V. (ed). Surgical Pathology of the Pituitary Gland. W. B. Saunders, Chapter 5, 1992 (In Press).
12. Lloyd, R.V.: Molecular biological analysis of pituitary disorders. In: Lloyd, R.V. (ed). Surgical Pathology of the Pituitary Gland. W. B. Saunders, Chapter 8, 1992 (In Press).
13. Lloyd, R.V. Ectopic Pituitary Adenomas. In: Lloyd, R.V. (ed). Surgical Pathology of the Pituitary Gland. W. B. Saunders, Chapter 11, 1992 (In Press).
14. Jin, L., Lloyd, R.V.: Metastatic neoplasms to the pituitary gland. In: Lloyd, R.V. (ed). Surgical Pathology of the Pituitary Gland. W. B. Saunders, Chapter 12, 1992 (In Press).
15. Lloyd, R.V.: Future prospects in the diagnosis and treatment of pituitary adenomas. In: Lloyd, R.V. (ed). Surgical Pathology of the Pituitary Gland. W. B. Saunders, Chapter 16, 1992 (In Press).
16. Lloyd, R.V.: Adrenal medulla and paraganglia. In: Gould, V., Lechago, J. (eds). Bloodworth's Endocrine Pathology, 3rd Edition. Williams & Williams, M.D., 1992 (In Press).
17. Lloyd, R.V., Jin, L.: Regulation of chromogranin A and B gene expression in human pituitary adenomas. 5th European Workshop on Pituitary Adenomas, Venice, 17-20 March 1991. Elsevier Science Publishers 1991 (In Press).

BOOKS:

1. Endocrine Pathology, Springer Verlag, New York, 1990.
2. Surgical Pathology of the Pituitary Gland. Saunders, Lloyd, R.V. (ed) (In Press) .

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Lloyd, R.V., Jin, L., Kulig, E., Fields, K., Camper, S.A., Frohman, L.A.: Progression from pituitary growth hormone (GH) cell hyperplasia to neoplasia in mice with the growth hormone releasing hormone (GHRH) transgene. Lab Invest 64:32A, 1991, Abstract 184.
2. Chang, A., Jin, L., Lloyd, R.V.: Expression of growth hormone releasing hormone (GHRH) in transgenic mice results in pancreatic islet beta cell hyperplasia. Lab Invest 64:32A, 1991, Abstract 181.
3. Horvath, E., Kovacs, K., Lloyd, R.V., Scheithauer, B.W., Stefaneanu, L. Changing perceptions of pituitary cell function. J Endocrinol Invest 14 (Suppl 1) pp. 31, 1991, Abstract OC6.
4. Stefaneanu, L., Kovacs, K., Horvath, E., Lloyd, R.V., Lancranjan, I., Buchfelder, M., Fahlbunch, R.: Effects of dopamine agonist therapy on morphology of prolactin-producing pituitary adenomas. J Endocrinol Invest 14 (Suppl 1), pp. 50, 1991, Abstract P4.
5. Lloyd, R.V., Jin, L., Chandler, W.F.: Regulation of chromogranin A and B gene expression in human pituitary adenomas. J Endocrinol Invest 14 (Suppl 1), pp. 8, 1991, Abstract 510.
6. Stefaneanu, L., Kovacs, K., Lloyd, R.V., Scheithauer, B.W.: Human pituitary in pregnancy: an in situ hybridization and immunocytochemical study. FASEB J 75th Ann Meeting Atlanta, GA, April 21-25, 1991, pp. 1391, Abstract 5920.
7. Wang, X., Tafra, L., Berezniak, R., Lloyd, R.V., Dafoe, D.C.: Success of composite fetal pancreas (FP) and fetal liver (FL) isografts transplanted to the intramuscular (IM) site in rats. Third International Congress on Pancreatic and Islet Transplantation. Symposium on Artifical Insulin Delivery System. Lyon France, June 6-8, 1991.
8. Stefaneanu, L., Horvath, E., Lloyd, R.V., Lancranjan, I., Buchfelder, M., Fahjlbusch, R.: Prolactin gene expression in human prolactin producing pituitary adenomas: effect of dopamine agonists. Endocrine Society 73rd Ann Meeting, Washington, D.C., June 19-22, 1991, pp. 393, Abstract 1450.
9. Jin, L., Kulig, E., Fields, K., Camper, S.A., Lloyd, R.V.: Regulation of PRL and Pit-1 expression in normal and neoplastic rat pituitary cells by FGF and estrogen. Endocrine Society 73rd Ann Meeting, Washington, D.C., June 19-22, 1991, pp. 169, Abstract 554.

10. In Situ Hybridization in Endocrine Pathology. Endocrine Pathol 1991; 2:1-3 (Editorial).

JOHN B. LOWE, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Clinical Immunology Diagnostic Service - sign out of serum and urine protein electrophoresis, immunofixation, and immunoelectrophoresis; terminal transferase immunofluorescence.

II. TEACHING ACTIVITIES:

A. Supervision of six postdoctoral fellows (Robert Larsen, Ph.D., Nozomu Hiraiwa, M.D.,Ph.D., Brent Weston, M.D., Marco Trinchera, M.D., Aron Thall, Ph.D. and Rosella Mollicone, Ph.D.) and one M.D., Ph.D. thesis student, (Mr. Kevin Gersten).

B. 1. Lecturer - Pathology 581
2. Lecturer - Pathology 850

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Analysis of the Roles of Oligosaccharides During Murine Embryogenesis". Source of award: Howard Hughes Medical Institute.

B. Principal investigator, "The Molecular Biology of Intracellular Lipid Transport", NIH DK-38482 (50% effort), $63,547/year direct cost ($317,737/five years), 8/1/86-7/31/91.

C. Sponsor, NRSA Postdoctoral Fellow, Brent Weston, M.D. "The Lewis Blood Group α(1,3/1,4) Fucosyltransferase Gene". Inclusive dates of funding: 12/1/90 - 11/30/92. Source of award: National Institutes of Health. Total direct costs = $62,300.00.

D. "Molecular Genetics of the Human Lewis and Lewis-Related Blood Group Loci". Source of Award: National Blood Foundation. Inclusive dates of funding: 7/1/91 - 6/30/93. Total direct costs = $19,500.00.

PROJECTS UNDER STUDY:

Structure and regulation of mammalian glycosyltransferase genes. Efforts are focused on the isolation and analysis of gene(s) for human and murine glycosyltransferases, using mammalian gene transfer techniques.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Resident Selection Committee.

REGIONAL AND NATIONAL:

B. Editorial Board, Journal of Biological Chemistry.

V. OTHER RELEVANT ACTIVITIES:

A. Howard Hughes Medical Institute, Assistant Investigator.

INVITED LECTURES AND SEMINARS:

1. Molecular genetics of human fucosyltransferase genes, International Symposium on the Biologic Function of Glycosphingolipids, Santa Barbara, California, July, 1990.
2. The molecular biology of human fucosyltransferase genes, Society for Complex Carbohydrates Conference, San Diego, California, October, 1990.
3. Molecular genetics of human fucosyltransferase genes, University of Tulsa, Tulsa, Oklahoma, October, 1990.
4. Mammalian genes that determine terminal glycosylation events, Jacques Monod Conference on the Chemistry, Biochemistry, and Molecular Biology of Glycoconjugates, Aussois, France, October, 1990.
5. ELAM-1-dependent cell adhesion to vascular endothelium determined by a transfected human fucosyltransferase cDNA, Genentech Corp., South San Francisco, California, November, 1990.
6. Cloning and expression of a fucosyltransferase cDNA that determines ELAM-1-dependent cell adhesion to vascular endothelium, Monsanto Corp., St. Louis, Missouri, December, 1990.
7. Cell adhesion determined by mammalian glycosyltransferase genes, Mount Sinai Hospital, Toronto, Canada, January, 1991.
8. Cloned fucosyltransferase genes that determine LEC-CAM-dependent cell adhesion, La Jolla Cancer Research Foundation, La Jolla, California, February, 1991.
9. Structural diversity in human fucosyltransferase genes, 1991 Gordon Conference on Complex Carbohydrates. Ventura, California, February, 1991.
10. ELAM-1-dependent cell adhesion to vascular endothelium determined by a transfected human fucosyltransferase cDNA, Biogen, Inc., Cambridge, Massachusetts, February, 1991.
11. Modification of mammalian cell glycosylation phenotype by glycosyltransferase gene transfection, Engineering Foundation Conference: Biochemical Engineering VII - Cellular and Reactor Engineering, Santa Barbara, California, March, 1991.
12. Endothelial adhesive events determined by transfected human fucosyltransferase cDNAs, University of Texas Southwestern Medical Center, Dallas, Texas, March, 1991.
13. A cloned fucosyltransferase cDNA determines ELAM-1 dependent cell adhesion to vascular endothelium, Vrije Universiteit Amsterdam, The Netherlands, April, 1991.
14. Molecular cloning of mammalian glycosyltransferases and construction of fusion proteins for synthesis of oligosaccharides, Rijksuniversiteit Leiden, The Netherlands, April, 1991.
15. Human fucosyltransferase genes and ELAM-1 dependent cell adhesion, Glaxo Group Research Limited, London, United Kingdom, April, 1991.
16. Structure and function of mammalian glycosyltransferases, Rijksuniversiteit Utrecht, The Netherlands, April, 1991.
17. Structure and regulation of mammalian glycosyltransferase genes, 1991 Meeting of the Biochemical Society, Reading, England, April, 1991.
18. Molecular genetics of human fucosyltransferases, Biochimie, Faculte de Pharmacie, Universite de Paris-Sud, Chatenay-Malabry, France, April, 1991.
19. Structure and function of human fucosyltransferase genes, 4th Symposium on Glycoconjugate Research, Tokyo, Japan, June, 1991.
20. Genetics of glycosyltransferases and implication in cell adhesion, Kyoto University, Kyoto, Japan, June, 1991.

21. Glycosyltransferase genes that determine expression of carbohydrate ligands for the selectin/LEC-CAM family of cell adhesion molecules, 1991 Gordon Conference on Phagocytes, Plymouth, New Hampshire, June, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Jefferson, J.R., Powell, D.N., Rymaszewski, Z., Kukowska-Latallo, J.F., Lowe, J.B. and Schroeder F.: Altered membrane structure in transfected mouse L-cell fibroblasts expressing rat liver fatty acid binding protein. J. Biol. Chem. 1990;265:11062-11068.
2. Kukowska-Latallo, J.F., Larsen, R.D., Rajan, V.P. and Lowe, J.B.: A cloned human cDNA determines expression of a mouse stage-specific embryonic antigen and the Lewis blood group α1,3/1,4 fucosyltransferase. Genes and Development. 1990;4:1288-1303.
3. Larsen, R.D., Ernst, L.K., Rajan, V.P. and Lowe, J.B.: Molecular cloning, sequence, and expression of a human GDP-L fucose:β-D-galactoside 2-α-L-fucosyltransferase cDNA that can form the H blood group antigen. Proc. Natl. Acad. Sci. USA 1990;87:6674-6678.
4. Lowe, J.B., Stoolman, L.M, Nair, R.J. Larsen, R.D., Berhend, T. and Marks, R.M.: ELAM-1-dependent cell adhesion to vascular endothelium determined by a transfected human fucosyltransferase cDNA. Cell 1990;63:475-484.
5. Nemecz, G., Hubbel, T., Jefferson, J.R., Lowe, J.B. and Schroeder, F.: Interaction of fatty acids with rat intestinal and liver fatty acid binding proteins expressed in E. coli. Arch. Biochem. Biophys. 1991;286:300-309.
6. Lowe, J.B., Kukowska-Latallo, J.F., Nair, R.P., Larsen, R.D., Marks, R.M., Macher, B.A., Kelly, R.J. and Ernst, L.K.: Molecular cloning of a human fucosyltransferase gene that determines expression of the Lewis x and VIM-2 epitopes but not ELAM-1-dependent cell adhesion. J. Biol. Chem.,In Press, 1991.
7. Lowe, J.B., Stoolman, L.M., Nair, R.P., Larsen, R.D., Berhend, T.L. and Marks, R.M.: A transfected human fucosyltransferase cDNA determines biosynthesis of oligosaccharide ligand(s) for endothelial leukocyte adhesion molecule I. Biochem. Soc. Transactions, In Press, 1991.
8. Lowe, J.B. Molecular cloning, expression, and uses of mammalian glycosyltransferases. Seminars in Cell Biology, In Press, 1991.

ARTICLES SUBMITTED OR IN PREPARATION:

1. Larsen, R.D., Ernst, L.K., Rajan, V.P. and Lowe, J.B.: Multiple transcripts generated by the human H blood group α1,2 fucosyltransferase gene.
2. Kelly, R., Ernst, L.K., Larsen, R.D. and Lowe, J.B.: The molecular basis for null alleles of the H blood group gene in a Bombay individual.
3. Hiraiwa, N. and Lowe, J.B.: Structure and expression of a murine α1,2 fucosyltransferase gene.
4. Weston, B.W., Nair, R.P. and Lowe, J.B.: Molecular cloning and expression of a human DNA restriction fragment encoding an α(1,3) fucosyltransferase homologous to the Lewis blood group α(1,3/1,4) fucosyltransferase.
5. Gersten, K. and Lowe, J.B.: Structure and expression of a murine α1,3 fucosyltransferase gene.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Lowe, J.B., Kelly, R.J., Larsen, R.D. and Ernst, L.K.: The molecular nature of a null allele of the H blood group α(1,2) fucosyltransferase gene in a Bombay (Oh) individual. Glycoconjugate J. 1990;7:24A.

2. Kelly, R.J., Ernst, L.K., Larsen, R.D. and Lowe, J.B.: Nonsense and missense mutations in the H blood group fucosyltransferase (FT) gene in Bombay and Parabombay individuals. FASEB J. 1991;4AA461.
3. Stoolman, L.M., Marks, R.M., Nair, R.P., Larsen, R.D., Bowen, B., Berhendt, T. and Lowe, J.B.: The role of fucosyltransferase in the generation of cell-surface ligands for ELAM-1 and other members of the LEC-CAM family. FASEB J. 1991;5:A1602.
4. Lowe, J.B., Weston, B.W., Kelly, R.M., Larsen, R.D., Ernst, L.K. and Nair, R.P.: Structural and functional diversity in human fucosyltransferase genes. Glycoconjugate J. 1991;8:4.2.
5. Prieto, P.A., Cummings, R.D., Lowe, J.B., Larsen, R.D. and Smith, D.F.: A CHO cell line transfected with cDNA for the human α1,2-fucosyltransferase synthesizes H antigen primarily on the poly-N-acetyl-lactosamine chains of Lamps. Glyconjugate J. 1991;8:4.6.

KENNETH D. MCCLATCHEY, M.D., D.D.S.
PROFESSOR AND ASSOCIATE CHAIRMAN
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
July 1, 1990 - June 30, 1991

I. CLINICAL ACTIVITIES

A. Surgical Pathology, consultant on all head and neck pathology cases.
B. Autopsy:
   1) Consultant on forensic odontology cases.
   2) Assistant Medical Examiner, Washtenaw County.
C. Director of Clinical Laboratories
D. Director of Clinical Microbiology Laboratory
E. Medical Director of Medical Technology Program; Eastern Michigan University.
F. Ann Arbor Veterans Administration Medical Center - monthly consultant.
G. Director, M-Labs, Department of Pathology, The University of Michigan.

II. TEACHING ACTIVITIES (Medical School/Hospitals)

A. Pathology 630/631; Course Director
   1) Five hours credit (M & W, 2-4:00 p.m.)
   2) 100 dental students, 25 medical technology and graduate students.
B. Oral Diagnosis 644; participant.
C. Pathology 600; lecturer, head and neck pathology.

III. RESEARCH ACTIVITIES

A. Consultant, Principal Investigator, Thomas E. Carey, Ph.D., Department of Otorhinolaryngology, The University of Michigan, Human Squamous Cell Carcinoma: Culture and Serology, NIH R01-CA28564-06, $139,388/year, $815,326/project period, 1985-90.
B. Consultant, Serologic Studies of Squamous Cell Carcinoma of the Head and Neck. Principal Investigator: Thomas E. Carey, Ph.D., Department of Otorhinolaryngology, The University of Michigan. NCI CA-49708-01, 6/1/89-3/31/92.
C. Consultant, Impact of Follow-Up on Control of High Blood Pressure and Cholesterol. Principal Investigator: Andrea Foote, Ph.D., Institute of Labor and Industrial Relations, The University of Michigan, 1988-present.
D. Veterans Administration Co-operative Studies Program, Executive Committee. G.T. Wolf, T.F. Beals, A.A. Forastiere, T. Carey, K.D. McClatchey, A. Flint, and J.L. Hudson: A New Strategy to Preserve the Voice Box in Advanced Laryngeal Cancer. Protocol 582-C, Clinical Research Center, The University of Michigan, 1985-present.

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL

A. Medical Service Plan Executive Committee, Department of Pathology, 1979-present.

MEDICAL SCHOOL/HOSPITAL

A. Ambulatory Care Committee, The University of Michigan Hospitals, 1980-present.
B. Advisor, Medical and Biological Illustration Program, The University of Michigan Medical School, 1986-present.
C. Infection Control Committee, The University of Michigan Hospitals, 1978-present.
D. Chairman, Laboratories Committee of the Medical Staff, The University of Michigan Hospitals, 1987-present.
E. Chairman, Quality Assurance Committee, The University of Michigan Hospitals, 1989-present.
F. Member, Claims Control Committee, The University of Michigan Hospitals, 1990-present.
G. Member, Patient Care Advisory Committee, The University of Michigan Hospitals, 1989-present.
H. Member, Transplant Program Task Force, The University of Michigan Hospitals, 1990-present.
I. Chairman, Department of Dermatology External Review Committee, The University of Michigan Hospitals, 1990-1991.

REGIONAL AND NATIONAL

A. College of American Pathologists, Fellow, 1975-present.
    1) Board of Governors, 1986-present.
    2) Liaison, Standards Committee, 1986-present.
    3) Chairman, Commission on Anatomic Pathology, 1986-present.
    4) Council on Government Relations, 1987-present.
B. National Committee for Clinical Laboratory Standards, Corresponding Membership, 1987-present.
    1) Council of the National Reference System for the Clinical Laboratory, 1987-present.
    2) Subcommittee on Cost Accounting, member, 1986-90.
    3) Chairman, Area Committee on General Laboratory Practice, 1986-90.
    4) International Relations Committee, member, 1988-present.
    5) Subcommittee on Standardization of the PAP Technique, 1988-present.
C. American Society of Clinical Pathologists, 1975-present.
    1) ASCP Advisory Council, 1984-present.
    2) ASCP Advisory Council, State Councilor, 1987-present.
D. Michigan Society of Pathologists, 1982-present.
    1) Editor, Newsletter, 1988-present.
E. Technical Advisory Committee, State of Michigan Department of Health, Bureau of Laboratory and Epidemiological Services, 1987-present.
F. American Society for Testing Materials (ASTM)
    1) Committee F31 on Health Care Services, member, 1988-present.
G. Member, National Fetal-Infant Mortality Review Program Steering Committee, 1990-present.

INTERNATIONAL

A. Secretariat, Commission on World Standards of World Association of Societies of Pathology, 1987-present.

V. OTHER RELEVANT ACTIVITIES

INVITED LECTURES/SEMINARS

1. Moderator, Scientific Session: Development and Application of Immuno Diagnostic Markers. Third International head and Neck Oncology Research Conference, Las Vegas, NV, September 26, 1990.
2. Visiting Professor, Emory University School of Medicine, Atlanta, GA. presentations include: 1) Paranasal Sinus, Salivary Gland, and Alveolar Bone Disease, 2) Laboratory Medicine in the '90's: Management Issues. October 8 & 9, 1990.
3. Moderator and lecturer of Residents' Seminar: Reimbursement in the Clinical Laboratories. CAP/ASCP Fall Meeting, Dallas, TX, October 20, 1990.
4. The Practice of Pathology in the '90's. Canadian-American Academy of Pathology/A.J. French Society Meeting, Chicago, IL, March 19, 1991.
5. The Joint Commission on Accreditation of Hospitals' Quality Assurance Process, With Discussion of the Entity "Total Quality". XVI World Congress of Anatomic and Clinical Pathology, Vancouver, British Columbia, June 24, 1991.
6. Future Goals for International Standardization (Commission on World Standards). XVI World Congress of Anatomic and Clinical Pathology, Vancouver, British Columbia, June 26, 1991.

VI. PUBLICATIONS

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Grenman, S.E., Van Dyke, D.L., Worsham, M.J., England, B., McClatchey, K.D., Hopkins, M., Babu, V.R., Grenman, R., and Carey, T.E.: Phenotypic Characterization, Karyotype Analysis and In Vitro Tamoxifen Sensitivity of New ER-Negative Vulvar Carcinoma Cell Lines, UM-SCV-1A and UM-SCV-1B. Int J Cancer, 45:920-927, 1990.
2. Grenman, S.E., Worsham, M.J., Van Dyke, D.L., England, B., McClatchey, K.D., Babu, V.R., Roberts, J.A., Maenpaa, J., and Carey, T.E.: Establishment and Characterization of UM-EC-2, a Tamoxifen-Sensitive, Estrogen Receptor-Negative Human Endometrial Carcinoma Cell Line. Gynecologic Oncology, 37:188-199, 1990.
3. Burkey, B.B., Hoffman, H.T., Baker, S.R., Thornton, A.F., McClatchey, K.D.: Chondrosarcoma of the Head and Neck. Laryngoscope, 100:1301-1305, 1990.
4. Zappia, J.J., Sullivan, M.J., and McClatchey, K.D.: Unilateral Multicentric Warthin's Tumors. J Otolaryngol, 20:93-96, 1991.
5. Wells, M.D., Hoffman, H.T., and McClatchey, K.D.: An Uncommon Case of Parotid Sialolithiasis. Ann Dent, 50:23-24, 1991.
6. Dept. of Veterans Affairs Laryngeal Cancer Study Group, Authors: Randomized Trial of Induction Chemotherapy for Larynx Preservation in Patients With Advanced Laryngeal Cancer. N Engl J Med, 324:1685-1690, 1991.
7. Zappia, J.J., Bradford, C.R., Winter, P.H., McClatchey, K.D.: Olfactory Neuroblastoma Associated With Kallman's Syndrome. J Otolaryngol, 1991 (accepted).

8. Grenman, R., Carey, T.E., McClatchey, K.D., Wagner, J.G., Pekkola-Heino, K., Schwartz, D.R., Wolf, G.T., Lacivita, L.P., Ho, L., Baker, S.R., Krause, C.J., and Lichter, A.S.: In Vitro Radiation Resistance Among Cell Lines Established From Patients With Squamous Cell Carcinoma of the Head and Neck. Cancer, March, 1991 (accepted).
9. Zappia, J.J., McClatchey, K.D.: Mucoepidermoid Carcinoma Associated With Acute Lymphoblastic Leukemia. J Ped Otorhinolaryngol, April, 1991 (accepted).
10. Zappia, J.J., Wolf, G.T., McClatchey, K.D.: Signet Ring Cell Adenocarcinoma Metastatic to the Maxillary Sinus. Oral Surg Oral Med Oral Pathol, June, 1991 (accepted).

ARTICLES SUBMITTED FOR PUBLICATION

1. Carroll, W.R., Niparko, J.K., Zappia, J.J., McClatchey, K.D.: Primary Adenocarcinoma of the Temporal Bone: A Case With Forty Year Follow Up. Archives of Otolaryngology-Head and Neck Surgery, July, 1990.
2. Carroll, W.R., Zappia, J.J., McClatchey, K.D.: Branchiogenic Carcinoma. Laryngoscope, November, 1990.
3. Truelson, J.M., Fisher, S.G., Wolf, G.T., Beals, T.E., McClatchey, M.D.: DNA Content and Histologic Growth Pattern Correlate With Prognosis in Patients With Advanced Squamous Cell Carcinoma of the Larynx. Cancer, January, 1991.

BOOKS AND CHAPTERS IN BOOKS

1. McClatchey, K.D. and McMahon Jr., L.F.: Laboratory Medicine, in Textbook of Internal Medicine, Kelley, Editor (2nd Edition). J. B. Lippincott, Philadelphia, Pennsylvania. Revised, 1990.

BOOKS OR JOURNALS EDITED

1. Clinical Laboratory Medicine, Williams & Wilkins (in preparation), 1989-present (publication in Spring, 1992).

PAMPHLETS

1. McClatchey, K.D., Dawson, J.B., Bernacki Jr., E.G., Kurtycz, D., Lukeman, J.M., Noller, K.L., Perna, V.P., Plott, A.E., Plowden, K., Richart, R.: Papanicolau Technique, NCCLS Proposed Guideline, NCCLS Publication GP15, Villanova, Pennsylvania, 1989-present.
2. Travers, E.M., Delahunty, D.C., Flanagan, J., McClatchey, K.D., Meyer, D., Rudar, J.M.: Cost Accounting in the Clinical Laboratory; Proposed Guidelines, Vol. 10, No. 13 (NCCLS Publication GP11-P). National Committee for Clinical Laboratory Standards, Villanova, Pennsylvania, 1990.

PAUL E. MCKEEVER, M.D., PH.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Examination of autopsy neuropathologic material - four months.
B. Daily surgical neuropathology and electron microscopic neuropathology - four months.
C. Consultations on surgical neuropathology from other hospitals - 12 months.
D. Ceroid Service, buffy coat division - 12 months.
E. Nerve and muscle biopsy services - four months.
F. Weekly Brain Tumor Board Review of Neurosurgery, Neuroradiology, Neuropathology and clinical-pathologic correlation - four months.
G. Diagnostic neuropathology consultant, Veterans Administration Hospital.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Neural and Behavioral Sciences 600, Neuropathology for Second Year Medical Students.
B. Neuropathology 858, Intensive laboratory-lecture course for beginning House Officers in Pathology and in several clinical services, Graduate Students and Faculty - 16 hours of instruction.
C. House Officers:
   1. Review of neuropathological postmortem material - four months.
   2. Review all neurosurgically removed material in this hospital in CME-approved biweekly conference - four months.
   3. Shared consultations in conference.
   4. Invited presentations of neuropathologic observations at joint Pathology-Neurology-Neurosurgery and clinical conferences.
   5. One month elective in Neuropathology.
   6. Pathology Resident's monthly Neuropathology Conference - four months.
   7. Weekly Neuromuscular Conference - four months.
   8. Individual daily instruction of Pathology House Officers over microscope.
D. Medical Students:
   Neuropathology electives - four students.
E. Teach laboratory techniques and writing skills to Neurohistologists and Research Staff.

REGIONAL AND NATIONAL:

A. 29th Annual AFIP Neuropathology Review, Armed Forces Institutes of Pathology, Washington, D.C., "New Methods of Brain Tumor Analysis", 1991.
B. Clinical Neuro-Oncology Course, University of Michigan Towsley Center, "Neuropathology and Labeling Index of Gliomas", 1991.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. National Institutes of Health Grant NIH CA-47558, "Antigenic Instabilities and Clonal Heterogeneity in Human Gliomas", Principal Investigator. Changes in malignancy and resistance to treatment of human gliomas, the most common and devastating group of brain tumors, are thought to be related in part to antigenic instabilities of these cells. Antigenic instabilities will be followed upon explantation of human glioma cells *in vitro* and correlated with studies designed to determine the mechanism of these instabilities. The extent of changes in antigens will be studied. Antigenic changes will be correlated with changes in cellular DNA over time intervals and correlated with changes in clones of cells from the gliomas of individual patients. 5/1/88 - 4/30/93.

B. National Institutes of Health Program Project NIH CA-42761,"Antimetabolite Selectivity: Regional Treatment and Modulation", Principal Investigator of Pathology Core Grant. 8/1/88 - 7/31/91.

C. National Institute of Health Program Project NS-15655, "PET Study of Biochemistry and Metabolism of the CNS" (Program Title). "Glioma Imaging with Benzodiazepine Analogs" (Section Title), Co-investigator. 12/1/89-11/30/94.

D. National Institutes of Health Grant NIH CA54104, "PET, Growth Kinetics and Neuropathology of Brain Tumors", Co-investigator. 5/1/91-4/30/95.

PROJECTS UNDER STUDY:

A. Growth, spread and antigenicity of ENU-induced gliomas in rats, with Constance D'Amato and Terry Hood. Submitted to Neurooncology.

B. Quantitative analysis of DNA in fresh and cultured cells of brain tumors, with Drs. William Ensminger, Parvin Shakui, William Chandler, and James Varani.

C. Extracellular matrix products and plasminogen activators of gliomas with Drs. James Varani, Robert Sitrin, Dario Caccamo, and Suzanne Fligiel.

D. Distribution of microspheres in tumor and normal tissues, three-dimensional tumor dosimetry for hepatic ^{90}Y microsphere therapy with Drs. William Ensminger, Peter Roberson and Randall Ten Haken.

E. Magnetic resonance diffusion and cross relaxation of brain tumors with Drs. Thomas Chenevert and Brian Ross. Grant pending.

F. Characterization of a basement membrane-associated protein expressed on bladder cancer cells with Drs. Monica Liebert and Barton Grossman. Submitted to International Journal of Cancer.

G. Clinical-pathologic correlations of intracystic hemorrhage in cervical ependymoma with Drs. Thomas Sweasy and William Chandler.

H. Characterization of Rosai-Dorfman disease in brain with Drs. Michael Boland and Karin Muraszko.

I. Prognostic potential of nuclear organizers in myxopapillary ependymoma with Dr. Donald Ross.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chief, Section of Neuropathology.

B. Member, Photography Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Organization and scheduling of Pathology, Neurology, Neuroradiology and Neurosurgery House Officer Neuropathology teaching conferences, individual instruction and consultation review.
B. Organization of call logistics, specimen handling, and schedules for coverage of diagnostic and postmortem neuropathology by staff.
C. Supervision of Neurohistologists and Neuropathology Laboratories, and quality control of histologic preparations.
D. Interaction with Chiefs and staff of other clinical services, particularly Neurosurgery, Neurology, Nuclear Medicine and Neuroradiology.
E. Quality control of ultrastructural and immunodiagnostic neuropathology.

REGIONAL AND NATIONAL:

A. Editorial Board, Critical Reviews in Neurobiology.
B. M-Lab Neuropathology Services.
C. Reviewer of NASA Program Project Grant application.
D. International Editorial Board, Cellular and Molecular Biology.
E. Primary Review Pathologist, Children's Cancer Study Group CCG 9891 nation wide study of childhood low grade gliomas.
F. Reviewer, American Journal of Surgical Pathology.
G. Reviewer, Archives of Pathology & Laboratory Medicine.
H. Reviewer, American Journal of Pathology.
I. Reviewer, Journal of Neuro-Oncology.
J. Reviewer, Neurosurgery.
K. Reviewer, Laboratory Investigation.
L. Reviewer, Journal of Histochemistry and Cytochemistry.

V. OTHER RELEVANT ACTIVITIES:

A. Faculty of Graduate Program of Department of Pathology.
B. Member of the University of Michigan Cancer Center.
C. Pathology Committee, Children's Cancer Study Group, Columbus, Ohio.
D. Member, International Academy of Pathology, 1972-
E. Member, Alpha Omega Alpha, Eta Chapter, 1972-
F. Member, American Association of Neuropathologists, 1978-
G. Member, New York Academy of Science, 1983-
H. Member, Society of Neuroscience, 1983-
I. Member, American Association of Pathologists, 1984-
J. Member, Children's Cancer Study Group, 1985-
K. Member, Histochemical Society, 1989-
L. Member, Constitution Committee, American Association of Neuropathologists, 1990-

INVITED LECTURES AND SEMINARS

1. "Phenotypic Alterations of Gliomas", Michigan State University, East Lansing, Michigan, 1990.
2. "Clinical Relevance of Changes in Glioma Antigens", Edward W. Sparrow Hospital, Lansing, Michigan, 1990.
3. "Phenotypic Alterations in Glioma Antigen Expression", Michigan Neuropathology Day, Henry Ford Hospital, 1990.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. McKeever, P.E., Feldenzer, J.A., McCoy, J.P., D'Amato, C.J., Laug, M., Chandler, W.F. and Varani, J.: Nuclear parameters as prognostic indicators in glioblastoma patients. J. Neuropathol. Exp. Neurol. 1990;49:71-78.
2. Silverstein, A.M., Quint, D.J. and McKeever, P.E.: Intradural paraganglioma of the thoracic spine. Amer. J. Neuroradiol. 1990;11:614-616.
3. Liebert, M., Wahl, R.L., Lawless, G., McKeever, P.E., Taren, J.A. and Beierwaltes, W.H.: Direct stereotactic intracerebral injection of monoclonal antibodies and their fragments: A potential approach to brain tumor radioimmunotherapy. Amer. J. Physiologic Imaging 1990;5:55-59.
4. Sackellares, J.C., Abou-Khalil, B.W., Siegel, G.J., Hood, T.W., Gilman, S., McKeever, P.E., Hichwa, R.D. and Hutchins, G.D.: Differences between lateral and mesial temporal metabolism interictally in epilepsy of mesial temporal origin. Neurology 1990;40:1420-1426.
5. Liebert, M., Wedemeyer, G., Chang, J.H.C., Stein, J.A., McKeever, P.E., Carey, T.E., Flint, A., Steplewski, Z., Buchsbaum, D.J., Wahl, R.L. and Grossman, H.B.: Comparison of antigen expression on normal urothelial cells in tissue section and tissue culture. J. Urol. 1990;144:1288-1292.
6. Sitrin, R.G., Gyetko, M.R., Kole, K.L, McKeever, P.E. and Varani, J.: Expression of heterogeneous profiles of plasminogen activators and plasminogen activator inhibitors by human glioma lines. Cancer Res. 1990;50:4957-4961.
7. Mukhopadhyay, S.K., McKeever, P.E., Greenberg, H.S., Junck, L., Chandler, W.F. and Ensminger, W.: Random sampling by glitter drop method. Life Sci. 1990;46:507-512.
8. Davenport, R.D., O'Donnell, L.J., Schnitzer, B. and McKeever, P.E.: Non-Hodgkin's lymphoma of the brain following Hodgkin's disease: An immunohistochemical study. Cancer 1991;67:440-443.
9. McKeever, P.E., Wahl, R.L., Shakui, P., Jackson, G.A., Letica, L.H., Liebert, M., Taren, J.A., Beierwaltes, W.H. and Hoff, J.T.: Products of cells from gliomas: VIII. Multiple-well immunoperoxidase assay of immunoreactivity of primary hybridoma supernatants with human glioma and brain tissue and cultured glioma cells. J. Histochem. Cytochem. 1990;38:815-822.
10. McDonald, J.W., Garofalo, E.A., Hood, T., Sackellares, J.C., Gilman, S., McKeever, P.E., Troncoso, J.C. and Johnston, M.V.: Altered excitatory and inhibitory amino acid receptor binding in hippocampus of patients with temporal lobe epilepsy. Ann. Neurol., In Press.
11. Lawrence, T.S., Davis, M.A., McKeever, P.E., Maybaum, J., Stetson, P.L., Normolle, D.P. and Ensminger, W.D.: Fluorodeoxyuridine-mediated modulation of iododeoxyuridine incorporation and radiosensitization in human colon cancer cells in vitro and in vivo. Cancer Res., In Press.
12. Pillai, K.M., McKeever, P.E., Knutsen, C.A., Terrio, P.A., Prieskorn, D.M. and Ensminger, W.D.: Microscopic analysis of arterial microsphere distribution in rabbit liver and hepatic VX2 tumor. Selective Cancer Therapeutics, In Press.

BOOKS AND CHAPTERS IN BOOKS:

1. Greenberg, H.S., Chandler, W.F., Ensminger, W.D., Junck, L., Page, M.A., Thornton, A., Sandler, H., Gebarski, S.S., McKeever, P.E., Papadopoulos, S., Stetson, P.L. and Tankanow, R.: Radiosensitization with carotid arterial infusion of bromodeoxyuridine (BUdR) ±5 fluorouracil biomodulation with external beam radiation for gliomas. European Rev. Biomed. Technology. Cardiostim 1990. Sepsi Publish., Paris, 1990, vol. 12.
2. McKeever, P.E., Davenport, R.D. and Shakui, P.: Patterns of antigenic expression in cultured glioma cells in, Nelson, J.S. (ed.), Critical Reviews in Neurobiology, CRC Press, Boca Raton, Florida, 1991, Vol. 6, pp. 119-147.

3. Greenberg, H.S., Chandler, W.F., Ensminger, W.D., Junck, L., Thornton, A., Sandler, H., Page, M.A., McKeever, P., Gebarski, S., Liang, B. and Tankanow, R.: Radiosensitization with carotid arterial infusion of bromodeoxyuridine (BUdR) ± 5 fluorouracil (5FU) biomodulation with focal external beam radiation (FEBT) for malignant gliomas. Neuro-Oncology, Kluwer Acad. Publish., Netherlands, 1991, pp. 217-219.
4. McKeever, P.E., Sima, A.A.F. and Blaivas, M.: Neoplasms of the sellar region, in, Lloyd, R.V. (ed.), Surgical Pathology of the Pituitary Gland. Major Problems in Pathology series. W.B. Saunders, In Press.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. McKeever, P.E., Genik, S.J., Rowe, J.M., Stetson, P.L., Prieskorn, D.M., Terrio, P.A., Knutsen, C.A., Knol, J.A. and Ensminger, W.D.: Quantitative immunohistochemistry (QIHC) of cellular and regional bromodeoxyuridine (BUdR) incorporations. J. Histochem. Cytochem. 1990;38:1028.
2. Lawrence, T.S., Sondak, V.K., McKeever, P.E., Stetson, P.L. and Ensminger, W.D.: The use of radiation therapy with IdUrd in the treatment of soft tissue sarcomas. Ninth annual meeting of the European Society for Therapeutic Radiology and Oncology, 1990, Montecatini, Italy.
3. Roberson, P.L., Ten Haken, R.K., Pillai, K.M., McKeever, P.E. and Ensminger, W.D.: Three-dimensional dose computation for hepatic microsphere therapy. J. Nucl. Med. 1990;31:28.
4. Buchsbaum, D.J., Greenberg, H., McKeever, P., Terry, V., Guilbault, D., Glatfelter, A. and Steplewski, Z.: Binding and localization of ^{125}I-labeled 425 antibody and F(ab')$_2$ fragments of human glioma. American Academy of Neurology Annual Meeting, 1990, Miami Beach, Florida.
5. Liebert, M., Wedemeyer, G., Stein, J.A., McKeever, P.E., Carey, T.E., Flint, A., Steplewski, Z., Buchsbaum, D.J., Wahl, R.L. and Grossman, H.B.: Antigen expression on normal urothelial cells cultured using a simplified technique. American Urological Association, Annual Meeting, 1990, New Orleans.
6. Mountz, J.M., Mountz, J.D., Sherman, P.S., McKeever, P.E. and Rowe, J.M.: ^{99m}Technetium autoradiographic analysis of brain lesions in T-cell receptor transgenic autoimmune mice. Soc. Neurosci. Abstr. 1990;16:1139.
7. McKeever, P.E. and Ross, D.A.: Review of book titled, "Stereotactic Brain Biopsy", by Parakrama T.Chandrasoma and Michael L.J. Apuzzo. Amer. J. Surg. Path. 1990;14:990.
8. Rowe, J.M., Hemperly, J.J., Sima, A.A.F., Gillard, M., Ross, D.A., McKeever, P.E.: Localization of neural cell adhesion molecules in human brain tumors. J. Neuropathol. Exp. Neurol. 1991;50:366.
9. McKeever, P.E., McLaughlin, P.W., Lawrence, T.S., Rowe, J.M., Stetson, P.L., Mukhopadhyay, S.K. and Ensminger, W.D.: Partial Growth arrest of glial fibrillary acidic protein (GFAP) positive cells in a solid human tumor. J. Neuropathol. Exp. Neurol. 1991;50:369.
10. Shakui, P., McKeever, P.E., Papadopoulos, S.M.: Separation of heterogeneous phenotypes of cells from human glioma tissue. Fed. Am. Soc. Exp. Biol. J. 1991;5:A1261.
11. McKeever, P.E., Rowe, J.M., McLaughlin, P.W., Genik, S.J. and Ensminger, W.D.: Double immunoperoxidase staining for bromodeoxyuridine and iododeoxyuridine. Soc. Neurosci. Abstracts 1991, In Press.
12. McKeever, P.E.: Computerized image analysis of distinct cell marker parameters of glial fibrillary acidic protein: Intensity of immunofluorescence and topography in human glioma cultures. First World Congress of Cellular and Molecular Biology, Paris, Sept. 1-7, 1991.

A. REES MIDGLEY, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Lectures:

1. Taught portion of Mammalian Reproductive Endocrinology, Physiology 581 (six hours lecture; ten contact hours).
2. April 17, 1991, Bioengineering 890 lecture: Real time monitoring of cellular activity; Aiming towards integrative biology.
3. October 2, 1990, Bioengineering 495 lecture: Monitoring the activity of living cells in real time.

B. Primary Supervsion of Two Postdoctoral Fellows:

1. Beverly Strassman, Postdoctoral fellow working on NIH F32 fellowship.
2. Daniel McConnell, Postdoctoral fellow working on chemiluminescence-based assays (applications for support pending to NIH and Lindburgh Fund).

C. Primary Supervision of five graduate students:

1. Mahmoud Ghazzi, Bioengineering (recipient of an NIH Physician Scientist Award; presented at the Society for the Study of Reproduction) - defense held 7/3/91.
2. Craig Halberstadt, Bioengineering - defense scheduled for 7/25/91.
3. Rhonda Brand, Bioengineering (presented at the Society for the Study of Reproduction) - defense probably in August.
4. Jane Wiesen, Cellular and Molecular Biology (presented at the Endocrine Society and to present at the Society for the Study of Reproduction) - defense probably in December.
5. Hal Cantor, Bioengineering (invited address before the Consortium for the Scientific and Industrial Use of the Macintosh; presented at the Society for the Study of Reproduction; presented at the Third International Meeting on Chemical Sensors.) - defense probably in December.

D. Service on Other Dissertation Committees:

1. Gyun Minn Lee, Ph.D. defense on 8/24/90, Chemical Engineering.
2. Soong Kwak, Ph.D. defence on 6/13/91 (Mental Health Research Institute.
3. Joanne Savinell, Ph.D. defense on 6/22/91, Chemical Engineering.

4. Kevin Fetteri, current, Biochemistry.
5. Dan Burdick, current, Music.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Gonadotrophin Control of the Ovary", NIH RO1 HD18018 (10%), $85,380 TDC current year. 3/1/88-11/30/91. This is my major source of research support. A competitive renewal was submitted on 6/29/91.
B. Principal Investigator, "Center for the Study of Reproduction", NIH P30 HD18258 (10%) (5% as Director of Administrative Core; 5% as Director, Standards and Reagents Core), $337,266 TDC year #3, 3/1/89-2/28/94 None of this is for my research support.
C. Mentor, "Training Program in Reproductive Endocrinology", NIH T32 HD-07048(5% maximum effort). None of my trainees are currently supported on this grant.
D. Co-investigator, "Site-Directed Bioreagent Immobilization for Development of Microbiosensor Assays", NSF ECS-8915497 (6%) (Principal Investigator Richard Brown, Departent of Electrical Engineering and Computer Science), 9/1/89-8/31/92, $181,811 2nd year total costs Role: My annual support from this grant, $13,199, is for one graduate research assistant, Hal Cantor.
E. Mentor, "The Reproductive Endocrinology of the Dogon," NIH F32 HD07480 (5%), Individual postdoctoral fellowship for Beverly I. Strassmann, 01/01/91-01/31/93. Cost shared.

