THE UNIVERSITY OF MICHIGAN

Department of Pathology

ANNUAL REPORT

1 July 1988-30 June 1989

THE UNIVERSITY OF MICHIGAN

DEPARTMENT OF PATHOLOGY

ANNUAL REPORT

1 JULY 1988 - 30 JUNE 1989

LIST OF FACULTY

LIST OF FACULTY

Name	Rank	Institutional Affiliation
Abell, Murray R.	Professor Emeritus	The University of Michigan
Abrams, Gerald D.	Professor and Director, Anatomic Pathology	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
Burkholder, Peter M.	Professor	Veterans Administration Medical Center
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
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

Name	Rank	Institutional Affiliation
Flint, Andrew	Associate Professor	The University of Michigan
Friedman, Bruce A.	Professor	The University of Michigan
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	The University of Michigan
Hinerman, Dorin L.	Professor Emeritus	The University of Michigan
Johnson, Kent J.	Professor	The University of Michigan
Judd, W. John	Associate Professor	The University of Michigan
Keren, David F.	Professor	The University of Michigan
Killen, Paul D.	Assistant Professor	The University of Michigan
Kunkel, Steven L.	Associate Professor	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.	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

Name	Rank	Institutional Affiliation
Naylor, Bernard	Professor	The University of Michigan
Nickoloff, Brian J.	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
Regezi, Joseph A.*	Associate Professor	The University of Michigan
Remick, Daniel G.	Assistant Professor	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
Shope, Thomas C.+	Associate Professor	The University of Michigan
Shu, Suyu+++	Associate Professor	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
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
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