PROPOSAL WRITING:

A. DOE Equipment proposal, October 1990: not selected for submission.
B. Michigan Memorial Phoenix Project: Development of a non-radiometric chemiluminescent energy transfer immunoassay: not funded.
C. OVPR Small Instrumentation Award for Ultralow Temperatre Freezer, funded.
D. NIHall Instrumentation Program: for Luminoskan microplate luminometer: funded ($27,700 from NIH; balance from RSP).
E. Equipment proposal to BRSG (Principal Investigator: Fred Karsch): Research in Reproductive Biology for Microtome and Microscope; Assisted with Preparation: microtome funded ($10,000).
F. NIH P30 Administrative supplemental request for P30 S&R Core: Denied for insufficient funds.
G. NIH K11 Physician Scientist Award Non-competitive renewal (Principal Investigator, Mahmoud Ghazzi): assisted: funded.
H. NIH P30 Center, Non-competitive renewal: funded.
I. NIH T32 training grant non-competitive renewal (Principal Investigator: Doug Foster): assisted with preparation: funded.
J. NASA: Assisted ERIM with development of a section of an application for studying the physiology of animals in space. Pending.
K. YSI, Yellow springs, Ohio: Equipment loan: Glucose-lactate analyzer for evaluating performance of bioreactors.
L.. NIH F32 fellowship application, Beverly Strassmann: The reproductive endocrinology of the Dogon.: funded.
M. NIH F32 fellowship application, Dan McConnell: Development of novel luminescence-based immunoassays: Submitted 5/8/91; Pending.
N. NIH P30 Center Competitive supplement for S&R Core (director of core): Submitted 5/29/91, Pending.

O. U54 Cooperative Consortium Infertility Center grant. Associate Director of Center; Principal Investigator of project: Gonadotrope-response to ovulation-controlling signals; Director of Assay Development Core. Submitted 6/1/91, Pending.
P. Charles A. Lindbergh Fund, Inc.: Reduction in use of radioisotopes, development of novel luminescence-based immunoassays (Principal Investigator: Dan McConnell): Submitted 6/17/92, Pending.
Q. NIH RO1 Competitive renewal, gonadotropin-control of the ovary: Submitted 6/29/91, Pending.

SCIENTIFIC COLLABORATIONS:

A. Biostatistics: Morton Brown and Dan Normolle: development and implementation of a new robust method for analysis of immunoassays involving maximum likelihood estimators.
B. Chemical Engineering: Bernhard Palsson: joint mentorship of Craig Halberstadt; mass culture of hybridoma cells.
Rane Curl: with Craig Halberstadt, development of a mathematical model describing a transtubular bioreactor.
C. Chemistry: Mark Meyerhoff: (with Richard Brown) NSF-funded project aimed at developing multisite, antibody-based solid state microelectrodes.
D. Electrical Engineering: Ken Wise: joint mentorship of Mahmoud Ghazzi; neuroelectric recording.
Richard Brown: (with Mark Meyerhoff) NSF-funded project aimed at developing multisite, antibody-based solid state microelectrodes.
E. Internal Medicine: David Humes: study of the ability of kidney stem cells to form tubules and, perhaps, to interact with endothelial cells to form glomeruli and an artificial kidney in a three dimensional transtubular bioreactor (aim of developing artificial organs).
F. Nursing: Nancy Reame: joint development of the U54 infertility center grant.
G. Pathology: Jim Varani: study of the ability of endothelial cells to form capillaries in a three dimensional transtubular bioreactor (aim of developing artificial organs).
H. Pediatrics: Vasantha Padmanabhan: joint development of a project to include in the U54 center application and a separate RO1 grant - concerning the responsiveness of pituitary cells to GnRH.
I. Carnegie Institute of Washington, Embryology and WSU, Anatomy: Bent Boving (retired): co-investigator in artificial organ development and perifusion programs.
J. ERIM: David Conrad: potential of using microsensors to monitor the physiology of animals in space.
K. Michigan State University, Animal Science: James Ireland: development of a solid state, two site chemiluminescence-based immunoassay for inhibin.
L. Wayne State University, Obstetrics and Gynecology: Ruth Moore: examination of the response of sheep pituitary cells in perifusion to GnRH.
M. Wayne State University, Chemistry: Paul Schaap: with Dan McConnell, development of new approaches for chemiluminescent immunoassays.

INTELLECTUAL PROPERTIES ACTIVITY:

A. Submitted Response to Final Office Action for Bioreactor System (UM File #136).
B. Submitted patent application, Bioreactor System with alginate matrix (UM File #548)

PROJECTS UNDER STUDY:

A. Development of a computer-controlled perifusion system for on-line analysis of cellular response to pulsatile and other controlled signalling.

B. Analysis of dynamic control of pituitary function by GnRH: the role of intercellular signalling.
C. Localization and regulation of mRNAs in rat granulosa cells.
D. Application of principles of cellular bioengineering to the growth and function of mammalian cells and the development of artificial organs.
E. Development of novel biosensors and immunoassays.
F. Examination of the relationships between changes in hormones, behavior and peer reactions during pre-adolescent development of children.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Director, Center for the Study of Reproduction.
B. Director, Standards and Reagents Core Facility.
C. Member, Selection Committee

UNIVERSITY:

A. Director, Reproductive Science Program.
B. Member, committee to Review IOG, CHGD and RSP.
C. Proposed the establishment of a Women's Health Initiative.
D. Initiated the establishment of a Michigan Reproductive Medicine Consortium (This led to submission of the U54 Consortium Center grant).
E. Interviewing candidates for Internal Medicine, Ob-Gyn, Perinatal Medicine, IOG.

REGIONAL AND NATIONAL:

A. Member, NIDDK Endocrinology Research Program Advisory Committee, 1986-.
B. Member, NIDDK Hormone Distribution Program Subcommittee, 1986-.
C. Member, NIH Reviewers Reserve, 1989-.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Member, Site visit team, P30 Center grant application, Harvard University/MGH, Boston, Massachusetts, July 23-25, 1990.
2. Center Directors meeting, Nashville, Tennessee.
3. 23rd Annual meeting of the Society for the Study of Reproduction.
4. Third International Meeting on Chemical Sensors, September 23-26, 1990.
5. Member, Site visit team, P30 Center grant application, University of Washington, Seattle, Washington, September 26-28, 1990.
6. Member, Site visit team, P01 Program Project grant application, Cornell University, Ithaca, New York, October 21-23, 1990.
7. Member, Site visit team, P30 Center grant application, University of Pittsburgh, Pittsburgh, Pennsylvania, November 8-10, 1990.
8. Presentation: ITI, Entrepreneurialship Forum, January 14, 1991.
9. Meeting of the NIDDK Endocrinology Research Program Advisory Committee and the Hormone Distribution Program subcommittee, Bethesda, Maryland, March 18, 1991..
10. Presentation: MTTC Entrepreneurialship Forum, May 15, 1991.
11. NICHD Center Directors meeting, San Antonio, Texas, May 19, 1991.

12. Attend Recent Advances in Reproductive Sciences workshop, San Antonio, Texas, May 20-21, 1991.

RELEVANT ACTIVITIES:

1. Developing an immunoassay analysis system to meet the needs of the Department of Pathology Ligand Assay Laboratory (Lig Anal).
2. Distributed to other scientists in the U.S. materials developed for presentation before Representative Carl Pursell regarding the funding crisis being faced by individual investigators and the unique problems of the NICHD (meeting held on April 11, 1990).
3. Implementing ELISA and chemiluminescence-based, solid state, two site immunoassays in Standards and Reagents Core as a partial replacement for radioimmunoassays (and thereby reduction in usage of radioactive isotopes).
4. Initiated collaboration with Lumigen, Inc., of Detroit, Michigan, the world leader in development of chemiluminescent substrates for immunoassays and molecular probes.
5. Assisted the National Hormone and Pituitary Program by evaluating collected antisera to cyclic AMP and preparing a pool for them to distribute for radioimmunoassay of cyclic AMP.
6. Met with Board of Directors or Scientific Advisory Board of BioQuant, Inc. on August 10, October 8, January 11, March 29, April 18.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Miyauchi, F. and Midgley, A.R., Jr.: Morphologically and functionally distinct subpopulations of steroidogenic cells in corpora lutea during pregnancy in rats. Endocrinol. Japan. 1990;37:649-663.
2. Cha, G.S., Liu, D., Meyerhoff, M.E., Cantor, H.C., Midgley, A.R., Goldberg, H.D. and Brown, R.B.: Electrochemical performance, biocompatibility, and adhesion of new polymer matrices for solid-state ion sensors. Analytical Chemistry, In Press. (September 1991).
3. Cantor, H.C. and Midgley, A.R.: Development of an active biosensor for real-time monitoring of neuroendocrine and gonadal humoral activity. Sensors and Actuators B. Chemical, In Press.

ARTICLES SUBMITTED:

1. Moenter, S.M., Brand, R.M., Midgley, A.R. and Karsch, F.J.: Dynamics of GnRH release during a pulse. Submitted to Endocrinology.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Cha, G.S., Brown, D.V., Meyerhoff, M.D., Cantor, H.C., Midgley, A.R., Goldberg, H.D. and Brown, R.B.: Performance, biocompatibility and adhesion of various polymer matrices for preparation of micro-ionbiosensor arrays, invited paper, Microsensor Symposium, FACSS 17th Annual Meeting, Cleveland, Ohio, October 7-12, 1990.
2. Cantor, H.C.: Utilization of a commercially available analog-digital data acquisition system with the Macintosh computer for studying real-time changes in circulating molecules in the living rat. Invited paper. Consortium for the Scientific and Industrial use of the Macintosh. October, 1990.

3. Meyerhoff, M.E., Cha, G.S., Ma, S.C., Goldberg, H.D., Brown, R.B., Midgley, A.R. and Cantor, H.C.: New polymeric membrane materials for fabricating potentiometric ion- and bio-selective sensors. Polymeric Material Science and Engineering Proceedings, American Chemical Society, Atlanta, Volume 64, pp.292-293, April 1991.
4. Poplawski, M.E., Cantor, H.C., Midgley, A.R. and Brown, R.B.: Microfabricated amperometric biosensors. Sixth International Conference on Solid-State Sensors and Actuators (Transducers '91), San Francisco, California, June 24-28, 1991.
5. Wiesen, J.F. and Midgley, A.R., Jr.: Localization of c43 GAP junction MRNA in rat ovary by in situ hybridization. 73rd Annual Meeting, Endocrine Society, June 19-21,1991.
6. Cantor, H.C., Brand, R.M., Boving, B.G., Ghazzi, M.N. and Midgley, A.R., Jr.: Monitoring dynamic responses of perifused tissue to hormonal stimuli instantaneously in real time. 24th Annual Meeting, Society for the Study of Reproduction, July 28-31, 1991.
7. Wiesen, J.F. and Midgley, A.R., Jr.: Loss of C43 GAP junction mRNA during follicular atresia. 24th Annual Meeting, Society for the Study of Reproduction, July 28-31, 1991.
8. Ghazzi, M.N., Wise, K.D., Anderson, D.J., Newman, S.W. and Midgley, A.R., Jr.: Use of silicon-based multichannel microelectrodes to characterize single-unit activity of neurons in the rat suprachiasmatic nucleus. Society for Neuroscience, November, 1991.

THESIS-RELATED MANUSCRIPTS NEARLY READY FOR SUBMISSION

1. Halberstadt, C.R., Lee, G.M., Palsson, B.O. and Midgley, A.R., Jr.: Hybridoma cell cultures. Ready for Biotechnology Progress.
2. Halberstadt, C.R., Lee, G.M., Palsson, B.O. and Midgley, A.R.: Enhanced antibody productivity and use of a serum-free, low-protein medium for long term hybridoma cell cultures using a transtubular bioreactor. Ready for Biotechnology and Bioengineering.
3. Halberstadt, C.R., Palsson, B.O., Midgley, A.R., Jr. and Curl, R.L.: Optimization of the transtubular bioreactor for the production of monoclonal antibodies in a serum-free, low-protein medium.
4. Brand, R.M., Canter, H.C., Ghazzi, M.N., Favreau, P.A., Boving, B.G. and Midgley, A.R., Jr.: Use of continuous, on-line pH monitoring To examine the flow dynamics of perifusion systems and cellular metabolism.
5. Brand, R.M., Williams, W.J. and Midgley, A.R., Jr.: Understanding the dynamics of perifusion systems: A method for improved interpretation of perifusion data.
6. Brand, R.M. and Midgley, A.R., Jr.: Continuous, on-line monitoring of cellular metabolism using a microperifusion system.
7. Wiesen, J.F. and Midgley, A.r., Jr.: Loss of c43 gap junction mRNA during follicular atresia.
8. Wiesen, J.F. and Midgley, A.R., Jr.: A decrease in ovarian c43 gap junction mRNA levels following the preovulatory surge of luteinizing hormone.
9. Ghazzi, M.N., Wise, K.D., Anderson, D.J. and Midgley, A.R., Jr.: Computer-assisted approach for analysis of single unit nerve cell activity extracted from multichannel, microprobe data.
10. Ghazzi, M.N., Wise, K.D., Najafi, K. and Midgley, A.R., Jr.: Performance of silicon-based multichannel microprobes in recording from deep brain structures.

RICHARD A. MILLER, PH.D., M.D.
PROFESSOR
DEPARTMENT OF PATHOLOGY
RESEARCH SCIENTIST
INSTITUTE OF GERONTOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. One session Pathology 581 (Kunkel).
      b. Eight sessions Physiology 604 (Faulkner).
      c. Pathology 620 (Miller), "Genetics and Cell Biology of Aging" scheduled for Fall, 1991.
   2. Ph.D. Thesis sponsor for Jia Shi (Pathology Department, Boston University).

B. Undergraduate students:
   a. None.

C. Postdoctoral Fellows:
   1. Duaine Jackola, Ph.D.
   2. Li Shaokang, U.S.
   3. Jacek Witkowski, Ph.D.
   4. Jagadananda Ghosh, Ph.D.
   5. Paul Turke, Ph.D.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Activation Defects in Aging T Cells", NIH AG-08904 (35%), $192,108/year ($1,292,667/five years), 8/1/90-7/31/95. MERIT Award. [Note: values given are total costs, i.e. Direct costs plus indirect costs projected at 59%.].

B. Principal Investigator, "T Cell Repopulation After Bone Marrow Transplantation", NIH CA-42148 (15%). $100,819/year, ($100,819/one year awarded to University of Michigan; continuation of grant from Bóston University), 9/30/90 - 3/31/92.

C Principal Investigator, "Aging Effects on IL-2 Secreting Helper T Cells", NIH AG-03978 (15%), $106,690/year ($106,690/one year awarded to University of Michigan; continuation of grant from Boston University), 8/10/90 - 7/31/91.

D. Training Supervisor, "Research Training Agreement: Postdoctoral Training in Aging and Growth Control", Boston University (NIH/NIA Prime) (0%), $20,304/year ($20,304/one year), 10/1/90 - 9/30/91).
E. Principal Investigator, "High Volume Scintillation Counter," University of Michigan Biomedical Research Support Grant (0%), $18,000/year ($18,000/one year).
F. Core Director, "Core Facility for Aged Rodents", NIH AG-08808 (10%), $78,278/year direct costs ($390,000/five years direct costs), 9/1/89 -8/30/94. [Component of Geriatric Research and Training Center, J. Halter, Program Director].

PENDING:

A. Principal Investigator, "Aging Effects on Il-2 Secreting Helper T Cells", NIH AG-03978 (25%), $294,294/year ($1,655,031/five years), 7/1/91-6/30/96.
B. Program Director, "Research Training in Experimental Immunopathology", NIH AI-07413, $122,966/year ($1,349,088/five years), 4/1/92-3/31/97.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Committee on Master Planning Analysis.

MEDICAL SCHOOL/HOSPITAL:

A. Institute of Gerontology: Faculty Executive Committee.
B. Geriatric Center and Institute of Gerontology: Director, Core Facility for Aged Rodents.
C. Member, Geriatric Center Research Operating Committee.

REGIONAL AND NATIONAL:

A. Board of Scientific Advisors, Buck Center for Research on Aging.
B. Research, Education and Practice Committee, Gerontological Society of America.
C. Immunobiology Study Section (ad hoc).
D. Elected Fellow, Gerontological Society of America.
E. Chair-Elect, Gordon Research Conference on "Biology of Aging".
F. Board of Scientific Advisors: American Federation for Aging Research.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Journal of Immunology.
B. Aging: Immunology and Infectious Disease.
C. Journal of Gerontology: Biological Sciences.

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, "Research Opportunities in the Biology of the Aging Immune System", National Institute on Aging Summer Workshop, Airlie, Virginia, July 23, 1990.
2. Invited Lecturer, "Activation Defects in T Lymphocytes from Aging Mice", Department of Microbiology, University of Kansas, Kansas City, October 25, 1990.
3. Invited Lecturer and Session Chair, "Activation Defects in T Lymphocytes from Aging Mice", Annual Meeting of the Gerontological Society of America, Boston, November 14-19, 1990.

4. Invited Lecturer, "Activation Defects in T Lymphocytes from Aging Mice", Division of Geriatric Medicine, Harvard University, December 7, 1990.
5. Invited Lecturer, "Activation Defects in T Lymphocytes from Aging Mice", Genentech, San Francisco, Calfornia, February 11, 1991.
6. Invited Lecturer, "Activation Defects in T Lymphocytes from Aging Mice", Department of Animal Science, University of Illinois, Springfield, Illinois, February 19, 1991.
7. Invited Lecturer, "Gerontology as Oncology: Research on Aging As The Key To The Understanding of Cancer", American Cancer Society Workshop on Cancer in the Older Person, Atlanta, Georgia, March 14-16, 1991.
8. Mini-Symposium Chair, "Memory vs. Anergy", Annual Meeting of the American Association of Immunologists, Atlanta, Georgia, April 21-15, 1991.
9. Invited Symposium Lecturer, "Activation Defects in T Lymphocytes from Aging Mice", Annual Meeting of the American Association of Immunologists, Atlanta, Georgia, April 21-25, 1991.
10. Invited Lecturer, "Immune Function in Diet Restricted Rodents", Symposium on Dietary Intervention in Aging, Volterra, Italy, April 27-30, 1991.
11. Round-Table Discussion Moderator, "Research Priorities in Aging", Gordon Conference on Biology of Aging, San Miniato, Italy, May 1-5, 1991.
12. Invited Lecturer, "Immune Function in Diet Restricted Rodents", Department of Physiology, University of Texas Health Science Center, San Antonio, Texas, May 27-28, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Meydani, S.N., Barklund, P., Liu, S., Meydani, M., Miller, R.A., Cannon, G.P., Morrow, F., Rocklin, R. and Blumberg, J.B.: Vitamin E supplementation enhances cell-mediated immunity in health elderly. Am. J. Clin. Nutrition 1990;52:557-563.
2. Patel, H. and Miller, R.A.: Analysis of protein phosphorylation patterns reveals unanticipated complexity in T lymphocyte activation pathways. J. Immunol. 1991;146:3332-3339.
3. Miller, R.A., Flurkey, K., Molloy, M., Luby, T., Ruger, J. and Stadecker, M.J.: Differential sensitivity of virgin and memory T lymphocytes to calcium ionophores suggests a buoyant density separation method and a model for memory cell unresponsiveness to Con A. J. Immunol. 1991, In Press.
4. Miller, R.A., Daley, J., Ghalie, R. and Kaizer, H.: Clonal analysis of T cell deficiencies in autotransplant recipients. Blood 1991;77:1845-1850.
5. Miller, R.A.: Short analytical review: accumulation of hyporesponsive, calcium extruding memory T cells as a key feature of age-dependent immune dysfunction. Clin. Immunol. Immunopath. 1991;58:305-371.
6. Miller, R.A.: Aging and immune function. International Review of Cytology 1991;124:187-216.
7. Miller, R.A., Flurkey, K. and Patel, H.: Signal transduction pathways in T lymphocytes from old mice. Aging. Immunology and Infectious Disease 1990;2:97-103.
8. Miller, R.A.: Gerontology as oncology: Research on aging as the key to the understanding of cancer. Cancer 1991, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Flurkey, K., Stadecker, M. and Miller, R.A.: Memory T lymphocyte hyporesponsiveness to non-cognate stimuli: a key factor in age-related immunodeficiency.
2. Patel, H. and Miller, R.A.: Age-associated changes in mitogen-induced protein phosphorylation in murine T lymphocytes.

3. Flurkey, K., Miller, R.A. and Harrison, D.E.: Cellular determinants of age-related decrements in the T cell mitogen response of B6CBAF1 mice.

BOOKS/CHAPTERS IN BOOKS:

1. Miller, R.A.: Limiting dilution assays for IL-2 and CTL precursor frequency, in, Coligan, J.E. et al. (eds.), Current Protocols in Immunology, Wiley-Interscience, New York, pp. 3.15.1-3.15.12, 1991.

RAJ S. MITRA, PH.D.
ASSISTANT RESEARCH SCIENTIST IN PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-Investigator, "Role of Adhesion Molecules in Psoriasis", National Institute of Health, Grant 1-RO1-AR40065, $416,759, direct cost, three years. (B.J. Nickoloff, Principal Investigator).
B. Co-Investigator, "Interaction of Interferon γ with Keratinocytes", National Institutes of Health, Grant AR-38957-03, $167,284, direct cost, three years, (B.J. Nickoloff, Principal Investigator).
C. Co-Investigator, "Dermal Dendrocytes and AIDS-Related Psoriasis", National Institutes of Health, Grant 1-RO1-AR-40488, $573,176, direct cost, three years, (B.J. Nickoloff, Principal Investigator).

PENDING:

A. Cytokine Network in Psoriasis; Competitive renewal of RO1-AR40065, (B.J. Nickoloff, Principal Investigator, R.S. Mitra, Co-Investigator)

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Responsible for smooth and productive daily operation of Dr. Nickoloff's laboratories.
B. Responsible for teaching theoretical as well as technical newcomers to the laboratory.

MEDICAL SCHOOL/HOSPITAL:

A. None.

REGIONAL AND NATIONAL:

A. None.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Nickoloff, B.J., Karabin, G.D., Barker, J.N.W.N., Griffiths, C.E.M., Sarma, V., Mitra, R.S., Elder, J.T., Kunkel, S.L. and Dixit, V.M.: Cellular localization of interleukin-8 and its inducer tumor necrosis factor in psoriasis. Am. J. Pathol. 1991;138:129-140.
2. Barker, J.N.W.N., Mitra, R.S., Griffiths, C.E.M., Dixit, V.M. and Nickoloff, B.J.: Keratinocytes as initiators of inflammation: A unifying explanation for diverse array of environmental stimuli to produce cutaneous inflammation. Lancet 1991;337:221.
3. Barker, J.N.W.N., Jones, M.L., Swenson, C.L., Sarma, V., Mitra, R.S., Ward, P.A., Johnson, K.J., Fantone, J.C., Dixit, V.M. and Nickoloff, B.J.: Monocyte chemotaxis and activating factor production by keratinocytes in response to γ-IFN. J. Immunol. 1991;146:1192.
4. Barker, J.N.W.N., Jones, M.L., Mitra, R.S., Fantone, J.C., Kunkel, S.L., Dixit, V.M. and Nickoloff, B.J.: Modulation of keratinocyte-derived interleukin-8 which is chemotactic for neutrophils and T lymphocytes. Am. J. Pathol. In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Mitra, R.S. and Nickoloff, B.J.: Epidermal growth factor and transforming growth factor-alpha decreases gamma interferon receptors and intercellular adhesion molecule on cultured keratinocytes. J. Cell. Physiol.
2. Nickoloff, B.J., Mitra, R.S., Barker, J.N.W.N., Karabin, G., Stoof, T. and Stoolman, L.M.: A comparative study of lymphocyte adhesion to keratinocytes, fibroblasts, and melanocytes reveal both LFA-1 (CD-18) dependent and independent pathways. J. Clin. Invest., Submitted, 1990.
3. Stoof, T.J., Mitra, R.S., Sarma, V., Dixit, V.S. and Nickoloff, B.J.: Keratinocyte activation following T lymphocyte binding.
4. Ribeiro, P.L., Mitra, R.S. and Bernstein, J.A.: Assessment of the role of DNA damage and repair in the survival of primary cultures of rat cutaneous keratinocytes exposed to Bio - (2-chloroethyl) sulfide. Toxicol. and Appld. Pharmacol. Submitted, 1991.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

BOOKS/CHAPTERS IN BOOKS:

1. Nickoloff, B.J., Varani, J. and Mitra, R.S.: Modulation of keratinocyte biology by gamma interferon: Revelance to cutaneous wound healing, in, Barbul, A. (ed.), Clinical and Experimental Approaches to Dermal and Epidermal Repair: Normal and Chronic Wounds, Alan R. Liss, Inc., New York, New York, 1991.

ABSTRACTS:

1. Barker, J., Griffiths, C.E.M., Mitra, R.S., Fisher, G. and Nickoloff, B.J.: Immunophenotypic modulation of cutaneous dendritic cell by various cytokines. Clin. Res. 1990;38:421.
2. Barker, J.N.W.N., Mitra, R.S., Griffiths, C.E.M., Dixit, V.M. and Nickoloff, B.J.: Keratinocyte production of pro-inflammatory molecules in response to known inducers of cutaneous inflammation. J. Cut. Path. 1990;17:286.
3. Barker, J.N.W.N., Griffiths, C.E.M., Mitra, R.S., Dixit, V.M. and Nickoloff, B.J.: Human epidermal keratinocytederived interleukin-8: Relevance to contact dermatitis. J. Invest. Dermatol. 1990;95:462.

4. Mitra, R.S. and Nickoloff, B.J.: Epidermal growth factor decreases gamma interferon receptors and induction of intercellular adhesion molecule-1. J. Invest. Dermatol. 1991;96,554.
5, Nickoloff, B.J., Stoof, J.J., Mitra, R.S., Griffiths, G.E.M., Aulieino, M. and Stoolman, L.M.: CD-18 (LFA-1) and CD-492 (VLA-4) mediate lymphocyte adherence to endothelial cells in rhus dermatitis. J. Invest. Dermatol. 1991;96,538.
6. Mitra, R.S., Barker, J.N.W.N., Stoof, J.J., Stoolman, L.M. and Nickoloff, B.J.: Comparison of lymphocyte adhesion to keratinocyte, fibroblast, melanocytes CD-18 (LFA-1) dependent and independent pathways. Clinical Research 1991;39.
7. Stoof, T.J., Mitra, R.S., Sarma, V.J., Dixit, V.M. and Nickoloff, B.J.: Binding by T lymphocytes triggers keratinocyte activation. 1991 Annual Meeting of the European Society for Dermatological Research, Copenhagen, June 1 - June 4, 1991.

BERNARD NAYLOR, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Cytopathology - 26 weeks.
B. Director, Cytopathology Laboratory - full time.
C. Consultation Service, Department of Pathology: Cytopathology, pulmonary pathology and gynecologic pathology - 12 months.
D. Necropsy service - on call coverage.
E. Consultant, Breast Care Center - 12 months.

II. TEACHING ACTIVITIES:

A. Pathology residents - supervision and teaching during cytopathology rotation and when covering necropsies.
B. Pathology residents - biweekly cytopathology conferences.
C. Senior medical students during pathology electives.
D. Sophomore medical students: class lectures.

III. RESEARCH ACTIVITIES:

A. Cytopathology, with particular reference to serous fluids, cytologic technique, and aspiration cytology.

PROJECTS UNDER STUDY:

A. Cross contamination in the cytologic staining circuit.
B. Cytologic manifestation of systemic lupus erythematosus.
C. The use of stained wet films in cytologic diagnosis.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director and Co-Director, Cytopathology Laboratory.
B. Chairman's Advisory Committee.
C. Advisory Committee on Appointments and Promotions.
D. Department of Pathology Medical Service Plan Executive Committee.

REGIONAL AND NATIONAL:

A. Secretary-Treasurer, American Society of Cytology.
B. North American Review Board, Acta Cytologica.

C. Editorial Board, The Cytotechnologist's Bulletin.
D. Editorial Board, Cytopathology.
E. Chairman, Editorial and Publications Committee, International Academy of Cytology.
E. Membership Committee, International Academy of Cytology.
F. Scientific Program Committee, International Academy of Cytology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Naylor, B.: Fine needle aspiration cytology of the breast: Obtaining the specimens, what they show, and is it worth it? Lecture, Symposium on Breast Diseases, University of Michigan, Grand Traverse Village, Michigan, July, 1990.
2. Naylor, B.: Fads and fashions in cytology. Papanicolaou Award Lecture, Annual Scientific Meeting of the American Society of Cytology, Washington, D.C., November, 1990.
3. Naylor, B.: Non-neoplastic entities in gynecologic cytology: A selection. Teleconference, American Society of Cytology, December, 1990.
4. Naylor, B.: A) Cytology of non-neoplastic entities, B) Cytology of effusions. Lectures & Workshops, 17th International Tutorial on Clinical Cytology, Tokyo, Japan, May, 1991.

HONORS AND AWARDS:

1. Papanicolaou Award for 1990 of the American Society of Cytology.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Naylor, B.: The pathognomonic cytologic picture of rheumatoid pleuritis. Acta Cytol. 1990;34:465-473.
2. Naylor, B.: Curschmann's spirals in pleural and peritoneal fluids. Acta Cytol. 1990;34:474-478.
3. Pennes, D.R., Naylor, B. and Rebner, M.: Fine needle aspiration biopsy of the breast: Influence of sample size on diagnostic yield. Acta Cytol. 1990;34:673-676.

BOOKS/CHAPTERS IN BOOKS:

1. Naylor, B.: Pleural, Peritoneal and pericardial Fluids, In, Bibo, M. (ed.), Comprehensive Cytopathology., Philadelphia, 1991, W.B. Saunders, 541-614.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Naylor, B.: Advertised positions for cytotechnologists: The first 26 years. Cytotechnol. Bull. 1990;27:19.

BRIAN J. NICKOLOFF, M.D., PH.D.
ASSOCIATE PROFESSOR OF PATHOLOGY AND DERMATOLOGY
DEPARTMENT OF PATHOLOGY
DEPARTMENT OF DERMATOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Dermatopathology, University of Michigan Hospitals.
B. Dermatopathology, M-Labs.
C. Dermatopathology, Private Consultations.
D. Dermatology, Melanoma Clinic.

II. TEACHING ACTIVITIES:

A. Pathology and Dermatology House Officers Lecture Series.
B. Clinical Pathology Orientation Lecture and Laboratory.
C. Five Week Medical Student (Year 2) Research Elective.
D. Year One Medical Student Dermatopathology Lecture Series.
E. Dermatology Grand Rounds - Dermatopathology Presentations.
F. Ten Week Undergraduate Student Research Elective.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIH First Award (50% effort: $90,000 Direct Costs; August, 1990-August, 1991): Interaction of Gamma Interferon with Keratinocytes.
B. NIH RO-1 (40% effort: $147,702 Direct Costs; June 1991-July 1992): Role of Adhesion Molecules in Psoriasis.
C. NIH RCDA (50% effort: $60,000 Direct Costs; July 1991-June 1994). Role of Adhesion Molecules in Skin Diseases.
D. NIH RO-1 (10% effort: $184,727 Direct Costs; July 1991-June 1994). Role of Dermal Dendrocytes in AIDS-Related Psoriasis.

PROJECTS UNDER STUDY:

A. Role of gamma interferon in modulating adherence reactions between resting and activated mononuclear leukocytes and keratinocytes.
B. Characterization of gamma interferon receptor on normal and psoriatic keratinocytes.
C. Gamma interferon activation of protein kinase C in benign and malignant keratinocytes.
D. Binding of lymphocytes to epidermis and vessels of frozen sections of psoriatic skin and other dermatoses.
E. Characterization of type of Beta Interferon produced by virally infected keratinocytes.
F. Interrelationship between gamma interferon, and tumor necrosis factor and PGE_2 and IL-1 production by keratinocytes and monocytes.

G. Characterization and biological significance of thrombospondin production by keratinocytes and melanocytes.
H. Role of extracellular matrix in adherence reactions involving resting and activated mononuclear leukocytes.
I. Characterization of epidermal growth factor receptor on normal and psoriatic keratinocytes.
J. Characterization of effect of cyclosporin A on phorbol ester induced cutaneous inflammation and hyperplasia.
K. Role of endothelial cell adhesion molecules (ICAM-1, ELAM-1, VCAM-1) in cutaneous leukocyte trafficking.
L. Role of Factor XIII a positive dermal dendrocytes in AIDS-related psoriasis.
M. Dissection of cytokine networks in psoriasis, allergic contact dermatitis to poison ivy, and mycosis fungoides.

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

A. Editorial Board - American Journal of Dermatopathology, Journal of Cutaneous Pathology, Autoimmunity Forum In Dermatology. Journal of American Academy of Dermatology.
B. Reviewer of articles for: Journal of Investigative Dermatology, Journal of Cutaneous Pathology, American Journal of Pathology, American Journal of Dermatopathology, Archives of Dermatology, Journal of American Academy of Dermatology, American Journal of Plastic Surgery, Journal of Cellular Physiology, American Journal of Pathology, British Journal of Dermatology, New England Journal of Medicine, Journal of National Cancer Institute, Journal of Clinical Investigation, Journal of Dermatological Science, Journal of Immunology.
C. Ad-hoc Review Committee - NIH Study Section - Skin Disease Research Center Grant Applications.
D. Member-General Medicine A Study Section, Subcomittee-1; NIH.
E. Ad-hoc Reviewer: University of Michigan Multipurpose Arthritis Center.
F. Ad-hoc Reviewer: University of Michigan Department of Surgery.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. The Histology and Immunophenotyping of Psoriasis. Invited Speaker. Clinical Dermatology in the Year 2000 Symposium, May 23, 1990, London, England.
2. The Pre-Eminent Role of the Keratinocyte in T-Cell Mediated Skin Diseases. Invited Speaker. Clinical Dermatology in the Year 2000 Symposium, May 24, 1990, London, England.
3. Adhesion Molecules for T Lymphocytes. Invited Speaker. Clinical Dermatology in the Year 2000 Symposium, Invited Speaker. May 25, 1990, London, England.
4. Role of ELAM-1 and VCAM-1 in Disorders of the Skin. Invited Speaker. Biogen Scientific Board of Directors Meeting on Endothelial Cells. June 3, 1990, Cambridge, Massachusetts.
5. Molecular, Immunologic and Pharmacologic Aspects of Psoriasis. Visiting Professor. Department of Dermatology. Johns Hopkins University. June 20, 1990, Baltimore, Maryland.
6. Role of IL-8 in Psoriasis. Visiting Professor, Department of Dermatology, Kiel University, August 17, 1990, West Germany.
7. The Cytokine Network in Psoriasis, Invited Speaker, Sandoz Forschanginstitut. August 20, 1990, Vienna, Austria.

8. Current Understanding of Psoriasis, Visiting Professor, Department of Dermatology, University of Wurzburg, August 21, 1990, Wurburg, West Germany.
9. Pathophysiology of Mycosis Fungoides, Invited Speaker, 15th International Cancer Congress, August 22, 1990, Hamburg, West Germany.
10. Molecular Basis for Growth Regulation and Inflammation in Psoriasis, Visiting Professor, Department of Pathology and Dermatology, University of Oklahoma Health Science Center, September, 25-26, 1990, Oklahoma City, Oklahoma.
11. Psoriasis Update, Invited Speaker, Extracellular Matrix Program, Department of Pathology Research Seminar Series, University of Michigan, October 23, 1990, Ann Arbor, Michigan.
12. Hair Follicle Interactions: Adhesion Molecules, Invited Speaker, NIH Research Workshop on Alopecia Areata, October 25, 1990, Bethesda, Maryland.
13. Detection of IFN-γ but not TNF-α mRNA in psoriatic epidermal sheets by PCR, Invited Speaker and Session Chairman, Central SID Meeting, November 2, 1990, Chicago, Illinois.
14. Molecular Basis for Growth Dysregulation and Inflammation in Psoriasis, Visiting Professor, Department of Dermatology, University of Alabama, November 16, 1990, Birmingham, Alabama.
15. Psoriasis Update and Dermatopathology Update, Visiting Professor, Department of Dermatology, University of Rochester, November 21, 1990, Rochester, New York.
16. Cytokine Network in Psoriasis, Invited Speaker, Annual Meeting of the American Society of Dermatopathology, November 29, 1990, Atlanta, Georgia.
17. Induction, Distribution, and Diminution of Keratinocyte Adhesion Molecules in Allergic Contact Dermatitis, Plenary Session Speaker and Co-Chairman, Annual Meeting-American Society of Dermatopathology, November 30, 1990, Atlanta, Geogia.
18. Role of Adhesion Proteins in Inflammatory Skin Disease, Convatec Skin Research-Scientific Advisory Board Meeting, December 14-15, 1990, Princeton, New Jersey.
19. The Cytokine Network in Psoriasis with Emphasis on TNF-α Inducible Genes., Invited Speaker-Collaborations Program Seminar Series, Genetech Inc, March 8, 1991, S. San Francisco, California.
20. The Cytokine Network in Psoriasis, Invited Speaker, Division of Rheumatology, Northwestern University April 15, 1991, Chicago, Illinois.
21. Molecular Basis of Inflammation and Growth Dysregulation in Psoriasis, Invited Speaker, Department of Biochemistry-MD/PhD Program Forum: Frontiers in Medical Sciences, April 15, 1991, Chicago, Illinois.
22. CD-18 (LFA-1) and CD-49d (VLA-4) Mediate Lymphocyte Adherence to Endothelial Cells in Rhus Dermatitis. Annual Meeting, Society for Investigative Dermatology, May 2, 1991, Seattle, Washington.
23. Topobiology and Investigative Dermatopathology, Invited Speaker, Howard Fox Lecture Series, Dept of Dermatology, New York University, June 7, 1991, New York, New York.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Barker, J.N.W.N., Sarma, V., Dixit, V. and Nickoloff, B.J.: Marked synergism between tumor necrosis factor-alpha and interferon-gamma in regulation of keratinocyte derived chemotactic and adhesion molecules. Rapid Communication J. Clin. Invest. 1990;85:605-608.
2. Bulengo, S., Brown, M.C., Dubin, H., Rasmussen, J.E., and Nickoloff, B.J.: Sweet's syndrome presenting in an unusual periorbital eruption. J. Am. Acad. Dermatol. 1991;24:140-141.
3. Eisen, D., Griffiths, C.E.M., Ellism C.N., Nickoloff, B.J. and Voorhees, J.J.: Cyclosporin wash for oral lichen planus. Lancet 1990;335:535-537.

4. Nickoloff, B.J. and Griffiths, C.E.M.: Lymphocyte trafficking in psoriasis: A new perspective emphasizing the dermal dendrocyte with active dermal recruitment mediated via endothelial cells followed by intraepidermal T-cell activation. J. Invest. Dermatol. 1990;95:35s-37s.
5. Elder, J.T., Klein, S.B., Tavakkol, A., Fisher, G.J., Nickoloff, B.J. and Voorhees, J.J.: Growth factor and proto-oncogene expression in psoriasis. J. Invest. Dermatol. 1990;95:7-9.
6. Nickoloff, B.J. and Griffiths, C.E.M.: Intraepidermal but not dermal T lymphocytes are positive for a cell-cycle associated antigen (Ki-67) in mycosis fungoides. Am. J. Pathol. 1990;136:261-266.
7. Nickoloff, B.J. and Griffiths, C.E.M.: Abnormal cutaneous topobiology: The molecular basis for dermatopathological mononuclear cell patterns in inflammatory skin disease. J. Invest. Dermatol. 1990;95:128-131.
8. Gupta, A.K., Cooper, K.D., Ellis, C.N., Nickoloff, B.J., Hanson, C.A. and Voorhees, J.J.: Lymphocyte infiltrates of the skin in association with cyclosporine A therapy. J. Am. Acad. Dermatol. 1990;23:1137-1141.
9. Fisher, G., Esmann, J., Griffiths, C.E.M., Talwar, H.C., Elder, J.T., Nickoloff, B.J., Karabin, G., Cooper, K.D. and Voorhees, J.J.: Cellular, biochemical and immunological characterization of topical retinoic acid treated human skin. J. Invest. Dermatol. 1991;96:699-707.
10. Varani, J., Shayevitz, J., Perry, D., Mitra, R.S., Nickoloff, B.J. and Voorhees, J.J.: Retinoic acid stimulation of human dermal fibroblast proliferation is dependent on extracellular Ca^{2+} concentration. Am. J. Pathol. 1990;136:1275-1281.
11. Nickoloff, B.J., Wood, G.S,, Griffiths, C.E.M., Chu, M. and Beckstead, J.H.: Disseminated dermal dendrocytomas: A new cutaneous fibrohistiocytic proliferative disease? Am. J. Surg. Path. 1990;14:867-871.
12. Nickoloff, B.J., Karabin, G.D., Barker, J.N.W.N., Griffiths, C.E.M., Sarma, V., Mitra, R.S., Elder, J.T., Kunkel, S.L. and Dixit, V.: Cellular localization of interleukin-8 and its inducer tumor necrosis factor-alpha in psoriasis. Am. J. Path. 1991;138:129-140.
13. Barker, J.N.W.N., Mitra, R.S., Griffiths, C.E.M., Dixit, V. and Nickoloff, B.J.: Keratinocytes as initiators of inflammation: A unifying explanation for diverse array of environmental stimuli to produce cutaneous inflammation. Lancet 1991;337:211-214.
14. Griffiths, C.E.M. and Nickoloff, B.J.: Induction, distribution, and diminution of leukocyte adhesion molecules (ELAM-1, ICAM-1, VCAM-1) T-cell chemotaxin (IL-8), and a modulatory cytokine (TNF-α) during the evolution of allergic contact dermatitis (Rhus Dermatitis). Br. J. Dermatol. 1991;124:519-526.
15. Nickoloff, B.J.: The human progenitor cell antigen (CD-34) is localized on endothelial cells, dermal dendritic cells, and perifollicular cells in formalin-fixed normal skin, and on proliferating endothelial cells and stromal spindle-shaped cells in Kaposi's Sarcoma. Arch. Dermatol. 1991;127:523-529.
16. Barker, J.N.W.N., Karabin, G.D., Stoof, T., Mitra, R.S., Sarma, V., Dixit, V.M. and Nickoloff, B.J.: Detection of gamma interferon mRNA in psoriatic epidermis by polymerase chain reaction. J. Dermatol. Sci. 1991;2:106-111.
17. Nickoloff, B.J.: Anti-β4 Integrin prominently stains nerves in psoriatic skin. Arch. Dermatol. 1991;127:271-272.
18. Barker, J.N.W.N., Jones, M.L., Swenson, C.L., Sarma, V., Mitra, R.S., Ward, P.A., Fantone, J.C. and Nickoloff, B.J.: Regulation of keratinocyte-derived monocyte chemotaxis and activating factor (MCAF) by interferon-gamma. J. Immunol. 1991;146:1192-1197.
19. Nickoloff, B.J. and Griffiths, C.E.M.: Aberrant intercellular adhesion molecule-1 (ICAM-1) by hair follicle epithelial cells and endothelial leukocyte adhesion molecule-1 (ELAM-1) by vascular cells are important adhesion molecule alterations in alopecia areata. J. Invest. Dermatol. 1991;96:91s-92s.
20. Nickoloff, B.J.: Cytokine network in psoriasis: Molecular pathway pointing to the psoriasis gene in mutant clones of epidermal keratinocytes. Arch. Dermatol. 1991;127:871-884.
21. Mahoney, S.E., Duvic, M., Nickoloff, B.J., Minshall, M., Smith, L.L., Griffiths, C.E.M., Paddock, S.W. and Lewis, D.E.: HIV transcripts indentified in HIV-related psoriasis and Kaposi's sarcoma lesions. J. Clin. Invest., In Press, 1991.

22. Barker, J.N.W.N., Jones, M.L., Mitra, R.S., Fantone, J.C., Kunkel, S.L., Dixit, V.M. and Nickoloff, B.J.: Modulation of keratinocyte-derived interleukin-8 which is chemotactic for neutrophils and T lymphocytes. Am. J. Pathol., In Press, 1991.

BOOKS/CHAPTERS IN BOOKS:

1. Nickoloff, B.J.: Leukocyte adhesion molecules and inflammatory cell migration pathways, in, Bos, J. (ed.), Skin Immune System, pp. 49-71, 1990. CRC Press, Inc, Boca Raton, Florida.
2. Nickoloff, B.J.: Role of epidermal T-cell migration in parapsoriasis and cutaneous T-cell lymphoma, in, Muller, A.S. (ed.), Proceedings of the First International Parapsoriasis Symposium, Mayo Clinic Press, pp. 85-93. 1991.
3. Nickoloff, B.J., Varani, J. and Mitra RS: Modulation of keratinocyte biology by gamma interferon: Revelance to cutaneous wound healing, in, Barbul, A. (ed.), Clinical and Experimental Approaches to Dermal and Epidermal Repair: Normal and Chronic Wounds, Alan R. Liss Inc., New York, New York, pp. 141-154, 1991.
4. Nickoloff, B.J.: Interferons and cutaneous metabolism, in, Biochemistry and Physiology of the Skin, Oxford University Press, New York, In Press, 1991.
5. Nickoloff, B.J.: Cytokine networks in skin disease, in, Kunkel, S. and Remick, D. (eds.), Cytokines in Health and Disease: Physiology and Pathophysiology. Marcel Dekker Inc., New York, New York, In Press, 1991.
6. Nickoloff, B.J.: Editor: Mast Cells, Macrophages and Dendritic Cells in Skin Disease, CRC Press, Inc., In Preparation. 1991.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR, ARTICLES PUBLISHED IN UNREFEREED JOURNALS:

1. Winterrowd, G.E., Fleming, W.E., Krezsicki, R.F., Nickoloff, B.J. and Sanders, M.E.: Mechanisms of memory T cell accumulation in inflamed tissues: Interleukin-2 induces naive to memory phenotype switch and enhanced adhesion. Clin. Res. 1990;38:390.
2. Fleming, W.E., Winterrowd, G.E., Krezsicki, R.F., Nickoloff, B.J. and Sanders, M.E.: Enhanced mechanisms of memory T cell enrichment in rheumatoid synovium: adhesion and altered phenotype of cytokine-treated T cells. Clin. Res. 1990;39:215.
3. Nickoloff, B.J.: Pathophysiology of cutaneous T cell lymphoma (Mycosis Fungoides). J. Cancer. Res. and Clin. Oncol. 1990;116:1176.
4. Barker, J.N.W.N., Griffiths, C.E.M., Mitra, R.J., Elder, J.T., Dixit, V., Kunkel, S. and Nickoloff, B.J.: Keratinocyte-derived interleukin-8: Regulation by TPA and urushiol and detection in inflamed skin. J. Invest. Dermatol. 1990;95:461.
5. Barker, J.N.W.N., Jones, M.L., Swenson, C., Mitra, R.J., Elder, J.T., Fantone, J., Ward, P.A., Dixit, V.M. and Nickoloff, B.J.: Keratinocyte production of a biologically active monocyte chemoattractant. J. Invest. Dermatol. 1990;94:505.
6. Fisher, G.J., Easmann, J., Griffiths, C.E.M., Duell, E.A., Elder, J.T., Karabin, G., Nickoloff, B.J. and Voorhees, J.J.: Cellular, immunological and biochemical characterization of topical all-trans-retinoic treated human skin. J. Invest. Dermatol. 1990;94:524.
7. Griffiths, C.E.M., Barker, J.N.W.N., Mitra, R.S. and Nickoloff, B.J.: The influence of ion exchange inhibitors and transforming growth factor beta on keratinocyte/lymphocyte interaction. J. Invest. Dermatol. 1990;94:531.
8. Karabin, G.D., Mitra, J.R., Stoolman, L. and Nickoloff, B.J.: Characterization of a model keratinocyte-lymphocyte adhesion system which is ediated by gamma interferon. J. Invest. Dermatol. 1990;94:541.
9. Mahoney, S.E., Duvic, M. and Nickoloff, B.J.: HIV transcripts detected in HIV-associated Kaposi's sarcoma and psoriasis. J. Invest. Dermatol. 1990;94:552.
10. Mitra, R.J., Karabin, G.D., Barker, J.N.W.N., Varani, J., Voorhees, J.J. and Nickoloff, B.J.: Molecular characterization of interaction between all-trans-retinoic acid, and gamma interferon on cultured human keratinocytes. J. Invest. Dermatol. 1990;94:556.

11. Nickoloff, B.J., Barker, J.N.W.N., Griffiths, C.E.M,, Elder, J.T., Kunkel, S. and Dixit, V.: Molecular and cellular localization of IL-8 and its inducer-TNF in psoriasis. J. Invest. Dermatol. 94:559, 1990.
12. Nickoloff BJ, Griffiths CEM, Barker JNWN, Kunkel S: Primary role for activated keratinocytes in rhus dermatitis. Clin Res 1990;38:525.
13. Barker, J.N.W.N., Griffiths, C.E.M., Mitra, R.J., Fisher, G. and Nickoloff, B.J.: Immunophenotypic modulation of cutaneous dendritic cell by various cytokines. Clin. Res. 1990;38:421.
14. Fivenson, D.P., Nickoloff, B.J, and Krull, E.A.: Thy-1+ Dermal dendrocytes in mycosis fungoides. Clin. Res. 1990;38:835.
15. Barker, J.N.W.N., Mitra, R.S., Griffiths, C.E.M., Dixit, V.M. and Nickoloff, B.J.: Keratinocyte production of pro-inflammatory molecules in response to known inducers of cutaneous inflammation. J. Cut. Path. 1990;17:286.
16. Nickoloff, B.J. and Griffiths, C.E.M.: Induction, distribution and diminution of leukocyte adhesion molecules (ELAM-1, ICAM-1, VCAM-1), A T cell chemotaxin (IL-8) and modulatory cytokine (TNF-α) in allergic contact dermatitis. J. Cut. Path. 1990;17:309.
17. Nickoloff, B.J., Barker, J.N.W.N., Karabin, G., Stoof, T., Sarma, V. and Dixit, V.: Detection of interferon-gamma but not tumor necrosis factor-alpha in mRNA in psoriatic epidermal sheets by polymerase chain reaction. Clin. Res. 1990;38:836.
18. Griffiths, C.E.M. and Nickoloff, B.J.: Modulation of leukocyte adhesion molecules, a T-cell chemotaxin (IL-8) and a regulatory cytokine in rhus dermatitis. Clin. Res. 1990;38:836.
19. Barker, J.N.W.N., Griffiths, C.E.M., Mitra, R.S., Dixit, V.M. and Nickoloff, B.J.: Human epidermal keratinocyte derived interleukin-8: Relevance to contact dermatitis. J. Invest. Dermatol. 1990;95:462.
20. Nickoloff, B.J., Stoof, T.S., Mitra, R.S., Griffiths, C.E.M., Aulicino, M. and Stoolman, L.M.: CD-18 (LFA-1) and CD-49J (VLA-4) mediate lymphocyte adherence to endothelial cells in Rhus Dermatitis. J. Invest. Dermatol. 1991;96:538.
21. Barker, J.N.W.N., Jones, M.L., Mitra, R.S., Elahe-Torabe, C., Fantone, J.C., Dixit, V.M. and Nickoloff, B.J.: Modulation of keratinocyte-derived interleukin-8 which is chemotactic for neutrophils and T cells. J. Invest. Dermatol. 1991;96:538.
22. Mitra, R.S. and Nickoloff, B.J.: Epidermal growth factor decreases gamma interferon receptors and induction of intercellular adhesion molecule-1 on keratinocytes. J. Invest. Dermatol. 1991;96:544.
23. Fivenson, D.P., Dunstan, R.W., Douglass, Mc., Nickoloff, B.J. and Moore, R.J.: Thy 1+ dermal dendrocytes in mycosis fungoides. J. Invest. Dermatol. 1991;96:599.
24. Stoof, T.J., Barker, J.N.W.N., Karabin, G.D., Sarma, V.J., Dixit, V.M. and Nickoloff, B.J.: Detection of interferon-gamma but not tumor necrosis factor mRNA in psoriatic epidermal sheets by polymerase chain reaction. J. Invest. Dermatol. 1991;96:614.
25. Nickoloff, B.J., Fivenson, D.P., Griffiths, C.E.M. and Modlin, R.: Preferential but not unique cutaneous endothelial cell expression of ELAM-1. Clin. Res. 1991;39:153.
26. Mitra, R.S., Barker, J.N.W.N., Stoof, T.J., Stoolman, L., and Nickoloff, B.J.: Comparison of lymphocyte adhesion to keratinocytes, fibroblasts, melanocytes: CD18 (LFA-1) dependent and independent pathways. Clin. Res. 1991;39:234.
27. Fivenson, D.P. and Nickoloff, B.J.: Adhesion molecule expression by Thy 1+/FXIIIa positive dermal dendrocytes in mycosis fungoides. Clin. Res. 1991;39:153.
28. Nickoloff, B.J. and Griffiths, C.E.M.: Not all spindled-shaped cells embedded in a collagenous stroma are fibroblasts: Recognition of the "collagen-associated dendrophage". J. Cut. Path. 1990;17:252-253.
29. Nickoloff, B.J. and Mitra, R.S.: Growth modulatory effects of tumor necrosis factor-alpha on human keratinocytes-response. J. Invest. Dermatol. 1991;96:397-398.
30. Barker, J.N.W.N., Allen, M.H., Griffiths, C.E.M., Nickoloff, B.J. and MacDonald, D.M.: Expression of the myelomonocytic antigens L1 and CD36 in human epidermis. Br. J. Dermatol. 1990;123:548-549.

31. Nickoloff, B.J. and Mitra, R.S.: Direct antiproliferative effects of cyclosporin A on cultured human keratinocytes and fibroblasts. Br. J. Dermatol. 1990;123:693.
32. Barker, J.N.W.N., Griffiths, C.E.M. and Nickoloff, B.J.: NAP/IL-8 immunoreactivity in normal and psoriatic skin. J. Invest. Dermatol., In Press, 1991.
33. Nickoloff, B.J.: Book Review-Tumors of the Epidermis by K. Hashimoto, A. Megregan, Butterworths. Am. J. Surg. Path., In Press, 1990.

GABRIEL NUNEZ, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Clinical Molecular Diagnostics Laboratory.
B. Autopsy Service.

II. TEACHING ACTIVITIES:

A. Supervised the following undergraduate students during the summer.
   a. Lauren K. Horton.
   b. Jeffrey Zacharias.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Functional Role of Bcl-2 and Antigenic Stimulation in the Development of Lymphoma," The University of Michigan Cancer Research Committee, 5% effort, $7,500, 7/1/91 - 7/1/92.

PENDING:

A. Principal Investigator, "Functional Role of Bcl-2 in B cell Development and Lymphoma," Cancer Research Institute, Investigator Award, 40% effort, $50,000/year, 7/1/91 - 7/1/95.
B. Principal Investigator, "Development of a Genotyping Core for CF Mutations," Cystic Fibrosis Foundation, (Core facility for the project "Gene Transfer Approaches to Cystic Fibrosis"), 10% effort, $25,000/year ($75,000/3 years) 9/1/91 - 8/31/94.

PROJECTS UNDER STUDY

A. Functional role of Bcl-2 in lymphocyte development and neoplasia.
B. Molecular cloning of genes involved in programmed cell death of B lymphocytes.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Molecular Diagnostics Laboratory.
B. Interviewer, postdoctoral candidates for fellowship in Anatomic Pathology.
C. Interviewer, postdoctoral candidates for research fellowships.

MEDICAL SCHOOL/HOSPITAL:

A. None.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Speaker, "Bcl-2 displays a restricted follicular localization and maintains B cell memory," Federation of American Society for Experimental Biology, Atlanta, Georgia, April, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Nunez, G., London, L., Hockenberry, D., Alexander, M., McKearn, J.P. and Korsmeyer, S.J.: Deregulated Bcl-2 gene expression selectively prolongs survival of growth factor deprived hematopoietic cell lines. J. Immunol. 1990;144:3602-3610.
2. McDonnell, T.J., Nunez, G., Platt, F.M., Hockenberry, D., London, L., McKearn, J.P. and Korsmeyer, S.J.: Deregulated Bcl-2-Ia transgene expands a resting but responsive IgM/IgD B cell population. Mol. Cell Biol. 1990;10:1901-1907.
3. Hockenberry, D.M., Nunez, G., Milliman, C., Screiber, R.D. and Korsmeyer, S.J.: Bcl-2, an inner mitochondrial membrane protein blocks programmed cell death. Nature (London) 1990;348:334-338.

ARTICLES ACCEPTED FOR PUBLICATION:

1. Nunez, G., Hockenberry, D., McDonnell, T.J., Zutter, M., Nahan, M. and Korsmeyer, S.J.: Bcl-2 demonstrates a restricted localization in germinal centers and maintains B cell memory, In Press.

BOOKS/CHAPTERS IN BOOKS:

1. Korsmeyer, S.J., McDonell, T.J., Nunez, G., Hockenberry, D. and Young, R.: Bcl-2: B cell life, death, and neoplasia, in Current Topics in Microbiology and Immunology, Mechanisms of B cell Neoplasia Conference, Bethesda, Maryland, Springer-Berlag, In Press.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Nunez, G., Hockenberry, D., McDonnell, T.J. and Korsmeyer, S.J.: Bcl-2 displays a restricted lymphoid localization and extends B cell memory. J. of Cellular Biochem. 1991;15A:268.
2. Nunez, G., Hockenberry, D., McDonnell, T.J., Nahm, M. and Korsmeyer, S.J.: Bcl-2 displays a restricted follicular localization and maintains B cell memory. FASEB J. 1991;5:1602.

HAROLD A. OBERMAN, M.D.
PROFESSOR OF PATHOLOGY
CO-DIRECTOR OF CLINICAL PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Co-Director, Section of Clinical Pathology, University Hospitals.
B. Director, Blood Bank, University Hospitals.
C. Diagnosis of surgical specimens from University Hospital patients.
D. Diagnosis of surgical specimens from M-Labs.
E. Diagnosis of consultation cases on surgical pathology of breast.
F. Medical coverage of Transfusion Service.
G. Medical coverage of Necropsy Service.
H. Member, University of Michigan Breast Care Center.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Lectures on breast pathology (two) and transfusion medicine (three) to sophomore class.
B. Postgraduate course, "Current Topics in Blood Banking", Planning Committee.
C. Course on Transfusion Medicine presented to Pathology and Hematology/Oncology House Officers.
D. Seminars and lectures on Pathology of Breast to Pathology House Officers.
E. Lecture to Section of Urologic Surgery, Department of Surgery: Appropriate use of blood components. July, 1990.
F. Presentation of Grand Rounds to Department of Internal Medicine: Indications and Complications of Blood Transfusion. July, 1990.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Significance of intraductal carcinoma and lobular carcinoma in-situ presenting in adenofibromas or in sclerosing adenosis.
B. Adenomyoepithelial neoplasms of breast.
C. Pleomorphic adenomas of breast.
D. New Ultrasound Methods for Cancer Diagnosis and Treatment (3-5 years at 5% effort).
E. Microvascular and Structural Imaging of Breast Cancer (3-5 years at 3% effort).

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

A. American Association of Blood Banks:
   1. Awards Committee, Chairman.
   2. Publications Committee.
B. American Society of Clinical Pathologists:
   1. Expert Review Panel in Anatomic Pathology.
   2. Search Committee for Editor, American Journal of Clinical Pathology.
C. International Academy of Pathology:
   1. Abstract Review Board.
D. Michigan Society of Pathologists:
   1. Medical Legislation Committee.
   2. Medical Care Insurance Committee.
E. Southeastern Michigan Red Cross Blood Program:
F. Consultant, Veterans Administration Hospital, Ann Arbor.
G. Test Committee on Blood Banking/Transfusion Medicine, American Board of Pathology.
H. Breast Cancer Task Force, Michigan Department of Public Health.

DEPARTMENTAL:

A. Co-Director, Division of Clinical Pathology.
B. Laboratory Communication Committee.
C. M-Labs Operation Committee.
D. Chairman's Advisory Committee.
E. Director, Fellowship program in Blood Banking/Transfusion Medicine.

MEDICAL SCHOOL/HOSPITAL:

A. Transufsion Committee, Chairman.
B. Breast Care Center.
C. Liver homotransplantation task force.
D. Bone marrow homotransplantation task force.
E. AIDS task force.
F. Advisory Committee on Appointments, Promotions and Titles of Medical School.
G. Mentor, M-1 students.
H. Hospital quality assurance committee.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Associate Editor, TRANSFUSION.
B. Editorial Board, American Journal of Surgical Pathology.
C. Editorial Board, American Journal of Clinical Pathology.
D. Editorial Board, Archives of Pathology and Laboratory Medicine.
E. Associate Editor, Critical Reviews in Clinical Laboratory Sciences.
F. Reviewer, American Journal of Medicine.
G. Reviewer, Cancer.
H. Reviewer, Journal of the American Medical Association.

INVITED LECTURES/SEMINARS:

1. Lecture, to Second World Week of Professional Updating in Surgery, Blood Transfusion in the U.S. and its Problems, Milan, Italy, July 20, 1990.
2. Lecture, to Department of Pathology, University of Bologna Medical School, "Stromal Tumors of the Breast", Bologna, Italy, July 23, 1990.
3. Visiting Professor, Rochester General Hospital, Rochester University School of Medicine, Rochester, New York, September 13, 1990.
4. "Problems in the Diagnosis and Management of Breast Cancer" American Society of Clinical Pathologists; Three day course organized and presented by Drs. Oberman and P.P. Rosen, St. Petersburg, Florida, December 5-7, 1990.
5. Lecture, "Hyperplasia and Atypical Hyperplasia of the Breast", Postgraduate course, Current Management of Breast Cancer, Northwestern University Medical School. Chicago, Illinois, December 12, 1990.
6. Lecture, "AIDS: An Update", Eastern Michigan University, Ypsilanti, Michigan, April 1, 1991.
7. Goldblatt Memorial Lecture, "Transfusion Medicine", Mt. Sinai Hospital, Cleveland, Ohio, May 22, 1991.
8. Lecture, "Medical-Legal Aspects of Blood Banking", University of Michigan Postgraduate Course, "Current Topics in Blood Banking", June 6, 1991.
9. Lecture, "The Role of the Pathologist in the Diagnosis and Management of Breast Carcinoma", University of Michigan Family Medicine postgraduate course, June 20, 1991.
10. Lecture, "Transfusion Medicine", University of Michigan Family Medicine postgraduate course, June 21, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Adler, D.D., Helvie, M.A., Oberman, H.A., Ikeda, D.M. and Bhan, A.O.: Radial sclerosing lesion of the breast: Mammographic features. Radiology, In Press.
2. Oberman, H.A. and Markey, B.A.: Noninvasive carcinoma of the breast presenting in adenosis. Mod. Pathol 1991;4:31-35.

BOOKS/CHAPTERS IN BOOKS:

1. Oberman, H.A.: Complications of blood transfusion, in, Greenfield, L. (ed.), Complications in Surgery and Trauma, J.B. Lippincott, Philadelphia, Pennsyvania, 1990.
2. Oberman, H.A.: Appropriate use of plasma and plasma derivatives, in, Summers, S.H., Smith, D.M., Agranenko (eds.), Arlington, Virginia, Transfusion Therapy: Guidelines for Practice, American Association of Blood Banks, 1990.
3. Goulet, J. and Oberman, H.A.: Blood and blood products in orthopaedic surgery. Chapter for orthopaedic textbook.
4. Rosen, P.P. and Oberman, H.A.: Tumors of the Breast, Fascicles of Tumor Pathology, Armed Forces Institute of Pathology, Universities Associated for Research and Education in Pathology, Inc.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR,

1. Book Review Editor, American Journal of Surgical Pathology.

(ILLNESS-RELATED ABSENCE, OCTOBER - NOVEMBER, 1990; SABBATICAL LEAVE, JANUARY - JUNE, 1991)

SEM H. PHAN, PH.D., M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Autopsy Service.

II. TEACHING ACTIVITIES:

A. Course Director, Pathology 650.
B. Soverin Karmiol, Ph.D. - Postdoctoral Fellow.
C. Mariano DiMiguel, M.D. - Postdoctoral Fellow.
D. Masud Malik, Undergraduate/Research.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Mechanisms and Genetic Regulation of Pulmonary Fibrosis", R01-HL28737-09.
B. Principal Investigator, "Macrophage Function in Lung Injury and Fibrosis", P01-HL31963, Section IV.
C. Principal Investigator, "Fibroblast Heterogeneity in Pulmonary Fibrosis", R01-HL39925.
D. Principal Investigator, "Crescentic Nephritis", P01DK38149, Section IV.
E. Co-Investigator, "Hepatic Ischemia-Induced TNF and Multiorgan injury", RO1-DK42455, Principal Investigator, D.G. Remick.

PROJECTS UNDER STUDY:

A. Lung macrophage/monocyte, recruitment and activation during lung injury and firosis.
B. Cytokine regulation of fibroblast function - in terms of chemotaxis, collagen metabolism and proliferation in fibrotic lesions of lung, kidney and skin.
C. Isolation and characterization of lung fibroblast clones from normal and fibrotic lung to examine extent of and mechanistic basis for heterogeneity.
D. Regulation of mesangial cell proliferation and collagen gene expression by mediators from diseased renal tissue and cells.
E. Regulation of production of fibrogenic mediators and cytokines by pulmonary endothelial cells and fibroblasts; and keratinocytes.
F. Production of monocyte chemotactic factors by alveolar macrophages and fibroblasts and endothelial cells, and its regulation by bleomycin and cytokines.
G. Mechanisms of xanthine dehydrogenase to oxidase conversion in rat pulmonary endothelial cells.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member, Departmental Research and Space Advisory Committee.
B. Member, Graduate Program Committee

MEDICAL SCHOOL/HOSPITAL:

A. Member, Medical Scientist Training Program Operating Committee.

REGIONAL AND NATIONAL:

A. Reviewer for the following journals: Journal of Clinical Investigation, American Review of Respiratory Diseases, Experimental Lung Research, American Journal of Pathology, Chest, Circulation Research.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Invited Seminar: "Modulation of TGF-β production in crescentric nephritis." Specialty Labs, Santa Monica, California, May 14, 1991.
2. Invited Lecture: "Mechanisms of neutrophil-induced endothelial cell injury." NHLBI/NIEHS Workshop on Environmental Lung Diseases, May 30, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Denholm, E.M. and Phan, S.H.: Specific bleomycin binding sites on rat macrophages. J. Leukocyte Biol. 1990;48:519-523.
2. Varani, J., Phan, S.H., Gibbs, D.F., Ryan, U.S. and Ward, P.A.: H_2O_2-mediated cytotoxicity of endothelial cells: Changes in ATP and purine products and effects of protective interventions. Lab. Invest. 1990;63:683-689.
3. Markey, B.A., Phan, S.H., Varani, J., Ryan, U.S. and Ward, P.A.: Inhibition of cytotoxicity by intracellular superoxide dismutase supplementation. Free Radical Biol. Med. 1990:9:307-314.
4. Merritt, S., Killen, P., Phan, S.H. and Wiggins, R.: Analysis of α1(I) procollagen, α1(IV) collagen and β-actin mRNA in glomerulus and cortex of rabbits with experimental antiglomerular basement membrane disease. Evidence for early extraglomerular collagen synthetic activity. Lab. Invest. 1990;63:762-769.
5. McClurkin, C. Jr., Phan, S.H., Hsu, C-H., Patel, S.R., Spicker, J.K., Kshirsagar, A.M., Yan, W. and Wiggins, R.C.: Colchichine-induced protection of renal function and reduction of fibrosis in a model of anti-GBM disease in the rabbit. J. Am. Soc. Nephrol. 1990;1:257-265.
6. Phan, S.H., Gharaee-Kermani, M., Wolber, F. and Ryan, U.S.: Stimulation of rat endothelial cell transforming growth factor-β production by bleomycin. J. Clin. Invest. 1991;87:148-154.
7. Coimbra, T.M., Wiggins, R., Noh, J.W., Merritt, S. and Phan, S.H.: Transforming growth factor-β production in antiglomerular basement disease in the rabbit. Am. J. Pathol. 1991;138-223-234.

8. Standiford, T.J., Kunkel, S.L., Phan, S.H., Rollins, B.J. and Strieter, R.M.: Alveolar macrophage-derived cytokines induce monocyte chemoattractant protein-1 expression from human pulmonary type II-like epithelial cells. J. Biol. Chem. 1991;266:9912-9918.
9. Phan, S.H. and Kunkel, S.L.: Lung cytokine production in bleomycin-induced pulmonary fibrosis. Exp. Lung Res. In Press, 1991..
10. Breen, E., Shull, S., Burne, S., Absher, M. Kelley, J., Phan, S.H. and Cutroneo, K.: Bleomycin regulation of TGF-β mRNA in rat lung fibroblasts. Am. J. Resp. Cell Molec. Biol. In Press.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Coimbra, T., Wiggins, R., Noh, J.W., Merritt, S. and Phan, S.H.: TGF-b mRNA and TGF-b latent and active protein in normal glomeruli and renal cortex and in anti-GMB disease in the rabbit, 23rd Annual Meeting of the American Society of Nephrology, December 2-5, Washington, D.C., 1990.
2. Phan, S.H., McGarry, B.M., Kunkel, S.L. and Ryan, U.S.: Modulation of endothelial cell transforming growth factor-b production by interleukin-1b and tumor necrosis factor-a. FASEB J. 1991;5:A517.
3. Karmiol, S., Remick, D.G. and Phan, S.H.: Effects of essential fatty acid deficiency on bleomycin-induced pulmonary fibrosis and alveolar macrophage cytokine production. FASEB J. 1991;5:A1441.
4. Phan, S.H. and Gannon, D.G.: Mechanism of xanthine dehydrogenase to oxidase conversion in endothelial cells. Am. Rev. Resp. Dis. 1991;142:A746.

CARL L. PIERSON, PH.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Associate Director, Clinical Microbiology Laboratory.
B. Coordinator, Infectious Disease Laboratory Rounds.

II. TEACHING ACTIVITIES:

A. Coordinator, Pathology House Officer Microbiology Laboratory rotation.
B. Lecturer, Clinical Pathology Ground Rounds.
C. Lecturer, Microbiology 201.
D. Lecturer, Microbiology 620.
E. Coordinator, Microbiology Laboratory Inservice.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "National survey of the susceptibility of the *Bateroides fragilis* group", Merck, Sharp & Dohme and Beecham Laboratories.
B. "Prevention of antibiotic-associated colitis with *Saccharomyces boulardii* administration," Biocodex.
C. "In Vitro susceptibility of hospital isolates to meropenon", ICI Pharmaceutical.
D. "Fleroxacin Multi-Center *In Vitro* Study", Hoffmann-LaRoche.
E. "Temafloxacin *In Vitro* Study", Abbott Labs.
F. Evaluation of "Dry Slide", Difco Labs.

PROJECTS UNDER STUDY:

A. Application of gas-liquid chromatography for rapid identification of microorganisms.
B. *In vitro* evaluation of meropenem.
C. *In vitro* evaluation of cefpirome.
D. Detection of verotoxin in patients with hemorrhagic enterocolitis.
E. Development of P.C.R. techniques for detection of Mycobacteria in patient specimens.
F. Evaluation of EIA Kits for detection of Clostridium difficile toxin A.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Clinical Pathology Laboratory Director's Committee.
B. M-Labs Technical Advisory Committee (Chairperson).

C. Clinical Microbiology Senior Staff Meeting (Chairperson).
D. Clinical Microbiology Inservice Program (Coordinator).

MEDICAL SCHOOL/HOSPITAL:

A. Hospital Infection Control Committee.
B. Task Force on AIDS (alternate).

REGIONAL/NATIONAL:

A. Co-chair, TriCounty Clinical Microbiology Association.
B. Alternate, Technical Advisory Committee, Bureau of Laboratory and Epidemiological Services, Michigan Department of Public Health.
C. Coordinator, Clinical Microbiology Laboratory Directors of Michigan Group meetings.
D. Treasurer, Michigan Branch, American Society for Microbiology.
E. Board member, South Central Association for Clinical Microbiology.

V. OTHER RELEVANT ACTIVITIES:

A. Reviewer, Journal of Clinical Microbiology.
B. Lecturer, Roche Pharmaceutical Training series.

INVITED LECTURES/SEMINARS:

1. Blythe, L. and Pierson, C.L.: "Evaluation of Syva enzyme immunoassay, GenProbe Pace 2 and Syva direct fluorescent test for Chlamydia trachomatis," South Central Association for Clinical Microbiology, 1991.
2. Fekety, R., Chang, L.W., and Pierson, C.L.: "Antibacterial activity of cefpirome against Staphylococcus aureus, Pseudomonas aeruginosa, Enterococcus faecalis and Clostridium difficile," West Berlin, Germany, 1991.

IV. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wakefield, T.W., Pierson, C.L., Schaberg, D.R., Messina, L.M., Lindenauer, M., Greenfield, L., Zelenock, G. and Stanley, J.: Artery, periarterial adipose tissue and blood microbiology during vascular reconstructive surgery". J. Vasc. Surg. 1990;11:624-628.
2. Cornick, N.A., Cuchural, G.J., Snydman, D.R., Jacobus, N.V., Iannini, P., Hill, P., Clearly, T., O'Keefe, J.P., Pierson, C.L. and Finegold, S.M.: The antimicrobial suspectibility patterns of the *bacteroides fragilis* group in the United States, 1987". J. Antimicrobial Chemotherapy 1990;25:1011-1019.
3. Reed, B.D. and Pierson, C.L.: Evaluation of a latex agglutination test for the identification of Candida species in vaginal discharge. J. Amer Board of Family Practice, Pn Press.
4. Brothers, T.E., Wakefield, T.W., Schaberg, D.R., Pierson, C.L., Graham, L.M. and Stanley, J.C.: Effect of controlled hemorrhage on tissue and serum cefazolin clearance. J of Surg Res, In Press.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Chapman, R.A., Custer, J.R., Pierson, C.L., Kratz, M., Brish, K., VandeKerkhove, J. and Bartlett, R.H.: ECLS circuits can be pre-assembled and primed for later use without risk of contamination, Children's National Medical Center ECMO Symposium, 1991.
2. Pierson, C.L., Hubbard, W. and Kratz, M.: The use of time-kill kinetics to determine the relative susceptibility of Enterococcus spp. to ampicillin/amunoglycoside combinations". American Society for Microbiology Annual Meeting, 1991, page 20.

CHARLES W. ROSS, M.D.
FELLOW/LECTURER IN HEMATOPATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Diagnostic Surgical Pathology, Hematopathology.
B. Clinical Flow Cytometry Laboratory.
C. Clinical Hematology Laboratory.
D. Clinical Molecular Diagnostics Laboratory.
E. Hematopathology Consultation Cases.

II. TEACHING ACTIVITIES:

A. Medical Students:
   1. Laboratory Instructor (2 sessions), Hematopathology - Pathology 600 course.
   2. M4 Clerkship, Hematology portion of Clinical Pathology Rotation.
B. House Officers:
   1. Sign-out of bone marrow biopsies, aspirates, blood smears, and body fluids in Hematology Laboratory.
   2. Sign-out of lymph node biopsies and review of hematopathology consultation material.
   3. Flow Cytometry sign-out.
   4. Molecular Diagnostics sign-out.
C. Hematopathology teaching:
   1. Hematopathology case conferences/biweekly.
   2. Leukemia conference/biweekly.
   3. Lymphoma conference/weekly.
   4. Molecular Diagnostics section conference/weekly.
D. Clinical Pathology Grand Rounds (one lecture).

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Detection of immunoglobulin gene rearrangements by the polymerase chain reaction.
B. Detection of Epstein-Barr virus in lymphoid lesions by polymerase chain reaction.
C. Immunophenotyping in chronic lymphoproliferative disorders.
D. Detection of *Toxoplasma gondii* in paraffin-embedded tissues by polymerase chain reaction.
E. Detection of *Mycobacterium tuberculosis* in sputum specimens by polymerase chain reaction.

IV. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ross, C.W., Stoolman, L.M., Schnitzer, B., Schlegelmilch, J.A. and Hanson, C.A.: Immunophenotypic aberrancy in adult acute lymphoblastic leukemia. Am. J. Clin. Pathol. 1990;94:590-599.
2. Ross, C.W., Schnitzer, B., Weston, B. and Hanson, C.A.: Chronic active Epstein-Barr virus infection and viral-associated hemophagocytic syndrome. Arch. Pathol. Lab. Med. 1991;115:470-474.
3. Hanson, C.A., Ross, C.W. and Schnitzer, B.: Anti-CD34 immunoperoxidase staining in paraffin sections of acute leukemia: Comparison with flow cytometric immunophenotyping. Human Pathol., In Press.
4. Hanson, C.A. and Ross, C.W.: The molecular genetics of the immunoglobulin and T-cell receptors: Applications in diagnostic hematopathology. Adv. Pathol. 1990;3:33-74.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Ross, C.W., Hanson, C.A. and Schnitzer, B.: CD30 (Ki-1)-positive large cell lymphoma mimicking gastrointestinal carcinoma.

BOOKS AND CHAPTERS IN BOOKS:

1. Hanson, C.A. Ross, C.W.: Clinical applications of molecular biology: Hematopoietic disorders, in, McClatchey, K.D. (ed.), Clinical Laboratory Medicine, Williams & Wilkins, Baltimore, Maryland, In Progress.

ABSTRACTS, BOOK REVIEW, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Ross, C.W., Schlegelmilch, J., Grogan, T., Schnitzer, B. and Hanson, C.A.: Detection of Epstein-Barr virus (EBV) genome in Ki-1 (CD30)-positive, large cell anaplastic lymphomas (LCAL) using the polymerase chain reaction (PCR). Lab. Invest. 64:83A, 1991.
2. Ross, C.W., Hanson, C.A., Appelman, H. and Schnitzer, B.: Ki-1 (CD30)-positive, anaplastic large cell lymphoma (ALCL) mimicking gastrointestinal carcinoma. Lab. Invest. 1991;64:40A.
3. Hanson, C.A., Ross, C.W. and Schnitzer, B.: CD34 immunoperoxidase (IP) staining in bone marrow paraffin sections: Correlation with flow cytometric (FC) studies. Lab. Invest. 1991;64:73A.
4. Hanson, C.A., Abaza, M., Ross, C.W., Sheldon, S., Schnitzer, B. and Stoolman, L.M.: Acute biphenotypic leukemia (ABL): Immunophenotyping (IPH), morphology, and cytogenetics. Lab. Invest. 1991;64:73A.
5. Sheldon, S., Farnen, J., Emerson, S.G., Ross and C.W., Hanson, C.A.: Chromosomal and growth factor abnormalities in leukemia: Utility of granulocyte macrophage-colony stimulating factor in cytogenetic analysis of chronic myeloproliferative disorders and acute myeloid leukemia, presented at American Association of Cancer Research, October 1990. Cancer Res. In Press, 1990.

NATHANIEL H. ROWE, D.D.S., M.S.D.
PROFESSOR OF PATHOLOGY, DENTISTRY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Intradepartmental

1. Oral Pathology Service Clinic, University Hospitals, Department of Dentistry and Oral Surgery.
2. Oral Pathology Biopsy Service Rotation, School of Dentistry.
3. Dental Faculty Associates, School of Dentistry.

B. Interdepartmental

1. Oral Pathology, clinical consultations on an as needed basis, The University of Michigan School of Dentistry Clinics.
2. Consult to VA Hospital, Ann Arbor.

II. TEACHING ACTIVITIES:

A. Oral Pathology, Course 516, to Freshmen Dental Students (course director).
B. Graduate Oral Pathology Seminar in Periodontics, Course 781 (course director).
C. General Pathology, Course 694.
D. Dental Hygiene, Course 220, to Freshmen Students.
E. Oral Pathology Course 624, to Sophomore Dental Students.
F. Oral Pathology, Course 818, to Senior Dental Students.
G. Dental Hygiene, Course 321, Senior Seminar.
H. Graduate Hospital Dentistry, Course 550.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Project Director, "Oral Zovirax for the Treatment of Recurrent HSV Labialis", 3% Effort, Burroughs Wellcome Company, 09/01/89 - 08/31/91, Total Direct Costs: $39,600.00.
B. Project Director, "Determination of the Feasibility and Economy of Central Coordination of the Collection and Disposal of Medical Waste", 10% Effort, A cooperative effort, Cosponsored by Delta Dental Plan of Michigan/Michigan Department of Public Health/Michigan Dental Association/the University of Michigan, 06/91 - 07/92, Total Direct Costs: $82,192.00.

UNDER CURRENT NEGOTIATION:

A. Project Director, "Topical Acyclovir in the Treatment of Recurrent Herpes Labialis", Burroughs Wellcome Co., 5% Effort, Amount approximately $50,000.00, 1 year.

IV. ADMINISTRATIVE ACTIVITIES:

A. Co-Director, Clinical Pathology Services, Department of Oral Medicine, Pathology, Surgery. Activities include:
   1. Provide Clinical Laboratory tests requisite to the needs of the intramural diagnostic and surgical program.
   2. Provide infection control monitoring services for the School of Dentistry.
   3. Provide, on a fee-for-service basis, infection control monitoring services for dental health care practitioners in the State of Michigan.

B. School of Dentistry Committees include:
   1. Merit and Raises Committee.
   2. Infection Control Committee, School of Dentistry.
   3. Hazardous Chemical Committee, School of Dentistry.

REGIONAL AND NATIONAL:

STATE OF MICHIGAN

A. Member, AIDS Speaker's Bureau, Michigan State Medical Society.
B. Member, Advisory Committee, Special Office on AIDS Prevention and the Disease Surveillance Section, Michigan Department of Public Health.
C. Member, Tobacco-Free Michigan Action Coalition, Michigan Department of Public Health.
D. Member, Executive Committee, American Cancer Society, Michigan Division.
E. Member, Board of Directors, American Cancer Society, Michigan Division.
F. Area Delegate Director, American Cancer Society, Michigan Division.
G. Member, Public Issues Committee, American Cancer Society, Michigan Division.
H. Member, By-Laws Revision Committee, American Cancer Society, Michigan Division.
I. Member, Professional Education Committee, American Cancer Society, Michigan Division.
J Consultant, Committee on Cancer and Infection Control, Michigan Dental Association.
K. Member, Special Committee on Health and Hazard Regulation, Michigan Dental Association.
L. Member, Research Screening Committee, Delta Dental Fund.
M. Member, Michigan Coalition on Smoking or Health.
N. Member, Coalition for Access to Health Care.

NATIONAL

A. Civilian Professor and Consultant, Office of the Surgeon General, United States Army.
B. National Board of Directors, American Cancer Society, Medical Delegate.
C. Member, National Public Issues Committee, American Cancer Society.
D. Member, National Credentials Committee, American Cancer Society.
E. Member, Science Information Committee, American Association for Dental Research.
F. Member, Council on Dental Therapeutics, American Dental Association.

INTERNATIONAL

A. External examiner in Oral Pathology, University of Malaysia, Kuala Lumpur, Malaysia.

V. OTHER RELEVANT ACTIVITIES:

A. Clinical and Patient Care
   1. Intradepartmental
      a. Oral Pathology Service Clinic, University Hospitals, Department of Dentistry and Oral Surgery.
      b. Oral Pathology Biopsy Service Rotation.
      c. Clinical Pathology Service, Co-Director.
   2. Interdepartmental
      a. Oral Pathology, clinical consultations on an as needed basis, The University of Michigan Medical School of Dentistry Clinics.
      b. Consultant, VA Hospital, Ann Arbor.

EDITORIAL BOARDS:

A.. Journal of the American Medical Association.
B. Journal of Oral Pathology.
C.. Journal of the American Dental Association.
Dd. Cancer.
E. Journal of the Academy of General Dentistry.

INVITED LECTURES/SEMINARS:

1. Michigan Association of Women Dental Students, "You, M.I.O.S.H.A., and the Law", October 6, 1990.
2. Continuing Education Course presented through University of Michigan Dental School, "Testing for and Recognition of Diseases in the Prosthodontic Patient", November 14, 1990.
3. Osaka Dental University, "Dental Caries", Osaka, Japan, July 10, 1990.
4. 26th Annual Burke Symposium, "A Strategy for Successful Dental Practice During the Coming Decade by the Integration of Biologic Therapeutic and Social Changes", Ft. Ord, California, July 26-27, 1991.
5. American Dental Association, "Management of Infections and Noninfectious Diseases in Dental Practice", Boston, Massachusetts, October 13, 1991.
6. Detroit Clinic Club, Perio Section, "Mucosal Disease", Orchard Lake, Michigan, October 17, 1991.
7. Michigan Academy of Pediatric Dentistry, "Thoughts on the Management of Oral Disease in Children", Lansing, Michigan, January 19, 1991.
8. Saginaw Valley Dental Society, "Compliance with Regulatory Requirements in the Control of Infection", Frankenmuth, Michigan, February 28, 1991.
9. Keynote speaker: First Turkish Endodontic Congress, "Periapical Healing", Istanbul, Turkey, April 22-26, 1991.
10. Flying Dentist Organization, "A Strategy for Successful Dental PracticE During the Coming Decade", Boyne Mountain, Michigan, June 24-25, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Rowe, N.H.: Glove use in dentistry. Part I: Preventing glove damage to hands. J. Mich. Dent. Assoc. 1990;72:147. Reprinted in the Florida Dental Journal, 1991. Reprinted in the Pennsylvania Dental Journal, 1991.

2. Rowe, N.H.: Providing health care to those who provide health care For others: Directive 1. J. Mich. Dent. Assoc. 1991;73:44-45.

BOOKS AND CHAPTERS IN BOOKS:

1. Rowe, N.H.: Jaw, Neuroectodermal Pigmented Tumor. Birth Defects Encyclopedia. #711.
2. Rowe, N.H.: Dental Caries (Revision), Chapter 17, in, Regezi, J.A. and Sciubba, J.J. (eds.), Oral Pathology, 2nd edition, W.B. Saunders Company, Philadelphia, In Press.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Spruance, S.J., Freeman, D.J., Stewart, J.C.B., McKeough, M.B., Wenerstrom, G., Krueger, G.G. and Rowe, N.H.: Experimental ultraviolet radiation (UVR)-induced herpes labialis: Early treatment with peroral acyclovir (ACV) markedly reduces the severity of incipient ;esions. Abstracts of the 1990 interscience Conference on Antimicrobial Agents and Chemotherapy. Abstract #202, p. 120, October 21, 1990.