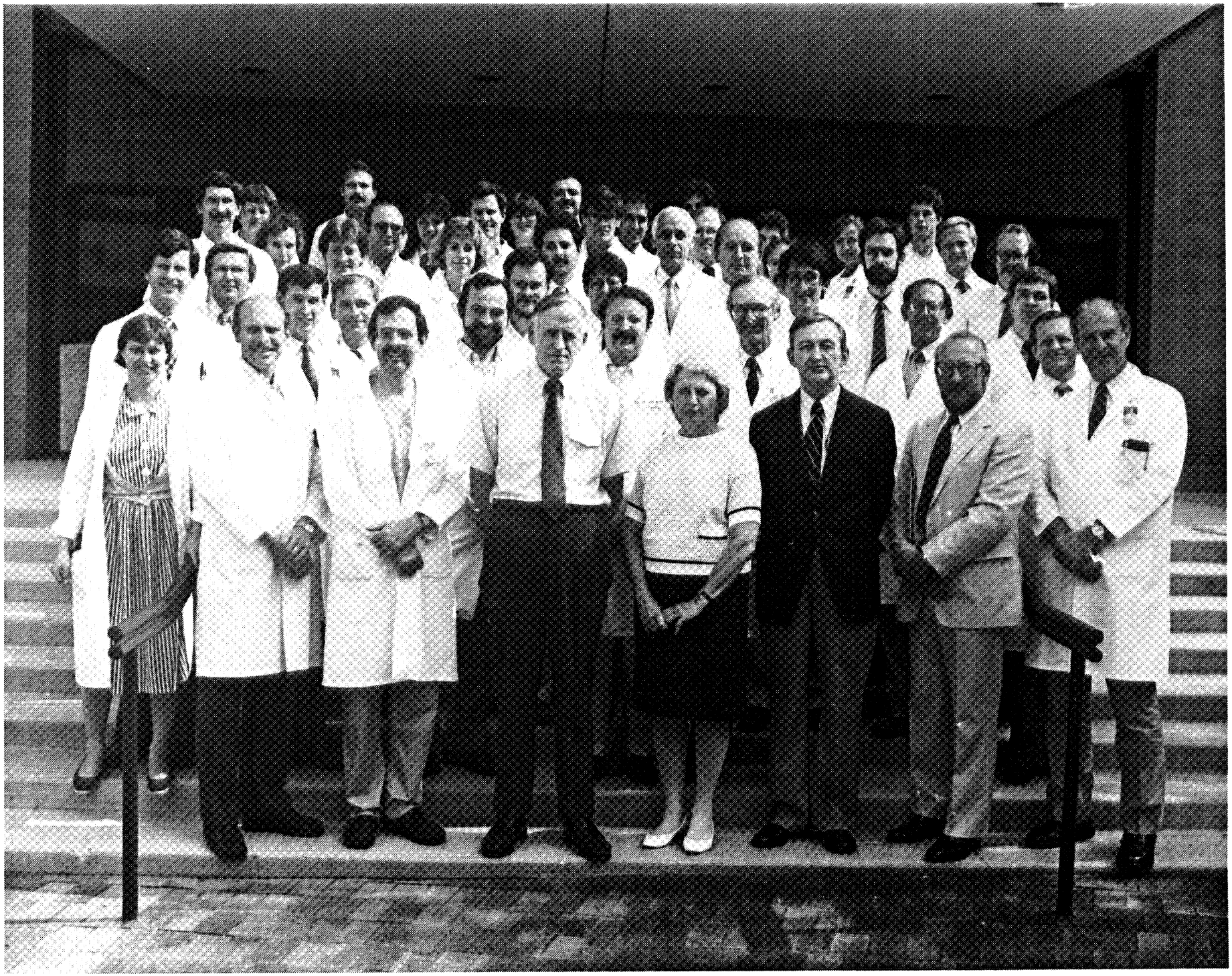


TABLE OF CONTENTS

TABLE OF CONTENTS

DEPARTMENTAL OVERVIEW

DEPARTMENTAL OVERVIEW
1988/89

For the better part of the current decade, change in the Department of Pathology has related to the laying of the foundations for a strong research program in the Department in a manner that the teaching and diagnostic programs of the Department will also be enhanced. This seems to have been accomplished. Beginning in 1980, a strong research program involving the areas of immunology and inflammation was developed by recruitment of a significant number of new faculty members. In the mid-1980's, coincident with establishment of The University of Michigan Howard Hughes Medical Institute, the Department of Pathology commenced recruitment of faculty members with strong credentials in the area of molecular genetics/biology and developed the Pathology Molecular Biology Program. As of Summer of 1989, with the arrival of Dr. Bernard Weiss from the Johns Hopkins School of Medicine, the Department has achieved a strong and well integrated research program.

Related to these accomplishments has been the exceptionally high quality of individuals being recruited into our Residency Training Program. Another result has been the inauguration of the Graduate Program in Experimental Pathology, approved by the Rackham Graduate School and scheduled for activation in the Fall of 1989. This program will allow the Department to achieve balance in the graduate-level activities, with a blend of Ph.D.-seeking candidates as well as the relatively large number (currently approximately 18) of postdoctoral fellows. The Ph.D. Program will also allow the Department for the first time to have access to students admitted to the Medical Scientist Training Program (M.D., Ph.D.).

The Department is in the process of adjusting the structure of the Pathology Residency Program to accommodate to the recommendations emanating from the Park City Retreat, which suggested that for combined AP/CP programs there should be a three year period core for training, followed by two years of elective experiences. A Departmental white paper has recently been developed in order to codify the Residency Training Program with respect to tracking options for residents. This document will formally state the number of slots available within each of the available options (e.g., combined AP/CP, AP only, CP only, etc.) This document will be discussed extensively within the Department prior to its becoming a policy document.

In 1989 the Department enters into a new phase in its development. As of August, 1989, Dr. Sharon W. Weiss joins our ranks as Director of the Division of Anatomic Pathology and Chief of Surgical Pathology. She brings to the Department new ideas and approaches as well as a professional record of being one of, if not the single most, distinguished surgical pathologist involving diagnosis of soft tissue tumors. Also joining the Surgical Pathology group will be Dr. Thomas S. Frank, who has recently completed a surgical pathology fellowship at the University of Pennsylvania, School of Medicine. In the Fall of 1989, Dr. Weiss will initiate a search process for recruitment of a third surgical pathologist, completing an increase by three in our group of surgical pathologists. The developments should enhance the functions in Surgical Pathology, which continues to see annual growth in the number of surgical pathology specimens. These changes in Surgical Pathology should provide additional diversity and strength to an already well-recognized resource in the Department of Pathology. One of the changes that will occur with Dr. Weiss's arrival will be the development of a Surgical Pathology Fellowship Program patterned after similar programs at Johns Hopkins University, Stanford University and the Mayo Clinic.

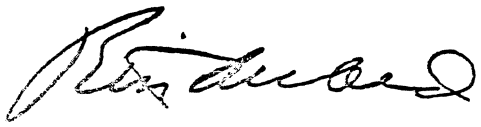
There is also a slow but steady build-up in faculty involved in the Clinical Pathology program in the Department. We have recently committed Departmental resources for the filling of Clinical Fellowships in the areas of Hematopathology and the Blood Bank. This recognizes the fact that there are two areas in which, because of substantial growth in the demands of increased clinical

volume and new program development. In the past year a new faculty position was also created in a manner that splits responsibilities between Clinical Immunology and research. Most recently new faculty positions related to Cytogenetics and Tissue Typing have also been created, the funding for which is provided both by the Department and by The University of Michigan Hospitals.

The commitment of Departmental resources to program expansions described above will strengthen the organization and allow us to meet the burgeoning institutional demands on our faculty. There is one note of concern. Over the past year, in spite of increased volume of activities in the area of Surgical Pathology, we have actually seen an effective fall in revenue for part B services. This is due to arbitrary reductions in payments by Blue Shield and by Medicare. The loss of revenue is equivalent to more than one-third of a million dollars per year. This, combined with the substantial costs related to recruitment of new clinical faculty, implies that we are approaching the point of diminished flexibility in our total Departmental budget. If there should be further reductions in reimbursement from payors such as Medicare and Blue Cross, or if we would realize an unexpected reduction in research revenue (which is not currently foreseen), we would be in a difficult situation. This underscores the importance of the upcoming contract negotiations with the University Hospitals. It also emphasizes the importance of the M-Labs Program which has assumed an important teaching role as well as providing important flexibility for academic program development.