BERTRAM SCHNITZER, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Director, Clinical Hematology Laboratory.
B. Director, University of Michigan Health Services Laboratories.
C. Diagnostic Surgical Pathology, Hematopathology.
D. Diagnostic Hematopathology Consultant, Veterans Administration Hospital.
E. Diagnostic Hematopathology of M-Lab clients.
F. Consultant for External and Transfer Hematopathology cases.
G. Review of Southwest Oncology Group (SWOG) cases (circa 150/year).
H. Review of lymphoma cases entered into Children's Cancer Study Group protocols.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Daily sign-out of bone marrow biopsies and aspirates.
B. Daily review of blood smears and body cavity and joint fluids in the Hematology Laboratory.
C. Daily review of in-house and consultation hematopathology cases and correlation with flow cytometry data and immunoperoxidase studies.
D. Daily review of outside consultation cases.
E. House Officer Conferences in Hematopathology. (Clinical Pathology Grand Rounds).
F. Biweekly House Office Hematopathology Conference.
G. Monthly lectures to house officers on acute leukemias and lymphomas.
H. Dental student lecture in Hematopathology.
I. Sophomore Medical student lectures in Hematopathology.
J. Sophomore Medical student laboratory sessions in Hematopathology.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Southwest Oncology Group (SWOG). Combination chemotherapy of unfavorable histology non-Hodgkin's lymphomas with CHOPP and CBV, with Dr. L. Dabich.
B. Southwest Oncology Group (SWOG). Combination chemotherapy of unfavorable histology non-Hodgkin's lymphomas with alternating regimens of CHOPP and CVB, with Dr. L. Dabich.
C. Pathology Coordinator, SWOG studies numbers 8515 and 8516.

SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Diagnostic Surgical Pathology, Hematopathology.
B. Diagnostic Clinical Pathology, Hematology.

MEDICAL SCHOOL/HOSPITALS:

A. Hematology Laboratory.
B. University of Michigan Health Service Laboratories.

REGIONAL AND NATIONAL:

A. President, Society for Hematopathology.
B. Society for Hematopathology, Executive Committee.
C. Southwest Oncology Group:
    1. Lymphoma Subcommittee.
    2. Leukemia Subcommittee.
D. Children's Cancer Study Group: Review of in-house cases of lymphoma cases.
E. Regional Center Review Pathologist, Southwest Oncology Group.
F. Member, Review Panel for Lymphomas, Southwest Oncology Group.
G. Member, Hematology Council, American Society of Clinical Pathologists.
H. Member, Hematology Workshop Review Committee, American Society of Clinical Pathologists.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARD:

A. Human Pathology.
B. Hematologic Pathology . Designated reviewer.
C. Arch. Pathol. Lab Med. Designated Reviewer

INVITED LECTURES/SEMINARS:

1. "A Practical Approach to Diagnostic Hematological Problems", ASCP Educational Course, Santa Fe, New Mexico, November, 1990. Lectures given included: a) Non-Hodgkin's Lymphomas; b) Hodgkin's Disease; c) A Practical Approach to the Diagnosis and Classification of Lymphomas and Leukemias by Flow Cytometry, and Electron Microscopy; d) Extranodal lymphomas; and e) Immunologic Classification of Acute Lymphoblastic Leukemias. Santa Fe, New Mexico.
2. "Hodgkin's Disease: Diagnosis and Differential Diagnosis", ASCP Workshop. October, 1990. Dallas, Texas.
3. Lecture on Hodgkin's Disease, lide Seminar, Greater Detroit Society of Pathologists. May 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ross, C.W., Stoolman, L.M., Schnitzer, B., Schlegelmilch, J.A. and Hanson, C.A.: Immunophenotypic aberrancy in adult acute lymphoblastic leukemia. Am. J. Clin. Pathol. 1990;94:590-599.
2. Hanson, C.A., Holbrook, E.A., Roth, M.S., Sheldon, S. and Schnitzer,B.: Detection of Philadelphia-chromosome positive cells from glass slide smears and paraffin sections using the polymerase chain reaction. Am J. Pathol. 1990;137:1-6.
3. Davenport, R.D., O'Donnell, L.R., Schnitzer, B. and McKeever, P.E.: Non-Hodgkin's lymphoma of the brain after Hodgkin's disease. An immunohistochemical study. Cancer 1991;67:440-443.
4. Hanson, C.A., Gribbin, T.E., Schnitzer, B, Schlegelmilch, J.A. Mitchell, B.S. and Stoolman, L.M.: CD11c (Leu M5) expression characterizes a B cell chronic lymphoproliferative disorder with features of both chronic lymphocytic leukemia and hairy cell leukemia. Blood 1990;76:2360-2367.
5. Ross, C.W., Schnitzer, B., Weston, B.R., and Hanson, C.A.: Chronic active Epstein-Barr virus infection and virus-associated hemophagocytic syndrome. Arch. Pathol. Lab. Med. 1991;115:470-474.

BOOKS AND CHAPTERS IN BOOKS:

1. Schnitzer B: Reactive lymphoid hyperplasia, in, Jaffe, E.S. (ed.), Surgical Pathology of the Lymph Nodes and Related Organs, 2nd Edition, WB Saunders Co., In Press.
2. Schnitzer B: Benign lymphoproliferative disorders, in, Knowles,D.M. (ed.), Neoplastic Hematopathology, Williams-Wilkins Co., In Press.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Ross, C.W., Hanson, C.A., Appelman, H. and Schnitzer, B: Ki-1 (CD30) positive anaplastic large cell lymphoma (ALCL) mimicking gastrointestional lymphoma. Mod. Pathol. 1991;4:40A. and Lab. Invest. 1991;64:40A.
2. Hanson, C.A., Abaza, M., Ross, C.W., Sheldon, S., Schnitzer, B. and Stoolman, L.L: Acute biphenotypic leukemia (ABL): Immunophenotyping (IPH), morphology, and cytogenetics. Mod. Pathol. 1991;4:73A and Lab. Invest. 1991;64:73A.
3. Ross, C.W., Schlegelmilch, J., Grogan, T., Schnitzer, B. and Hanson, C.A.: Detection of Epstein-Barr Virus (EBV) genome in Ki-1 (CD-30) positive, large cell anaplastic lymphomas (LCAL) using the polymerase chain reaction (PCR). Mod. Pathol. 1991;4:83A and Lab. Invest. 1991;64:83A.
4. Grogan, T., Spier, C., Braziel, R., Wirt, D., Montiel, M., Kerrington, D., Schnitzer, B., Tubbs, R., Levy, N., Cossman, J., Berman, M., Fisher, R. and Miller, T.: Refined working formulation categorization of lymphomas using phenotypic and genotypic analysis: A SWOG central repository study. Mod. Pathol. 1991;4:73A and Lab. Invest. 1991;64:73A.

SUZANNE M. SELVAGGI, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Cytopathology - 26 weeks.
B. Gynecologic Pathology (transfer cases) - 12 months.
C. Consultation service, Department of Pathology: Cytopathology and Gynecologic Pathology - 12 months.

II. TEACHING ACTIVITIES:

A. Daily microscopic sessions in Cytopathology with pathology residents and cytopathology fellow.
B. Instruction of pathology residents and cytopathology fellow in the performance and interpretation of fine needle aspirates.
C. Pathology residents - monthly cytopathology conference.
D. Cytotechnologists - cytopathology conference (6X/yr).
E. Gynecologic Oncology Tumor Board Conference - weekly.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Cytologic indicators of cervical smear adequacy.
B. Transplant cytology.
C. Computer applications to cytology.
D. Cytomorphology of human breast cancer cells grown in tissue culture (with S. Ethier, Department of Radiation Oncology).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Co-Director, Cytopathology Laboratory.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Quality Assurance/Quality Control Committee.

REGIONAL AND NATIONAL:

A. Reviewer, Diagnostic Cytopathology

B. Committee Member, National Cancer Institute's second workshop on the proposed Bethesda Nomenclature System for Cervicovaginal Cytology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Factors Influencing Fine Needle Aspiration Cytology in the Management of Recurrent Gynecologic Malignancies", Poster, Spring Scientific Meeting of the American Society of Clinical Pathology, San Francisco, California, 1990.
2. "Diagnostic Accuracy of Fine Needle Aspiration Cytology in Persistent or Recurrent Gynecologic Malignancies, Poster, Annual Scientific Meeting of the American Society of Cytology, Washington, D.C., November, 1990.
3. Comparison of Smears and Cell Blocks in the Fine Needle Aspiration Diagnosis of Recurrent Gynecologic Malignancies, Poster, Annual Scientific Meeting of the American Society of Cytology, Washington, D.C., November, 1990.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Selvaggi, S.M.: Cytology of non-neoplastic cysts of the ovary. Diagn. Cytopathol. 1990;6:77-85.
2. Selvaggi, S.M. and Migdal, S.: Cytologic features of atypical mesothelial cells in peritoneal dialysis fluid. Diagn. Cytopathol. 1990;6:22-26.
3. Zalupski, M.M., Ensley, J.F., Ryan, J., Selvaggi, S.M., Baker, L.H. and Wolman, S.R.: A common cytogenetic abnormality and DNA content alternations in dedifferentiated chondrosarcoma. Cancer. 1990;6:1176-1182.
4. Smith, R., Deppe, G., Selvaggi, S.M. and Lall, C.: Benign teratoma of the omentum and ovary coexistent with an ovarian neoplasm. Gynecol. Oncol. 1990;39:204-207.
5. Selvaggi, S.M.: Fine needle aspiration cytology of ovarian follicle cysts with cellular atypia from reproductive-age patients. Diagn. Cytopathol. 1991;7:189-192.
6. Wojcik, E.M. and Selvaggi, S.M.: Goblet cell carcinoid tumor in peritoneal fluid: A case report. Diagn. Cytopathol. 1991;7:155-157.
7. Selvaggi, S.M. and Malviya, V.: Efficacy of the modified Ayre spatula/Zelsmyr Cytobrush versus the modified Ayre spatula/bulb aspirator in the collection of cells from the uterine cervix. Diagn. Cytopathol., In Press.
8. Jacques, S.M. and Selvaggi, S.M.: Multiple peritoneal cytologies collected during laparotomy for gynecologic malignancy. Diagn. Cytopathol., In Press.
9. Wojcik, E.M. and Selvaggi, S.M.: Factors influencing fine needle aspiration cytology in the management of recurrent gynecologic malignancies. Acta Cytol., In Press.
10. Wojcik, E.M. and Selvaggi, S.M.: Comparison of smears and cell blocks in the fine needle aspiration diagnosis of recurrent gynecologic malignancies. Acta Cytol., In Press.
11. Selvaggi, S.M.: Cytologic features of malignant ovarian monodermal teratoma with an ependymal component in pelvic washings. Int. J. Gynecol. Pathol., In Press.

CHAPTERS IN BOOKS:

1. Selvaggi, S.M. and Lawrence, W.D.: Cytopathology of the uterine cervix, in, Jordan, J.A., Blackledge, G.R. (eds.s), Textbook of Gynecology Oncology, Grune Stratton Ltd., Chapter 26, 1991.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Wojcik, E.M. and Selvaggi, S.M.: Factors influencing fine needle aspiration cytology in the management of recurrent gynecologic malignancies. Am. J. Clin. Pathol. 1990;93:444.
2. Wojcik, E.M. and Selvaggi, S.M.: Diagnostic accuracy of fine needle aspiration cytology in persistent or recurrent gynecologic malignancies. Acta Cytol. 1990;34:730.
3. Wojcik, E.M. and Selvaggi, S.M.: Comparison of smears and cell blocks in the fine needle aspiration diagnosis or recurrent gynecologic malignancies. Acta Cytol. 1990;34:729-730.
4. Book Review: Comprehensive Cytopathology, Bibbi, M. (ed.), W.B. Saunders Co., 1991; Am. J. Surg. Pathol., In Press.

SUSAN SHELDON, Ph.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Clinical Cytogenetics Laboratory.

II. TEACHING ACTIVITIES:

A. Pathology house officers:
   1. Instruction in genetics and cytogenetics.
   2. Weekly review of bone marrow and relevant peripheral blood cases with house officers on Hematopathology rotation.

B. Medical Genetics fellows and medical students.
   Instruction in cytogenetics as it relates to both genetic and acquired disease.

C. Hematology/Oncology fellows.
   Instruction in cytogenetics as it relates to hematologic disease.

D. Clinical Pathology Grand Rapids.

E. Medical Genetics Rounds, weekly participant, two lectures.

F. Leukemia Conference, biweekly.

G. Genetic Counseling graduate students:
   1. One lecture.
   2. Individual tutorials.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Role of the use of growth factors and mitogens for cytogenetic examination of hematologic malignancies in a clinical laboratory.

B. Use of growth factors to elaborate expression of a Philadelphia chromosome.

C. Use of intercalating agents to enhance resolution of chromosome bands.

D. Correlation of ploidy with expression of differentiated function.

E. Role of deletions of 12p in eosinophilia.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Assistant Director, Clinical Cytogenetics Laboratory.

MEDICAL SCHOOL/HOSPITAL

A. Director, Clinical Research Center Cell Immortalization Facility.

REGIONAL AND NATIONAL:

A. Planning Committee, Cytogenetics Technologist Program, Eastern Michigan University.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Cytogenetics and Molecular Genetics", lecture to advanced genetics class at University of Michigan, Flint, Michigan.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Sheldon, S., Farnen, J., Emerson, S., Ross, C. and Hanson, C.A.: Utility of granulocyte-macrophage colony stimulating factor in cytogenetic analysis of chronic myeloproliferative disorders and acute myeloid leukemia. Presented at American Association of Cancer Research, October 1990. Cancer Res. 1990, In Press.
2. Hanson, C.A., Abaza, M., Ross, C.W., Sheldon, S., Schnitzer, B. and Stoolman, L.M.: Acute biphenotypic leukemia (ABL): Immunophenotyping (IPH), morphology, and cytogenetics. Lab. Invest. 1991;64:73A.

SUYU SHU, PH.D.
ASSOCIATE PROFESSOR OF SURGERY
DEPARTMENT OF SURGERY
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Director, Oncology Laboratory.
B. Establishment of a clinical laboratory for culture and immunologically stimulated human T lymphocytes for cancer treatment.

II. TEACHING ACTIVITIES:

A. Supervision of two postdoctoral fellows.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Adoptive T Cell Immunotherapy of Nonimmunogenic Tumors", National Cancer Institute, Grant 1 RO1 CA47285, June, 1988 to May 1993, Total award of $796,763 (direct cost).
B. Co-Principal Investigator, "Adoptive Therapy of Human Cancer with Sensitized T Cells", National Cancer Institute, RO1 CA51220, October 1, 1990 to September 30, 1993. Total award $474,437.
C. Program Preceptor, "Surgical Oncology Training in Tumor Immunology", National Cancer Institute, T32 Training Grant, July 1991 to June 1996, Total direct cost $940,561.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interview candidates for faculty positions in Division of Surgical Oncology.
B. Participate in surgical resident research program.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Cancer Center of the University of Michigan.

REGIONAL AND NATIONAL:

A. Reviewer for the following journals: Cancer Research, Journal of Immunology, Cancer Immunology and Immunotherapy.

V. OTHER RELEVANT ACTIVITIES:

A. Member, Experimental Therapeutics II Study Section, NCI, NIH, 1989-.
B. Editorial Board (Currently Active) Journal of Immunotherapy, Vaccine Research.
C. Consultant: Fenwal Division, Baxter Healthcare Corporation, Consulting Immunologist.

INVITED LECTURES AND SEMINARS:

1. Visiting Scientist, "Generation of Immune T Lymphocyte with Reactivity Toward Autochthonous Tumors, Fenwal Division, Baxter Healthcare Corporation, Santa Ana, California, July 25, 1990.
2. Invited Speaker, "T Cells as Therapeutic Agent for Treatment of Cancer", International Conference on Biological Treatment of Melanoma and Other Cancers, Newcastle, Australia, September 4-7, 1990.
3. Invited Speaker, "Generation of Tumor Immune T Lymphocytes by Active Immunization Followed by In Vitro Sensitization: Experimental Models and Clinical Trial", 82nd Annual Meeting, American Association for Cancer Research, Houston, Texas, May 18, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Sakai, K., Chang, A.E. and Sju S.: Phenotype analyses and cellular mechanisms of pre-effector T lymphocyte response to progressive murine sarcoma. Cancer Res. 1990;50:4371-4376.
2. Sakai, K., Chang, A.E. and Shu, S.: Effector phenotype and immunologic specificity of T cell mediated adoptive therapy for a murine tumor that lacks intrinsic immunogenicity. Cell. Immunol. 1990;129:241-255.
3. Vander Woude, D.L., Shu, S. and Chang, A.E.: Differential activity of interferon-alpha on the function of sensitized T cells in adoptive immunotherapy. Surgical Forum 1991;XLUL:436-438.
4. Vander Woude, D.L., Wagner, P.D., Shu, S. and Chang, A.E.: Enhanced antitumor reactivity of tumor-sensitized T cells by interferon-alfa. Arch. Surg. 1991;126:307-313.
5. Sondak, V.K., Wagner, P.D., Shu, S. and Chang, A.E.: Suppressive effects of visceral tumor on the generation of antitumor T cells for adoptive immunotherapy. Arch. Surg. 1991;126:442-446.
6. Yoshizawa, H., Sakai, K., Chang, A.E. and Shu, S.: Activation by anti-CD3 of tumor draining lymph node cells for specific adoptive immunotherapy. Cell. Immunol. 1991;134:473-479.
7. Yoshizawa, H., Chang, A.E. and Shu, S.: Specific adoptive immunotherapy mediated by tumor-draining lymph node cells sequentially activated with anti-CD3 and IL-2. J. Immunol., In Press.
8. Wagner, P.D., Shu, S. and Chang, A.E.: Divergent effects of TNF_{α} in the adoptive immunotherapy of a murine sarcoma. J. Surg. Res., In press.

BOOKS/CHAPTERS IN BOOKS:

1. Shu, S., Yoshizawa, H., Sakai, K. and Chang, A.E.: In vitro activation of T cells from tumor-draining lymph nodes for adoptive immunotherapy, in, Lotze, M.T. and Finn, O.J. (eds.), Cellular Immunity and the Immunotherapy of Cancer, UCLA Symposia on Molecular and Cellular Biology, New Series, Vol. 136, Editors, Wiley-Liss, Inc., New York, New York, pp. 255-266, 1990.

2. Chang, A.E., Yoshizawa, H., Sakai, K. and Shu, S.: Generation of sensitized T lymphocytes for adoptive immunotherapy, in, Lotze, M.T. and Finn, O.J. (eds.), Cellular Immunity and the Immunotherapy of Cancer, UCLA Symposia on Molecular and Cellular Biology, New Series, Vol. 135, Wiley-Liss, Inc., New York, New York, pp. 315-320, 1990.
3. Shu, S. and Chang, A.E.: Sensitization of T lymphocytes for cancer therapy, in, Hersey, P. and Mitchwll, M.S. (eds.), Proceedings of the International Conference on Biological Treatment of Melanoma and Other Cancers, The Royal Newcastle Hospital Press, 1990.

ABSTRACTS, BOOK REVIEWS, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Shu, S., Yoshizawa, H. and Chang, A.E.: Adoptive T cell immunotherapy mediated by in vitro activated tumor-bearing lymph node cells. Res. Cancer Conference, Michigan Division of the American Cancer Society, 1990.
2. Shu, S., Yoshizawa, H. and Chang, A.E.: In vitro activation of tumor-draining lymph node cells for generation of tumor-specific T lymphocytes. International Conference on Biological Treatment of Melanoma and Other Cancers. Newcastle, Australia, September, 1990.
3. Hoshizawa, H., Chang, A.E. and Shu, S.: Cellular mechanisms of tumor regression mediated by specific T cells generated by anti-CD3/IL-2 activation. Federation of American Societies for Experimental Biology (Annual Meeting). Abst. 5574, 1991.
4. Chang, A.E., Yoshizawa, H. and Shu, S.: Sensitized T cell therapy of human cancer. American Association for Cancer Research (Annual Meeting). Abst. 1486, 1991.
5. Shu, S. Generation of tumor immune T lymphocytes by active immunization followed by in vitro sensitization: Experimental models and clinical trial. American Association for Cancer Research (Annual Meeting). Symp. 14, 1991.
6. Geiger, J.D., August, D.A., Shu, S. and Chang, A.E.: Anti-CD3 activated lymphocytes in adoptive immunotherapy. Society of University Surgeons (Annual Meeting), 1991.
7. Geiger, J.D., Shu, S. and Chang, A.E.: Enhanced generation of tumor sensitized T cells for adoptive immunotherapy using a bacterial adjuvant. American Cancer Society Research Conference (Annual Meeting), 1991.
8. Geiger, J.D., Shu, S. and Chang, A.E.: Enhanced generation of effector T cells for adoptive immunotherapy. Association for Academic Surgery (Annual Meeting), 1991.

LAWRENCE SILBART, PH.D.
RESEARCH INVESTIGATOR IN PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Eastern Michigan University:
   1. Immunotoxicology lecture, 2/19/91 for Chem 412 (Toxicology II).

B. University of Michigan Medical School:
   1. Pathology 650, two week instruction on immunochemical methods.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

1. "The Mucosal Immune Response to Aflatoxin B_1", Department of Health and Human Services, Public Health Service, National Institutes of Health, National Cancer Institute, 5/1/89 to 4/31/92. Total costs, $276,367.00.
2. "Continued Development of Mucosal Vaccines for Carcinogens", Smokeless Tobacco Research Council, Inc, 7/1/90 to 6/31/93. Total costs, $274,989.00.

PENDING:

1. "The Preston Connecticut Incinerator Project", Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institutes for Environmental Health Science. $171,714 Total costs.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL: None.

MEDICAL SCHOOL/HOSPITAL: None.

REGIONAL AND NATIONAL: None.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS: None.

INVITED LECTURES/SEMINARS:

1. "Development of non-toxic (anti-idotypic) mucosal vaccines to block the absorption of the chemical carcinogen 2-acetylaminofluorene (AAF)", American Association of Immunologists (AAI); 4/23/91, Atlanta, Georgia (FASEB). .

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Silbart, L.K., Keren, D.F., McDonald, R.A., Goslinoski, L., Miller, B., Clements, J.D. and Smart, J.: Strategies for eliciting a mucosal immune response to the chemical carcinogens 2-acetylaminofluorene (AAF) and aflatoxin B_1 (AFB_1). Frontiers of Mucosal Immunology 2:469-470.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Silbart L.K., McDonald, R.A, Lincoln, P.M., Goslinoski, L. and Keren. D.F.: The adjuvant effect of cholera toxin and its B subunit on the elicitation of a mucosal immune response to 2-AAF-thyroglobulin conjugates.
2. Silbart L.K., McDonald, R.A., Lincoln, P.M. Goslinoski, L. and Keren, D.F.: Elicitation of a secretory immune response to the carcinogen 2-acetylaminofluorene (2-AAF) is enhanced by conjugation to the mucosal immunogen cholera toxin.

BOOKS/CHAPTERS IN BOOKS:

1. Keren, D.F. and Silbart, L.K. Strategies to Achieve Mucosal Immunity, Submitted.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Silbart, L.K., Keren, D.F., McDonald, R.A., Goslinoski, L., Brownlee, B.E., Lash, C. and Smart, J.B.: Development of non-toxic (anti-idiotypic) mucosal vaccines to block the absorption of the chemical carcinogen 2-acetylaminofluorene (AAF). FASEB J. 1991;5:A966.
2. Miller, B.F., Toth, C.M., Silbart, L.K., McDonald, R.A., Keren, D.F. and Smart, J.B.: Radioimmunoassay (RIA) for the detection of secretory antibodies to the carcinogen aflatoxin B_1 (AFB_1) in rabbit and mouse intestinal secretions. FASEB J. 1991;5:A881.

EUGENE M. SILVERMAN, M.D.
CLINICAL ASSOCIATE PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Coverage of M-Labs cases including most cases from:
   1. Albion Community Hospital, Albion, Michigan.
   2. Thorn Hospital, Hudson, Michigan.
   3. University of Michigan Health Service, Ann Arbor, Michigan.
   4. Falzone Laboratories.
   5. Perry Health Net.
   6. Other various institutions.

B. Autopsy Coverage for Albion Community Hospital, Albion, Michigan, and Thorn Hospital.

C. Rotation with other staff pathologists.
   1. Six weeks coverage at the University Hospital of weekend autopsy call.

II. TEACHING ACTIVITIES:

A. Supervise residents in gross cutting of M-Labs cases and review microscopic material with residents in all interesting cases.

B. Read out some M-Labs autopsies and some University of Michigan autopsies with residents.

III. RESEARCH ACTIVITIES:

A. Investigation of hepatic fatty change in exogenous obesity and following gastric exclusion surgery.

B. Investigation of malacoplakia of the endometrium.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Associate Director, M-Labs.
   1. Participate in planning, marketing, and implementation of M-Labs programs.

B. Director, Laboratory at Albion Community Hospital, Albion, Michigan.

C. Chairman, Tissue/Transfusion Committee, Albion Community Hospital, Albion, Michigan.

D. Chairman, Infection Control Committee, Albion Community Hospital, Albion, Michigan.

E. Member of Surgery Committee, Albion Community Hospital.

F. Director of Laboratories, Thorn Hospital, Hudson, Michigan.

G. Chairman, Tissue/Transfusion Committee, Thorn Hospital, Hudson, Michigan.

H. Chairman, Infection Control Committee, Thorn Hospital, Hudson, Michigan.

I. Director of Laboratories, Lapeer Regional Hospital, Lapeer, Michigan.
J. Member, Tissue/Transfusion Committee, Infection Control Committee, Lapeer Regional Hospital, Lapeer, Michigan.

V. **OTHER RELEVANT ACTIVITIES:** None.

VI. **PUBLICATIONS:** None.

ANDERS A.F. SIMA, M.D., PH.D.
PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Neuropathology Service, 33%.

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Neuropathology 858 — 6 hours;
      b. CME accredited Conferences
         Brain Conference — 16 hours;
         Brain Tumor Conference — 16 hours;
         Neuromuscular Conference — 16 hours;
         Neuropath Conference for house staff — 16 hours.

B. Undergraduate students:
   a. Neuropathology (NSB 600) — 4 hours.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Pathology of the Node of Ranvier in Diabetic Neuropathy", RO1-DK 43884-01 (40%), National Institutes of Health, with Tennekoon, G. and Rotkowski, J.L. $1,472,882/5 years, 4/1/91 - 3/31/96.

B. Principal Investigator, "The Role of Trophic Factors and Their Synthesis in Diabetic Neuropathy", #1901122, Juvenile Diabetes Foundation International, $47,801.00/year, 7/1/90 - 6/30/92.

C. Equipment grant, Wyeth-Ayerst, Radon, Pennsylvania, $570,000.00, 1991.

D. Principal Investigator, "The Long Term Preventional and Interventional Effect of Statil on Diabetic Neuropathy in the BB-Rat", ICI-RDN-3, ICI, Great Britain, $212,104.74/3 years, 1988-91.

E. Co-Investigator, and Sima, A.A.F. "Synthesis and Responsiveness to Trophic Factor by Diabetic Nerve of the BB-Rat", Murphy, L.J., Principal Investigator, Medical Research Council of Canada, $141,180.00/year, 4/1/88-3/31/93.

PENDING:

A. "Molecular Elements, Neurocircuits and Mental Illness", National Institute of Mental Health, Sima, A.A.F. (10% effort), Watson, S. (PI), $5,166,343.00/five years.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. CERAD representative, Michigan Dementia Program.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Executive Committee, Michigan DRTC.
B. Director, Image Analysis core, Michigan DRTC.
C. Director, Animal Core, Michigan DRTC.

REGIONAL, NATIONAL AND INTERNATIONAL:

A. Member, Medical Advisory Board, Juvenile Diabetes Foundation International, New York, New York.
B. Member, Organizing Committee, International Diabetes Federation Satellite symposium on Diabetic Neuropathy, New York, New York.
C. International Scientific Coordinator 3rd LAD, Jerusalem, Israel.
D. Executive Committee, LAD, Jerusalem, Israel.
E. Member, Council on Diabetic Complications, ADA, New York, New York.
F. Abstract Review Board, ADA, Alexandria, Virginia.
G. Member, Specialty Committee Neuropathology, Royal College of Physicians and Surgeons of Canada, Ottawa, Canada.
H. Scientific Advisor, Wyeth-Ayerst, Radon, Pennsylvania.
I. Scientific Advisor, Endocrinology Section FDA, Rockville, Maryland.

V. OTHER RELEVANT ACTIVITIES;

EDITORIAL BOARDS:

A. Journal of Neuropathology and Experimental Neurology.
B. Diabetes Research and Clinical Practice.
C. Lessons from Animal diabetes.
D. International Diabetes News.
E. Ad hoc Reviewer for nine journals (Neuropathology and Diabetes).
F. Study sections
   1. Medical Research Council of Canada
   2. Juvenile Diabetes Foundation International
   3. American Diabetes Association

INVITED LECTURES/SEMINARS:

1. Scheie Eye Institute, University of Pennsylvania, Philadelphia 1990.
2. Wyeth-Ayerst France, Paris, France, 1990.
3. Miles Pharmaceutical Inc., New Haven, Connecticut, 1990.
4. Simposia International, Neuropatia Diabetica, Ixtapa, Mexico, 1991.
5. Department of Medicine, University of Utrecht, Holland, 1991.
6. Italian Diabetes Association, Taromina, Italy, 1991.
7. Investigators meeting, Wyeth-Ayerst, Miami Beach, FL, 1991
8. Symposium on Diabetic Neuropathy, Oosterbeek, Holland, 1991.
9. Department of Endocrinology, University of Catania, Italy, 1991.

10. Symposium on Diabetic Polyneuropathy, IDF, Washington, 1991.
11. IDF Satellite Symposium on Controversies in Etiology and Treatment of Diabetic Neuropathy, New York, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Chakrabarti, S. and Sima, A.A.F.: The presence of anionic sites in basement membranes of cerebral capillaries. J. Microvasc. Res. 1990;39:123-127.
2. Greene, D.A., Sima, A.A.F., Pfeifer, M.A. and Albers, J.W.: Diabetic neuropathy, Ann. Rev. Med. 1990;41:303-317.
3. Sima, A.A.F., Prasher, A., Zhang, W-X, Chakrabarti, S. and Greene, D.A.: The preventive effect of long term aldose reductase inhibition (Ponalrestat) on nerve conduction and sural nerve structure in the spontaneously diabetic BB-rat. J. Clin. Invest. 1990;85:1410-1420.
4. Zhang, W-X, Chakrabarti, S., Greene, D.A. and Sima, A.A.F.: Diabetic autonomic neuropathy in BB-rats: The effect of ARI-treatment on heart-rate variability and vagus nerve structure. Diabetes. 1990;39:613-618.
5. Multiauthor. Consensus statement: Diabetic neuropathy. Diabetes Care 1990;13:47-52.
6. Sima, A.A.F.: Diabetic neuropathy. Man. Med. 1990;59:154-156.
7. Sima, A.A.F. and Greene, D.A.: Neuropathies diabetiques - histopathologie. Diab. Metabol. 1990;16:346-347.
8. Greene, D.A. and Sima, A.A.F.: Pathogenie de la neuropathie diabetique. Diab. Metabol. 1990;16:357-358.
9. Chakrabarti, S., Sima, A.A.F., Lee, J., Brachet, P. and Dicon, E.: Nerve growth factor (N DF), proNGF, and NGF receptor-like immunoreactivity in diabetic and non-diabetic BB-rat retina. Brain Res. 1990;523:11-5.
10. Chakrabari, S., Ma N. and Sima, A.A.F.: Anionic sites in diabetic basement membranes and their possible role in diffusion barrier abnormalities. Diabetologia 1991;34:301-306.
11. Sima, A.A.F.: Structural and morphometric assessment of diabetic neuropathy. 1991;IPJ 6:29-32.
12. Sima, A.A.F., Nathaniel, V., Prashar, A., Brill, V. and Greene, D.A.: Endoneurial microvessels in human diabetic neuropathy: Endothelial cell dysjunction: and lack of treatment effect by an aldose deductase inhibitor. Diabetes, In Press.
13. Chakrabarti, S., Ghahary, A., Murphy, L.J. and Sima, A.A.F.: Insulin-like growth factor-I expression in the retina of diabetic BB/W-rats. Diab. Res. Clin. Prac., In Press.
14. Simmons, Z., Albers, J.W. and Sima, A.A.F.: Perineuritis presenting as mononeuropathy multiplex: A case report. Muscle and Nerve, In Press.
15. Ghahary, A., Chakrabarti, S., Murphy, L.J. and Sima, A.A.F.: The effect of insulin and statil on aldose reductase expression in the diabetic rat. Diabetes, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Lindstrom, P., Brismar, T. and Sima, A.A.F. Impaired recovery after anoxic conduction block in diabetic (BB/W)-rat nerve in vivo. Ann. Neurol. Submitted.
2. Sima, A.A.F., Zhang, W-X and Chakrabarti, S.: Impaired visual evoked potentials and primary axonopathy of the optic nerve in the diabetic BB/W-rat. Diabetes. submitted.
3. Sutherland, G.R., Loew, D., Peeling, J., Auty, A. and Sima, A.A.F.: A multiple sclerosis plaque studies using 'H nuclear magnetic resonance spectroscopy and histopathology. Can. J. Neurol. Sci. Submitted.
4. Peeling, J., Sutherland, G.R. and Sima, A.A.F.: "H NMR Spectroscopy of tissue metabolism in the diabetic BB-rat. Mag. Res. Med. Submitted.

5. Sutherland, G.R., Bose, R., Pinsky, C. and Sima. A.A.F.: The variable status of the radical-scavenging systems in primary intracranial neoplasms. Brain Research. Submitted.
6. Sima, A.A.F., Nathaniel, V., Bril, V., Brown, M. and Greene, D.A.: Overt diabetic neuropathy: repair of axo-glial dysjunction and axonal atrophy by aldose reductase inhibition and its correlation to improvement in nerve conduction velocity. Diabetologia. Submitted.
7. Sima, A.A.F., Brown, M.B., Prashar, A., Chakrabarti C., Laudadio, C. and Greene, D.A.: The reproducibility and sensitivity of sural nerve morphometry in the assessment of diabetic peripheral polyneuropathy. Diabetes. Submitted.
8. Sima, A.A.F., Green, D.A., Brown, M.B., Hohman, T. and Gonen, B.: Effect of long-term treatment with the aldose reductase inhibitor tolrestat on the sural nerve biochemistry and morphometry in advanced diabetic peripheral neuropathy. Diabetes. Submitted.

BOOKS/CHAPTERS IN BOOKS:

1. Sima, A.A.F., Yagihashi, S. and Greene, D.A.: Morphological features of human and animal diabetic nerve, in, Ward, J. and Gogo, Y. (eds), Diabetic Neuropathy. John Wiley & Sons Ltd, England, Chapt. 2,pp17-28, 1990.
2. Yagihashi, S., Ido, Y., Kamijo, M. and Sima, A.A.F.: Distal axonal degeneration in the diabetic nerve: A dynamic process in insulin-deficient diabetic rats, in, Ward, J. and Goto, Y. (eds), Diabetic Neuropathy. John Wiley & Sons Ltd, England, Chapt. 7,pp91-97, 1990.
3. Greene, D.A., Lattimer, S.A. and Sima, A.A.F.: Tissue-specific metabolic alterations in the pathogenesis of diabetic peripheral neuropathy, in, Belfiori, F., Malinatti, G.M. smf Reaver, G.M. (eds). Tissue Specific Metabolic Alterations in Diabetes. Karger. Gasel. pp.83-96, 1990.
4. Greene, D.A., Bril, V. and Sima, A.A.F.: The relevance and efficacy of aldose reductase inhibitors in human diabetic neuropathy, in, Ward, J. and Goto, Y. (eds), Diabetic Neuropathy. John Wiley & Sons Ltd, England, Chapt. 13,pp 113-142, 1990.
5. Tagihashi, S. and Sima, A.A.F.: Effect of methylcobalamin on the autonomic nerve lesions in the spontaneously diabetic BB rat: Ultrastructural and morphometric study, in, Ward, J. and Goto, Y. (eds), Diabetic Neuropathy. John Wiley & Sons Ltd, England, Chapt. 52,pp447-450, 1990.
6. Sima, A.A.F. and Greene, D.A.: Structural changes in diabetic neuropathy, in, Brownlee, M. and Sherwood, L.M. (eds), Diabetes Mellitus and Its Complications: Pathogenesis and Treatment, Hanley & Belfus, Inc., Philadelphia, pp.103-115, 1990.
7. Greene, D.A. and Sima, A.A.F.: The sorbitol-myo-inositol hypothesis, in, Brownlee, M. and Sherwood, L.M. (eds), Diabetes Mellitus and Its Complications: Pathogenesis and Treatment, Hanley & Belfus, Inc., Philadelphia, pp.15-29, 1990
8. Greene, D.A. and Sima, A.A.F.: The polyol pathway and diabetic neuropathy, in, Andreani, D., Gueriguran, J.L. and Stenler, G.E. (eds), Diabetic Complications: Epidemiology and Pathogenetic Mechanisms, Serono Symposia Publications from Raven Press, New York 67: pp. 283-301, 1991.
9. Sima, A.A.F. and Chakrabarti, S.: Chronic diabetic complications, in, Tze, W.J., Sima, A.A.F., (eds), Insulin Dependent Diabetes Mellitus Current Concepts and Approaches, Radar Publ. Inc., Montreal, pp. 43-72, 1991.
10. Sima, A.A.F.: Early detection and therapeutic approach to chronic complications. Diabetic neuropathy, in, Tze, W.J. and Sima, A.A.F., (eds), Insulin Dependent Diabetes Mellitus Current Concepts and Approaches. Radar Publ. Inc., Montreal, pp.233-244, 1991.
11. Greene, D.A. and Sima, A.A.F.: La via dei polioli e la neuropatia diabetica in Neuropatia diabetica attulita in tema di patogenesi clinical e terapia. D. Cucinotta (ed). Editoriale Bros s.a.s., Consenza, pp.51-59, 1991.
12. Sima, A.A.F. and Greene, D.A.; Morfologia dei nervi in Neuropatia diabetica attulita in tema di patogenesi clinica e terapia. D. Cucinotta (ed). Editoriale Brow s.a.s., Consenza, pp.61-70, 1991.

13. Chakrabarti, S., Ma N. and Sima, A.A.F.: Basement membrane anionic sites in the BB-rat, in, Shafrir, E., Vardi, P. and Sima, A.A.F., (eds), Frontiers in Diabetes Research: Lessons from Animal Diabetes III, John Libbey Company, London, pp. 453-455, 1991.
14. Murphy, L.J., Ghahary, A., Chakrabarti, S. and Sima, A.A.F.: Aldose reductase gene expression in the BB-rat, in, Shafrir, E., Vardi, P. and Sima, A.A.F., (eds), Frontiers in Diabetes Research: Lessons from Animal Diabetes III, John Libbey Company, London, pp.439-443, 1991.
15. Sima, A.A.F. and Greene, D.A.: Preventive effect of aldose reductase inhibitors on the neuropathy in the BB-rat, in, Shafrir, E., Vardi, P. and Sima, A.A.F., (eds), Frontiers in Diabetes Research: Lessons from Animal Diabetes III, John Libbey Company, London, 448-452, 1991.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Sima, A.A.F., Chakrabarti, S., Ghahary, A. and Murphy, L.J.: Aldose rductase gene expression and the effect of insulin and aldose reductase inhibition. 3rd Internatl. Workshop. Lessons from Animal Diabetes, Tokyo, Japan, 1990.
2. Chakrabarti and S., Sima, A.A.F.: Retinal capillary basement membrane thickening in diabetes: effects of euglycemia, aldose reductase inhibition and dmyo-inositol supplementation. 3rd Internatl. Workshop. Lessons from Animal Diabetes, Tokyo, Japan, 1990.
3. Sima, A.A.F., Chakrabarti, S. and Zhang, W-X: Optic neuropathy in the diabetic BB-rat. 3rd Internat. Workshop. Lessons from Animal Diabetes, Tokyo, Japan, 1990.
4. Greene, D.A., Bochenek, W., Harati, Y., Sima, A.A.F., Hohman, T., Hicks, D., Beg, M., Gonen B. and the Tolrestat Study Group: Biochemical and Morphometric Response to Tolrestat in Human Diabetic Nerve. European Association for the Study of Diabetes, Copenhagen, September, 1990.
5. Lattimer S., Chakrabarti, S., Greene, D.A. and Sima, A.A.F.: Metabolic correction with myoinositol retards the development of chronic diabetic neuropathy in the BB-W rat. Diabetes 40: Suppl. 1,267A.
6. Greene, D.A. and Sima, A.A.F.: Aldose reductase inhibitor (ARI) treatment normalized axo-glial dysjunction and improves nerve fiber pathology in advanced diabetic neuropathy. Diabetes, 40: Supp. 1,9A.
7. Sima, A.A.F. and Greene, D.A.: Sural nerve fiber density and normality predict clinical sensory deficits and electrophysiology in chronic diabetic neuropathy. Diabets, 40: Supp. 1, 554A.
8. Sima, A.A.F. and Greene, D.A.: Correlations between nerve morphometry, electrophysiology and sensory score in diabetic neuropathy, and their implications for the design of aldose reductase clinical neuropathy trials. US-Japan Aldose Reductase Workshop, Hawaii, 1991.
9. Greene, D.A. and Sima, A.A.F.: Neuropathy: Clinical features and biopsy study. US-Japan Aldose Reductase Workshop, Hawaii, 1991.
10. Sima, A.A.F.: The effect of ponalrestat on the development of somatic and autonomic neuropathy in the BB-rat. US-Japan Aldose Reductase Workshop, Hawaii, 1991.
11. Gonen, B., Sima, A.A.F., Greene, D.A., Beg, M. and Bochenek, W.: The effect of tolrestat on nerve morphometry in patients with diabetic neuropathy. US-Japan Aldose Reductase Workshop, Hawaii, 1991.
12. Bochenek, W., Beg, M., Hohman, T., Sima, A.A.F., Greene, D.A., Hicks, D. and Gonen, B.: The effects of tolrestat on activity of polyol pathway in diabetic neuropathy. US-Japan Aldose Reductase Workshop, Hawaii, 1991.
13. Sima, A.A.F. and Greene, D.A.: Via de los polioles y complicaciones cronicas de la diabetes mellitus. Simp. International: Neuropatia diabetica: Ixtapa. Mexico, January, 1991.
14. Sima, A.A.F.: Tolrestat: Nuevos hallozgos en biopsia de nervio human. Introduction e resultados. Simp. International: Neuropatia Diabetica: Ixtapa, Mexico, January, 1991.
15. Rowe, J.M., Hemperly, J.J. and Sima, A.A.F.: Localization of neural cell adhesion molecules in human brain tumors. J. Neuropath. Exp. Neurol 50: 366, 1991.