At present, we can take pride in the progress of the Department. the recent success in program development and faculty recruitment within the Department will enhance our stature and help us to move closer to the ultimate objective of academic pre-eminence in the field of Pathology.

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
DIRECTOR OF ANATOMIC PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Services - 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:
ICS-500 Sequence Coordinator and Lecturer, "Basic Concepts of Disease" - 22 contact hours
B. Sophomore Medical Class:
1. ICS 600 - Clinicopathologic Conferences - 8 contact hours
2. Pathology 600 - lecture - 8 contact hours
C. 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 - 4 contact hours
3. Biology 262 - (LS&A Lecturer) - 2 contact hours
D. Hospital Conferences:
1. Cardiovascular Pathology Conference - monthly
2. Internal Medicine CPC - monthly
3. Internal Medicine Necropsy Review - monthly
4. Gynecologic Pathology, Non-oncologic - monthly
E. House Officers:
Training in Surgical and necropsy Pathology
F. Invited Lectures:
1. "The uses of endomyocardial biopsy" Department of Pathology, Siriraj Hospital, Mahidol University, Bangkok, Thailand. Feb 22, 1989.
2. "Serial lectures on cardiac pathology" Department of Pathology, Jinan University Medical College, Guangzhou, China. Feb 27 - March 2, 1989.
3. "Early cancer and precancer" Central Michigan Community Hospital, Mt. Pleasant, MI, April 2, 1989.
G. Class of 1991 - Excellence in Teaching Award

III. RESEARCH ACTIVITIES

PROJECTS UNDER STUDY:

A. Recovery from myocardial infarction - Anatomic and functional aspects (with K. Gallagher, et. al.)
B. Toxicity of mitometh (with D.E. Schteingart)
C. Natural history of myocarditis (multi-center myocarditis study)
D. Toxicity of zinc (with G. Brewer)
E. Effect of gastrointestinal flora on body temperature (with M. Kluger)
F. Radiologic/Pathologic correlation in pancreatic neoplasms (with I. Francis)
G. Director - Tissue procurement core - U of M Cancer Center

IV. SERVICE ACTIVITIES

DEPARTMENTAL:

A. Director, Division of Anatomic Pathology, Surgical Pathology
B. Member, Historical Collections Committee, Medical School
C. Chair, Standing Committee for Investigation of Misconduct in Research, Medical School
D. Member, Ethics Committee, Hospital
E. Member, General Surgery Search Committee
F. Member, Medical School Committee to Develop Guidelines For the Responsible Conduct of Research

REGIONAL AND NATIONAL

A. Deputy Medical Examiner, Washtenaw County
B. President, Gastrointestinal Pathology Society, IAP
C. Member, Expert Panel, Performance Improvement Program, CAP
D. Abstract Reviewer, International Academy of Pathology
E. Editorial Board, "Modern Pathology"

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Hanson CA, Boling SF, Stoolman LM, Schlegelmilch JA, Abrams GD, Miska PT, Deeb GM: Cytoimmunologic monitoring and Heart Transplantation. J.Ht.Tsplt. 1988; 7, 424-429.
2. Yuzbasiyan-Gurkan V, Brewer GJ, Abrams GD, Main B and Giacherio D: Treatment of Wilson's disease with Zinc: V: Changes in serum levels of lipase, amylase, and alkaline phosphatase in Wilson's disease patients. J Lab & Clin Med; In press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Medical Students:
   1. Lecturer, Pathology 600 Course
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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Microbore Applications to the analysis of drugs.
B. Distribution of cyclosporine and metabolites in blood and tissues.
C. Lactate production during myocardial ischemia.
D. Esoteric analysis of drugs by gas chromatography/mass spectrometry.
E. Measurement of cyclosporine by radioimmunoassay.

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, Michigan Section, American Association for Clinical Chemistry.
B. Education Committee, Michigan Section, American Association for Clinical Chemistry.
C. Past Chairman, American Association for Clinical Chemistry, Michigan Section.
D. College of American Pathologists Chemistry Reference Laboratory.
E. Member, NCAA Drug Testing Team.
F. Executive Committee, Therapeutic Drug Monitoring Clinical Toxicology Division, AACC.
G. ETS Advisory Board, Syva Corporation.
H. Member, Academy of Clinical Laboratory Physicians and Scientists.
I. Member, American Association of Pathologists.
J. Member, American Association for Advancement of Science.
K. Member, Clinical Ligand Assay Society.

V. OTHER RELEVANT ACTIVITIES:

A. Biomedical Chromatography, Editorial Board, 1988--
B. Therapeutic Drug Monitoring and Clinical Toxicology Newsletter, Editorial Board, 1988--

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.