16. D'Amato, C.J., Sima, A.A.F., Foster, N.L., Dickson, D.W. and Hicks, S.P.: Cerebral lewy bodies with progressive supranuclear palsy. J. Neuropath. Exp. Neurol. 50:308, 1991.
17. Sima, A.A.F.: Morphometric responses to aldose reductase inhibitor treatment in human diabetic nerve. Oosterbeek, Holland, 1991.
18. Sima, A.A.F. and Greene, D.A.: Morphological changes in diabetic neuropathy and responses to ARI-treatment. Italian Diabetes Assoc. Ann. Meeting. Italy, 1991.
19. Sima, A.A.F., Chakrabarti, S. and Zhang, W.: Optic neuropathy in the BB-W Rat. International Diabetes Foundation - Satellite Symposium. New York, 1991.
20. Sima, A.A.F. and Charkrabarti, S.: Long term postprandial glycemic lowering prevent diabetic neuropathy in the BB-W rat. International Diabetes Foundation - Satellite Symposium. New York, 1991.
21. Sima, A.A.F., Bril, V. and Greene, D.A.: Endoneurial microvessels in human diabetic neuropathy: "endothelial cell dysjunction" and lack of treatment effect by an ARI. International Diabetes Foundation - Satellite Symposium. New York, 1991.
22. Sima, A.A.F. and Greene, D.A.: Sorbinil and tolrestat neuropathy study groups: Sural nerve fiber density and normality predict clinical sensory deficits and electrophysiology in chronic diabetic neuropathy. International Diabetes Foundation-Satellite Symposium. New York, 1991.
23. Greene, D.A. and Sima, A.A.F.: Efficacy of aldose reductase inhibitors in human sural nerve. International Diabetes Foundation - Satellite Symposium New York, 1991.
24. Lindstrom, P., Brismar, T. and Sima, A.A.F.: Impaired recovery after anoxic conduction block in diabetic (BB-Wistar) rat nerve in vitro. International Diabetes Foundation - Satellite Symposium, New York, 1991.
25. Greene, D.A., Brown, M.B., Laudadio, C. and Sima, A.A.F.: Reproducibility and sensitivity of sural nerve morphometry in the assessment of diabetic peripheral neuropathy. International Diabetes Foundation - Satellite Symposium, New York, 1991.
26. Charkrabarti, S., Sima, A.A.F., Ghahary, A., Murphy, L.J., Dicou, E. and Brachet, P.: Nerve growth factor (NGF), insulin-like growth factor-I (ICF-1) and their receptors in the retina of diabetic and non-diabetic BB-rats. International Diabetes Foundation. Washington, D.C. 1991.
27. Green, D.A. and Sima, A.A.F.: The potential effect of aldose reductase inhibitor on the complications of diabetes. Symposium on Diabetic Neuropathy, causal therapies. Oosterbeck, Holland, 1991.
28. Paro, M., Prosdocimi, M., Fiori, M.G. and Sima, A.A.F.: Autonomic innervation of the bladder in two models of experimental diabetes in the rat; function abnormalities, structural alterations and effects of ganglioside administration. 15^{o} Congresso Nationale della Societa Italiani di Urodinaurica, Padova, 1991.
29. Fratkin, J.D., Jones, M.S., D'Amato, C.J., Foster, N., Remick, D., Dragovic, L., Garcia, J.H., Ho, K.O., Huang, T.E., Sima, A.A.F. and Lovell, K.L.: Michigan dementia postmortem examination program: neuropathological effects toward morphological standardization of dementia diagnosis. J. Neuropath. Exp. Neurol. 50:38A, 1991.

LLOYD M. STOOLMAN, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Flow Cytometry Diagnostic Service - interpretation of cell surface marker studies and cellular DNA analyses in the evaluation of hematologic disorders, primary and secondary immune deficiencies and autoimmune processes.

B. Hematopathology Diagnostic Service - interpretation of peripheral smears, body fluid cytologies, bone marrow aspirates and biopsies, cytochemical stains.

II. TEACHING ACTIVITIES:

A. Research supervisor for undergraduate, graduate and postdoctoral investigators:

1. Jim Grober, M.D., Rheumatology Fellow, Department of Internal Medicine, University of Michigan, School of Medicine- recipient of NIH post-doctoral fellowship to study the adhesion.molecules mediating attachment of leukocytes to the endothelium of rheumatoid synovium.
2. R. Situ, M.D. Chairman, Department of Pathology, Jinan University, Guangzow, PRC- visiting scholar studying the expression of receptors for the extracellular matrix in cultured human T-lymphoblastic leukemias.
3. Terry Behrend, B.A., Medical Student (M1), University of Michigan, School of Medicine (summer 1990 and 1991) - recipient summer research grant focusing on the regulation of carbohydrate ligand(s) for ELAM-1 on leukocytes. Initial work on this project culminated in co-authorship on paper demonstrating the role of fucosyl-transferases in construction of ligands for ELAM-1.
4. Judy Shih, Undergraduate student, University of Michigan School of Arts and Sciences (summer 1990) - co-investigator with Dr. J. Grober studying expression and function of endothelial adhesion molecules in rheumatoid synovitis.

B. Small group seminar leader, Microbiology and Immunology-Experimental program in which the basic science are taught in the context of a clinically relevant case study.

C. Laboratory Instructor, Organ Systems Pathology (Pathology 600) - joined group of ten instructors as permanent faculty in the course. Instructors selected for interest and skill in teaching.

D. Lecturer, Experimental Pathology (Pathology 580 and 581).

E. Daily sign-out of cases in flow cytometry and hematopathology with pathology residents and medical students (3-4 months).

F. Weekly case-studies/seminars on the clinical applications of flow cytometry for the residents, fellows and medical students.

G. Preceptor, Senior medical student (M4) elective in Pathology.

H. Pediatric/Adult Leukemia Conferences.

I. Adult Lymphoma Conferences.

J. Speaker, Rheumatology, Hematology/Oncology and Cancer Center Research Seminars.

III. RESEARCH ACTIVITIES:

SPONSORED RESEARCH:

FUNDED:

A. Principal Investigator, "Endothelial Binding Lectins of Lymphoid Malignancies", NIH, RO1 ($425,000), three years, 30 September 1989 through 31 August 1992-30% effort).
B. Principal Investigator, "The Role of Lymphocyte Migration in Chronic Inflammatory Arthritis", NIH, Multipurpose Arthritis Center, Development and Feasibility Grant ($143,469), three years, 1 February 1988 through 31 January 1991 - 15% effort).
C. Co-Principal Investigator, "Mechanisms of Lymphocyte Recruitment to the Lungs", NIH, SCOR in Occupational and Immunologic Lung Diseases, P50 HL 46487-01 project #4, $650,000, five years, 1 December 1991 through 31 November 96, 15% effort.

SUBMITTED:

A. Co-Principal Investigator, "Cytokine Network in Psoriasis" (with Dr. Brian Nickoloff, Department of Pathology, University of Michigan), NIH, RO1, 15% effort.

IN PREPARATION:

A. Principal Investigator, "LEC-CAM (selectin) and integrin mediated adhesion in the spread of lymphoid malignancies", NIH, R01, 40% effort, competitive renewal.
B. Principal Investigator, "LEC-CAM (selectin) mediated adhesion in delayed-type hypersensitivity diseases of synovium and skin", NIH, RO1, 30% effort.
C. Principal Investigator, "LEC-CAM (selectin) mediated leukocyte recruitment in animal models of inflammatory arthritis", NIH SCOR in Rheumatologic Diseases, 15% effort.

PROJECTS UNDER STUDY:

A. Transmembrane signalling and the control of LECAM-1/LAM-1 during lymphocytic migration and activation.
B. Synthesis of high avidity ligands for the LEC-CAM (selectin) family of cell adhesion molecules.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Coordinator, M4 clerkship in clinical pathology.
B. Member, Quality Assurance Committee.
C. Member, Equipment and Space Allocation Committee.

MEDICAL SCHOOL HOSPITAL:

A. Co-director, Clinical Flow Cytometry Laboratory: Negotiated the purchase and managed the implementation of a new generation of cost effective instruments for acquisition and analysis of flow cytometry data.

V. OTHER RELEVANT ACTIVITIES:

PATENT APPLICATIONS:

A. U.S. Application #07/603.018
Title: Agents and methods for binding to ELAM-1.
Status: Co-inventor.

INVITED LECTURES AND SEMINARS:

1. Lecturer and Visiting Scholar, "Functional Epitopes and Regulation of the Human Endothelial Binding Lectin (LEC-CAM1): A Homing Receptor of Lymphoid Cells", University of California at San Francisco, Immunology Program, San Francisco, California.
2. "Functional Epitopes and Regulation of the Human Endothelial Binding Lectin (LEC-CAM1): A Homing Receptor of Lymphoid Cells", Minisymposium presentation, American Association of Immunologists Annual Meeting, New Orleans Convention Center, New Orleans, Louisiana.
3. "The Role of Fucosyl-Transferase in the Generation of Cell-Surface Ligands for ELAM-1 and Other Members of the LEC-CAM Family", FASEB Annual Meeting, minisymposium presentation, Atlanta Convention Center, Atlanta, Georgia.
4. lecturer and instructor, "Immunophenotyping of Acute Leukemias and Chronic Myelogenous Leukemia in Blast Crisis", American Society of Clinical Pathologists, Annual Clinical Flow Cytometry Workshop, Chicago, Illinois.
5. "LEC-CAM Mediated Adhesion in Leukocyte Recruitment and Lymphocyte Recirculation", Warner-Lambert Research Seminar Series, Ann Arbor, Michigan.
6. "Monocyte-Endothelial Interactions in Rheumatoid Synovitis", Proctor and Gamble Research Seminar Series, Cincinnati, Ohio.
7. "Regulation of LECAM-1 on T-cells", 2nd International Titisee Symposium on Leukocyte Adhesion Molecules, Titisee, Germany.

MANUSCRIPT/GRANT REVIEWS:

A. Journal of Clinical Investigation.
B. Journal of Laboratory Investigation.
C. American Journal of Pathology.
D. Journal of Cell Biology.
E. Journal of Biological Chemistry.
F. Journal of Leukocyte Biology.
G. Journal of Immunology.
H. Immunology Today.
I. Journal of Cellular Biochemistry.
J. National Heart, Lung and Blood Institute, consultant for site visit (program project), University of Minnesota, Minneapolis, Minnesota.
K. Renal Center Program Project, University of Michigan, Member of Internal Review Committee.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Strahler. J.R., Kuick, R., Eckerskorn, Lottspeich, F., Richardson, B.D., Fox, D.A., Stoolman, L.M., Hanson, C.A., Nichols, D., Tueche, H.J. and Hanash, S.M.: Identification of two related

markers for common acute lymphoblastic leukemia as heat shock proteins. J. Clin. Invest. 1990;85;200.

2. Hanson, C.A., Thamilarasan, M., Ross, C.W., Stoolman, L.M. and Schnitzer, B.: Kappa light-chain gene rearrangement in T-cell acute lymphoblastic leukemia. Am. J. Clin. Path. 1990;91(4):563.
3. Ross, C.W., Stoolman, L.M., Schnitzer, B., Schlegelmilch, J.A. and Hanson, C.A.: Immunophenotypic aberrancy in adult acute lymphoblastic leukemia. Am. J. Clin. Path. 1990;94:590.
4. Hanson, C.A., Gribbin, T.E., Schnitzer, B., Schlegelmilch, J.A., Mitchell, B.S. and Stoolman, L.M.: CD11c (LeuM5) expression characterized a B-cell chronic lymphoproliferative disorder with features of both chronic lymphocytic leukemia and hairy cell leukemia. Blood. 1990;76:2360.
5. Lowe, J.B., Stoolman, L.M., Nair, R.P., Larsen, R.D., Behrend, T. and Marks, R.M.: ELAM-1-dependent Cell Adhesion to Vascular Endothelium Determined by a Transfected Human Fucosyltransferase cDNA. Cell. 1990;63:475.
6. Varani, J., Stoolman, L.M., Wang, L., Schuger, L., Flippin, C., Dame, M., Dixit, V.M., Johnson, K.J., Todd III, R.F., Ryan, U.S. and Ward, P.A.: Thrombospondin production and thrombospondin-mediated adhesion in U937 cells. Exp. Cell Res., 1991, In Press.
7. Stoolman, L.M.: LEC-CAMs (selectins): lectin-like receptors involved in lymphocyte recirculation and leukocyte recruitment, in, Fukuda, M. (ed.), CRC Critical Reviews-Cell Surface Carbohydrates and Cell Development, CRC Press, Inc. (New York, 1991, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Stoolman, L.M., Situ, R., Wang, L. and Varani, J.: Regulation of fibronectin and laminin binding activity in human T-lymphoblastic cell lines.
2. Stoolman, L.M.: Lectin-like adhesion receptors in leukocyte recruitment. Laboratory Investigation, Invited Review, In Preparation.
3. Stoolman, L.M.: The hematogenous spread of malignancies-lessons from leukocyte recruitment. Invasion and Metastasis, Invited Review, In Preparation.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Hanson, C.A., Stoolman, L.M., Gribben, T.E. and Schnitzer, B.: CD11c expression in B-cell chronic lymphoproliferative disorders (CLPD) distinct from hairy cell leukemia (HCL). Lab. Invest. 1990;62:42A.
2. Stoolman, L.M., Ebling, H. and Debelak, D.: Regulation of the human endothelial-binding lectin LEC-CAM1 (Leu8/TQ1/LAM1/DREG/gp90mel14 homolog) in peripheral blood lymphocytes and cultured T-lymphoblasts. FASEB J. 1990;4:A911.
3. Grober, J., Ebling, H., Fox, D.A., Todd, R.F., Riedy, B.P. and Stoolman, L.M.: Monocyte-microvascular adhesive interactions in chronic rheumatoid arthritis. FASEB. J. 1990;4(3):A1139.
4. Jones, M.L., Karabin, G., Stoolman, L.M., Nickoloff, B. and Fantone, J.: Monocyte chemoattractant mRNA expression and activity production in the human Jurkat cell line clone JS9-78. FASEV J. 1990;4:A349.
5. Grober, J., Ebling, H., Fox, D.A., Todd, R.F., Riedy, B.P. and Stoolman, L.M.: Monocyte-endothelial adhesive interactions in chronic rheumatoid arthritis, American College of Rheumatology, Central Regional Meeting, Chicago, Illinois, selected for symposium presentation and Outstanding Investigator Award, 1990.
6. Stoolman, L.M., Hanson, C., Holbrook, E.A. and Ebling, H.: Functional epitopes and regulation of the human endothelial binding lectin (LEC-CAM1): a homing receptor of lymphoid cells, ASBMB/AAI Annual Meeting, selected by minisymposium presentation, 1990.

7. Karabin, G.D., Mitra, R.S., Stoolman, L.M. and Nickoloff, B.J. Characterization of a model keratinocyte-lymphocyte adhesion system which is modulated by gamma interferon (IFN-gamma). J. Invest. Dermatol. 1990;94:541.
8. Grober, J., Fox, D.A., Todd, R.F. and Stoolman, L.M.: Monocyte-endothelial adhesive interactions in chronic rheumatoid arthritis, Selected for minisymposium presentation at the American College of Rheumatology National Meeting, Seattle, Washington, October, 1990.
9. Stoolman, L.M., Marks, R.M., Nair, R.P., Larsen, R.D., Bowen, B., Berhrendt, T. and Lowe, J.B.: The role of fucosyl-transferase in the generation of cell-surface ligands for ELAM-1 and other members of the LEC-CAM family, Presented at the annual FASEB Meeting, Atlanta, Georgia, April, 1991.
10. Nickoloff, B.J., Stoof, T.J., Mitra, R.S., Griffiths, C.E.M., Aulicino, M. and Stoolman, L.M.: CD-18 (LFA-a) and CD49d (VLA-4) mediate lymphocyte adherence to endothelial cells (ECa) in Rhus Dermatitis, presented at the Annual Society for Investigative Dermatology, Seattle, Washington May, 1991.
11. Gober, J.S., Fox, D.A., Bowen, B. and Stoolman, L.M.: LEC-CAM (selectin) mediated monocyte-endothelial adhesion in chronic rheumatoid arthritis, submitted for 55th Annual Scientific Meeting, American College of Rheumatology, Boston, Massachusetts, 1991.

GERD O. TILL, M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Functional tests of neutrophils isolated from patient blood samples.

II. TEACHING ACTIVITIES:

A. Dental and graduate students (Course 630, ten one hour sessions).
B. Postdoctoral fellows, residents, undergraduate students.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

1. Principal Investigator, "Thermal Injury, ATP Depletion and Oxygen Radicals", GM-39397.
2. Co-Principal Investigator, "Thermal Injury, Complement and Leukocyte Dysfunction", GM-28499, (with Peter A. Ward).
3. Co-Principal Investigator, "Lung Injury Produced by Oxygen Metabolites", GM-29507), (with Peter A. Ward).

PROJECTS UNDER STUDY:

A. Pathophysiology of acute pulmonary injury: Role of complement, neutrophils, histamine, xanthine oxidase, and toxic oxygen species.
B. Experimental thermal injury: Role of complement, leukocytes, mast cells, xanthine oxidase, and oxygen radicals in the pathophysiology of edema formation and secondary organ injury.
C. Mechanisms of ischemia-reperfusion injury of the eye.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interviewed candidates for faculty positions.
B. Participation in undergraduate research program.

MEDICAL SCHOOL/HOSPITAL:

A. Interviewed candidates for faculty positions.
B. Consultant for clinical research programs.
C. Reviewer of intra-departmental grant proposals.

REGIONAL AND NATIONAL:

A. Reviewer for the following scientific journals: American Journal of Physiology, American Review of Respiratory Disease, FASEB Journal, Infection and Immunity, International Archives of Allergy and Applied Immunology, Journal of Applied Physiology, Journal of Laboratory and Clinical Medicine, Journal of Leukocyte Biology.

V. OTHER RELEVANT ACTIVITIES:

Member Editorial Advisory Board Immunobiology.

INVITED LECTURES/SEMINARS:

1. Invited Speaker, International Cartilage Project (ICP) Conference on "Understanding Osteoarthritis (OA) and the Anti-OA Effects of Diclofenac (Voltaren)". Ascot, Great Britain, November 4-7, 1990.
2. Invited Speaker, Teaching Conference on "Complement" at Division of Rheumatology, University of Michigan Medical School, 19 December 1990.
3. Invited Speaker, Second International Congress on "The Immune Consequences of Trauma, Shock and Sepsis - Mechanisms and Therapeutic Approaches". Munich, FRG, March 6-9, 1991.
4. Invited Speaker and Symposium Chair, Second International Conference on Shock, "Free Radical Scavengers in Experimental Shock and Trauma", Vienna, Austria, June 2-6, 1991

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Till, G.O., Friedl, H.P. and Ward, P.A.: Antioxidant treatment in experimental thermal injury. Adv. Exp. Med. Biol. 1990;264:543-550.
2. Thomson, P.D., Till, G.O., Paul, J., Woolliscroft, J.O., Prasad, J.K. and Smith, D.J.: Superoxide dismutase prevents lipid peroxidation in burn patients. Burns 1990;16:406-408.
3. Ward, P.A. and Till, G.O.: Pathophysiological events related to thermal injury of skin. J. Trauma 1990;30:S75-S79.
4. Friedl, H.P., Till, G.O., Smith, D.J., Thomson, P.D., Trentz, O. and Ward, P.A.: Zur Pathogenese Tourniquet-induzierter Ischämie-Reperfusionsschäden beim Menschen. Chirurg. Forum 1990;333-336.
5. Marak, G.E., Till, G.O. and Ward, P.A.: Xanthine oxidase generation of toxic oxygen metabolites in acute uveitis. Int. Ophthalmol. 1990;14:345-347.
6. Wilkins, E.G., Punch, J., Rees, R.S., Cashmer, B., Smith, D.J. and Till, G.O.: Evidence of xanthine oxidase activity in human free flaps following reperfusion. Surg. Forum 1990;41:672-675.
7. Friedl, H.P., Trentz, O., Toledo-Pereyra, L.H. and Till, G.O.: Zur Pathogenese von Reperfusionsschäden nach partieller Leberischämie mit internem Shunt. Hefte Unfallheilkunde 1990;212: 472-473.
8. Smith, D.J., Punch, J.D., Wilkins, E.G., Cashmer, B., Till, G.O. and Rees, R.S.: Xanthine oxidase: Its role in the no-reflow phenomenon. Surg. Forum 1990;41:519-521.
9. Friedl, H.P., Till, G.O., Trentz, O. and Ward, P.A.: Komplementsystem, Histamin und Xanthinoxidase als initiale Triggermechanismen des akuten Leberversagens. Hefte Unfallheilkunde 1990;212:475-476.
10. Wolter, J.R. and Till, G.O.: Granulocyte invasion related to detachment and degeneration of corneal endothelium in acute kerato-uveitis. Cornea 1990;9:347-353.

11. Thomson, P.D., Till, G.O., Moore, N.P., Prasad, J.K. and Smith, D.J.: Enhancement of humoral immunity by heterologous lipid peroxidation products from burn injury. J. Burn Care Rehabil. 1991;12:38-40.
12. Hatherill, J.R., Till, G.O. and Ward, P.A.: Mechanisms of oxidant-induced changes in erythrocytes. Agents Actions 1991;32:351-358.
13. Till, G.O., Friedl, H.P. and Ward, P.A.: Lung injury and complement activation: role of neutrophils and xanthine oxidase. Free Rad. Biol. Med. 1991;10:379-386.
14. Ward, P.A., Till, G.O. and Warren, J.S.: Pathophysiology of leukocyte-mediated tissue injury. J. Critical Care 1991;6:112-116.
15. Punch, J., Rees, R., Cashmer, B., Wilkins, E., Smith, D.J. and Till, G.O.: Xanthine oxidase: Its role in the no-reflow phenomenon. Surgery, In Press.
16. Rees, R., Punch, J., Wilkins, E., Cashmer, B., Till, G.O. and Smith, D.J.: Acute lung injury following hind limb ischemia-reperfusion in the rat. J Trauma, In Press.
17. Thomson, P.D., Till, G.O. and Smith, D.J.: Modulation of IgM antibody formation by lipid peroxidation products from burn plasma. Arch. Surg., In Press.
18. Till, G.O.: Startreaktionen des traumatischen Schocks: experimentelle Ergebnisse. Hefte Unfallheilkunde, In Press.
19. Friedl, H.P., Frank, J., Trentz, O.A., Bauch, U., Till, G.O. and Trentz, O.: Reperfusions-schaden durch toxische Sauerstoffradikale nach Tourniquet-induzierter Ischämie beim Menschen. Hefte Unfallheilkunde, In Press.
20. Winn, W.C., Davis, G.S., Durda, J.P. and Till, G.O.: The effect of neutropenia on experimental Legionella pneumonia. Infec. Immun., In Press.
21. Ward, P.A., Till, G.O., Gannon, D.E., Varani, J. and Johnson, K.J.: The role of iron in injury of endothelial cells in vitro and in vivo. Oxygen Rad. Biol. Med., In Press.
22. Yang, V.C., Port. F.K., Kim, J.-S., Teng, C.-L.C., Till, G.O. and Wakefield, T.W.: The use of immobilized protamine in removing heparin and and preventing protamine-induced complications during extracorporeal blood circulation. Anesthesiology, In Press.
23. Wakefield, T.W., Kirsh, M.M., Till, G.O., Brothers, T.E., Hantler, C.B. and Stanley, J.C.: Absence of complement-mediated events in cardiopulmonary bypass patients undergoing protamine reversal of heparin anticoagulation. Surgery, In Press.

BOOKS AND CHAPTERS IN BOOKS:

1. Ward, P.A., Friedl, H.P. and Till, G.O.: Role of oxygen radicals in experimental shock, in, Coran, A.G. and Harris, B.H. (eds.), Pediatric Trauma, Proceedings of the Third National Conference, J.B. Lippincott Co, Philadelphia, pp. 50-57, 1990.
2. Ward, P.A., Till, G.O. and Johnson, K.J.: Oxygen-derived free radicals and inflammation, in, Leadbetter, W.B., Buckwalter, J.A. and Gordon, S.L. (eds.), Sports-Induced Inflammation: Clinical and Basic Science Concepts, Chapter 18, pp. 315-324, American Academy Orthopaedic Surgery, Park Ridge, Illinois, 1990
3. Till, G.O., Friedl, H.P. and Ward, P.A.: Histamine-dependent modulation of oxygen radical production, in, Farr, C.H. (ed.), Proceedings of the Second International Conference of Bio-Oxidative Medicine, In Press.
4. Till, G.O. and Ward, P.A.: Complement-induced lung injury, in, Said, S.I. (ed.), The Pulmonary Circulation and Acute Lung Injury, 2nd Edition. Futura Publishing, Co., In Press.
5. Ward, P.A., Warren, J.S., Till, G.O., Varani, J. and Johnson, K.J.: Free radicals in lung disease. in, Rice-Evans, C. (ed.), Proceedings on Free Radicals, Diseased States and Anti-Radical Interventions, The Richelieu Press, London, In Press.
6. Morganroth M.L., Till, G.O. and Ward, P.A.: Pathophysiology of ischemia-reperfusion lung injury, in, Das, D.K. (ed.), Pathophysiology of Reperfusion Injury , CRC Press, Inc., In Press.
7. Till, G.O. and Ward, P.A.: Antioxidants in shock and ischemic injury, in, Perspectives in Shock Research: Progress in Clinical and Biological Research, In Press.

8. Till, G.O.,Varani, J., Phan, S.H. and Ward, P.A.: Oxygen radical-mediated endothelial cell injury, in, The Immune Consequences of Trauma, Shock and Sepsis. Springer Verlag, Heidelberg, In Press.
9. Till, G.O.: Oxygen radical-mediated thermal skin damage, in, Fuchs, J. and Packer, L. (eds.), Oxidative Stress in Dermatology, Marcel Dekker, Inc., New York, In Press.
10. Till, G.O.: Inflammation, in, Mortillaro, N.A. and Taylor, A.E. (eds.), The Pathophysiology of the Microcirculation, CRC Press, Inc., In Press.
11. Ward, P.A., Till, G.O., Gannon, D.E., Varani, J. and Johnson, K.J.: The role of iron in injury of endothelial cells in vitro and in vivo, in, Oxygen Radicals in Biology and Medicine, In Press.
12. Ward, P.A., Warren, J.S., Till, G.O., Varani, J. and Johnson, K.J.: Modification of disease by preventing free radical formation: A new concept in pharmacologic intervention, in, Clinical Hematology, Vol. 2, In Press.
13. Friedl, H.P., Till, G.O., Trentz, O. and Ward, P.A.: Role of oxygen radicals in tournoquet-related ischemia-reperfusion injury of human patients, Sringer Verlag, Heidelberg, In Press.
14. Friedl, H.P., Trentz, O., Till, G.O. and Ward, P.A.: Role of oxygen radicals in multiple organ failure, in, The Immune Consequences of Trauma, Shock and Sepsis. Springer Verlag, Heidelberg, In Press.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Thomson, P.D., Till, G.O. and Smith, D.J.: Enhancement of humoral immunity by products of lipid peroxidation in burn plasma. Proceedings Western Surgical Association, November 11-14, 1990.
2. Friedl, H.P., Till, G.O., Frank, J., Trentz, O.A., Ward, P.A. and Trentz, O.: Effect of diclofenac on in-vivo activation of plasma xanthine oxidase activity of human patients subjected to ischemia-reperfusion injury. Proceedings of the International Cartilage Project Conference, Ascot, Great Britain, November 4-7, 1990.
3. Till, G.O., Friedl,H.P., Paul, J.B. anf Ward, P.A.: Effect of diclofenac on rat xanthine oxidase activity. Proceedings of the International Cartilage Project Conference, Ascot, Great Britain, November 4-7, 1990.
4. Mahrougui, M., Till, G.O. and Ward, P.A.: Diverse signal transduction pathways in rat pulmonary artery endothelial cells. FASEB J. 1991;5:924A.
5. Till, G.O., Mahrougui, M. Elner, V.M., Marak, G.E. and Elner, S.G.: Inflammatory mediator-induced hydrogen peroxide production by retinal pigment epithelial cells. Invest. Ophthalmol. Vis. Sci. 1991;32:2541A.
6. Friedl, H.P., Till, G.O., Decurtins, M., Toledo-Pereyra, L.H. and Trentz, O.: Experimental ischemia-reperfusion injury of liver: role of xanthine oxidase. Proceedings of the XXth Annual Meeting of the European Histamine Research Society, Marburg, FRG, May 8-12, 1991.
7. Prasad, J.K., Oman, G.M., Till, G.O., Taddonio, T.E., Moore, N.P. and Thomson, P.D.: The role of lipid peroxidation products (conjugated dienes) in the modulation of polymorphonuclear leukocyte function. Proc. Amer. Burn Assoc. 1991;23:68.
8. Thomson, P.D., Till, G.O. and Smith, D.J.: Modulation of humoral immune function by homologous products of lipid peroxidation from burn plasma. Proc. Amer. Burn Assoc. 1991;23:72.
9. Till, G.O.: Oxygen radical-mediated cell injury. Abstracts, 2nd International Congress on the Immune Consequences of Trauma, Shock and Sepsis. Mechanisms and Therapeutic Approaches. PL7, Munich, March 6-9, 1991.
10. Till, G.O.: Antioxidant treatment of inflammatory tissue injury. Circ.Shock 1991;34:144.
11. Friedl, H.P., Frank, J., Trentz, O.A., Till, G.O., Ward, P.A. and Trentz, O.: Xanthine oxidase activity in a human model of ischemia reperfusion injury. Circ.Shock 1991;34:149.

JAMES VARANI, PH.D.
ASSOCIATE PROFESSOR OF MICROBIOLOGY AND IMMUNOLOGY
DEPARTMENT OF PATHOLOGY
UNIVERSITY OF MICHIGAN

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Lecturer, Pathology 580.
B. Lecturer, Pathology 581.
C. Course Director, Pathology 850.
D. Member, Dissertation committee of Mr. Todd Kroll
E. Member, Dissertation committee of Mr. Zwehi Soong.
F. Mentor for students who worked in my laboratory over the past year including four post-doctoral fellows, six undergraduate students, one graduate student and one high school student.
G. Mentor, Small group tutorials in Microbiology for medical students.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Monocyte Recognition of Target Cells", American Cancer Society IM-432.
B. Principal Investigator, "Biochemical Control of Microcarrier Culture", NIH CA33052.
C. Co-Investigator, "Thrombospondin Receptors on Squamous Carcinoma Cells", American Cancer Society PDT-324.
D. Co-Investigator, "Protease-Oxidant Interactions in Lung Inflammation", NIH HL42607.
E. Principal Investigator on Project 10, "Retinoic Acid and Cells of the Skin", Johnson and Johnson Corporation.

PROJECTS UNDER STUDY:

A. The development of substrates for optimum growth of cells in large-scale culture.
B. Mechanisms by which monocytes recognize and interact with the endothelium and with squamous epithelial cells.
C. The role of thrombospondin in the biology of human squamous carcinoma cells.
D. Influence of retinoic acid on proliferation and matrix production by dermal fibroblasts and epidermal keratinocytes.
E. Mechanisms of endothelial injury in lung inflammation and kidney inflammation.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Member, Departmental Advisory Committee on Appointments, Promotions and Tenure.
B. Member, Departmental Space and Research Committee.
C. Member, Department of Pathology Graduate Program Committee.
D. Member, Departmental Pathology Human Resource Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Member, University Committee on Use and Care of Animals.
B. Member, Jody C. Ungeleiter Award Selection Committee.
C. Chairman, Jody C. Ungeleiter Award Selection Committee.
D. Member, Medical School Committee on Summer Research Opportunities.
E. Program Director, University of Michigan Cancer Center Program on Tumor Cell Metastasis and the Extracellular Matrix.
F. Member, University of Michigan Cancer Center Basic Research Committee.
G. Member, Cancer Biology Research Training Grant Scientific Steering Committee.
H. Director, Pathology Research Seminar Series.

REGIONAL AND NATIONAL:

A. Editorial Board of Invasion and Metastasis.
B. Manuscript reviewer for: Cancer Research, Journal of the National Cancer Institute, International Journal of Cancer, American Journal of Pathology, Laboratory Investigation, Experimental Cell Research, Clinical and Experimental Metastasis, Invasion and Metastasis, Science, Proceedings of the National Academy of Sciences.
C. Grant reviewer for the Medical Research Council of Canada and for the Veterans Administration.
D. NIH Study Section Member: National Drug Development Cooperative Grants review panel.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, Department of Pathology, Wayne State University, October 17, 1990.
2. Invited Lecturer, Department of Pathology, University of Nebraska, November 13, 1990.
3. Invited participant, Symposium on Endothelial Cell injury, Medical College of Ohio, Toledo, Ohio, November 5-6, 1990.
4. Invited Lecturer, Symposium on Retinoids - Ten years of Research, Geneva, Switzerland, November 16-17, 1990.
5. Invited Lecturer, Department of Pathology, VAMC - Wayne State University, December 11, 1990.
6. Invited participant, UCLA Symposium on Oxygen Radicals, Big Sky, Montana, January 28 - February 4, 1991.
7. Invited Lecturer, FASEB Symposium on Oxygen Radicals and Ischemia, Atlanta, Georgia, April 24, 1991.
8. Invited Lecturer, Maine Cytometry Research Institute, Portland, Maine, May 20-21, 1991.
9. Invited Lecturer, Johnson and Johnson Symposium on Retinoids and Skin, Raritan, New Jersey, May 27-28, 1991.

PATENTS:

1. U.S. Patent No. 4,994,338. Collagen-coated Microcarrier Beads. Issued: February 19, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Sitrin, R.G., Gyetko, M.R., Kole, K.L., McKeever, P.E. and Varani, J.: Expression of heterogeneous profiles of plasminogen activators and plasminogen activator inhibitors by human glioma lines. Cancer Res. 1990;50:4957-4961.
2. Varani, J. and Chakrabarty, S.: Modulation of fibronectin synthesis and fibronectin binding during transformation and differentiation of mouse AKR fibroblasts. J. Cell Physiol. 1990;143:449-454.
3. Chakrabarty, S., Fan, D. and Varani, J.: Modulation of differentiation and proliferation in human colon carcinoma cells by transforming growth factor beta 1 and beta 2. Int. J. Cancer 1990;46:493-499.
4. Varani, J., Shayevitz, J., Perry, D., Mitra, R.S., Nickoloff, B.J. and Voorhees, J.J.: Retinoic acid stimulation of human dermal fibroblast proliferation is dependent on suboptimal extracellular Ca^{2+} concentration. Am. J. Path. 1990;136:1279-1281.
5. Schuger, L., Dixit, V.M., Carey, T.E. and Varani, J.: Modulation of squamous carcinoma cell growth, morphology, adhesiveness and extracellular matrix production by interferon-γ and tumor necrosis factor-α. Immunopathology. 1990;58:279-286.
6. Gannon, D.E., He, X., Ward, P.A., Varani, J. and Johnson, K.J.: Time-dependent inhibition of oxygen radical-induced lung injury. Inflammation. 1990;14:509-522.
7. Varani, J., Phan, S.H., Gibbs, D.F., Ryan, U.S. and Ward, P.A.: H_2O_2-mediated cytotoxicity of rat pulmonary endothelial cells: Changes in ATP and purine products and effects of protective interventions. Lab. Invest. 1990;63:683-689.
8. Schuger, L., O'Shea, S. and Varani, J.: Development of an organotypic model of embryonic lung morphogenesis: role of the basement membrane. Development 1990;110:1091-1099.
9. Markey, B.A., Phan, S.H., Varani, J., Ryan, U. and Ward, P.A.: Inhibition of H_2O_2 and neutrophil-induced cytotoxicity by intracellular superoxide dismutase supplementation. Free Rad. Biol. Med. 1990;9:307-314.
10. Chakrabarty, S., Jan, Y. and Varani, J.: Differentiation-related alterations in the plasma membranes of chemically-transformed murine fibroblasts. Cancer Res. 1990;10:1319-1328.
11. Varani, J., Gibbs, D.F., Inman, D.R., Shah, B., Fligiel, S.E.G. and Voorhees, J.J.: Inhibition of epithelial cell adhesion by retinoic acid: Relationship to reduced extracellular matrix production and alteration in Ca^{2+} levels. Am. J. Path. 1991;138:887-895.
12. Castle, V., Varani, J., Fligiel, S.E.G., Prochownik, E.V. and Dixit, V.M.: Antisense-mediated reduction in thrombospondin reverses the malignant phenotype of a human squamous carcinoma. J. Clin. Invest., In Press.
13. Shayevitz, J.R., Varani, J., Ward, P.A. and Knight, P.R.: Halothane and isoflurane increase pulmonary artery endothelial cell sensitivity to oxidant-mediated injury. Anesthesiology, In Press.
14. Varani, J., Ginsburg, I., Gibbs, D.F., Mukhopadhyay, P.S., Sulavik, C., Johnson, K.J., Weinberg, J.M., Ryan, U.S. and Ward, P.A.: Hydrogen-peroxide-induced cell and tissue injury: Protective effects of Mn^{2+}. Inflammation, In Press.
15. Schuger. L., Skubitz, A.P.N., O'Shea, K.S., Chang, J.F. and Varani, J.: Identification of laminin domains involved in branching morphogenesis: Effects of anti-laminin monoclonal antibodies on mouse embryonic lung development. Develop. Biol., In Press.

16. Varani, J., Stoolman, L., Wang, T.L., Schuger, L., Flippen C., Dame, M., Johnson, K.J., Todd, R.F., Ryan, U.S. and Ward, P.A.: Thrombospondin production and thrombospondin-mediated adhesion in U937 cells. Exp. Cell Res., In Press.
17. Rao, R.C., Varani, J. and Soong, H.K.: FGF promotes corneal stromal fibroblast motility. Invest. Ophthalmol., In Press.
18. Petryniak, J., Varani, J., Ervin, P.R. and Goldstein, I.J.: Differential expression of glycoproteins containing α-D-galactosyl groups on normal human breast epithelial cells and MCF-7 human breast carcinoma cells. Cancer Lett., In Press.
19. Yamamoto, T., Varani, J., Soong, H.K. and Lichter, P.R.: Effects of 5-fluorouracil and mitomycin-C on cultured rabbit subconjunctival fibroblasts. Ophthalmology., In Press.
20. Weinberg, J.M., Venkatachalam, M.A., Roeser, N.F., Davis, J.A., Varani, J. and Johnson, K.J.: Amino acid protection of cultured kidney tubule cells against calcium ionophore-induced lethal cell injury. Lab. Invest., In Press.
21. Weinberg, J.M, Varani, J., Johnson, K.J., Roeser, N.A., Dame, M.K., Davis, J.A. and Venkatachalma, M.A.: Protection of human umbilical vein endothelial cells by glycine and structurally similar amino acids against calcium and hydrogen peroxide-induced lethal cell injury. Am. J. Path., In Press.
22. Mulligan, M.S., Varani, J., Dame, M.K., Lane, C.L., Smith, C.W., Anderson, D.C. and Ward, P.A.: Role of ELAM-1 in neutrophil-mediated lung injury in rats. J. Clin. Invest., In Press.
23. Varani, J., Inman, D.R., Gibbs, D.F., Fligiel, S.E.G. and Voorhees, J.J.: Modulation of Ca^{2+} levels in keratinocytes by all-trans retinoic acid. Immunopathology., In Press.
24. Varani, J., Gendimenico, G.J., Shah, B., Gibbs, D.F., Capetola, R.J., Mezick, J.A. and Voorhees, J.J.: A direct comparison of the pharmacologic effects of retinoids on skin cells in vitro and in vivo. Skin. Pharmacol., In Press.
25. Fligiel, S.E.G., Inman, D.R., Talwar, H.S., Fisher, G.J., Voorhees, J.J. and Varani, J.: Modulation of growth in normal and malignant melanocytic cells by all-trans retinoic acid. J. Cutan. Pathol., In Press.
26. Varani, J., Jones, J., Dame, M.K., Sulavik, C., Gibbs, D.F. and Johnson, K.J.: Effects of all-trans retinoic acid on neutrophil-mediated endothelial cell injury and immune complex injury in rats. Am. J. Path., In Press.
27. Varani, J., Astrom, A., Griffiths, C.E.M. and Voorhees, J.J.: Induction of proliferation of growth-inhibited keratinocytes and fibroblasts by sodium lauryl sulfate: Comparison with all-trans retinoic acid. J. Invest. Dermatol., In Press.

BOOKS AND CHAPTERS IN BOOKS:

1. Ward, P.A. and Varani, J.: Mechanisms of neutrophil-mediated killing of endothelial cells. J. Leuk. Biol. 48:97-102, 1990.
2. Ward, P.A., Warren, J.S., Till, G.O., Varani, J. and Johnson, K.J.: Free radicals in lung disease, in, Rice-Evans, C. (ed.)., Free Radicals, Disease States and Anti-Radical Interventions. London, England, pp. 57-77. 1989.
3. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: Cytokines, Toxic oxygen products and cell injury. Molecular Aspects of Medicine., In Press.
4. Varani, J.: Leukocyte-endothelial cell interactions, in, Catravas, J. and Ryan, U. (eds.), Vascular Endothelium: Physiological Basis of Clinical Problems., In Press.
5. Varani, J.: Extracellular matrix production and squamous cell differentiation, in, Weiss, L., Buchanan, M. and Orr, F.W. (eds.), The Microcirculation and Cancer Metastasis, CRC Press Inc., In Press).
6. Ward, P.A., Warren, J.S., Johnson, K.J. and Varani, J.: Inflammation, oxygen radicals and tissue injury, in, Oxidative Damage and Repair: Clinical, Biological and Medical Aspects, In Press.
7. Nickoloff, B.J., Varani, J. and Mitra, R.S.: Modulation of keratinocyte biology by gamma interferon: Relevance to cutaneous wound healing, in, Clinical and Experimental Approaches to Dermal and Epidermal Repair: Normal and Chronic Wounds., Wiley-Liss, Inc. pp. 141-154, 1991.

8 Varani, J., Fligiel, S.E.G. and Voorhees, J.J.: All-transretinoic acid modulation of proliferation and adhesion in epithelial cells and fibroblasts is associated with alterations in extracellular matrix production and Ca^{2+} metabolism, in, Retinoids J. H. Saurat (ed.)., Karger, Basel, Switzerland, In Press.

9. Varani, J. and Johnson, K.J.: Modulation of endothelial cell injury by cell-trans retinoic acid (RA): Role in anti-inflammatory effects of RA, in, Jesaitis (ed.), Molecular Basis of Oxidative Damage by Leukocytes, CRC Press, In Press.

10. Johnson, K.J., Varani, J. and Smolen, J.E.: Neutrophil activation and function in health and disease, in, Coffey, R.D. (ed.), Granulocyte Response to Cytokines: Basic and Clinical Research, Marcell Dekker, Inc., N.Y., In Press.

11. Varani, J. and Ward, P.A.: Neutrophil-endothelial interactions, in, Maini, R.N. and Zvaifler, N.J. (eds.), Rheumatology, Gower Medical Publishing, London, In Press.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Schuger, L., Skubitz, A.P.N., O'Shea. L.S. and Varani. J.: Identification of laminin domains involved in epithelial branching morphogenesis: effects of anti-laminin monoclonal antibodies on mouse embryonic lung morphogenesis. J. Cell Biol. 1990;111:400a.

2. Mitra, R., Schuger, L., Chang, J.F. and Kunkel, S.: Expression of TNFα in mouse placenta. FASEB.J. 1991;5:A1621.

3. Johnson, K.J., Jones, J., Dame, M.K., Gibbs, D.F. and Varani, J.: In vitro modulation of the acute inflammatory response by all-trans retinoic acid. J. Cell Biochem. 1991;(Suppl. 15c):220.

4. Varani, J., Gibbs, D.F., Mukhopadhyay, P.S., Sulavik, C., Johnson, K.J., Weinberg, J.M., Ginsburg, I. and Ward, P.A.: Hydrogen peroxide-induced cell and tissue injury: Protective effects of manganese. J. Cell Biochem. 1991;(Suppl. 15c):223.

5. Shayevitz, J.R., Williams, B. and Varani, J.: Halothane modulation of endothelial cell Ca^{2+} exchange. FASEB J. 1991;5.

6. Johnson, K.J., Sulavik, C., Gibbs, D. and Varani, J.: In vivo suppression of immune complex injury by all-trans retinoic acid. FASEB J. 1991;15.

7. Inman, D.R., Fligiel, S.E.G. and Varani, J.: Retinoic acid (RA) inhibits proliferation but not differentiation in human melanocytic cells. FASEB J. 1991;5.

8. Varani, J., Ginsburg, I., Johnson, K.J., Gibbs, D.F., Weinberg, J.M. and Ward, P.A. Amino acids and metal ions protect endothelial cells from lethal injury. FASEB J. 1991;5.