INVITED LECTURES/SEMINARS:

1. "Effects of Blood Parameters and Metabolites on the Distribution of Cyclosporine in Blood", Mayo Clinic, Rochester, Minnesota, July 1988.
2. "Use of Cardiac Drugs in the Elderly", National Meeting of the American Association for Clinical Chemistry, New Orleans, Louisiana, July 1988.
3. "Instrumentation Update", American Society for Medical Technology Annual Meeting, Detroit, Michigan, September 1988.
4. "Impact of Organ Transplantation on the Clinical Laboratory in Chemistry", American society for Medical Technology Annual Meeting, Detroit, Michigan September 1988.
5. "Therapeutic Drug Monitoring and Toxicology: Issues for the 90's", International TDM Meeting, Chicago, Illinois, October 1988.
6. "Special Considerations for Geriatric Drug Monitoring", International TDM Conference, Chicago, Illinois, October 1988.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Nelson, S.D., Kou, W.H., Annesley, T., DeBuitleir, M., and Morady, F.: Significance of ST segment depression during paroxysmal supra ventricular tachycardia. J. Amer. Coll. Cardiol. 1988; 12: 383-387.
2. Fisher G., Duell E.A., Nicholoff B.J., Annesley T.M., Ellis C.N., and Vorhees J.J.: Levels of cyclosporine in epidermis of treated psoriasis patients differentially inhibit growth of keratinocytes cultured in serum free versus serum containing media. J. Invest. Derm. 1988; 91: 142-146.
3. Annesley, T.M., and Judd, W.J.: Bleach and LISS: A potential hazard. J Med. Labor. Scie. 1989;46:83-85.
4. Annesley, T.M.: Geriatric Therapeutic Drug Monitoring. Clin. Chem 1989;35:In Press.
5. Annesley, T.M.: Extending the clinical laboratory into forensic drug testing. J. Clin. Immunoassay 1989; 12: Accepted for Publication.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

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 - 5 full class lectures.
   2. Lab Instructor Pathology 600 - 1 semester.
   3. Pathology 630 (dental) - 3 full class lectures.
   4. Senior medical student electives - 6 month instruction in surgical pathology in the reading room.
   5. Senior medical student elective in pathology rotation, supervisor 1 month.

B. House Officers:
   1. Surgical Pathology Conference - 1 hour per week.
   2. Autopsy service tutoring, 5-6 weekends and gross autopsy conference twice a week.
   3. Surgical pathology diagnosing room instruction for assigned house officer - 5 1/2 months.
   4. Gastrointestinal and hepatic pathology tutoring - full time.
   5. Mentor for one house officer in gastrointestinal and liver pathology subspecialty - 1 month total.
   6. Formal Lectures on GI and Liver Pathology - 7 hours.

C. Interdepartmental:
   1. Medical Gastrointestinal Pathology 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 Campylobacter-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.
F. Liver Transplantation for Hepatitis B Disease with Mike Lucey, Keith Henley and Bob Merion.
G. Prognostic Markers in Colorectal Cancer, with David Graham.

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. Member, Program Committee, Michigan Society of Pathologists.
B. Reviewer of papers for Archives of Pathology and Laboratory Medicine, Human Pathology, Gastroenterology, and Am J of Gastroenterology.
C. Chairman, Publications Committee and Member, Executive Committee, Gastrointestinal Pathology Club.
D. Expert Pathologist, Large Bowel and Anal Canal Neoplasms and Gastric Neoplasms Panels, College of American Pathologists Performance Improvement Program.
E. Coordinator for Pathology, Randomized Therapeutic Trail in Cancer of the Esophagus, International Organization for Statistical Studies of Diseases of the Esophagus, Paris, France.
F. Visiting Pathologist for Regional Workshops on Pathologic Diagnosis in Inflammatory Bowel Disease, sponsored by the National Foundation for Ileitis and Colitis and the Johns Hopkins Medical Institution. Seminars conducted:
   1. New Orleans, LA, November 12, 1988.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Visiting Professor Lecture: Carcinoma and dysplasia in IBD. Indiana University School of Medicine, Department of Pathology, Indianapolis, Indiana, September 15, 1988.
2. Lecture: New staging methods in colon cancer. Annual fall meeting: Michigan Tumor Registrars Association, The University of Michigan Medical Center, October 28, 1988.
3. Lecture: Carcinoma and dysplasia in IBD and Seminar in G-I Pathology. Wisconsin Society of Pathologists, Fall Meeting, Oshkosh, Wisconsin, October 1, 1988.
4. Lecture: Adenoma Carcinoma Sequence in the Colon. Pontiac General Hospital, Department of Surgery, Pontiac, MI, November 14, 1988.