9. Dame, M.K., Varani, J., Weinberg, J.M. and Ward, P.A.: Neutrophil killing of human umbilical vein endothelial cells is oxygen radical-mediated and enhanced by TNFα. FASEB J. 1991;5.

10. Varani, J., Gibbs, D.F., Dame, M.K. and Voorhees, J.J.: Stimulation of proliferation and inhibition of adhesion in keratinocytes by retinoic acid is associated with a decrease in intracellular and total Ca^{2+}. J. Invest. Dermatol. 1991;96:581.

PETER A WARD, M.D.
PROFESSOR AND CHAIRMAN
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. These have been chiefly related to administrative responsibility for all clinical service functions of the Department.
B. Autopsy Service.

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Blair A.Walker, M.D. , Postdoctoral Fellow.
      b. Michael S. Mulligan, M.D., Postdoctoral Fellow.
      c. Cheryl Swenson, D.V.M., Ph.D. Postdoctoral Fellow
      d. Hedwig Murphy, M.D., Postdoctoral Fellow
      e. Jonathon W. Homeister, Ph.D. Dissertation Committee member.
      f. Mary C. Mancini, M.D., Medical College of Ohio, Dissertation Committee member.
      g. Susan A. Moore, M.S., Dissertation Committee member.
   2. Indirect supervision of four Research Scientists.
   3. Gross Autopsy Conference, 25 hours.

B. Undergraduate students:
   a. Lawrence E. Stern, research mentor for Honors Project.
   b. Lecture, ICS 600, two hours.
   c. Two hour lecture to Alpha Omega Alpha members, April, 1990.
   d. Lecture, College Honors Seminar 250, February, 1991.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Thermal Injury, Complement, and Leukocyte Dysfunction", NIH GM-28499 (10%), $111,434/year ($577,063/five years), 1/1/86-12/31/91.
B. Principal Investigator, "Lung Immunopathology", NHLBI HL-07517 (5%), $286,684/year ($1,291,531/five years), 7/1/86-5/31/91.
C. Principal Investigator, "Leukocyte Chemotaxis", NIH HL-28442 (10%), $88,449/year ($505,936/five years), 7/1/86-6/30/91.
D. Principal Investigator, "Lung Injury Produced by Oxygen Metabolites", NIH GM-29507 (20%), $120,486/year ($507,078/five years), 7/1/82-6/30/92.
E. Principal Investigator, "Inflammatory Cells and Lung Injury", NHLBI HL-31963 (35%), $628,780/year ($3,876,003/five years), 3/1/84-2/28/94.

F. Co-Investigator, "Mechanisms of Glomerular and Tubular Injury", NIH-DK39255 (5%), $39,398 (Project V only), 9/1/87-8/31/92.
G. Principal Investigator, "Lung Immunopathology", NHLBI-HL07517 (5%), $287,958 ($1,444,250/five years), 6/1/91-5/31/96.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chief, Section of General Pathology.
B. MSP Executive Committee.
C. Pathology Associates.

MEDICAL SCHOOL/HOSPITAL:

A. Ambulatory Care Strategic Planning Steering Committee, The University Hospitals, 1991--
B. Advisory Committee for the Howard Hughes Medical Institute, 1984--
C. Board of Directors, M-Care, 1986--
D. Center Advisory Committee for The University of Michigan Multipurpose Arthritis Center, 1987---
E. Clinical Quality Improvement Lead Team, 1991--
F. Committee to Review VA FTE's, The University of Michigan Medical School, October, 1988--
G. Dean's Advisory Council, 1985--
H. Dean's Council of Clinical Chairmen, 1985-1990
I. Executive Advisory Committee for Gene Expression and Gene Transfer in the Cardiovascular System, August, 1991--
J. Executive Director's Advisory Council, 1988--
K. Feasibility Study for Multifloor Medical Research Facility Attached to Medical Science II Committee, Director
L. Geriatric Center Steering Committee, 1990--
M. Guilford Upjohn Endowed Chair in Internal Medicine and Oncology, Department of Internal Medicine, Hematology and Oncology Unit, the Universit of Michigan, 1987--
N. Hospital Advisory Group, 1988-91
O. Internal Medicine Advisory Committee for the University of Michigan George M. O'Brien Renal and Urologic Center, 1991--
P. Medical Sciences Research Building (MSRB) Task Force, Chairman
Q. Medical Science Research Building III Project, September, 1990--
R. Medical Service Plan Advisory Committee, 1987--
S. Medical Service Plan Executive Committee, 1987-91
T. Michigan Diabetes Research and Training Center Policy Committee, 1981--
U. Michigan Eye Bank Research Review Committee, 1980--
V. National Task Force on Organ Transplantation, 1985--
W. Pathology Associates, 1980--
X. Presidential Initiatives Fund, The University of Michigan, March, 1987--
Y. University of Michigan Geriatrics Center Steering Committee, 1990--
Z. University of Michigan Medical School Executive Committee, September 1, 1990--

REGIONAL AND NATIONAL:

A. American Association for Advancement of Science.
B. American Association of Immunologists.
C. American Association of Pathologists.
    1. Nominating Committee, 1985-present.

2. Executive Committee, Intersociety Pathology Council and Universities Associated for Research and Education in Pathology, Inc.
3. Representative to the Universities Associated for Research and Education in Pathology, 1988-89.
4. Steering Committee for the Federal Demonstration Project, 1990--.
5. Future Directions Committee, 1989--.

D. American Board of Pathology, effective January 1, 1988..
1. Trustee, 1980--
2. Immunoathology Test Committee, 1980-85, 1988- Vice-Chairman
3. Anatomic Pathology Examination Committee, 1988--
4. By-Laws Committee, 1988--
5. Examination Evaluation Committee, 1988--
6. Professional Qualification/Competence Committee, 1988--
7. ABP/ABPRF Research Committee, 1989--
8. Residency Review Committee for Pathology

E. American Federation for Clinical Research
F. American Heart Association, Cardiopulmonary Division.
G. America Lung Association.
H. American Society for Clinical Investigation.
I. American Pathology Foundation.
J. American Thoracic Society.
K. Association of American Physicians.
L. Association of Pathology Chairmen.
M. Center for Alternatives to Animal Testing, Johns Hopkins University.
N. Cytogen, 1983--.
O. A. James French Society of Pathologists, 1988--.
P. Health Policy Agenda for the Amerian People, Advisory Committee.
Q. Institute of Medicine, July 1, 1990
R. International Academy of Pathology.
1. Council Member, April 1, 1986-1989.
2. Member, Finance Committee, April 1, 1986-1990.
3. Vice-President, 1990.
4. President-Elect, 1991.

S. Mallinckrodt, Inc., Advisory Board, 1984--.
T. Michigan Society of Pathologists.
U. Michigan Thoracic Society, 1988--.
V. The New York Academy of Sciences.
1. Committee on Human Rights, Correspondent.

W. The Oxygen Society, 1988--
X. Phi Rho Sigma, President, The University of Michigan Chapter, September, 1988
Y. Society of Medical Consultants to the Armed Forces.
1. President, 1988

Z. Universities Associated for Research and Education in Pathology, Inc., Board of Directors.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. American Journal of Pathology, Editorial Board, 1982--.
B. American Review of Respiratory Diseases, Consulting Editor, 1977--.
C. Archives of Pathology and Laboratory Medicine, Reviewer, 1973--.

D. Arthritis and Rheumatism, Consulting Editor, 1975--.
E. Cancer Research, Associate Editor, 1987--.
F. Clinical Immunology and Immunopathology, Consulting Editor, 1977--.
G. CRC Critical Reviews in Free Radical Research, Advisory Board, 1986--.
H. CRC Critical Reviews in Toxicology, Advisory Board, 1986--.
I. Experimental Cell Research, Consulting Editor, 1980--.
J. Experimental Lung Research, Consulting Editor, 1980--.
K. Human Pathology, Consulting Editor, 1980--.
L. Infection and Immunity, Editorial Board, 1978--.
M. Journal of Clinical Investigation, 1982--.
N. Journal of Experimental Cell Research, Consulting Editor.
O. Journal of Experimental Lung Research, Consulting Editor.
P. Journal of Experimental Pathology, 1986--.
Q. Journal of the Reticuloendothelial Society, Consulting Editor.
R. Journal of Clinical Investigation, Consulting Editor.
S. Laboratory Investigation, Editorial Board, 1981--.
T. Nature, Consulting Editor, 1980--.
U. New England Journal of Medicine, Consulting Editor, 1980--.
V. Journal of Critical Care, Editorial Board.
W. Review Committee for new Editor-in-Chief, Human Pathology, April 1987--.
X. Toxicologic Pathology, Editorial Board, 1988--.

INVITED LECTURES/SEMINARS:

1. Moderator, Workshop 5, "The Resident as an Investigator", Aspen Lung Conference, Resident Training, Recruitment, Curriculum, Certification, and Accreditation, Aspen, Colorado, July 25-29, 1990.
2. Invited Lecturer, Second Year Medical Students, "Immunologic Lung Disease" and "Cytokines and Endothelial Cell Injury", Hahnemann Medical College, Philadelphia, Pennsylvania, October 5, 1990
3. Invited Lecturer, "Mediator Interactions with Endothelial Cells", Chicago Lung Association, Chicago, Illinois, October 18, 1990.
4. Invited Lecturer, "Damage of Endothelial Cells by Toxic Oxygen Products of Neutrophils", Medical Forum, "Oxidants and Antioxidants: Pathophysiological Determinants and Therapeutic Agents", sponsored by the Zambon Group, Don Carlos Hotel, Marbella, Spain, October 26-27, 1990.
5. Invited State-of-the-Art Lecturer, "Role in Lung Injury of Products of Neutrophils, Macrophages and Endothelial Cells", to the Second Annual Midwest American Federation for Clinical Research at the Drake Hotel, Chicago, Illinois, November 1, 1990.
6. Review Committee Member, Pathology Site Visit at Case Western Reserve University, Cleveland, Ohio, November 11-12, 1990.
7. Invited Lecturer, "Oxygen Products and Tissue Damage", at the Fifth Biennial Meeting on Oxidative Damage and Repair, Pasadena, California, September 17-19, 1990.
8. Invited Lecturer, "Amplification and Control of Tissue by Leukocyte Oxidant Production", Keystone Symposia on Molecular and Cellular Biology, Big Sky, Montana, January 31st thru February 3, 1991.
9. Invited Speaker, Monsanto Company Seminar Series, "Role of Adhesion Molecules in Acute Inflammation", and "ARDS and Antioxidant Strategies", Monsanto Company, St. Louis, Missouri, February 18-20, 1991
10. Invited Lecturer, "Complement, Cytokines and Tissue Injury" and "Role of ELAM in Inflammation In Vivo", and Co-Chair session, "Cell Adhesion Molecules", at the 2nd International Congress on The Immune Consequences of Trauma, Shock and Sepsis, Munich, Germany, March 4th through 10th, 1991.
11. Participant, External Advisory Committee, New Mexico Cancer Research and Treatment Center, Albuquerque, New Mexico, March 27-29, 1991.
12. Invited Participant, Joint Committee on Health Policy, sponsored by the Association of American Universities, at the Park Hyatt Hotel, Washington, D.C., April 16, 1991.
13. Participant, Advisory Board for "HIV - Alveólar Macrophage Program Project Grant" for Richard M. Rose, M.D., Deaconess Hospital, Boston, Massachusetts, April 17, 1991.

14. Chair Session, "Oxygen Toxicity in Reperfusion Injury", at the FASEB Meetings, Atlanta, Georgia, April 22, 1991.
15. Chair Satellite Symposium, "RJR Pulmonary Research Scholars", at the FASEB Meetings, Atlanta, Georgia, April 22, 1991.
16. Cochair Symposium, "Complement Proteins and Complement Receptors in Immunopathology", with H.J. Muller-Eberhard, at the FASEB Meeting, Atlanta, Georgia, April 24, 1991.
17. Invited Lecturer, "Oxygen Radicals in Acute Lung Injury", sponsored by the Department of General Surgery, the University of Ulm, at the Reisenberg Castle in Ulm, Germany, April 24-27, 1991.
18. Invited Lecturer, "Complement Activation and Lung Injury - Protection by sCRI", in the conference, New Advances in the Treatment of Endotoxemia and Sepsis, held at the Ritz-Carlton, Philadelphia, Pennsylvania, May 6, 1991.
19. Invited Lecturer, "Acute Reversible and Irreversible Response to Injury in the Lung", NHLBI/NIEHS Workshop on Environmental Lung Disease, held at the Holiday Inn Crown Plaza, Rockville, Maryland, May 29, 1991.
20. Invited Lecturer, "Upregulation of ELAM-1 *In Vivo* and its Functional Consequences", in the session entitled Endothelial Cell Modulation of Vascular Smooth Muscle, at the International Society for Heart Research Meeting, Cincinnati, Ohio, May 30, 1991.
21. Invited Lecturer, "Antioxidants and Deferoxine", in Session VII, Prevention of and Interventions for Ischemia-Reperfusion Injury", in the Conference, Biology of Lung Preservation for Transplantation, sponsored by the National Institutes of Health, Bethesda, Maryland, June 11, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Friedl, H.P., Smith, D.J., Thomson, P.D., Louis, D.S., Till, G.O. and Ward, P.A.: Histamine and xanthine oxidase activity in a human model of ischemia-reperfusion injury. Surg. Forum 1989;15:587-589.
2. Friedl, H.P., Till, G.O., Ward, P.A. and Trentz, O.: Role of xanthine oxidase in microvacular damage following thermal injury of skin. Chirurgisches Forum 1989;59-62.
3. Ginsburg, I., Ward, P.A. and Varani, J.: Lysophosphatides enchance superoxide responses of stimulated human neutrophils. Inflamm. 1989;13:163-174.
4. Marks, R.M., Todd, R.F., III and Ward, P.A.: Rapid induction of neutrophil-endothelial adhesion by endothelial complement fixation. Nature 1989;339:314-317.
5. Phan, S.H., Gannon, D.E., Varani, J., Ryan, U.S. and Ward, P.A.: Xanthine oxidase activity in rat pulmonary artery endothelial cells and its alteration by activated neutrophils. Amer. J. Pathol. 1989;134:1201-1211.
6. Shuger, L., Varni, J., Marks, R.M., Kunkel, S.L., Johnson, K.J. and Ward, P.A.: Cytotoxicity of tumor necrosis factor-α for human umbilical vein endothelial cells. Lab. Invest. 1989;61:62-68.
7. Strieter, R.M., Kunkel, S.L., Showell, H.J., Remick, D.G., Phan, S.H., Ward, P.A. and Marks, R.M.: Endothelial cell gene expression of a neutrophil chemotactic factor by TNF-α, LPS, and IL-1b. Science 1989;243:1467-1469.
8. Sullivan, J.L., Till, G.O. Ward, P.A. and Newton, R.B.: Nutritional iron resticiton diminishes acute complement-dependent lung injury. Nutrition Res. 1989;9:625-634.
9. Till, G.O., Friedl, H.P., Ward, P.A. and Trentz, O.: Role of complement in xanthine oxidase-mediated thermal injury of skin. Chirurgisches Forum 1989;55-58.
10. Ward, P.A., Cunningham, T.W. and Johnson, K.J.: Signal transduction events in stimulated rat neutrophils: Effects of adenine nucleotides. Clin. Immunol. Immunopathol. (Elmer Becker Symposium) 1989;50:30-41.
11. Warren, J.S., Kunkel, R.G., Simon, R.H., Johnson, K.J. and Ward, P.A.: Ultrastructural cytochemical analysis of oxygen radical-mediated immunoglobulin A immune complex induced lung injury in the rat. Lab. Invest. 1989;60:651-658.

12. Friedl, H.P., Till, G.O., Smith, D.J., Thomson, P.D., Trentz, O. and Ward, P.A.: Zur pathogenese touriquet-induzierter ischamie-reperfusionsschaden beim menschen. Chirurg. Forum 1990;333-336.
13. Guice, K.S., Oldham, K.T., Caty, M.G., Johnson, K.J. and Ward, P.A.: Neutrophil-dependent oxygen radical mediated lung injury associated with acute pancreatitis. Ann. Surg. 1990;210:740-747.
14. Guice, K.S., Oldham, K.T., Johnson, K.J. and Ward, P.A.: Mechanisms of capillary endothelial cell injury in acute pancreatitis. Ann. Surg. 1990;210:740-747.
15. Hagenlocker, B.E., Walker, B.A.M. and Ward, P.A.: Superoxide responses of immune complex-stimulated rat alveolar macrophages: Intracellular calcium and priming. J. Immunol. 1990;144:3898-3906.
16. Marak, G.E., Jr., Till, G.O. and Ward, P.A.: Xanthine oxidase generation of toxic oxygen metabolites in acute uveitis. Int. Ophthalmology 1990;14:345-347.
17. Markey, B.A., Phan, S.H., Varani, J., Ryan, U.S. and Ward, P.A.: Inhibition of cytotoxicity by intracellular superoxide dismutase supplementation. Free Rad. Biol. Med. 1990;9:307-314.
18. Morganroth, M.L., Schoeneich, S.O., Till, G.O., Ward, P.A., Horvath, S.J. and Glovsky, M.M.: $C3a_{57-77}$, a C-terminal peptide, causes thromboxane-dependent pulmonary vascular constriction in isolated perfused rat lungs. Amer. Rev. Resp. Dis. 1990;141:296-300.
19. Riva, C.M., Morganroth, M.L., Ljungman, A.G., Schoeneich, S.O., Marks, R.M., Todd, R.F., III, Ward, P.A. and Boxer, L.A.: Iloprost inhibits neutrophil-induced lung injury and neutrophil adherence to endothelial monolayers. Amer. J. Resp. Cell Molec. Biol. 1990;3:301-309.
20. Shlafer, M., Brosamer, K., Forder, J.R., Simon, R.H., Ward, P.A. and Grum, C.M. Cerium chloride as a histochemical marker of hydrogen peroxide in reperfused ischemic hearts. J. Mol. Cell Cardiol. 1990;22:83-97.
21. Till, G.O., Friedl, H.P. and Ward, P.A.: Antioxidant treatment in experimental thermal injury. Adv. Exp. Med. Biol. 1990;264:543-550.
22. Varani, J., Phan, S.H., Gibbs, D.F., Ryan, U.S. and Ward, P.A.: H_2O_2-Mediated cytotoxicity of rat pulmonary endothelial cells: Changes in ATP and purine products and effects of protective interventions. Lab. Invest. 1990;63:683-689.
23. Walker, B.A.M., Hagenlocker, B.E., Douglas, V.K. and Ward, P.A.: Effects of adenosine on inositol 1,4,5-triphosphate formation and intracellular calcium changes in Formyl-Met-Leu-Phe-stimulated human neutrophils. J. Leukocyte Biol. 1990;48:281-283.
24. Ward, P.A. and Till, G.O.: Pathophysiological Events Related to Thermal Injury of Skin. J. Trauma 1990;30:S75-S79.
25. Ward, P.A., Walker, B.A.M. and Hagenlocker, B.E.: Functional consequences of interactions between human neutrophils and ATP, ATPγS, and adenosine. Ann. N.Y. Acad. Sci. 1990;603:108-119.
26. Ward, P.A. and Varani, J.: Review: Mechanisms of neutrophil-mediated killing of endothelial cells. J. Leukocyte Biol. 1990;48:97-102.
27. Warren, J.S., Johnson, K.J. and Ward, P.A.: PAF and immune complex-induced injury. J. Lipid Mediators. 1990;2:S229-S237.
28. Warren, J.S., Yaboroff, K.R., Mandel, D.M., Johnson, K.J. and Ward, P.A.: Role of $O_2^{-\cdot}$ in neutrophil recruitment into sites of dermal and pulmonary vasculitis. Free Rad. Biol, Med. 1990;8:163-172.
29. Yu, G.H. and Ward, P.A.: Structural requirements for binding of adenosine-5'0-(3-thiotriphosphate) (ATPγS) to human neutrophils. Immunopharmacol. 1990;20:175-182.
30. Barker, J.N.W.N., Jones, M.L., Swenson, C.L., Sarma, V., Mitra, R.S., Ward, P.A., Johnson, K.J., Fantone, J.C., Dixit, V.M. and Nickoloff, B.J.: Monocyte chemotaxis and activating factor production by keratinocytes in response to IFN-γ. J. Immunol. 1991;146:1192-1197.
31. Hatherill, J.R., Till, G.O. and Ward, P.A.: Mechanisms of oxidant-induced changes in erythrocytes. Agents and Actions 1991:32;351-358.
32. Mulligan, M.S., Hevel, J.M., Marletta, M.A. and Ward, P.A.: Tissue injury caused by deposition of immune complexes is L-argenine dependent. Proc. Natl. Acad. Sci. 1991;88:6338-6342.
33. Shayevitz, J.R., Varani, J., Ward, P.A. and Knight, P.R.: Halothane and isoflurane increase pulmonary artery endothelial cell sensitivity to oxidant-mediated injury. Anest. 1991;74:1067-1077.
34. Till, G.O., Friedl, H.P. and Ward, P.A.: Lung injury and complement activation: Role of neutrophils and xanthine oxidase. Free Rad.Biol.Med. 1991;10:379-386..

35. Varani, J., Ginsburg, I., Gibbs, D.F., Mukhopadhyay, P.S., Sulavik, C., Johnson, K.J., Weinberg, J.M., Ryan, U.S. and Ward, P.A.: Hydrogen peroxide-induced cell and tissue injury: Protective effects of Mn^{2+}. Inflammation 1991;15:291-301.
36. Varani, J., Stoolman, L., Wang, T., Schuger, L., Flippen, C., Dame, M., Johnson, K.J., Todd, R.F., III, Ryan, U.S. and Ward, P.A.: Thrombospondin production and thrombospondin-mediated adhesion in U937 cells. Exp. Cell Res. Exp. Cell Res. 1991;195:177-182.
37. Walker, B.A.M., Hagenlocker, B.E., Douglas, V.K., Tarapchak, S.J. and Ward, P.A.: Nucleotide responses of human neutrophils. Lab. Invest. 1991;64:105-112.
38. Walker, B.A.M., Hagenlocker, B.E., Stubbs, E.B., Jr., Sandborg, R.R., Agranoff, B.W. and Ward, P.A.: Signal transduction events and FcγR engagement in human neutrophils stimulated with immune complexes. Journal of Immunology 1991;146:735-741.
39. Walker, B.A.M., Hagenlocker, B.E. and Ward, P.A.: Superoxide responses to formyl-methionyl-leucyl-phenylalanine in primed neutrophils: Role of intracellular and extracellular calcium. J. Immunol. 1991;146:3124-3131.
40. Ward, P.A., Till, G.O. and Warren, J.S.: Pathophysiology of leukocyte-mediated tissue injury. J. Crit. Care 1991;6:112-116.
41. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: PAF, cytokines, toxic oxygen products and cell injury. Molec. Aspects Med. 1991;12:169-174.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Gannon, D.E., He, X., Ward, P.A., Varani, J. and Johnson, K.J.: Time-dependent inhibition of oxygen radical-induced lung injury. Inflammation, In Press.
2. Morganroth, M.L., Schoeneich, S.O., Till, G.O., Pickett, W. and Ward, P.A.: Complement and neutrophil-mediated injury of perfused rat lungs. Lab. Invest., In Press.
3. Mulligan, M.S., Varani, J., Dame, M.K., Lane, C.L., Smith, C.W., Anderson, D.C. and Ward, P.A.: Role of ELAM-1 in neutrophil-mediated lung injury in rats. J. Clin. Invest., In Press.
4. Oldham, K.T., Guice, K.S., Till, G.O. and Ward, P.A.: Evidence of local complement activation in cutaneous thermal injury in rats. Adv. Shock. Res., In Press.
5. Rao, N.A., Sevanian, A., Faure, J.-P., Kozak, Y., Ward, P.A., Till, G.O. and Marak, G.E.: The participation of reactive oxygen metabolites in the pathogenesis of experimental allergic uveitis. Invest. Ophthalmol. Vis. Sci., In Press.
6. Till, G.O., Friedl, H.P. and Ward, P.A.: Role for histamine and xanthine oxidase in complement- and oxidant-mediated acute lung injury. Free Rad. Biol. Med., In Press.
7. Till, G.O. and Ward, P.A.: Immunologic and phagocytic cell defects in thermally injured patients. J. Crit. Care Med., In Press.
8. Varani, J., Ginsburg, I., Johnson, K.J., Gibbs, D.F., Weinberg, J.M. and Ward, P.A.: Amino acids and metal ions protect endothelial cells from lethal injury. FASEB J., In Press.
9. Walker, B.A.M., Seiler, A.J., Becker, C.A., Hagenlocker, B.E. and Ward, P.A.: Absence of FMLP receptors on rat macrophages. Submitted to the Journal of Leukocyte Biology.
10. Ward, P.A.: The wound environment - Local and systemic perturbations: Inflammation and the burn wound. J. Burn Care & Rehab. In Press.
11. Ward, P.A.: Free radicals and lung injury: Implications for therapy. Proceedings of the International Conference on Oxygen Free Radicals in Health and Disease, In Press.
12. Ward, P.A. and Johnson, K.J.: Lung inflammatory mechanisms. J. Human Path., In Press.
13. Ward, P.A., Johnson, K.J. and Till, G.O.: Mechanisms of lung injury. Prax. Klin. Pneumonol., In Press.
14. Yu, G.H., Tarapchak, Walker, B.A.M. and Ward, P.A.: Adenosine-5'-0-(3-thiotriphosphate) (ATPSγS) binding to human neutrophils: Evidence for a common nucleotide receptor. Lab. Invest., In Press.

BOOKS/CHAPTERS IN BOOKS:

1. Till, G.O., Friedl, H.P. and Ward, P.A.: Antioxidant treatment in experi mental thermal injury, Emerit, I., Packer, L. and Auclair (eds), in, Antioxidants in Therapy and Preventive Medicine, Plenum Press, New York, New York, pp. 543-549, 1990.

2. Till, G.O., Friedl, H.P. and Ward, P.A.: Mechanisms of phagocytic cell-mediated injury and its relationship to ischemic injury, in, Zelenock, G.B., D'Alecy, L.G., Fantone, III, J.C., Shlafer, M. and Stanley, J.C.(eds, Clinical Ischemic Syndromes: Mechanisms and Consequences of Tissue Injury, Chapter 19, Mosby Co., St. Louis, pp. 327-345, 1990.
3. Ward, P.A., Morganorth, M.L., Senior, R.M., and Campbell, E.J.: Inflammatory mediators of pulmonary tissue injury, Chapter 13, in, Bray, M. and Anderson, W. (eds.), Mediators of Pulmonary Inflammation, Chapter in series, Lung Biology in Health and Disease, pp. 533-591, 1991.
4. Ward, P.A., Till, G.O. and Johnson, K.J.: Oxygen-derived free radicals and inflammation. Chapter 18, in, Leadbetter, W.B., Buckwalter, J.A. and Gordon, S.L. (eds), Sports-Induced Inflammation: Clinical and Basic Science Concepts, American Orthopaedic Society for Sports Medicine Symposium presented in Bethesda, Maryland, May, 1989, American Academy of Orthopaedic Surgeons, pp. 315-324, 1990.
5. Ward, P.A., Walker, B.A.M. and Hagenlocker, B.E.: Functional consequences of interactions between human neutrophils and ATP, ATPγS, and adenosine, Dubyak, G.R. and Fedan, J.S. (eds), Biological Actions of Extracellular ATP, Annals of the New York Academy of Sciences, New York, New York, pp. 108-119, 1990.
6. Ward, P.A. and Warren, J.S.: Neutrophils, macrophages and cytokines, in, Pozzi, E. (ed), International Symposium on Pathophysiology of Pulmonary Cells, Proceedings of the Symposium, Turin, Italy, Masson, Milano, pp. 31-36, 1990.
7. Warren, J.S., Johnson, K.J. and Ward, P.A.: 7.2.4 Consequences of oxidant injury, Crystal, R.G., West, J.B., Barnes, P.J., Cherniack, N.S. and Weibel, E.R. (eds), The Lung: Scientific Foundations, Raven Press, New York, pp. 1829-1838, 1991.
8. Warren, J.S., Johnson, K.J. and Ward, P.A.: 7.5.2 Immunoglobulin and complement mediated immune injury, Crystal, R.G., West, J.B., Barnes, P.J., Cherniack, N.S. and Weibel, E.R. (eds), The Lung: Scientific Foundations, Raven Press, New York, pp. 1939-1946, 1991.
9. Warren, J.S., Ward, P.A. and Johnson, K.J.: The inflammatory response, in, Williams, W.J. (ed), Hematology, 4th Edition, McGraw-Hill, New York, New York, pp. 63-70, 1990.
10. Ward, P.A. and Warren, J.S.: Neutrophils, macrophages and cytokines, in, Baggiolini, M., Pozzi, E., and Semenzato, G. (eds), Neutrophils, Lymphocytes and Lung, Meetings on "Pathophysiology of Pulmonary cells", Turin, Italy, February 16-17, 1990, Masson, Milan, Italy, pp. 31-36, 1991.
11. Ward, P.A.: Flow cytometric analysis of the immune and phagocytic cells, in Newcombe, D.S., Rose, N.R. and Bloom, J.C. (eds), Clinical Immunotoxicology, Raven Press, New York, 1992.
12. Warren, J.S., Johnson, K.J. and Ward, P.A.: Consequences of oxidant injury, in, Crystal, R.G. and West, J.B. (eds), The Lung: Scientific Foundations, Raven Press, New York, New York, pp. 1829-1838, 1991.
13. Warren, J.S., Johnson, K.J. and Ward, P.A.: 7.5.2 Immunoglobulin and complement mediated immune injury, in, Crystal, R.G. and West, J.B. (eds), The Lung, Scientific Foundations, Raven Press, New York, New York, pp. 1939-1946, 1991.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Craig, R.A., Walker, B.A.M., Hagenlocker, B.E. and Ward, P.A.: FMLP-induced superoxide responses in PAF primed human neutrophils in the absence of increased intracellular Ca^{2+}. FASEB J. 1991:5;A587.
2. Dame, M.K., Varani, J., Weinberg, J.M. and Ward, P.A.: Neutrophil killing of human umbilical vein endothelial cells is oxygen radical-mediated and enhanced by TNF–α. FASEB J. 1991:5;A888.
3. Jones, M.L., Grande, J.P., Killen, P.D., Yoshimura, T. and Ward, P.A.: Regulation of monocyte chemoattractant protein (MCP-1) mRNA expression in rat mesangial cells. FASEB J. 1991:5;A975.
4. Jones, M.L., Ward, P.A. and Warren, J.S.: Cloning of rat MCP1 and its expression in a baculovirus system. Third International Workshop on Cytokines Meeting from November 10 to 14, 1991, in Stressa, Italy.100.
5 Mahrougui, M., Till, G.O. and Ward, P.A.: Diverse signal-transduction pathways in rat pulmonary artery endothelial cells. FASEB J. 1991:5;A530.
6. Murphy, H.S., Shayman, J.A. and Ward, P.A.: Signal transduction in endothelial cells stimulated by C5a. FASEB J. 1991:5;A1340.

7. Owens, C.A., Grande, J.P., Yu, G.H., Killen, P.D. and Ward, P.A.: Adenine nucleotide binding to cultured human mesangial cells. FASEB J. 1991:5;A909.
8. Varani, J., Gibbs, D.F., Mukhopadhyay, P.S., Sulavik, C., Johnson, K.J., Weinberg, J.M., Ginsburg, I. and Ward, P.A.: Hydrogen peroxide-induced cell and tissue injury: Protective effects of manganese. J. Cell Biochem. 1991;Suppl. 15c:223.
9. Varani, J., Ginsburg, I., Johnson, K.J., Gibbs, D.F., Weinberg, J.M. and Ward, P.A.: Amino acids and metal ions protect endothelial cells from lethal injury. FASEB J. 1991:5;A887.
10. Walker, B.A.M., Owens, C.A. and Ward, P.A.: Absence of FMLP receptors in rat macrophages. FASEB J. 1991:5;A549.

JEFFREY S. WARREN, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Director, Clinical Immunopathology Laboratory.
B. Autopsy pathology, staff coverage (one weekend).
C. Diplomate, Immunopathology subspecialty certification; August, 1990.

II. TEACHING ACTIVITIES:

A. Pathology 631 (60 contact hours).
B. ICS 600
   "Autoimmunity" (10/18/90).
   "Multiple Myeloma" (1/18/91).
C. Clinical Pathology Grand Rounds:
   "Complement I" (11/23/90).
   "Complement II" (11/30/90).
   "Antinuclear antibody testing" (12/07/90).
D. Immunopathology journal club (one hour; biweekly).
E. Immunopathology signout: Pathology residents, M-4 medical students, EMU medical technology students (daily; every other week).
F. Supervision of research activities for:
   1. Michael L. Jones, Ph.D. candidate - postdoctoral fellow; (4/1/89-present).
   2. Craig Flory, Ph.D. - postdoctoral fellow; (6/15/90 - present).
   3. Peter A. Barton (M-2 medical student); (6/1/90 - 8/25/91) (sponsored by American Heart Association of Michigan summer fellowship).
   4. James Baker (M-2 medical student); (6/1/91 - 7/31/91) (sponsored by J.C. Fantone III, M.D.).

III. RESEARCH ACTIVITIES:

A. Role of cytokines (tumor necrosis factor, interleukin 1) in immune complex lung injury.
B. Platelet-activating factor in immune complex alveolitis.
C. Homozygous C5 deficiency in pathogenesis of endotoxic shock.
D. Cloning and expression of rat monocyte chemoattractant protein 1 (MCP1) in a baculovirus system.

SPONSORED SUPPORT:

A. Principal Investigator, NIH (R29 - HL40526), (50% effort), "Monocyte-Macrophage Cytokines in Immune Complex Lung Injury": 4/1/89 - 3/31/94 ($350,000; direct costs).

B. Principal Investigator, American Heart Association of Michigan Grant-in-Aid, (10% effort), "Platelet-Activating Factor in Immune Alveolitis": 7/1/89 - 6/30/91 ($44,400; direct costs).
C. Biomedical Research Support Grant; (5% effort), "Homozygous C5 Deficiency in the Endotoxin-Triggered Shock Response": 5/1/91 - 7/1/92 ($8,000) (pilot study).
D. Principal Investigator, American Heart Association of Michigan Grant-in-Aid, (10% effort), "Activated endothelium influences monocyte function": 7/1/91-6/30/92 ($25,500; direct costs).
E. NIH(RO1) "Monocyte Chemoattractant Protein 1 in Pulmonary Granulomatosis": (Submitted 6/30/91).

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

A. Medical School Admissions Committee.

DEPARTMENTAL:

A. Member search committee for biochemistry section director.
B. Interviewer, graduate pathology program applicants.
C. Interviewer, pathology residency applicants.

REGIONAL AND NATIONAL:

A. Ad hoc referee for following journals: American Journal of Pathology; Laboratory Investigation; Journal of Applied Physiology; Blood; Journal of Leukocyte Biology; Pediatric Research; Chest; American Review of Respiratory Disease; American Journal of Respiratory Cell and Molecular Biology; Journal of Pharmacology and Experimental Therapeutics; Lung; Human Pathology; Journal of Laboratory and Clinical Medicine; Circulation; Ophthalmology; Clinical Immunology and Immunopathology; Circulation Research.
B. Preparation of immunopathology subspecialty board exam questions.

V. INVITED LECTURES/SEMINARS:

1. Warren, J.S.: Oxygen radicals and cytokine mediators of inflammation, ASCP Pathology Update 1990, Chicago, Illinois, September 12, 1990 (Postgraduate course).

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Warren, J.S., Johnson, K.J. and Ward, P.A.: PAF and immune complex induced injury. J. Lipid Mediators 1990;2:S229-S237.
2. Warren, J.S., Barton, P.A., Mandel, D.M. and Matrosic, K.: Intrapulmonary tumor necrosis factor triggers local platelet-activating factor production in rat immune complex alveolitis. Lab. Invest. 1990;63:746-754.

3. Portz, D.M., Elkins, T.E., White, R., Warren, J.S., Adaevah, S. and Randolph, J: Oxygen free radicals and pelvic adhesion formation: I. Blocking oxygen free radical toxicity to prevent adhesion formation in an endometriosis model. Int. J. Fertil. 1991;26:39-42.
4. Warren, J.S., Barton, P.A. and Jones, M.L.: Contrasting roles for tumor necrosis factor in the pathogenesis of IgA and IgG immune complex lung injury. Am. J. Pathol. 1991;138:581-590.
5. Warren, J.S.: Intrapulmonary interleukin 1 mediates acute immune complex alveolitis in the rat. Biochem. Biophys. Res. Commun. 1991;175:604-610.
6. Barker, J.N.W.N., Jones, M.L., Mitra, R.S., Crockett-Torabe, E., Fantone, J.C., Kunkel, S.L., Warren, J.S., Dixit, V.M. and Nickoloff, B.J.: Modulation of keratinocyte-derived interleukin-8 which is chemotactic for neutrophils and T lymphocytes. Am. J. Pathol., In Press.
7. Warren, J.S. and Barton, P.A.: In vitro analysis of pulmonary inflammation using rat lung organ cultures. Exp. Lung. Res., In Press.

SUBMITTED FOR PUBLICATION:

1. Mulligan, M.S., Varani, J., Warren, J.S., Till, G.O., Smith, C.W., Anderson, D.C., Todd, R.F. and Ward, P.A.: Roles of rat β2 integrins of neutrophils in complement-and oxygen radical-mediated acute inflammatory reactions. Submitted for publication.
2. Jacobs, J.C., McNeeley, S.G., Elkins, T.E., Warren, J.S. and Hoeft-Loyer, C.M.: Rabbit model for polymicrobial upper genital infections. Submitted for publication.
3. Warren, J.S.: Disparate roles for TNF in the pathogenesis of acute immune complex alveolitis and dermal vasculitis. Submitted for publication.
4. Jones, M.L., Grande, J.P., Killen, P.D., Yoshimura, T., Ward, P.A. and Warren, J.S.: Regulation of monocyte chemoattractant protein-1 mRNA expression in rat mesangial cells. Submitted for publication.
5. O'Donnell, L.R., Kaminski, M.S. and Warren, J.S.: Factitious paraproteinemia in a patient receiving monoclonal antibody therapy. Submitted for publication.
6. Mulligan, M.S., Warren, J.S. Smith, C.W., Anderson, D.C and Ward, P.A.: Mediation of lung injury following deposition of IgA immune complexes. Submitted for publication.
7. DeForge, L.E., Kenney, J.S., Jones, M.L., Warren, J.S. and Remick, D.G.: Biphasic production of IL-8 in LPS-stimulated human whole blood: Separation of LPS-cytokine-stimulated components using anti-TNF and anti-IL-1 antibodies. Submitted for publication.
8. Jones, M.L. and Warren, J.S.: Monocyte chemoattractant protein 1 in a rat model of pulmonary granulomatosis. Submitted for publication.
9. Warren, J.S.: Complementary roles for interleukin 1β and platelet-activating factor in the pathogenesis of acute immune complex alveolitis in the rat. Submitted for publication.
10. Elkins, T.E., Warren, J.S., Portz, D. and McNeeley, S.G.: The interaction of peritoneal macrophages and current adhesion-preventing solutions in the production of oxygen free radicals and the early inflammatory response. Submitted for publication.

BOOKS/CHAPTERS IN BOOKS:

1. Keren, D.F. and Warren, J.S.: Diagnostic Immunology: Laboratory Diagnosis of Immunologic Diseases, Williams and Wilkins, Baltimore, Maryland, In Press.
2. Warren, J.S., Ward, P.A. Johnson, J.K.: The inflammatory response, in, Williams, W.J. (ed.), Hematology, 4th Edition, McGraw-Hill, New York, New York, pp. 63-70, 1990.
3. Warren, J.S., Johnson, K.J. and Ward, P.A.: Immunoglobulin and complement mediated immune injury, in, Crystal, R.G. and West, J.B. (eds.), The Lung: Scientific Foundations, Raven Press, New York, New York, pp. 1939-1946, 1991.
4. Warren, J.S., Johnson, K.J. and Ward, P.A.: Consequences of oxidant injury, in, Crystal, R.G. and West, J.B., (eds.), The Lung: Scientific Foundations, Raven Press, New York, New York, pp. 1829-1838, 1991.

5. Ward, P.A., Warren, J.S., Till, G.O., Varani, J. and Johnson, K.J.: Free radicals in lung disease, in, Rice-Evans, C. (ed.), Free Radicals, Diseased Stated and Anti-Radical Interventions, Proceedings of the Special Colloquium, London, England, In Press.
6. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: PAF, cytokines, toxic oxygen products and cell injury, in, Molecular Aspects of Medicine, Proceedings of the VIIth Annual Inflammation Meeting, Birmingham, United Kingdom, Pergammon Press, In Press.
7. Ward, P.A. and Warren, J.S.: Neutrophils, macrophages, and cytokines, in, Pozzi, E., (ed.), International Symposium on Pathophysiology of Pulmonary Cells, Proceedings of the Symposium, Turin, Italy, Masson, Milano, pp. 31-36, 1990.
8. Warren, J.S.: Role of cytokines in experimental lung injury, in, Remick, D.G. and Kunkel, S.L. (eds.) Cytokines in Health and Disease, Marcel Dekker, Inc., New York, New York, In Press.
9. Ward, P.A., Warren, J.S., Johnson, K.J. and Varani, J.: Inflammation; oxygen radicals and tissue injury, in, Oxidative Damage and Repair: Clinical, Biological and Medical Aspects, Proceedings of the 5th Biennial Meeting of the International Society for Free Radical Research. Pasadena, California, Pergammon Press, In Press.
10. Ward, P.A., Mulligan, M.S. and Warren, J.S.: Neutrophils, cytokines, oxygen radicals and lung injury. The Immune Consequences of Trauma, Shock and Sepsis - Mechanisms and Therapeutic Approaches, Proceedings of the Symposium. Munich, Germany, Springer-Verlag, In Press.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFERRED JOURNALS:

1. Ward, P.A., Till, G.O. and Warren, J.S.: Pathophysiology of leukocyte-mediated tissue injury. J. Crit. Care 1991;6:1-5.
2. Warren, J.S.: Cytokine mediators of inflammation. Clin, Immunol. Newsl., In Press.
3. Warren, J.S., Barton, P.A., Mandel, D.M. and Matrosic, K.: Intrapulmonary tumor necrosis factor triggers endogenous platelet-activating factor in acute immune complex alveolitis. American Heart Association of Michigan, Lansing, Michigan, September 11, 1990 (abstract).
4. Jones, M.L., Grande, J.P., Killen, P.D., Yoshimura, T., Ward, P.A. and Warren, J.S.: Regulation of monocyte chemoattractant protein (MCP-1) mRNA expression in rat mesangial cells. FASEB, 1991.
5. Barton, P.A. and Warren, J.S.: In vitro analysis of pulmonary inflammatory processes using rat lung organ cultures. FASEB, 1991 (minisymposium).
6. Warren, J.S., Jones, M.L. and Yoshimura, T.: Monocyte chemotactic activity in a rat model of pulmonary granulomatosis. FASEB, 1991 (minisymposium).

LEE WEATHERBEE, M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Chief, Laboratory Service, Veterans Administration Medical Center, Ann Arbor, Michigan and Vetrans Administration Outpatient Clinic, Toledo, Ohio.
B. Consultant for referred bone pathology cases at University of Michigan.
C. Surgical pathology, Veterans Administration Medical Center.
D. Autopsy pathology, Veterans Administration Medical Center.
E. Cytopathology - occasional coverage Veterans Administration Medical Center.