5. Seminar on Neoplastic Diseases of Intestine, American Society of Clinical Pathologists, course on Surgical Pathology of the Gastrointestinal Tract, San Antonio, Texas, April 28, 1989.
6. Lecture: Gastritis and Campylobacter. Michigan Society of Histotechnologists Annual Symposium/Convention, Ann Arbor, Michigan, May 13, 1989.
7. Visiting Professor Lecture: Gastritis. University Hospital, Department of Pathology, State University of New York, Stony Brook, New York, June 9, 1989.
8. Lecture: Stromal Tumors of the Gut, Grand Rounds, Department of Pathology, UCLA, Los Angeles, CA, June 28, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lynch HT, Smyrk T, Lanspa SJ, Marcus JN, Kriegler M, Lynch JF, and Appelman HD: Flat adenomas in a colon cancer-prone kindred. J Natl Cancer Inst 80:278-282, 1988.
2. Johnson TL, Barnett JL, Appelman HD, and Nostrant T: Candida hepatitis: histopathologic diagnosis. Am J Surg Pathol 12:716-720, 1988.
3. Plke AM, Lloyd RV, and Appelman HD: Cell markers in gastrointestinal stromal tumors. Hum Pathol 19:830-834, 1988.
4. Cooper HS, Dayal Y, Gourley WK, Kelly JK, Madara JL, Petras RE, Snover DC, and Appelman HD: Diagnostic nonproblems in gastrointestinal biopsy pathology. Proceedings of the 1988 subspecialty conferences on gastrointestinal pathology at the USCAP. Mod Pathol 2:244-259, 1989.
5. Flint A, Apppelman HD, and Beckwith AL: DNA analysis of gastric stromal tumors: Correlation with pathologic features. Accepted for pulication Surg Pathol.
6. McQuillan AC and Appelman HD: Superficial Crohn's disease: A study of 10 patients. Accepted for publication, Surg Pathol.
7. Brewer GJ, Yuzbasiyan-Gurkan V, Lee D-Y and Appelman HD: The treatment of Wilson's disease with zinc. VI. Initial treatment studies. Accepted for publication in J Lab Clin Med.
8. Barnett JL, Behler EM, Appelman HD, and Elta GH: Campylobacter pylori is not associated wtih gastroparesis. Accepted for publication in Diag Dis Sci.

BOOKS AND CHAPTERS IN BOOKS:

1. Antonioli DA and Appelman HD: Anus and Perianal Area. Chapter 36 in Sternberg Stephen S., ed. Diagnostic Surgical Pathology, Raven Press, Ltd, New York, 1989.
2. Appelman HD: Mesenchymal Tumors of the Gut: Historical Perspectives, New Approaches, New Results, and Does It Make Any Difference? Ch 6 in Goldman H, Appelman HD and Kaufman N, eds. Gastrointestinal Pathology. USCAP Monograph. Williams and Wilkins, Baltimore. In Press.
3. Appelman HD: Barrett's Esophagus: Morphologic Considerations. In Orringer MB, ed.: Surgery of the Alimentary Tract - The Esophagus. W B Saunders, Philadelphia. In Press.
4. Appelman HD: Mesenchymal Tumors of the GI Tract. Chapter 15 in Pathology of the Gastrointestinal Tract, Ming S-C and Goldman H., eds. W.B. Saunders, Philadelphia. In Press.

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

1. Mutchnick MG, Lee HH, Haynes GD, Hoofnagle JH and Appelman HD: Thymosin treatment of chronic active hepatitis B (CAHB): A preliminary report on a controlled, double blind study. Hepatology 8:1270, 1988.
2. Su Y-L, Appelman HD and Mutchnick MG: Absence of Thymosin B4 in bile ducts of liver tissue from patients with cholestatic liver disease. Hepatology 8:1291, 1988.
3. Graham DM and Appelman HD: Crohn's type lymphoid reaction in colon carcinoma. Lab Invest 60:34A, 1989.
4. Lanspa SJ, Lynch HT, Smyrk TC, Strayhorn P, Watson P, Lynch J, Appelman H: Initial results of a colonoscopy screening program in Lynch syndrome. Gastrointestinal Endoscopy 35:173, 1989.
5. Wolber R, Owen MB, DelBuono L, Appelman H: Lymphocytic gastritis in patients with celiac sprue or sprue-like disease. Lab Invest 106A, 1989.
6. Lucey MR, Sorenthal S, Martin P, DiBisceglie A, Burtch G, Nostrant T, Appelman HD: Liver transplantation for hepatitis B viral infection. Gastroenterology 96:A624, 1989.
7 Book Review: The Liver: Biology and Pathobiology, ed. 2, edited by Irwin M. Arias, William R. Jakoby, Hans Popper, et al. in Arch Pathol Lab Med 112:1167, 1988 (Book Review).
8. Book Review: Inflammatory Bowel Disease, 3rd Ed, Kirsner JB and Shorter, RG eds. 1988. In: Am J Surg Pathol 13:434, 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

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. Lecturer, Blood Bank Introductory Lecture Series.
   2. Coordinator, Introductory Blood Bank Seminar Series for Pathology House Officers.
   3. 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:

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.
B. Co-chairman, Education Committee, Michigan Association of Blood Banks.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "New Developments in Leuko Poor Products", Michigan Association of Blood Banks , Education Committee. Technical Workshop, Lansing, Michigan, May 4 and 5, 1989.
2. "Ask Your Peers", Panel Discussion at MABB Technical Workshop, Lansing, Michigan, May 4 and 5, 1989.