II. TEACHING ACTIVITIES:

A. House officers - VA Medical Center surgical and autopsy pathology.
B. Clinicopathologic conference - monthly, Veterans Administration Medical Center.
C. Veterans Administration Medical Center Tumor Board - weekly.
D. Dental Student lectures (three) in bone pathology.
E. Medical student lectures (two) in bone pathology.
F. Medical student - second year pathology laboratory.
G. Medical student - fourth year rotation at the Veterans Administration Medical Center.
H. Gross pathology seminar for house officers at University of Michigan.

III. RESEARCH ACTIVITIES:

COOPERATIVE STUDIES: Ongoing: With Environmental Epidemiology Service, Department of Veterans Affairs, Agent Orange and non-Hodgkin's lymphoma.

SPONSORED SUPPORT: None.

IV. ADMINISTRATIVE ACTIVITIES:

LOCAL:

A. Overall responsibility for Veterans Administration Medical Center Laboratory Service and for Laboratory at Veterans Administration Outpatient Clinic, Toledo, Ohio.
B. Executive Faculty, The University of Michigan Medical School.
C. Admissions Committee, The University of Michigan Medical School.
D. Clinical Executive Board, Veterans Administration Medical Center.
E. Dean's Committee, Veterans Administration representative.
F. Quality Assurance Board, Veterans Administration Medical Center.
G. Professional Standards Board, Veterans Administration Medical Center.
H. Radiation Safety Committee, Veterans Administration Medical Center.
I. Search Committee for Veterans Administration Medical Center; Chief, Psychiatry.

J. Resident Selection Committee, University of Michigan Department of Pathology.

REGIONAL AND NATIONAL:

A. Red Cross Medical Advisory Board, Southeastern Michigan Region.

V. OTHER RELEVANT ACTIVITIES:

A. Inspector for College of American Pathologists Inspection and Accreditation Program.
B. Deputy Medical Examiner, Washtenaw County.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Dalager, N., Kang, H., Bunt, V. and Weatherbee, L.: Non-Hodgkin's lymphoma among Vietnam veterans. J. Occupat. Med. 1991;33:7.

BERNARD WEISS, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES: None.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Tutor, Microbiology small group session.
B. Supervised research of medical student (Vernon Stevenson) and two postdoctoral fellows (Jie Wu and Linghua Wang).
C. Student Seminar Evaluation Committee, Cellular and Molecular Biology Training Program.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. American Cancer Society, Mutants for DNA Enzymes, NP770-S.
B. National Science Foundation, Prevention and Repair of DNA Damage in Bacteria, DMB-8922562.

PROJECTS UNDER STUDY:

A. The consequences of replacing thymine with uracil in DNA.
B. A gene of *Escherichia coli* affecting DNA and pantothenate biosynthesis.
C. A superoxide response regulon of *Escherichia coli.*

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Co-director, Graduate Training Program in Pathology.

REGIONAL AND NATIONAL:

A. Ad hoc grant reviewer for National Science Foundation and National Institutes of Health.
B. Referee for the following journals:
   1. Nucleic Acids Research.
   2. Journal of Biological Chemistry.
   3. Journal of Bacteriology.
   4. Molecular and General Genetitcs.
   5. Molecular Microbiology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECURES/SEMINARS:

1. International Society for Free Radical Research, Symposium on Oxidative Damage and Repair, Pasadena.
2. University of New Mexico Medical School, Department of Cell Biology.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PURLICATION IN REFEREED JOURNALS:

1. Tsaneva, I.R. and Weiss, B.: *soxR*, a locus governing a superoxide reponse regulon in *Escherichia coli* K-12. J. Bacteriol. 1990;172:4197-4205.
2. Wu, J. and Weiss, B.: Two divergently transcribed genes, *soxR* and *soxS*, control a superoxide response regulon of *Escherichia coli*. J. Bacteriol. 1991;173:2864-2871.

BOOKS/CHAPTERS IN BOOKS:

1. Weiss, B., Tsaneva, I.R. and Wu, J..: A superoxide response regulon in *Escherichia coli*. UCLA Symp. Mol. Cell Biol. New Ser. 1990;136:287-295.
2. Weiss, B. and Wu, J.: Control of a superoxide response regulon of *Escherichia coli*, in, Davies, K.J.A. (ed.), Oxidative Damage & Repair: Clinical, Biological, and Medical Aspects, Pergamon, New York, 1991, In Press,

SHARON W. WEISS, M.D.
PROFESSOR OF PATHOLOGY
DIRECTOR OF ANATOMIC PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Service - four months.
B. Consultant for Bone and Soft Tissue - 12 months.
C. Secondary Consultant for Breast Pathology - 12 months.
D. Necropsy Service - one week.
E. M-Labs Surgical Pathology Service - as needed.

II. TEACHING ACTIVITIES

A. Sophomore Medical Class:
Pathology 600 - lecture - two contact hours.
B. House Officers:
1. Training in Surgical Pathology.
2. Lectures, - three hours.
C. Hospital Conferences:
1. Sarcoma Conference - monthly.
D. Graduate Student:
Responsible for training of Dr. Mark Smith, Imperial Cancer Research Fund, London England - 7/90-11/90; Dr. Patricia Perosio, 1/91-6/91; Dr. John Geiss, University of California San Francisco.

III. RESEARCH ACTIVITIES

SPONSORED SUPPORT:

A. Southwest Oncology Group, SWOG study 9055 ($3,197).

PROJECTS UNDER STUDY:

A. Dedifferentiation in low grade liposarcoma.
B. Epithelioid malignant Schwannoma.
C. Angiomatosis.
D. Prognostic factors in retroperitoneal sarcoma.
F. Sarcoma amplified sequence in sarcomas.
G. Tumor necrosis factor in neoplasms.

IV. SERVICE ACTIVITIES

DEPARTMENTAL:

A. Director, Division of Anatomic Pathology, Surgical Pathology.
B. Member, Chairman's Advisory Committee.
C. Member, Photography Committee.
D. Member, Program Committee, Residency Training Program.
E. Director, Surgical Pathology Fellowship Program.
F. Member, Tissue and Invasive Procedures Committee.

REGIONAL AND NATIONAL

A. Chairman, WHO Committee for Classification of Soft Tissue Tumors.
B. US-Canadian Academy of Pathology:
   1. Councillor
   2. Benjamin Castleman Award Committee.
   3. International Vice President - North American Division.
C. American Society of Clinical Pathology:
   1. Anatomic Pathology Council.
D. Association of Directors of Anatomic Pathology:
   1. Program Chairman.
   2. Executive Council.
E. Chairman, Sarcoma Pathology Subcommittee, Southwest Oncology Group.
F. Editorial Board, American Journal of Surgical Pathology.
G. Editorial Board, American Journal of Dermatopathology.
H. Editorial Board, American Journal of Clinical Pathology.
I. Editorial Borad, Human Pathology.
J. Editorial Board, Seminars Diagnostic Pathology.
K. Editorial Board, Journal of the National Cancer Institute.
L. Editorial Board, AFIP Fascicles (3rd Series).
M. Consultant in Pathology, National Institutes of Health.
N. Member, Michigan Society of Pathologists.
O. Member, Arthur Purdy Stout Society of Surgical Pathologists.

V. INVITED LECTURES

1. 23rd Annual Meeting of Japanese Orthopaedic Association Musculoskeletal Tumor Society, Osaka, Japan, July 1990.
2. "Diagnostic Pathology '90", sponsored by the United States and Canadian Academy of Pathology, Inc., Ann Arbor, Michigan, August, 1990.
3. Speaker, International Skeletal Society, Salzburg, Austria, September, 1990.
4. "Diagnostic Problems in Surgical Pathology," American Society of Clinical Pathologists, Dallas, Texas, October, 1990.
5. Moderator, Annual Program Meeting, Association of Directors of Anatomic Pathology, Chicago, Illinois, October, 1990.
6. Speaker, Rhabdomyosarcoma Study Group, Columbus, Ohio, December, 1990.
7. Speaker, California Society of Pathologists, San Francisco, California, December, 1990.
8. Speaker, Michigan Society of Pathologists, Ann Arbor, Michigan, December, 1990.
9. Speaker, Detroit Society of Pathologists, February, 1991.
10. Speaker, Detroit Pathology Residents, William Beaumont Hospital, Royal Oak, Michigan, February, 1991.
11. Faculty, Surgical Pathology Specialty Conference, US-CAP, Chicago, Illinois, March, 1991.

12. Moderator, Bone and Soft Tissue Specialty Conference, US-CAP, Chicago, Illinois, March, 1991.
13. Speaker, Annual Meeting, Arthur Purdy Stout Society of Surgical Pathologists, Chicago, Illinois, March, 1991.
14. Speaker, Arizona Society of Pathologists, Tucson, Arizona, April, 1991.
15. Visiting Professor, Eleanor Humphrey Memorial Lecture, University of Chicago, Chicago, Ilinois, April, 1991.
16. Speaker, French Society of Pathologists, University of Paris, Paris, France, May, 1991.
17. Speaker, Department of Pathology, Wayne State Medical School, Detroit, Michigan, May, 1991.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Kao, G.F., Laskin, W.B. and Weiss, S.W.: Eccrine spiradenoma occurring in infancy: mimicking mesenchymal tumor. J. Cut. Pathol. 1990;17:214-219.
2. Luthringer, D.J., Virmani, R., Weiss, S.W. and Rosai, J.: A distinctive cardiovascular lesion resembling histiocytoid hemangioma: Report of 11 cases. Amer. J. Surg. Pathol. 1990;14:993-1000.
3. Costa, M.J. and Weiss, S.W.: Angiomatoid malignant fibrous histiocytoma: A long-term follow-up study of 108 cases with evaluation of histologic predictors of outcome. Amer. J. Surg. Pathol. 1990;14:1126-1132.
4. Fetsch, J.F. and Weiss, S.W.: Observations concerning the pathogenesis of epithelioid hemangioma. Mod. Pathol., In Press.
5. Laskin, W.B. and Weiss, S.W. and Bratthauer, G.L.: Epithelioid varant of peripheral nerve sheath tumor (malignant epithelioid schwannoma). Amer. J. Surg. Pathol., In Press.
6. Becker, R.L., Venzon, Lack, E., Mikel, U., Weiss, S.W. and O'Leary, T.O.: Flow cytometry and morphometry of malignant fibrous of the extremities: Prognostic prediction for recurrence and survival. Amer. J. Surg. Pathol., In Press.
7. Smith, M.E.F., Costa, J. and Weiss, S.W.: Evaluation of CD68 and other histiocytic antigens in angiomatoid malignant fibrous histiocytoma. Amer. J. Surg. Pathol., In Press.

BOOKS AND CHAPTERS IN BOOKS

1. Laskin, W.B. and Weiss, S.W.: Benign fibrous lesions of upper limb, in, Bogumull, G.P. and Fleegerl, E.S. (ed.), Tumors of the Hand and Upper Limb, Churchill Livingstone, London, In Press.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS

1. Budd, G.T., Metch, B., Weiss, S.W., Stephens, R., Fabian, C. and Balcerzak, S.: Ifosfamide (IFl) + cisplatin in the treatment of metastatic soft tissue sarcoma (STS) ASCD: 1990;9:316(#1222).
2. Enzinger, F.M., Weiss, S.W. and Liang, C.Y.: Author's Reply. Amer. J. Surg. Pathol. 1990;14:1169.
3. Weiss, S.W. and Rao, V.K.: Well-differentiated liposarcoma of deep soft tissue: A follow-up study of 95 cases with analysis of the incidence of dedifferentiation. Lab. Invest. Mod. Pathol. 1990;4:9A(#44).
4. Weiss, S.W.: Contemporary issues in the diagnosis nomenclature, and behavior of lipomatous tumors. Jap. J. Orthop. Surg. (Abstract), July, 1990.

SECTION REPORTS

DIVISION OF ANATOMIC PATHOLOGY

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1990 - 30 JUNE 1991

This academic year witnessed the completion of our series of faculty recruitments. Dr. Suzanne Selvaggi joined our ranks as the new Co-Director of the Cytology Service, bringing us additional expertise in gynecologic pathology, while Dr. Elizabeth del Buono will join the surgical pathology staff in the coming academic year sharing with us her interest in liver pathology and diagnostic molecular biology. Dr. Robert Schmidt officially concludes his active academic appointment but will assume a role as Emeritus Professor.

Our educational activities within the division have flourished and acquired added dimensions. In its first year, the surgical pathology fellowship program was an unqualified success. Drs. Elizabeth Del Buono and David Graham performed in a superlative fashion strengthening both the resident and faculty support for this fledgling program. We look forward to the second year with Drs. Randall Shannon, Steven Mandell, and Dr. Lawrence Zukerberg from the Massachusetts General Hospital. Dr. Denise Sulavik served with distinction as the cytopathology fellow and will be followed this coming year by Dr. Paul Mazzara. Our division hosted the Third Annual Diagnostic Pathology course for the US-CAP during the month of August. Our residents freely availed themselves of this week long course which earned excellent reviews from the participants not only for its content but also for the opportunity it provided for the registrants to tour our facilities. Dr. Robert Scully, Professor of Pathology of the Massachusetts General Hospital, accepted our invitation to be the Second Annual Residents' Visiting Professor delivering a lecture on Serous Borderline Tumors of the Ovary and a slide seminar. In addition, Drs. Kamal Ishak (Armed Forces Institute of Pathology) and Robert Kurman (Johns Hopkins Hospital) shared their expertise with us in their respective areas of liver and gynecologic pathology.

The anatomic pathology laboratories, now under the capable direction of Ms. Ada Tillman following the retirement of Elizabeth Binns, faced new and difficult challenges in responding to budgetary cuts. Although it is inevitable that we will lose some of our flexibility in responding to emergent requests for stat biopsy procedures, we view this as an opportunity to critically and creatively evaluate our entire operation and to devise ways to improve our efficiency. Toward this end we initiated a System Analysis Review which identified a need for changes in our accessioning process, handling of personal consultations, and retrieval and tracking of slides. Although these issues will be addressed over the coming year a series of changes were initiated in January which should improve the efficiency of all of the laboratories. These included deletion of microscopic descriptions in surgical pathology reports on a routine basis, centralization of staining procedures in the histopathology laboratory, utilization of computer-generated slide labels, training sessions for staff and housestaff in accessioning procedures, decrease in the number and stains performed on a routine basis for special procedures (e.g., endomyocardial biopsies), a QA/QC tracking system to ensure timely completion of cases, and integration of personal consultations into our network database. The success of these efforts was acknowledged by the overall excellent performance of our laboratories during the recent CAP inspection.

Our diagnostic sophistication has improved over the past year with the addition of molecular biological techniques to our diagnostic armamentarium. Identification of selected infectious agents (CMV, atypical mycobacteria) represent our initial accomplishments attributable largely to the efforts of Dr. Tom Frank. We look to an expansion of these activities as well as a close working relationship with our Flow Cytometry and Cytogenetic Laboratories.

Although budgetary issues have of necessity consumed a great deal of our time this year, our division is equally concerned about ensuring the viability of academic pathology. Toward that end we all remain committed to the nurturing and education of medical students, housestaff, and junior faculty.

Sharon W. Weiss, M.D.
Director, Anatomic Pathology

AUTOPSY SERVICE

DEPARTMENT OF PATHOLOGY
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The Autopsy Service of the Department of Pathology continues its service function of performing autopsies on University of Michigan patients, as well as the Medical Examiner cases for Washtenaw County.

I. Alzheimer's Disease:

A. The University of Michigan. In order to provide the highest quality tissue for researchers of the Alzheimer's Disease Research Center (ADRC), the Department of Pathology has established an on-call system to harvest brains between the hours of 8 PM and 4 AM. The ADRC coordinator makes the arrangements to bring the body to the morgue and the Pathology on-call house officer performs an *in situ* inspection and removes the brain with the assistance of the on-call dieners. The ADRC is paying the costs of this program, which was instituted on March 1, 1991.

B. State of Michigan. Working closely with the Dementia Subcommittee of the Michigan Department of Public Health, a state-wide program has been initiated to make brain-only autopsies available to the people of the State of Michigan. The neuropathologists at The University of Michigan, Michigan State University, Oakland County Medical Examiner's Office, and William Beaumont Hospital are participating in the program. Under this program, a person with documented dementia will make prior arrangements with a local pathologist for removal of the brain; the local pathologist will then send the entire brain to a neuropathologist for diagnosis. Important components of the program are:

1. An adequate premortem neurological assessment must have been made, in order to correlate the histologic findings with the clinical information.
2. Prior arrangements must have been made with a funeral director and local pathologists.
3. The program is available to anyone who wishes to participate, but the funeral director, local pathologist, and neuropathologist must all be paid by the family. State funding for the program is essentially non-existent.

II. Medical Examiner Cases:

Difficulty with medical examiner's cases continues. We have worked closely with the Michigan Association of Medical Examiners (MAME) to establish a working solution to the problem that arises when injury occurs in one county and death occurs in another county. A compromise has been reached which has the support of both The University of Michigan and MAME. Legislation is presently being written that will be jointly sponsored by Representative Kirk Profit, and the State legislator from the Grand Haven area, the district which previously opposed us. The bill will permit us to charge the county of injury for the cost of the autopsy if death occurs within 24 hours after arrival in the county of death. This legislation will be introduced in the Fall of 1991, and we do not anticipate any difficulty with its passage.

III. Future plans for the Autopsy Service:

At the recent CAP inspection, the Autopsy Service was again cited for: i.) failure to complete autopsy reports in a timely manner, and, ii:) lack of a system to code and retrieve diagnoses. Both of these issues are being addressed vigorously. A carefully analysis is being performed to determine the cause of the delay in obtaining brain reports, since this remains the single slowest component of the service. Pathology Data Systems is working to develop a module to transfer data; hopefully this system will be operational in the near future.

Total University of Michigan Autopsies	385
M-Labs Cases	11
Medical Examiner Cases	60
In-Hospital Cases	18
Outside Cases	42
Percent of University of Michigan Autopsies (includes Teratology cases)	45%
Number of Faculty Participating on the Autopsy Service	21

Daniel G. Remick, M.D.
Director, Autopsy Service

CYTOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
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The laboratory began the year in difficult circumstances: a severely depleted technical staff resulting in an unprecedented backlog of unexamined specimens. Because of the nation-wide shortage of cytotechnologists, it was not easy to extricate ourselves from this situation. It required an inordinate amount of overtime by our technical staff as well as sending specimens to outside laboratories to get them read and reported. Gradually, our technical staff have been replaced, and we are now up to full complement.

The outside laboratory that supplied 50% of our annual total of 40,000 gynecologic specimens recently stopped sending specimens to our laboratory. These specimens imposed a large burden on the laboratory, not only because of their number but also because of the administrative and logistical disadvantages we labored under with a distant client. Furthermore, for the two years we had been receiving these extra 20,000 specimens we had dealt with them without any increase in technical staff or pathologists.

In September, 1990 additional Federal regulations came into effect governing the practice of gynecologic cytology. They have created extra work, especially for the cytotechnologists, in that we have to carry out additional quality assurance measures, some of dubious value.

Dr. Suzanne M. Selvaggi, formerly of Wayne State University and Hutzel Hospital in Detroit, joined the faculty in December, 1990 to replace Dr. Robert W. Schmidt, who retired. She brings to the position wide experience in cytopathology and gynecologic pathology.

Bernard Naylor, M.D.
Director, Cytopathology Laboratory

DERMATOPATHOLOGY SERVICE
DEPARTMENT OF PATHOLOGY

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The Dermatopathology Service receives diagnostic case material from five different sources: (1.) UMMC (ID) cases; (2.) outside contractural (MD) cases; (3.) personal consultations (HE) cases; and (4.) outside slides reviewed for referred patients (TD) cases; and informal consultations (intramural, VAH, and MU) cases:

Work load volume is as follows:

	1989 - 1990	1990-1991
HE	790	822
ID	NA	NA
MD	NA	NA
TD	NA	NA
Informal	NA	350

Correlative activities included participation in Melanoma Clinics (biweekly), Cutaneous Lymphoma Conference (monthly) and Dermatology Grand Rounds (weekly).

Teaching included scheduled presentations to medical and dental students.

1990-1991 continued the gradual trend for an increased workload.

John T. Headington, M.D.,
Director, Dermatopathology Service

Brian J. Nickoloff, M.D., Ph.D.

ELECTRON MICROSCOPY SERVICE
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
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The electron microscopy laboratory continues to provide an important service and research function for the Department of Pathology as well as the Medical Center. For example, during this past year 482 clinical specimens were submitted. This number is up dramatically from the previous year when 391 clinical specimens were processed. Of this total, 140 were renal biopsies while the remainder were tumors of various types as well as nerve and muscle biopsies. This marked increase in clinical electron microscopy cases is in marked contrast to what is seen nationally where most EM services have seen a marked decrease in volume.

The most dramatic growth in electron microscopy continues to be in the area of research. During this past year over 20 investigators from virtually every department in the medical school have utilized this facility. During this past year 356 samples were submitted for actual ultrastructural analysis. This is derived from over 800 samples submitted in total, many of which required only thick sectioning and not complete EM analysis. This high volume continues to tax our capability particularly with the development of newer methodologies such as in-situ hybridization and immunoelectron microscopy. It is a tribute to the laboratory personnel; in particular Ms. Robin Kunkel, that we continue to offer rapid turn around time while providing the most up-to-date techniques for the investigators using this facility.

During this past year there has been several personnel changes. In the Clinical EM area Ms. Cindy Lamm left after three years with us to pursue graduate studies. In addition, in the research area Mr. Bradley Nelson also left to pursue an advanced degree. We have added two new individuals to take their places. In the clinical laboratory we have added Dr. Yin Ru Sieracki and in the research laboratory Ms. Lisa Riggs. In addition, Ms. Barbara Rogers has been made supervisor of the clinical laboratory. It is a tribute to the personnel in the laboratory that the specimens continued to be processed in a timely fashion in spite of all of the laboratory turnover. In particular, I would like to site the efforts of Ms. Rogers who made a major effort to get the clinical laboratory into compliance for a recent CAP inspection which was passed with flying colors. Her efforts included a complete rewriting of many areas of the procedure manual as well as instituting a comprehensive quality control program.

It is anticipated that during this coming year that demands on the EM service will continue to increase; particularly in the research area. Plans are underway to develop a computerized morphometric analysis system that would allow for precise quantification of ultrastructural alterations by the use of image analysis. Therefore, it appears as if concerns about the future of EM in modern pathology are unfounded. In fact, as our degree of understanding on the molecular basis of disease increases, correlative ultrastructural studies using specific molecular probes will assume increasing importance.

Kent J. Johnson, M.D.
Director
Electron Microscopy Service

NEUROPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
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The Laboratory of Neuropathology continues to have three interrelated functions: Laboratory diagnostic service, teaching and research. Dr. Samuel P. Hicks was on Active Emeritus status, and made significant contributions to the Autopsy Neuropathology Service. Dr. Anders A.F. Sima joined the service this year. Dr. Mila Blaivas, Ms. Constance J. D'Amato, and Dr. Paul E. McKeever, also contributed to the Neuropathology Service. .

CLINICAL ACTIVITIES:

The following examinations were completed with the support of our neurohistology, electron microscopic, general histology, immunohistology, and secretarial staff.

1. There were 536 neurosurgical cases examined this year from Main, Mott and outside hospitals in consultation. 47 cases were referrals from other institutions, a portion of which were part of interdepartmental collaborative NIH funded studies of PET scanning and BUDR radio-sensitization of gliomas. One hundred sixty-eight surgical specimens required special neurohistologic procedures.
2. There were 342 brains examined out of 396 autopsies which is 86% of all autopsies at this Medical Center. An additional 24 brains were examined from other institutions and hospitals. While all neuropathology faculty have participated, Dr. Hicks and Ms. D'Amato collaborated to prepare descriptions of most UM autopsy brains, and other brains referred for consultation.
3. There were 169 muscle biopsies (a 17% increase over the previous year), nearly all with histochemistry, some with electron microscopy. There were 66 peripheral nerve biopsies. Teased fiber preparations and electron microscopy were performed on appropriate nerve biopsies. The combination of nerve teasing, muscle histochemistry, electron microscopy and morphometry make the service regionally competitive for diagnostic consultation. Dr. Blaivas examined 47 cases from other hospitals in consultation.
4. Faculty interpreted 169 cases in semithin section and electron micrographs of 112 cases (32% increase). The majority were nerve, pediatric muscle, and neurosurgical biopsy cases.
5. The ceroid service, buffy coat division, reported four cases.
6. The Brain Tumor Board of the University of Michigan Cancer Center and Hospitals reviewed neuropathology and clinical aspects of more than 120 difficult neurooncology cases.

TEACHING ACTIVITIES:

1. Medical Students: This year the faculty taught the regular Neuropathology sequence to our medical students (13 hours) in the Neural and Behavioral Sciences (NBS) 600 curriculum. NBS Neuropathology consists of lectures, handouts, and posters for all second year medical students. In addition to being Director of the NBS Program for 40% of her time, Ms. D'Amato conducted 12 hours of brain cutting sessions for small groups of the second year students.
2. House Officers, Graduate Students, Postgraduate and other students and faculty: These include a conference every other month with Neurology; twice monthly Continuing

Medical Education (CME) accredited conferences where all biopsies are presented and interpreted; a conference where abnormal brains are examined with all clinicians invited weekly; three types of nerve and muscle biopsy conferences (one weekly, one twice a month and one monthly) accredited for CME; individual instruction on autopsies and biopsy material; Neuropathology 858, an 18 hour laboratory-lecture course; and bimonthly conferences with Neuroradiology and Pediatric Neurology.

3. Electives: One neurosurgery resident and four medical students chose elective rotations on the Neuropathology Service.

RESEARCH ACTIVITIES:

1. Dr. Hicks and Ms. D'Amato's experimental work concerned the role of fetal rat brain phagocytes in repair after radiation injury, and the association of thrombospondin with the development of astrocytic gliosis after surgical brain injury in adult rats. They also provided neuropathologic diagnostic support for Drs. Anne Young and John Penney's biochemical study of Alzheimer's disease and other human dementias.
2. Dr. Blaivas and associates investigate ocular muscle (normal and abnormal). She is also investigating musculature related to cleft palates in children and mice. She is investigating normal and diseased musculature of the face and the pelvic floor.
3. Dr. Sima and collaborators are examining the regulation of all adhesive molecules and junctional molecules in diabetic nerve and retina to elucidate the etiology to defects occurring in axo-glial junctions and endothelial cell tight junctions in diabetes. Furthermore they are examining the interaction between nerve growth factors (NGF, IGF-1) and nerve regeneration in diabetes.
4. Dr. McKeever and associates are determining the extent and cause of differences in antigens in brain tumor tissue versus cells in culture. These differences may result from a separate population of cells within brain tumors or from instability of antigen expression by neoplastic cells. They are measuring DNA content and BUdR labeling indices in tumor specimens *in vivo* and *in vitro*.
5. Groups of the University of Michigan Cancer Center faculty and staff with clinical research interests in brain tumors, met and generated a number of project considerations from Pathology, Neurosurgery, Nuclear Medicine, Neuropathology, Neurology and Neuroradiology collaborations.
6. Collaboration with Neurology, Michigan State University, The State of Michigan Department of Public Health, the Alzheimer's Association, Henry Ford Hospital, and Beaumont Hospital proposes to establish a registry for dementias and Alzheimer's disease.

Paul E. McKeever, M.D., Ph.D.
Director
Neuropathology Service

PEDIATRIC PATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1990 - 30 JUNE 1991

The activities of this service were carried out as in the past, primarily by Kathleen P. Heidelberger, M.D. and Mason Barr, Jr., M.D.

Necropsy figures are as follows:

M/W/H Unit Deaths (20 weeks gestation or any live born, to 18 years)	=194
Necropsies on Above	=144
Necropsy Percentage	=61%

Of the 144 posts, 52 patients' bodies were released to Anatomy for study and disposal. These gross posts were performed by Mason Barr, Jr., M.D., with necessary histology by Dr. Heidelberger Ninety-two patients were posted by the residents and senior staff in Pathology, primarily Dr. Heidelberger. Necropsies categorized in the adult general hospital statistics as "Medical Legal" posts included 14 posts on pediatric patients including SIDS cases, child abuse cases and trauma cases, most of which were classified as inpatient deaths.

A total of 438 necropsies for UMMC Hospitals patients was performed (including the 14 pediatric "Medical Legals"), 52 by Dr. Barr in the Teratology Unit and 386 by the Pathology Department Staff. Thus, 33% of the total posts at the UMMC were pediatric posts.

It should be noted that as a regional center, with a wide range of subspecialities, the total number of cases examined in the Teratology Unit was 182 - including both all referred fetuses and infants and newborn fetal losses at less than 20 weeks' gestational age.

The total number of pediatric surgical specimens (including placentas) examined is almost 2,500. This represents an increase of over 8.5% from the previous academic year.

Kathleen P. Heidelberger, M.D.
Director
Pediatric Pathology Service

SURGICAL PATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
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The Surgical Pathology Service witnessed one of the steepest volume increases last year. Our annual hospital-based work volume increased by 14% and our personal consultation by 22%, bringing our total annual accessions to 31,116 cases. This volume identifies us as one of the most active university hospital services in the country. The imminent opening of the Medical Procedures Unit is projected to further increase our annual volume by 10%. Although the increasing volumes coupled with personnel and budgetary constraints have forced some inevitable cutbacks, we have met the foregoing challenges, for the most part, with programmatic changes such that only minor curtailment of services has resulted. We continue to search for other ways of improving our efficiency in order to support our clinical services.

Our staff looks with immeasurable pride on the accomplishments of our first surgical pathology fellows who completed their training at the conclusion of this year. Their acceptance by our staff and clinical colleagues attests to the highly level of competence which they displayed throughout their fellowship year. The success of this first year has secured a firm place for this fellowship experience within our educational programs.

We continue to expand our diagnostic armamentarium utilizing newer technologies. We are able to identify certain infectious agents by molecular diagnostic techniques, and will soon offer flow cytometric and cytogenetic analysis of some solid neoplasms as a standard laboratory procedure.

Sharon W. Weiss, M.D.
Chief,
Surgical Pathology

CLINICAL PATHOLOGY LABORATORIES

DEPARTMENT OF PATHOLOGY
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Clinical laboratory personnel continued to be busy in the past year with increased volume, in addition to consolidation of laboratories and continued new initiatives in the areas of quality assurance and cost effective management. Additionally, the M-Labs program continued to develop. Specific laboratory activities can be found on the following pages, yet certain activities of the clinical laboratories are worthy of special mention.

In the face of ever-increasing laboratory volume, the clinical laboratory staff met the challenge of further consolidation of special limited function laboratories, including the consolidation of the Histocompatibility Laboratory. In addition to the consolidation of the laboratory, Dr. James Baker was hired as director of the laboratory.

A College of American Pathologists (CAP) inspection was successfully carried out this spring. The inspection was passed with only a few minor deficiencies. In addition, the Clinical Toxicology Laboratory passed a CAP forensic drug testing lab inspection.

The laboratories responded to the present cost containment program with a program that demonstrated cost savings in personnel (FTEs), commodities, and programs. Implementation of the cost savings is now in effect, including the development of utilization review programs in areas where clinical programs are growing the fastest; for example, in blood products.

The Quality Assurance Committee, made up of members of the laboratory staff and coordinated for Dr. McClatchey by Suzanne Butch, Chief Technologist for the Blood Bank, continues to show a visionary approach to quality assurance in the clinical laboratories, both intra- and inter-laboratory. The development of indicators is now directed at programs where patient outcome can be affected.

The M-Labs program in the clinical laboratories is continues to be a part of the daily routine. The M-Labs program is constantly monitored by the M-Care/M-Labs Quality Improvement Committee, which is made up of selected laboratory personnel to ensure the quality performance of the M-Labs program. One of the many positive outcomes of the M-Labs programs has been a stronger commitment by laboratory professionals to a high quality, extremely cost efficient laboratory system.

Kenneth D. McClatchey, M.D., D.D.S.
Director,
Clinical Pathology Division

UNIVERSITY HOSPITALS BLOOD BANK AND TRANSFUSION SERVICE

DEPARTMENT OF PATHOLOGY
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PATIENT CARE:

The usage of blood products in the last year increased, with the exception of Red Blood Cells. This was effected by programmatic changes as well as utilization review, particularly in cardiac surgery. Red Blood Cell usage was 90 per cent of the previous year (figures based on 10-month usage, July 1990 through April 1991). The usage of cryoprecipitate increased 115 per cent, Fresh Frozen Plasma increased 123 per cent, and platelet concentrates increased 107 per cent compared to the previous year. Use of 5 per cent albumin increased 135 per cent, due to increased activity in plasmapheresis.

Laboratory activity increased commensurately with blood products. The volume of type-and-screen procedures increased 109 per cent, antibody identifications increased 111 per cent compared to the previous year. Crossmatches were stable at 98 per cent of previous annual activity.

Significant increases were seen in laboratory activities related to the Bone Marrow Transplantation Program. Ninety stem cell harvest procedures were performed compared to one in the previous year. One hundred twenty-three bone marrow freezing and storage procedures were performed, compared to 19, and 20 marrow separation procedures compared to 9 in the previous year.

Activity in the Transfusion and Apheresis Service also increased. Outpatient transfusions increased 112 per cent, and plasmapheresis procedures increased 136 per cent. The Cobe 2991 apheresis instruments were replaced by Cobe SPECTRA instruments. This is anticipated to increase reliability and decrease set-up time require for each procedure.

The utilization review program conducted with the Section of Thoracic Surgery continued to show positive results. Blood usage in cardiac surgical procedures decreased by approximately one-third in terms of average number of components used and average donor exposures. In addition, the number of patients undergoing cardiac surgical procedures utilizing no homologous blood increased significantly. This utilization review program, which involves peer review within the Section of Thoracic Surgery based upon data provided by the Blood Bank/Transfusion Service, has served as a model for development of comprehensive review procedures within the institution.

EDUCATIONAL ACTIVITIES:

The medical, technical and nursing staff of the Blood Bank/Transfusion Service were active in education at the departmental, institutional, regional and national levels. All first-year Pathology House Officers in Clinical Pathology participated in the Blood Bank orientation course. Daily teaching rounds were held for House Officers assigned to the Blood Bank. Dr. Oberman, Dr. Davenport and Mr. Judd presented Pathology Grand Rounds throughout the year. In addition, Fellows in Pediatric Hematology rotated through the Blood Bank. The nursing staff of the Transfusion and Apheresis Service presented regular education services for nursing at the University of Michigan Hospitals on the topics of blood product administration and adverse transfusion reactions.

The eighteenth annual postgraduate course "Current Topics in Blood Banking" was held June 5, 6 and 7, 1991. Mr. Judd and Ms. McCoy-Pardington were program directors. The course continues to be one of the largest continuing education programs in Blood Banking in the nation. Members of the

Blood Bank and Transfusion Service staff presented Workshops on management, serologic problems and treatment of coagulopathies. Ms. Steiner presented the Ron Scherdt Memorial Lecture entitled, "Is It Auto or Is it Allo?" Mr. Judd presented a lecture entitled, "Pretransfusion Testing: What Else Can Go?"

Presentations by the Blood Bank and Transfusion Service faculty and staff at the American Association of Blood Banks included management, medical and serologic topics. Dr. Davenport presented posters on tumor necrosis factor production in hemolytic transfusion reactions and prophylactic transfusion before liver biopsy. Mr. Meade presented "Availability of Standard Operating Procedures on the Inpatient Unit: A Nursing Practice Quality Assurance Audit." Ms. Barnes presented "Reducing Nonindicated Pretransfusion Prophylactic Medication through Physician Education." Ms. Butch presented "Reducing Donor Exposures: Effectiveness of RBC Syringes." Mr. Judd presented "Acute Intravascular Hemolysis Due to Anti-i." Ms. Knafel presented "Is Autologous Blood Overutilized?" Mr. Judd presented invited lectures at the Rhode Island Blood Bank Society Annual Meeting, Ortho Diagnostics, Michigan Association of Blood Banks Travelling Seminar Series, Central Michigan Community Hospital, Port Huron Hospital, Indiana Association of Blood Banks Annual Meeting and the Michigan Society for Medical Technology. Ms. Steiner presented invited lectures at the Ontario Medical Technology Convention, Region VI of the American Society for Medical Technology, the Ortho Forum, the Chicago Medical Technology meeting, Michigan Society for Medical Technology, and the Michigan Association of Blood Banks. Ms. Butch presented invited lectures at the Michigan Association of Blood Banks, Region VI of the American Society for Medical Technology, and the American Association of Blood Banks.

PROFESSIONAL ACTIVITIES:

Staff at the Blood Bank and Transfusion Service continued to be active at the regional and national levels. Ms. Butch served as Chairperson of the Education Committee of the Michigan Association of Blood Banks; Chair, Director Examination Subcommittee of the Examination Council of the National Certification Agency for Clinical Laboratory Personnel; Historian of the Publications Committee of the Michigan Society for Medical Technology; and Chairperson of the Blood Bank Special Interest Group of Cerner PathNet Users Group. Ms. Barnes served as Inspector for the Inspection and Accreditation Program of the American Association of Blood Banks. Ms. Steiner served as a Member-at-Large of the Executive Board of the Michigan Association of Blood Banks; Chair, By-laws and Policy Manual Committee; and Annual Meeting Committee of the Michigan Association of Blood Banks. Ms. Steiner also served on the Reference Laboratory and Rare Donor File Committee of the American Association of Blood Banks. Mr. Judd served as Chairman of the Specialist in Blood Banking Program, member of the Annual Meeting Program Committee, and member of the Spring Workshop Committee of the Michigan Association of Blood Banks. Mr. Judd also served as North Central District Representative on the Board of Directors of the American Association of Blood Banks. Ms. Butch served as Co-Editor of the Journal, "Clinical Laboratory Science". Dr. Oberman served as Associate Editor of the Journal, "Transfusion".

RESEARCH ACTIVITIES:

The faculty and staff of the Blood Bank and Transfusion Service are actively pursuing ongoing research activities in the pathophysiology of transfusion reactions, pretransfusion testing, the genetic basis of blood group antigens, and strategies for reduction of donor exposures. Completed publications in peer-reviewed journals by the faculty and staff of the Blood Bank and Transfusion Service in the past year include the following:

1. Butch SH. Computer software quality assurance. Lab Med, 1991;22:18-22.
2. Judd WJ. Are there better ways than the crossmatch to detect ABO incompatibility? Transfusion 1991;31:192-4.

3. Nugent CE, Gelinas JR, Judd WJ, Steiner EA. Anti-Yt^a does not cause hemolytic disease of the newborn. Obstetr Gynecol. In Press.
4. Judd WJ, Butch SH. When is blood transfused relative to its date of expiration? Transfusion 1991;31:464-5.
5. Judd WJ, Steiner EA. Multiple hemolytic transfusion reactions caused by anti-Do^a (letter). Transfusion 1991;31:477.
6. Judd WJ, Steiner EA. Adsorption of anti-Cr^a by human platelet concentrates (letter). Transfusion 1991;31:286.
7. Davenport RD, Strieter RM, Standiford TJ, Kunkel SL: Interleukin-8 production in red cell incompatibility. Blood 1990;76:2439-42.
8. Davenport RD, Strieter RM, Kunkel SL: Red cell ABO incompatibility and production of tumor necrosis factor-alpha. Br J Haematol, In Press.

Harold A. Oberman, M.D.
Director,
Blood Bank and Transfusion Service

CLINICAL CYTOGENETICS LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

The Clinical Cytogenetics Laboratory has continued to expand, both in numbers and complexity of samples processed and in personnel. In the last year, approximately 875 amniotic fluids, 60 tissues (skin, POC, etc.), 345 peripheral blood specimens, 145 fragile-X analyses, 67 prophase analyses, 6 breakage studies and 273 bone marrows were completed for a total of 1,771. Increases were seen in all areas, particularly bone marrow and prophase analysis. It is important to note that more than half of the non-prenatal specimens required special processing and analysis. With expanded staffing, the use of the laboratory computer and daily sign out, the turn-around time for the prenatal cases has gone from 3 to 4 weeks to 14 days or less.

The laboratory as a whole is planning to continue to decrease turn-around times and expand the extent of its analyses, as this appears to be the direction that the field of cytogenetics is taking. A collaborative effort with a group from Maternal-Fetal Medicine resulted in the institution of a program of earlier prenatal diagnoses by chorionic villus biopsy. Approximately 100 cases are expected during the first year (which began in May, 1991), and these are not expected to replace any of the amniocenteses being performed now.

Bone marrow cytogenetic analyses continue to increase; this trend is expected to continue as the Bone Marrow Transplant program grows. A number of studies are underway to determine the value of various mitogens and growth factors for stimulation of abnormal clones for bone marrow analyses. In addition, some solid tumors, primarily sarcomas, have been analyzed and this type of analysis is now available clinically.

Some molecular cytogenetic analysis is being offered by the clinical laboratory. Using fluorescent *in situ* hybridization, chromosomes X, Y, 13, 14, 15, 21, and 22 can now be identified, a procedure which is useful in ascertaining the origin of certain "marker" chromosomes. These studies undoubtedly will be expanded in the future.

Thomas W. Glover, Ph.D.
Director,
Clinical Cytogenetics Laboratory

Susan Sheldon, Ph.D.
Assistant Director

CLINICAL FLOW CYTOMETRY LABORATORY

DEPARTMENT OF PATHOLOGY
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1 JULY 1990 - 30 JUNE 1991

The Clinical Flow Cytometry Laboratory has enjoyed a stable and productive year without significant changes in overall operation. The laboratory has continued its active role in diagnostic clinical pathology and indeed has continued to show growth in all areas of the laboratory. A total of 2400 immunophenotyping specimens were handled by the laboratory over the past 12 months, which is an increase of 25% from the previous year. This included approximately 1200 specimens for monitoring T-cell subsets in patients with acquired or inherited immunodeficiencies or in patients receiving organ transplants. Approximately 600 specimens were processed for cell surface markers for possible hematologic disorders, including acute or chronic leukemias. The remaining 600 specimens were studied for platelet-associated immunoglobulins or neutrophil-specific antibodies. An additional 5000 reticulocyte counts were also performed by flow cytometry. This was the first complete year of our laboratory routinely performing reticulocyte counts, which are analyzed Monday thru Saturday in the laboratory. Stat reticulocyte requests (less than 5/year) are performed in the hematology laboratory.

Each immunophenotyping specimen analyzed in the laboratory requires anywhere from 6 to 30 individual staining, quantitation, and analytic procedures. Quality control and calibration procedures further add to the specimen load. Thus, the laboratory staff conducted approximately 37,000 individual marker studies in fiscal year 1990/1991. The laboratory continues to provide 12 to 24 hour turn-around studies on acute leukemia and selected transplant patients. Overall, Part B billings continue to increase without a significant change in commodity expenses.

The Flow Cytometry Laboratory continues to implement changes to enhance the operational efficiency of the laboratory, to maintain commodity expenses, and academically still be at the forefront of clinical flow cytometric applications. Two-color immunophenotypic analysis has become a routine standard in the laboratory. During the past year, we have implemented two-color staining for all non-acute leukemia work-ups and have made significant progress in implementing two-color analysis for our acute leukemias. Once this is accomplished, no single-color assays will be routinely performed in the laboratory. Although two-color reagents are more expensive, the marked reduction in preparation and analysis time has allowed us to handle the continuing increase in laboratory requests without increasing personnel. Other changes in the laboratory have included the development of leukemic cell lines as sources of normal controls and evaluation of nuclear and cytoplasmic antigens in acute leukemia specimens.