VI. PUBLICATIONS: None.

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 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Medical Director, Myelodysplasia Unit: inpatient and outpatient services for children with spina bifida, 362 Clinic Visits.
B. Attending Physician Pediatrics Infant Ward: 4 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 4 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. OB/GYN Grand Rounds

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: 202 fetal/neonatal examinations

COLLABORATIVE RESEARCH:

1. Collection and allocation of fetal tissues for research projects in the Departments of Pediatrics, Pathology, Obstetrics, Anatomy, Orthopedics, Internal Medicine, Genetics, and Howard Hughes Institute. Loan of fetal material for research investigations in the Department of Radiology.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Departmental - Pathology: none.
B. Departmental - Pediatrics: Editorial Board, Pediatric Rounds; House Officer Selection Committee, House Officer Work Group, chairman.
C. Steering Committee for DSCC-funded Cost of Comprehensive Care Study.
D. Standardization and product evaluation committee, member; Infant care review committee

REGIONAL AND NATIONAL:

A. Reviewer for journals: Teratology, Pediatric Pathology, American Journal of Public Health and New England Journal of Medicine.
B. Section Editor (Clinical Teratology), Public Affairs Committee, Teratology.
C. Publications Committee, Teratology Society.
D. Editorial Board, Birth Defects Encyclopedia.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. The tetrad of abnormal development. In 6th Annual Refresher Course, Teratology Society. Richmond, Virginia, June 3-4, 1989.
2. Turner's syndrome from conception to birth: Fetal pathology studies. In: Turner Syndrome: A Life Cycle Perspective. Livonia, Michigan, November 11, 1988.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Dasouki, M., Barr, M., Erickson, R. and Cox, B.: Translocation (1:22) in a child with bilateral oblique facial clefts. J. Med. Genet., 25:427-429, 1988.
2. Siebert, J.R., Barr, M., Jackson,J.C., Benjamin, D.R.: Ebstein's anomaly and extracardiac defects. Am J Dis Child 143:570-572, 1989.

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

1. Blane, C.E., Barr, M., DiPietro, M.A., Sedman, A.B., Bloom, D.A.: Fetal and newborn renal obstructive dysplasia: Diagnosis and therapeutic implications. Presented to Pediat Radiol., 1989.
2. Barr, M., Oman-Ganes, L.: Turner syndrome and small heart: A cause of death in utero. Presented to Soc. Pediatr. Pathol. Buffalo, NY, Oct. 1-2, 1988. Pediatric Pathology, 1988; 8:657-8.
3. Barr, M., Oman-Ganes, L.: Subnormal heart weight and hydropic Turner syndrome in midgestation: A cause of death. Presented to D.W. Smith Workshop on Malformations and Morphogenesis. Oakland, CA, Aug. 1988.
4. Barr, M.: Morphometric profiles in trisomy 21 at midgestation: The effects of edema and cardiac malformation. Presented to Teratology Society, Richmond VA, June 4-8, 1989. Teratology, 1989; 39:440-441.
5. Barr, M.: Turner's syndrome from conception to birth: Fetal pathology studies. Presented at Turner Syndrome Conference, Livonia, MI, Nov. 11, 1988. Adoles. Pediat. Gynecol, Aug. 1989; 2(3), in press.
6. Johnson, M.P., Barr, M., Qureshi, F., Drugan, A., Evans, M.I.: Symmetrical intrauterine growth retardation is not symmetrical: The ontogeny of organ specific gravimetric deficits in midtrimester and neonatal trisomy 18. Presented to Soc. Gynecol. Invest. San Diego, CA, Mar. 15-18, 1989.
7. (Letter) Barr, M.: Comments on "Origin of abnormality in a human simelian foetus..." Teratology, 1988; 38:487-488.
8. (Book Review) Barr, M.: The Malformed Fetus and Stillbirth: A Diagnostic Approach by R.M. Winter et al. Teratology 1989; 39 (in press).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Associate Chief of Laboratory Service, Veterans Administration Medical Center.
B. Director, Diagnostic Electron Microscopy Unit, Veterans Administration Medical Center.
C. Cytopathology, Veterans Administration Medical Center.
D. Coordinator of Decentralized Hospital Computer Program in Laboratory Service, Veterans Administration Medical Center.
E. Fine Needle Aspiration, Veterans Administration Medical Center.
F. Surgical/Autopsy Pathology, Veterans Administration Medical Center.
G. Washtenaw County Deputy Medical Examiner.
H. Consultant: Diagnostic electron microscopy. Veterans Administration Medical Center, Allen Park.
I. Consultant: Cytopathology, Veterans Administration Medical Center, Battle Creek.

II. TEACHING ACTIVITIES:

A. Pathology 600, Medical School, Veterans Administration Laboratory Section.
A. Pathology House Officer monthly elective: Diagnostic Electron Microscopy, 7 months.
C. Diagnostic Electron Microscopy Case Conference, bi-weekly.
D. Pathology House Officers, fine needle aspiration technique and interpretation.
E. Thesis Committee for graduate student in School of Public Health.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-Investigator: Adjuvant Chemotherapy in Laryngeal Cancer (G. Wolf, Principal Investigator).
B. Pathologist for: VA Cooperative Study #268. A New Strategy to Preserve the Larynx in the Treatment of Advanced Laryngeal Cancer.
C. Marijuana-Bronchoscopy Project (Tashkin/Gong/Fligiel), NIH.
D. Crescentic Nephritis -Core B- NIH Program Project, Consultant (Wiggins, Johnson).
E. Cytoskeletal alterations from cellular oxidant injury. VA Merit Review, Consultant (Hinshaw).

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. Automatic Scanning Light Microscopy in Morphometric Analysis of Immunologically Labeled Cells.
E. Surface Markers for Antigen Localization in Scanning and Transmission Electron Microscopy.
F. Morphometric analysis of pneumocyte cultures (with P. Weinhold).
G. Growth and Differentiation of Rat Renal Tubular Epithelial Cells in Culture (with D. Humes).
H. DNA Cytomorphometry of Laryngeal Squamous Cell Carcinomas (with G. Wolf).

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 Oversight Committee, VA Medical Center.
E. Medical School Admission Committee.

REGIONAL AND NATIONAL:

A. Veterans Administration Central Office Electron Microscopy Review Group.
B. Practice of Pathology Committee, Michigan Society of Pathology.
C. Association of Veterans Administration Pathologists, Secretary-Treasurer.

V. OTHER RELEVANT ACTIVITIES:

A. Lecture to Pulmonary Division: Cytopathology and Electron Microscopy.
B. Diagnostic Electron Microscopy Unit at the Veterans Affairs Medical Center was designated as EM Center of Excellence.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hinshaw, D.B., Armstrong, B.C., Beals, T.F., Hyslop, P.A.: A cellular model of endothelial cell ischemia. J. Surg. Res. 44:527-537, 1988.
2. Wolber, R.A., Beals, T.F., Lloyd, R.V., Maassab, H.F.: Ultrastructural localization of viral nucleic acid by In Situ hybridization. Lab. Invest. 59:144-151, 1988.
3. Hinshaw, D.B., Armstrong, B.C., Burger, J.M., Beals, T.F., Hyslop, P.A.: ATP and microfilaments in cellular oxidant injury. Am. J. Pathol. 132:479-488, 1988.
4. Chensue, S.W., Remick, D.G., Shmyr-Frosch, C., Beals, T.F., Kunkel, S.L.: Immunohistochemical demonstration of cytoplasmic and membrane-associated tumor necrosis factor in murine macrophages (cover illustration). Am. J. pathol. 133:564-672, 1988.
5. Wolber, R.A., Beals, T.F., Maassab, H.F.: Ultrastructural localization of Herpes Simplex virus RNA with in situ hybridization. J. Histo. Cytochem. 37:97-104, 1989.
6. Viscardi, R.M., Weinhold, P.A., Beals, T.F., Simon, R.H.: Cholinephospate cytidylytransferase in fetal rat lung cells: Activity and subcellular distribution in response to dexamethasone, triiodothyronine, and fibroblast conditioned medium. Exp. Lung Res., 1988.
7. Solomon, A.R., Beals, T.F.: Malignant dermal cylindroma. Am. J. Derm. 1989.
8. Gilsdorf, J.R., Wilson, K., Beals, T.F.: Bacterial colonization of intravenous catheter materials in vitro and in vivo. Accepted in Surgery, 1989.

CHAPTERS IN BOOKS:

1. Fliegel, S.E.G., Beals, T.F., Vemkat, H., Toth, S., Gong, H., Tashkin, D.: Pulmonary Pathology in Marijuana Smokers. in, Marijuana: An International Research Report. Proceedings of the Melburne Symposium on CAnnabis. 1987. Monograph Series #7. G. Chester, P. Consroe and R. Musdy eds Australian Gov. Publ. Service, Camerra, pp43-48, 1988.
2. Wolber, R.A., Beals, T.F.: Chapter 19. Streptavidin-Gold Labeling for Ultrastructural In Situ Nucleic Acid Hybridization. in, Colloidal Gold Methods and Applications. Vol. 2 ed. M.A. Hayat. Van Nostrand Reinhold Co., N.Y., 1989 (in press).

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

1. Hinshaw, D., Burger, J., Armstrong, B., Beals, T., Omann, G., Hyslop, P.: Actin and Glutathione in Oxidant Injury. Fed. Am. Soc. Exp. Biol., 1989.
2. Beals, T.F., Fligiel, S.E.G., Stuth, S., Tashkin, D.P.: Morphological Alterations of Alveolar Macrophages from Marijuana Smokers. Am. Rev. Respir. Dis. 139:A336, 1989.
3. Fligiel, S.E.G., Tashkin, D.P., Beals, T.F., Barbers, R.G., Gong, H. Jr.: Comparison of Inflammatory Cell Components Seen in Bronchial Biopsies with those in Bronchoalveolar Lavage Fluid from Smokers and Non-Smokers. Am. Rev. Respir. Dis. 139:A336, 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Muscle biopsies and nerve biopsies done for the University of Michigan and other hospitals in and out of state.
B. Six rotations in Autopsy Service.
C. Neuropathology service coverage during Dr. Paul E. McKeever's absences.
D. Visits to the Chelsea Community Hospital Laboratory, Albion Community Hospital, and coverage of M-Labs surgical pathology at the University of Michigan Hospital.
E. Occasional consultant cases of brain biopsies and rheumatology cases.