The Flow Cytometry Laboratory has continued to enhance the efficiency of its daily operation. The generation of final reports by pathologists and technologists has been greatly simplified requiring less paper work and professional time. The development of a computer database of immunophenotyping results has been a tremendous help in both the day-to-day operation in the laboratory, as well as in its academic mission. This database is relatively unique to a clinical laboratory and provides an instantaneous source of important patient information, which we continue to modify and enhance. It has also enabled us to maintain a more accurate record of cryopreserved leukemia samples.

The laboratory has continued to develop its quality assurance program. The pathologists staffing the laboratory are actively involved in deciding the appropriateness of requested immunophenotyping studies. Only those cases which warrant phenotypic analysis will be processed by the laboratory. Approximately 150 tissue specimens and over 200 blood and bone marrow samples were cancelled

without instrument analysis as a result of pathologist's triage. This aspect emphasizes the continuing need and importance for the pathologist's daily involvement in the laboratory.

New developments in the Flow Cytometry area in the upcoming year will be concentrated on adapting many of our assays to the new Becton-Dickinson FACSCAN flow cytometer. Approximately 1/2 of our assays can now be performed on the FACSCAN. Continued development on this instrument will happen during the course of the year along with development of appropriate database changes. The laboratory will also closely look at commodity expenses to significantly reduce that portion of its overall budget. The laboratory continues to provide backup service to the hematopathology portion of the Molecular Diagnostic Laboratory. Further description of the Molecular Diagnostic component is discussed separately (see Clinical Molecular Diagnostic Laboratory).

Curtis A. Hanson, M.D.

Lloyd M. Stoolman, M.D.
Directors
Clinical Flow Cytometry Laboratory

CLINICAL HEMATOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
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LABORATORY ACTIVITIES:

A. There was an overall increase in the total number of tests from 463,000 in 1988-1989 to 475,000 in 1989-1990, and to 538,000 in 1990-1991 (13.3% increase from 89-90)..

B. There was 7.7% increase in the number of tests requiring review by hematopathologists, from 3900 cases in 1989-1990 to 4200 cases in 1990-1991. This review included cases with abnormal peripheral blood smears and abnormal body cavity fluids including differential white cell counts and screening for malignant cells.

C. In December 1990 the automatic verify by the Cerner system of negative results from the Rapimat urinalysis instrument was implemented. This change was our first main step in using the Cerner system to enhance the efficiency of the laboratory.

D. In March 1991 implementation of reporting automated differential counts from the STKS instruments in the Main Hematology Laboratory was effected, reducing the number of manual differential white blood cell counts by 41%. In June 1991, implementation of reporting of automated differential counts in the Taubman Stat Laboratory was accomplished, leading to a 39% reduction in the number of manual differentials performed. Implementation was accomplished by dual-reporting manual and automated differentials for a six week interval. During this time, all data (over 10,000 comparisons) were collected on the computer system. Currently, we are in a collaborative project with Biostatistics and the Cancer Center to evaluate and eventually publish these data.

E. On April 1, 1991, we implemented a cooperative protocol with the Microbiology Laboratory for detection and reporting of intracellular bacteria in body fluids.

F. A computer database is being established to keep track of all bone marrow and pertinent reviewed cases. This will allow for better tracking and organization of material.

G. Daily bone marrow signout with house officers and fellows.

H. Daily signout of in-house and UM clients' cases, abnormal smears and body and joint fluids takes place 7 days per week.

I. A quality assurance program has continued in the area of bone marrow cytochemical stains for leukemia and other labor intensive "specialty" tests within the laboratory. This program has led to a substantial decrease in the number of special tests and cytochemical stains performed, resulting in improved utilization of resources.

TEACHING ACTIVITIES:

A. Pathology House Officers and Hematopathology Fellows participated in the following activities:
   1. Daily review of abnormal blood smears, body fluids, joint fluids for crystals, bone marrow aspirates and bone marrow biopsies.
   2. Daily review of in-house and transfer consultation cases in hematopathology (lymph node biopsies, bone marrow biopsies, aspirates, splenectomy specimens, etc.).
   3. Daily review of outside consultation cases of Drs. Schnitzer and Hanson.
   4. Correlation of morphology with special studies (cytochemistry, flow cytometry, immunoperoxidase and occasionally electron microscopy).
   5. Daily review of abnormal blood smears from M-Labs clients.
   6. A formal teaching conference for House Officers has been continued.
   7. Review of SWOG cases.

8. Weekly Interdepartmental Lymphoma Conference.
9. Biweekly Interdepartmental Leukemia Conference.
10. Pediatric Hematology/Oncology Fellows participate in signouts.

B. Hematopathology Fellowship Program
C. Continuing medical education for medical technologists - monthly.

FY 91/92 GOALS:

A. Implementation of cost-containment programs.
B. Review and development of laboratory utilization.
C. Implement limits on repetitive differential requests.
D. Continue to liberalize automated differential criteria.
E. Preliminary studies of limiting WBC requests from intensive care units.
F. Continue to enhance the overall efficiency of the laboratory operation.

Bertram Schnitzer, M.D.

Curtis A. Hanson, M.D.

Directors
Clinical Hematology Laboratory

CLINICAL IMMUNOPATHOLOGY LABORATORY

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OVERVIEW:

Jeffrey Warren, M.D. assumed the role of laboratory director on September 1, 1989 when David Keren, M.D. departed by become the Director of Warde Medical Laboratories. Dr. Keren continues to provide invaluable advice as an ad hoc consultant. John Lowe, M.D. has increased his level of service commitment to aid in filling the void left by Dr. Keren's departure. Kent Johnson, M.D., and Kevin Cooper, M.D. (Dermatology) continue to signout tissue immunofluorescence studies.

CLINICAL SERVICES:

As the fiscal year approached its conclusion, the laboratory had experienced a modest increase in total volume (approximately 2%) despite the setbacks incurred by the nursing strike during the summer of 1989. Particularly gratifying has been the growth in several relatively new assays; these include the neutrophil cytoplasmic antibody (NCA) test, prealbumin assay, and immunoglobulin G subclass determinations. Neutrophil cytoplasmic antibody determinations have increased from approximately 20/month to more than 40/month, prealbumins have increased three-fold and immunoglobulin G subclass determinations have increased by approximately 50%. In addition, we instituted the microalbuminuria assay as a clinical test.

RESEARCH AND DEVELOPMENT:

The laboratory has participated in an ongoing methods comparison study of microalbuminuria assays. This study is being conducted by Dr. Patricia Mueller at the Centers for Disease Control in Atlanta. Involvement in this study has been an outgrowth of our support of ongoing clinical studies of ambulatory diabetic patients being carried out by Dr. William Herman (Department of Medicine, University of Michigan) and Dr. Mindy Smith (Department of Family Practice, University of Michigan). We initiated laboratory support of a clinical study of atypical antinuclear antibodies in conjunction with Dr. Joseph McCune (Department of Medicine, University of Michigan). We are currently setting up the Western immunoblot technique in order to examine the specificities of anti-neutrophil cytoplasmic antibodies. Finally, after conducting a method comparison study of IgG subclasses quantitated by microELISA versus radial immunodiffusion, we have recently switched to the later method. The RID method should prove to be more reliable and the laboratory should realize a significant annual cost savings.

QUALITY ASSURANCE:

The laboratory completed two QA projects. These relate to proper specimen procurement for CSF oligoclonal bands and proper screening requests for Bence Jones proteins.

TEACHING/PROFESSIONAL:

Residents, M4 medical students, and medical technology students from Eastern Michigan University rotated through the laboratory. Immunopathology journal club for medical technologists and on-service house officers were conducted biweekly. Four clinical pathology grand rounds were presented by Drs. Lowe and Warren. Other professional activities of faculty and staff in the laboratory are summarized under individual faculty reports.

Jeffrey S. Warren, M.D.
Director
Clinical Immunopathology Laboratory

CLINICAL MICROBIOLOGY LABORATORY

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CLINICAL ACTIVITIES:

The volume of tests performed during the year increased 9% compared to last year with requests for CSF, blood and chlamydia increasing greater than 15%. MLabs specimen requests increased 15.8% over last year and accounted for 13% of total laboratory test volume. Several new tests were implemented during the year including the use of DNA probes for the direct detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* and an EIA method to enhance detection of *Giardia lamblia*. Considerable effort was put toward the training of phlebotomists stationed in the ER to perform Strep A EIA tests and toward monitoring activities at the M-Care laboratories. Several Quality Assurance projects were carried out including the monitoring of blood and stool cultures for correct usage. Toward the end of the fiscal year, much effort was directed toward the Cost Containment program. The CAP inspection was completed successfully in June. The laboratory provided continuous data and information to Infection Control Services for their daily investigations of potential nosocomial infections.

TEACHING ACTIVITIES:

A more extensive Pathology Resident raining program was developed and instituted for the 13 residents who spent 1-2 months in the laboratory. In addition, several Pediatric residents received on-site training in the lab. Infectious Disease laboratory rounds were conducted each weekday attended by fellows, residents and medical students during which interesting cases were discussed and lab demonstrations performed by the assigned Pathology resident. Several of our senior technologists participated in several national and regional conferences. Culture data was supplied to several residents to assist them in preparing for educational presentations.

RESEARCH ACTIVITIES

Most of the research efforts during the year were directed toward the development and evaluation of more rapid and sensitive diagnostic techniques and the comparative evaluation of new antimicrobials. Automated EIA methods for the detection of *Chlamydia, Clostridium difficile* toxin A and *Rubella* IgG were performed. An automated method for the screening of urines was evaluated with the results presented at the annual ASM meeting. A research antimicrobic panel was developed and used to evaluate the activity of several new beta-lactam and fluoroquinolone antimicrobics. Appropriate data were suppled to the hospital P&T committed to assist their evaluation of new antimicrobics considered for the formulary. Laboratory personnel assisted investigators from other departments by providing laboratory expertise and cultures for their investigations. Examples include the isolation and characterization of yeast isolates for a member of the Dept. of Family Practice and the isolation, identification and new drug susceptibility of organisms for the Dept. of Obstetrics and

Gynecology. An exciting new development is the utilization of PCR for the direct detection of *Mycobacterium tuberculosis* in clinical specimens. This investigation is being conducted with the Molecular Diagnostic Unit and shows great promise.

Kenneth D. McClatchey, M.D., D.D.S.
Director
Clinical Microbiology Laboratory

Carl L. Pierson, Ph.D.
Associate Director
Clinical Microbiology Laboratory

HISTOCOMPATIBILITY AND IMMUNOGENETICS LABORATORY

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This has been a year of intense change for the Histocompatibility Laboratory; the personnel, techniques and administrative functions were all reorganized in an attempt to make the laboratory run more efficiently. Despite these changes, the laboratory's clinical activity was maintained, and in some cases, increased. The new personnel and techniques were incorporated in the lab without any disruption in accreditation or quality of service.

CLINICAL ACTIVITIES:

Clinical Activity in the Histocompatibility Laboratory showed a general increase in the number of tests done during the past year. Tissue typings for both Class I and Class II antigens stayed at approximately 1,200 analysis per year, while antibody screenings and crossmatches each had approximately a 10% increase in the number of tests. Mixed Lymphocyte Cultures (MLC's) showed an enormous increase of approximately 2,000% such that now approximately 60 MLC's are done each year.

Personnel changes during the year involved the appointment of a new Director, Dr. James Baker, on January 1, 1991 and the hiring of two new employees, Catherine Boik (a Medical Technologist) and Maxine Lipon (a Medical Technician).

Improvements in technical functions in the laboratory involved changes in the procedures for most of the assays. The technique for performing Class II typing was changed to florescence microscopy, with two-color dye labelling and magnetic bead separation of cells. This allowed the time required for the Class II typing to shrink from approximately 48 to 4 hours, while increasing the likelihood that typing could be accomplished on individuals with low lymphocyte counts. The equipment and techniques for MLC's were improved to reduce background and increase the viability of the cultures. In addition, University of Michigan typing trays were developed to reduce reliance on commercial vendors and increase the specificity of the antigen assignments. This also allowed for a projected savings of approximately 20% of the budget as compared to the cost of commercial trays.

An extended effort was made to automate the functions of the laboratory and this was completed in late June of 1991. A local area network was installed and managed by Jeff Hayward, the Data Supervisor the Laboratory, in conjunction with Pathology Data Services. Activities including data analysis, archiving, retrieval and report generation were automated, and techniques were introduced which allowed direct billing through Pathnet. Because the laboratory was dependent on paper records up until this point, an extensive program of microfiche was undertaken to archive all of the past records of the laboratory. These activities will reap tremendous benefits in efficiency and cost savings in the coming years.

TEACHING ACTIVITIES:

Every member of the laboratory was involved in the teaching activities of the laboratory and these activities were markedly expanded over previous years. The laboratory was involved in the instruction of Pathology Residents, Allergy Fellows, Renal Fellows and the rotation for Hematology Fellows from the Department of Medicine. Dr. Baker, the Laboratory Director, initiated a program for reevaluation of the procurement activities of the Transplant Society of Michigan and this has resulted in

a new and more efficient manner for state-wide matching of organs with recipients. Ms. Cynthia Schall, the Laboratory Supervisor, was involved in teaching review courses at the Henry Ford Hospital, University of Michigan, and the Biotest International Symposium. She also oversaw the teaching activities of the Laboratory for both the Residents and two "Women In Science" Interns.

NEW GOALS:

Goals of the laboratory in the coming year involve the development of HLA typing by DNA analysis using the Polymerase Chain Reaction, in order to better support the bone marrow program. In addition, it is hoped to develop a basic-science research program in Transplantation Immunology to support both the Transplant Surgery Service in the Department of Surgery and the Transplantation Medicine Program in the Department of Medicine.

James R. Baker, Jr., M.D.
Director
Histocompatability and Immunogenetics Laboratory

LIGAND ASSAY LABORATORY

DEPARTMENT OF PATHOLOGY
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CLINICAL ACTIVITIES:

The Ligand Assay Laboratory is continuing to migrate to non-radioisotoic methodologies as acceptable replacements become available. We are also engaged in an active effort to improve turnaround time. The acquisition of a robot pipetting system (TECAN) enables us to reduce significantly technical pipetting time and more utilization of semi-automated analyzers (e.g., the Abbott IMx) has increased our efficiency. Such efforts have enabled us to absorb an increase of greater than 15% test volume this fiscal year (bringing our volume to over 150,000) without a corresponding increase in the number of FTEs or requiring additional overtime.

Specific changes in the procedures used in the Ligand Laboratory are the conversion of the LH, FSH, Prolactin and B_2 Microglobulin assays from RIA procedures to the IMx fluorescent analyzer; conversion of Anti-DNA assay from an in-house ^{3}H method to a simpler ^{125}I kit; and changing the Estrogen Progesterone Receptor assays from a ^{3}H binding method to an enzyme immunoassay (EIA). New tests initiated in this fiscal year include: Hepatitis C antibody, Insulin Growth Factor - 1 (IGF-1) Progesterone and Estradiol. The Estradiol assay was brought over from the Gynecologic Endocrine Laboratory. Progesterone and Estradiol are now done seven days a week. Finally, the PAP assay was brought in-house from send-out.

By the end of July it is projected that we will have set-up and run a Ciba-Corning ACS:180 analyzer that will allow us to convert several more of our assays to chemiluminescence methodology. This analyzer has pipetting capabilities and can read bar code on patient samples, thus significantly reducing the potential for identification error and improve turnaround time. Employing these instruments in large or technician time intensive assays allows us to continue to handle the ever increasing test volume and the development and evaluation of newer assays and analytes without increasing staff levels or overtime. The incorporation of newer assays and analytes gives us the ability to reduce the number of duplicate samples and standard curves that we are running. This results in a significant reduction in our per-test cost.

Migration of data analysis from PDP 11/44 to a Macintosh based system is nearing completion. The hardware is in place and the software is running but is not yet in its final form. Besides the usual opportunities afforded to the Pathology Residents to observe and participate in the Ligand Laboratory Function, we also extend this opportunity to Medical Technology students from Eastern Michigan University.

Barry England, Ph.D.
Director
Ligand Assay Laboratory

PATHOLOGY DATA SYSTEMS

DEPARTMENT OF PATHOLOGY
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1 JULY 1990 - 30 JUNE 1991

The activities of Pathology Data Systems for the past year can be divided into three separate categories: (1) PathNet hardware and software upgrades; (2) new hardware and applications to support the data processing needs of users; (3) educational activities.

PATHNET HARDWARE AND SOFTWARE UPGRADES:

In the first category, the most important change was the hardware upgrade of the VAX cluster, with replacement of the old processors with VAX models 8820 and 6510. The capacity of the processors on the cluster was approximately doubled as a result of this upgrade. Two state-of-the-art "optical" disk drives (RV20s) were also installed. Based on WORM technology (write one, ready many times), these drives provide greatly enhanced storage capabilities. As the result of their installation, cost savings are already being realized by the elimination of WAR reports on microfiche.

Software changes on the VAX cluster included two separate upgrades of VMS, the VAX operating system, as well as an upgrade to Version 304 of the PathNet software. WP-LINK was also installed and is now in the final stages of testing. This latter product will allow surgical pathology reports and personal faculty consultations to be generated in WordPerfect software running on distributed PCs in the department, with the final reports uploaded and integrated into the unified departmental data base.

Version 304 of PathNet supports bar code labeling which is now being implemented across all laboratories. Every test tube label generated in Central Distribution will include bar-code information relating to the patient, including name/hospital registration number, tests ordered, and the PathNet accession number. The presence of bar-coded labels will streamline laboratory operations because incoming specimens can be "wanded" to indicate specimen availability. Tubes can be then fed in random order into those automated laboratory instruments with the ability to input bar-code information.

Extensive progress has been made in the development of the test system (verification environment) which is use to test new and untried software before it is brought up on the live PathNet system. More specifically, we have developed software to copy actual patient test results to the test data base so that new software can be stressed in a test environment more closely mimicking the live environment. Accreditation agencies are now placing greater emphasis on the quality of such a test environment.

NEW HARDWARE AND SOFTWARE APPLICATIONS:

A new test inquiry program, POC, was developed locally to allow physician users to retrieve test results from the PathNet data base. This application was a major improvement over the preexisting Cerner software called PRI in that it is more user-friendly and it supports patient list management by physicians. This means that the physician is required to enter the name and registration number of a

patient into the system only once. The computer will then remember the information for subsequent retrieval of test results. Cerner has decided to make this software available to their other client sites.

Progress continues to be made in terms of locally developed CCL applications (Cerner command language; an SQL-type application) to query the data base and provide *ad hoc* reports. For example, a recurring report is sent to the Obstetrics-Gynecology Clinic containing a list of "non-negative" Pap smear results as a follow-up to the standard patient reports. Other examples of CCL reports include a chart-reprinting feature for those clinics which follow their patients on a long-term basis such as Hematology-Oncology and a feature for automatically extracting screening test results from the data base and generating letters to be sent by clinics to their patients.

A rule-based decision-support system was deployed on PathNet. This is a tool to utilize locally developed rule to facilitate laboratory work and support user needs. Currently the application is being used to support an auto-verify function whereby the system will review test results for reasonableness and then verify them if they fall within preestablished parameters. The system is also being used to support reflexive testing within various laboratories whereby additional tests are automatically ordered for a patient if the results for selected tests are initially positive.

As an R&D project using PDS research funds, a VAX "server" (model 4200) was purchased to which a portion of the laboratory data base is being copied. This server uses relational data base technology and has the capability to respond to SQL queries from users connected to the network throughout the hospital. The basic strategy here is to develop a prototype of a client-server architecture in PDS. Data base queries from users can then be shifted to the server from the production VAX cluster, which can then be used primarily to support the real-time production work of the laboratories. Discussions are ongoing with personnel in various clinical units who wish to have access to this server. This client-server project will be supported by Cerner and will also serve as a "showcase" for DEC.

The departmental centralized word-processing system (IBM 5520) was replaced with high-performance Novell network and PCs running WordPerfect. The choice of this word-processing software was driven by the need to integrate the system with WP-LINK which will be used to upload surgical pathology reports into the PathNet data base. This network has some sophisticated features, including the ability to back-up the PCs disk drives to servers installed on the network. A number of Novell servers were also installed in MSRB, including one to integrate the Macintosh and DOS environments.

The Tissue Typing Laboratory was brought-up using locally developed software and a Novell-based microcomputer network. This was a significant development in that it is an example of the development and integration of a network into the PathNet system when the Cerner-supplied software is not ideally suited to support the mission of the laboratory.

The Maternal and Child Health Center was activated, entailing computer support from PDS personnel. Preliminary plans were made to convert reporting in Cytology to the "Bethesda system." This new reporting system will be accompanied by automatic SNOMED coding of cytology reports. Preparatory work was also done to activate order-entry, result-reporting of test results via the mainframe computer using the HealthQuest software.

EDUCATIONAL ACTIVITIES:

PDS personnel supported the ninth annual Laboratory Information System Symposium in June. The conference attracted 210 registrants from 30 states, including Alaska, and Canada. Some 28 LIS vendors were in attendance. The conference was moved to the Power Center this year because the Towsley Center was no longer large enough to accommodate the annual conference.

Four members of the PDS staff presented posters at the annual PathNet Users Group in Kansas City in May. Bruce Friedman was installed as the Chairman of the Executive Council of the PathNet Users Group. PDS also continues to be support site visits from hospital groups considering the purchase of Cerner software.

Bruce A. Friedman, M.D.
Director,
Pathology Data Systems

PHLEBOTOMY SERVICES AND CENTRAL DISTRIBUTION

DEPARTMENT OF PATHOLOGY
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PHLEBOTOMY SERVICES:

The major change during the past year regarding phlebotomy services has been an extension of the range and type of services offered to hospital physicians. Beginning in April, 1990, as a new service on the midnight shift, collection of *stat* specimens and blood cultures was begun. Beginning in May, 1990, phlebotomists working in the Emergency Department and the Pediatrics Walk-in Clinic also began to draw blood and blood cultures. They also began to perform a limited range of laboratory tests in the Emergency Department such as glucose by glucometer, urine dip sticks, strep testing, and hematocrit.

Another significant expansion of phlebotomy services occurred in October, 1990, when phlebotomists began to draw blood from indwelling catheters on patient unit 8B. This pilot project has been judged to be successful, so there are now plans underway to extend the service to the outpatient pediatric population. This procedure has generally been recognized as a specialized nursing function, both locally and nationally, prior to the implementation of the program here at the University of Michigan Hospitals.

CENTRAL DISTRIBUTION:

In Central Distribution, a collection/handling fee was initiated for research specimens. the number of such specimens had grown precipitously in recent months, and the workload was beginning to effect routine patient specimens. The fee was set a a minimum level, and designed only for cost-recovery.

The workflow of the "sendout" and MLabs specimens in Central Distribution was intensively scrutinized by personnel in Central Distribution. As a result of this study, a new clinical coordinator position was established at the senior technologist level to supervise and rationalize both sendout and MLabs activities.

Finally, intensive planning took place to prepare both Central Distribution and the Phlebotomy Team for the deployment of labortory-wide bar-coded labels. Such labels will be computer-generated within Central Distribution, and then placed on all phlebotomist-drawn specimens. This machine-readable label will expedite specimen logging into the Central Distribution. Specimens can also be loaded in random order into the various automated analyzers in the laboratories which are capable of reading bar-coded labels.

Bruce A. Friedman, M.D.
Director,
Pathology Data Systems

ADMINISTRATIVE/FINANCIAL AFFAIRS DIVISION

DEPARTMENT OF PATHOLOGY
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The Administrative and Financial Affairs Division, which is under the auspices of the Office of the Chairman and his designee, includes five sections which are organized as follows:

A. ADMINISTRATIVE SUPPORT CENTER - PATHOLOGY LABORATORIES:

- Nancy A. Coray, Financial Analyst and Billing Coordinator
- Deborah Day Jansen, Administrative Coordinator for Pathology Laboratories
- Thomas D. Morrow, Assistant Administrator for Finance and Administration
- Beverly J. Smith, Administrative Assistant, Personnel and Payroll functions

Surgical Pathology Transcription:

- Robin O'Connor, Office Manager
- June M. Possley, Office Supervisor

B. CLINICAL FACULTY OFFICES, UNIVERSITY HOSPITALS:

- Holly A. Wagner, Office Supervisor

C. MEDICAL SERVICE PLAN BILLING OFFICE:

- Douglas M. Kennedy, Manager
- John J. Gilbert, Financial Analyst

D. OFFICE OF RESEARCH AND EDUCATION ADMINISTRATION:

- Maria A. Ceo, Administrative Associate
- Kathleen L. Atkins, Student Services Assistant

E. OFFICE OF THE CHAIRMAN:

- Laura D. Blythe, Staff Assistant
- Mary Anne Tishma, Staff Assistant

In addition to the management of daily activities, each of the units completed major projects.

ADMINISTRATIVE SUPPORT CENTER:

1. The M-Labs Program has gained several new physician clients this past year including one from Advanced Medical/Metpath Laboratories; one from the Lapeer area.
2. Coordinated an inspection of the Laboratories and of the UMMC Satellite Clinics by the College of American Pathologists.
3. Several staff have completed Team Leader Training for the Hospitals' Total Quality Program and initiated development of quality improvement teams in the Pathology Laboratories.

4. Participated in the planning for the renovation and remodeling to the Blood Bank was completed to resolve a citation issued by the Michigan Department of Public Health which included the reconfiguration of space for the Apheresis Center and the addition of an enclosed counseling area for the Directed Donor Program.
5. Participated with PDS staff in the development of an on-line process for surgical consults using a Cerner product titled, WP Link, which is now being piloted in the Faculty Support areas.

CLINICAL FACULTY OFFICES:

1. All secretarial support staff have completed classes in WordPerfect in preparation for the implementation of the WPLink surgical consult processing.
2. Two additional faculty members have been added to the Division of Surgical Pathology, Drs. Suzanne Selvaggi and Elizabeth DelBuono. A reorganization of the secretarial support staff was initiated in support of these faculty members.
3. Assisted in the development of standards for the department and Holly Wagner participated as a member of the Word Processing Committee.

MEDICAL SERVICE PLAN OFFICE:

1. Implemented automated entry of professional fee charges , Surgical and Cytopathological, for hospital patients using the Pathology Laboratory Computer System.
2. Coordinated a training program for WordPerfect for departmental clerical support staff.
3. Implemented tape to tape claim submission to Medicaid for all professional fee charges.
4. Implemented the Metropolitan Medicare System which included new claim requirements, remittance forms and action codes.
5. Updated computer equipment for Billing Office staff allowing access to the Pathology Laboratory Computer system for charge entry and report viewing in addition to access to the IDX system.
6. Coordinated the minor renovation of several research laboratory as well as the initiation of a major renovation to the Flow Cytometry Research and Molecular Diagnostics laboratories.
7. Participated in the presentation of the All Funds Budget for Fiscal Year 1991 as requested by the Medical School.

OFFICE OF RESEARCH AND EDUCATION ADMINISTRATION:

1. Coordinated the purchase of all equipment and supplies necessary for the research laboratory of Dr. Gabriel Nunez, a new faculty member in the Department.
2. Participated in the revision of a three year budget of all funds.
3. Participated in the development of the annual All Funds Budget.
4. Coordinated the quarterly publication of the Pathology Telephone Directory.
5. Developed and implemented insurance coverage for specific scientific equipment through the Hospitals which resulted in significant savings to the research programs.
6. Coordinated the renovation and remodeling project for the clerical support area and one faculty office in the MSRBI complex.

GENERAL:

1. Developed a plan for implementation of the Cost Reduction Program for the University Hospitals and Medical School, reducing all budgeted funds by 7.6% or $1,800,000 which included a staff reduction of 29.5 FTEs..
2. Prepared a forecast of the impact of the change in Medicare regulations (RBRVS) effective 1 January 1992 and developed revenue alternatives for professional income.
3. Participated with the Chairman to initiate expense reduction associated with all Departmental budgets.

4. Assisted in the development of a plan for the reorganization of the M-Labs Program due to a change in the directorship and the loss of several major clients.
5. Coordinated the plans for the Second Scientific Meeting of the A. James French Society of Pathologists which will be held in October 1991 and will be attended by over 100 pathologists from all areas of the country.
6. Began the planning process to initiate a fundraising campaign to endow a chair in honor of A. James French, M.D.

SUMMARY OF FINANCIAL DATA:

1. Grants and contracts:

101 active grants, contracts and other accounts		
Total Direct Expenditures	$4,698,302	
Indirect Research Expenditures	$2,037,124	
Total Sponsored Projects		$6,735,427
Other Expenditures (General Funds, MSP subaccounts, gifts, accounts - 27)		$2,346,723

2. Medical Service Plan:

Average number of active accounts	13,662
Number of charge entries	76,552
Gross Billings - Anatomic & Clinical Pathology	$10,302,842
Net Collections - Anatomic & Clinical Pathology	$4,671,147
Part A Payment	$2,572,667

3. Pathology Laboratories:

Number of fee code procedures	3,222,177
Number of reportable laboratory test results (est.)	12,800,000
Gross Revenue Pathology Laboratories	$92,176,528
Direct Expenses Pathology Laboratories	$20,211,435

Respectfully submitted

Eugene J. Napolitan
Administrator

EDUCATIONAL ACTIVITIES

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

The Department of Pathology has continued to offer a number of diverse programs within the Medical School Dental School, School of Public Health, College of Literature, Science and the Arts, and the Rackham School of Graduate Studies. These include courses requiring formal lecture and laboratory exercises, as well as providing for senior medical student pathology elective clerkships. Many faculty continue to serve on graduate student thesis committees and supervise medical student research experiences. Within the Medical Center context, Departmental teaching activities extend not only to medical students, but also house officers and the staff of many clinical departments in the form of regularly scheduled formal conferences. Departmental teaching also extends to practitioners in the region and nation through courses given through Continuing Medical Education Programs of The University of Michigan and the International Association of Pathologists (IAP).

MEDICAL AND DENTAL STUDENT PROGRAMS:

This past year, the Department of Pathology initiated a summer clinical/research program for underrepresented minority medical students. The goal of this program is to provide M1 and M2 students the opportunity to participate in Departmental clinical and research activities and promote the integration of Basic Science studies with patient-oriented clinical problems or focused research programs. In addition, it is hoped that the early exposure to the multiple opportunities available in Pathology will encourage students to consider careers in the specialty. Eleven students participated in the program and preliminary evaluations indicate that the program is viewed very positively by the students.

The Sophomore Pathology Course (Path 600) continues to be the primary focus of faculty teaching of medical students. The structure of the course is predicated on the students' acceptance of a significant responsibility for their own education, under faculty guidance. Formal evaluation indicated that the course continues to function smoothly and is well accepted by the students. Efforts to closely correlate the Introduction to Clinical Sciences Course (ICS-601) with the Sophomore Pathology Course continues to function to enhance the students' educational experience and reinforce "core material". The primary area of concern of faculty and students continues to be the relative lack of contact time that the faculty have with students within the Medical School curriculum. During the past year a new clinical rotation in Laboratory Medicine was developed and will be offered to fourth year medical students. This rotation will complement our current fourth year Pathology clerkship (which is more oriented toward anatomic pathology) and medical student research rotations.

The Department of Pathology continues to have primary responsibilities for the teaching of general and systemic pathology to dental students. This includes the presentation of formal lectures (Pathology 630) and preceptors of laboratory sessions (Pathology 631). Formal student evaluation indicates that the course functions smoothly and is well received by the students.

DOCTORAL PROGRAM:

The graduate program in Pathology was initiated two years ago and currently has six students enrolled. The primary goal of the Doctoral in Pathology Program is to train individuals for careers as independent scientific investigators with a focus on the study of the cellular and molecular basis of

disease processes. Five graduate level courses are offered by the Department, including a new course on the Genetics and Cell Biology of Aging.

Graduate Medical Education

The Department of Pathology provides formal advance training to M.D.s and Ph.D.s through the Residency Training Program, clinical fellowships and postdoctoral research fellowships. These programs are integrated to provide trainees the greatest opportunity for clinical and research training in their chosen discipline and to foster academic excellence.

Residency Training

The Department of Pathology offers high quality resident training in both anatomic and clinical pathology with opportunities to pursue basic research training in experimental pathology. The program continues to be exceedingly competitive with 113 completed applications received, and 32 candidates invited to interview in the Department this past year. Six outstanding residents were recruited to the Department: Philip J. Boyer, M.D., Ph.D., Walter H. Henricks, III, M.D., Margaret M. Moll, M.D., Patricia M. Perosio, M.D., Scott G. Silveira, M.D., and Robert A. Stern, M.D..

Currently, there are 27 residents in the Department, 25 of whom are receiving training in both anatomic and clinical pathology and 2 receiving training in anatomic pathology alone. Three residents graduated from the program this past year. Two graduates assumed positions as staff pathologists at the University of Michigan, Department of Pathology, and Butterworth Hospital, Grand Rapids, Michigan. The third resident will continue training in Forensic Pathology, Sacramento, California.

A significant number of residents continue to be involved in both clinical and experimental research projects which have resulted in the presentation of their work at national meetings, as well as publications in peer-reviewed journals. The residents again this year took the American Society of Clinical Pathologists' in-service examination and performed very well.

Clinical Fellowships

The Department provides advanced training in surgical pathology, cytopathology, hematology, and transfusion medicine through formal fellowship programs. Five positions are currently supported and the clinical fellowships are closely integrated with the Residency Training Programs (see Anatomic and Clinical Pathology Sections).

Postdoctoral Research Training

The Department of Pathology provides advanced research training for approximately 24 postdoctoral fellows which includes Pathology residents seeking advanced training in experimental pathology. Fellows are located within the faculty research laboratories of the Department. Support is provided by an NIH-funded Lung Immunopathology Training grant (HL-07517, P.A. Ward, Principal Investigator) and externally-funded faculty research grants. This past year five fellows completed their training and have assumed the following positions:

1. Elahe Crockett-Torabi, Ph.D., Assistant Research Investigator, Department of Pathology, The University of Michigan Medical School (NIH FIRST Award)
2. Joseph P. Grande, M.D., Ph.D., Senior Associate Consultant, Department of Pathology, Mayo Clinic Medical School
3. Joseph W. Francis, Ph.D., Assistant Research Investigator, Department of Pediatrics, The University of Michigan.
4. Cheryl Swenson, D.V.M., Ph.D.,Assistant Professor, Michigan State University.

5. Theresa Bacon-Baguley, Ph.D., Assistant Professor, Department of Health Science, Grand Valley State University.

Formal courses given within the Department include:

I. COURSES IN THE MEDICAL CURRICULUM

A. ICS 500:
   1. Introductory Lectures on General Pathology (15 contact hours).

B. ICS 600/601:
   1. Immunopathology Sequence (15 contact hours).
   2. Clinicopathologic Conferences (10 contact hours).
   3. Selected Topics in Surgical Pathology.

C. NBS 600:
   1. Neuropathology (25 contact hours).

D. Pathology 600:
   1. 68 hours of whole-class lecture, 74 hours of laboratory (in each of six sections) (142 contact hours).

E. Pathology Clerkships:
   1. Elected by 47 students at University Hospitals.

F. Summer Clinical/Research Programs in Pathology for Underrepresented Minority Students

II. COURSES IN THE DENTAL CURRICULUM

A. Pathology 630:
   1. General Pathology Lectures (45 contact hours).

B. Pathology 631:
   1. Pathology Laboratory (60 contact hours) each of two sections (assisted by Oral Pathology staff).

III. GRADUATE COURSES IN PATHOLOGY

A. Pathology 580: General Pathology for Biologic Scientists
B. Pathology 581: Cellular and Molecular Basis of Disease
C. Pathology 583: General Pathology Laboratory - Histopathology
D. Pathology 620: Genetics and Cell Biology of Aging
E. Pathology 650: Laboratory Techniques in Experimental Pathology
F. Pathology 850: Special Topics in Pathology
G. Pathology 599: Non-Dissertation Research
H. Pathology 990: Pre-Candidate Dissertation Reseach
I. Pathology 995: Candidate Dissertation Research

IV. POSTGRADUATE MEDICINE/CONTINUING MEDICAL EDUCATION:

A. Current Topics in Blood Banking Symposium, June 5 - June 7, 1991.
B. Clinical Laboratory Computers Symposium, June 12 - June 14, 1991.
C. Pathology 858:
   1. Neuropathology (18 contact hours).

V. CLINICAL CONFERENCES:

The Department of Pathology provides an important educational service to many other clinical departments through regular participation in interdepartmental working/teaching

conference. The Department is involved in many such conferences on a weekly, bi-weekly, and monthly basis. The units served include:

Internal Medicine

- Gastroenterology
- Nephrology
- Hematology/Oncology
- Nuclear Medicine
- Pulmonary Medicine
- Arthritis
- Cardiology
- General (Necropsy Review, CPC)

Dermatology

Thoracic Surgery

Urology

Pediatrics

- Cardiology
- Oncology
- Gastroenterology
- General (Death Conference, CPC)

Obstetrics and Gynecology

- Oncology

Oral Surgery

General Surgery (Breast, GI)

Otorhinolaryngology

Joseph C. Fantone, M.D.
Coordinator,
Educational Activities

THE UNIVERSITY OF MICHIGAN MEDICAL SCHOOL DEPARTMENT OF PATHOLOGY HOUSE OFFICERS 1990 - 1991

Elizabeth A. Del Buono, M.D.
Chief Resident
House Officer IV
(4th Year)

David M. Graham, M.D.
House Officer V
(5th Year)

Michael J. Caplan, M.D.
House Officer IV
(4th Year)

Randall J. Shannon, M.D.
House Officer IV
(4th Year)

Denise E. Sulavik, M.D.
House Officer IV
(4th Year)

Paul F. Mazzara, M.D.
Assistant Chief Resident
House Officer IV
(4th Year)

Cynthia A. Hegg, M.D.
House Officer V
(4th Year)

Steven H. Mandell, M.D.
House Officer IV
(4th Year)

Barbara A. Markey, M.D.
House Officer III
(3rd Year)

Loretta R. O'Donnell, M.D.
House Officer III
(3rd Year)

Cheryl A. Utiger, M.D.
House Officer III
(3rd Year)

Sarah E. Campbell, M.D.
House Officer III
(3rd Year)

Philip L. Perkins, M.D.
House Officer IV
(3rd Year)

Kyle A. Carr, M.D.
House Officer II
(2nd Year)

Suzanne M. Cook, M.D.
House Officer II
(2nd Year)

John R. Goldblum, M.D.
House Officer II
(2nd Year

Eric P. Kaldjian, M.D.
House Officer II
(2nd Year)

Priscilla R. Lindley, M.D.
House Officer II
(2nd Year)

Sonya K. Brown, M.D.
House Officer I
(1st Year)

Jane S. Chen, M.D.
House Officer I
(1st Year)

Eric D. Hsi, M.D.
House Officer I
(1st Year)

Charles J. Hunter, M.D.
House Officer III
(1st Year)

Jeffrey P. Pearson, M.D.
House Officer I
(1st Year)

David A. Start, M.D.
House Officer I
(1st Year)

M-LABS

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

The M-Labs program continues to grow in both Anatomic and Clinical Pathology. In addition to increased volume, the profit margin of the M-Labs program continues to improve based on increased efficiency and maturation of the clinical laboratory system to a reference laboratory system within the central pathology laboratories.

M-Labs is carefully evaluating its function in the face of recent budget reductions. Presently, the program has not had to alter client service.

M-Labs has over 100 clients, of which approximately 20 can be considered major clients. These clients include hospital accounts and large doctor office accounts. M-Labs has lost a major reference lab client to a regional lab group operating in western Wayne County.

M-Labs' maintenance of the laboratory quality improvement programs in all the M-Care sites has matured to include proficiency testing and preparation for accreditation proceedings.

The forecast for the coming year for M-Labs is for slow growth with no foreseeable increase in costs of the program.

Kenneth D. McClatchey, M.D., D.D.S.
Director,
M-Labs Program

VETERANS ADMINISTRATION MEDICAL CENTER
LABORATORY SERVICE

DEPARTMENT OF PATHOLOGY - UNIVERSITY OF MICHIGAN
ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

INTRODUCTION:

The Veterans Administration Medical Center Laboratory Service is closely affiliated with the Department of Pathology at the University of Michigan Medical Center. The Faculty have academic appointments and participate in departmental activities in a manner similar to other Sections. Recruitment efforts are combined and candidates are evaluated for academic potential as well as professional competence similar to any departmental candidate. There are four full-time pathology staff positions available although a vacancy has existed from some time despite continued recruitment efforts. Three resident positions are available and are filled by university pathology residents on monthly rotations in Surgical Pathology, Autopsy Pathology and electives including Electron Microscopy and special study areas in Surgical Pathology. The Chief, Laboratory Service is a voting member of the Dean's Committee.

ANATOMIC PATHOLOGY:

A. Surgical Pathology: 4,881 surgical cases have been received and reported during this time. The resident assigned to surgical pathology acts as coordinator of this section and in that capacity examines all material grossly and microscopically under the close, one-to-one, supervision of the staff pathologist. The resident has the opportunity to coordinate the findings with the clinical staff and medical students. An extensive quality assurance program includes consultation with AFIP, University of Michigan and review of frozen sections, amended diagnoses and surgical appropriateness.

B. Autopsy Pathology: 63 autopsies were completed during this period of time. The resident performs the autopsy, prepares the gross pathologic diagnosis, presents the case at the autopsy conference and then cuts tissue for slides and microscopic diagnosis. All of the steps are supervised by staff pathologists including the performance of the dissection as well as microscopic diagnosis. The residents also presented the findings of selected autopsies at Medicine Morbidity and Mortality Conference. Twenty-two cases were presented during this time.

C. Cytology: 2,491 specimens were diagnosed during this period. Close correlation with surgical pathology is made as appropriate and the residents are encouraged to review cytologic material during their surgical and autopsy rotation.

D. Electron Microscopy: 336 electron microscopy cases were reported. An elective rotation is available for pathology residents in_discipline. Informally, residents may familiarize themselves with electron microscopy techniques and interpretation through consults with Dr. Beals regarding many cases for which electron microscopy is appropriate. Dr. Beals presents biweekly seminars for the residents at the University during the academic year. As a VA "Center of Excellence" this electron microscopy section serves as consultant to other VA medical centers and to some other hospitals.

CLINICAL PATHOLOGY:

1,610,000 tests were done in the sections of chemistry, hematology, microbiology and immunohematology. Although there is not a formal "clinical" pathology rotation available for the use of

residents, continuing education conference are also presented requently and are available for residents participation even as a teacher. Dr. Chensue is director of clinical pathology.

EDUCATION AND TEACHING:

One-on-one teaching of residents is the daily procedure in surgical pathology. A surgical pathology conference is held biweekly. An autopsy conference with the entire staff is held the day following every autopsy. All residents participate in informal conferences, consultation episodes. The scheduling is such that the residents are generally permitted time to attend conferences, lectures and seminars at University of Michigan.

The entire VA staff participates in laboratory teaching of medical students on a yearly basis. Dr. Weatherbee lectures in bone pathology. Dr. Beals and Weatherbee give a gross pathology conference periodically.

RESEARCH:

Dr. Chensue continues as a member of the VA Research and Development Committee and a strong funded research program as well. The other staff are participating in clinical studies in collaboration with a variety of investigators.

SUMMARY:

The Veterans Administration Medical Center Laboratory Service is committed to the practice of high quality medicine and the appropriate care of patients. We feel that the close association with the University of Michigan enables us to accomplish that goal by establishing a stimulating academic environment in which research and teaching are encouraged. Every effort is made to improve the professional interchange between the two institutions. During this year there has been steady progress toward the clinical addition to this medical center that will more than double the present space of the Laboratory Service.

Lee Weatherbee, M.D.
Chief, Laboratory Service
Ann Arbor VA Medical Center