II. TEACHING ACTIVITIES:

A. Taught residents, fellows and staff in Neurology, Rheumatology and Pediatrics on muscle and nerve biopsies.
B. Taught pathology residents how to perform and read out autopsies.
C. Lectured on muscle and nerve pathology to residents in Pathology, Neurology and sophomore medical students.
D. Monthly conference on muscle and nerve cases with Neurology and Rheumatology departments.
E. Biweekly muscle and nerve 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 (coinvestigator on the MI Eye-bank and Transplantation Center Grant: 1988-1989; $10,000).
B. Peripheral nerve grafting (pilot study for the future grant).
C. Mitochondrial systemic disorders.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Continuing improvement of interdepartmental coordination of muscle and nerve biopsy service. Installment of the new software for Bioqunt.

MEDICAL SCHOOL:

A. Member of the Admission Committee

REGIONAL AND NATIONAL:

A. Visits to Chelsea Laboratory.
B. Visits to Albion Community Hospital Laboratory.
C. Member, American Association of Neuropathologists, IAP, ASCP, AAAS, AMA.

V. OTHER RELEVANT ACTIVITIES:

A.. Participated in weekly brain cutting conference.
B. Participated in Dr. P.E. McKeever's conferences for neurosurgeions and brain tumor boards

INVITED LECTURES/SEMINARS:

1. Attended PNAA meeting in Nova Scotia - 1 week
2. Attended IAP meeting taking a long course in neuropathology and several short courses - 1 week
3. Attended American Association of Neuropathologists meeting in Dallas - 4 days.

VI. PUBLICATIONS:

ARTICLES SUBMITTED:

1. Silbergleit R., Gebarski S.S., McGillicudy J., Blaivas M.: Lumbar synovial cyst: correlation of myelographic, CT, MRI, and pathologic findings. To: Radiology.
2. Higgs J.B., Blaivas M., Alber J.W.: McArdle's disease presenting as treatment rsistent polymyositis. Rebusmitted to: Arthritis and Rheumatism.

BOOKS AND CHAPTERS IN BOOKS:

1. McKeever, P.E., Blaivas, M.: The brain, spinal cord and meninges (Chapter 9) in, Stephen S. Sternberg (ed), Diagnostic Surgical Pathology, Raven Press, New York, New York, pp. 315-369, 1989.

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

1. Jaradeh, S., Ball, R., Blaivas, M. and Albers, J.W.: Conduction block in hereditary neuropathies. The American Neurological Association Meeting, March, 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Invited Presentations:
   1. Baylor College of Medicine, Institute of Molecular Genetics and the Howard Hughes Medical Institute, Weekly Seminar, 1989.
   2. Biomedical Research Council Forum on Transgenic Animal Models of Disease, The University of Michigan, 1989.

B. Formal Courses
   1. Lecturer, Pathology 600.
   2. Lecturer, Pathology 580.
   3. Lecturer, Biochemistry 501.
   4. Pathophysiology, Fifth Block, Baylor College of Medicine (Invited lecturer, Inherited Connective Tissue Disease).

C. Supervision of three postdoctoral fellows (Thomas Saunders, Ph.D., Eric Patterson, Ph.D., and Gopa Majmudar, Ph.D.).

D. Mentor in the Minority High School Student Summer Research Program.

E. Mentor, Kellogg Foundation High School Teacher Summer Research Program, University of Michigan.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principle 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).

PROJECTS UNDER STUDY:

A. We are interested in the relationship between structure and function for type I collagen, a fibrous protein that resides in the extracellular matrix (ECM) of most tissues. Type I collagen was chosen in part because of a larger interest in the contribution of the ECM to tissue assembly during development. By focusing on a major ECM component, our goal is to define this contribution in molecular terms.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

A. Member, Planning Committee, University of Michigan Skeletal Dysplasia Clinic.

DEPARTMENTAL:

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

V. OTHER RELEVANT ACTIVITIES:

A. The Journal of Clinical Investigation
B. The Journal of Biological Chemistry

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Byers, P.H., Tsipouras, P., Bonadio, J.F., Starman, B.J. and Schwartz, R.C. (1988). Am. J. Hum. Genet. 42, 237.
2. Patterson, E., Smiley, E., and Bonadio, J. (1989) RNA sequence analysis of a perinatal lethal osteogenesis imperfecta mutation. J. Biol. Chem. (In Press).

PETER M. BURKHOLDER, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Staff Pathologist for Anatomic Pathology Services at the Ann Arbor Veterans Administration Medical Center.
B. Chief, Microbiology Laboratory, Ann Arbor Veterans Administration Medical Center.

II. TEACHING ACTIVITIES:

A. Pathology 600 - Laboratory, Veterans Administration team.
B. Supervision of first year residents in surgical and autopsy pathology at the Ann Arbor VA Medical Center.
C. Presentation of pathology case material at Tumor Board, Morbidity and Mortality Conferences, and Nephrology Conferences, the Ann Arbor Veterans Administration Medical Center.

III. RESEARCH ACTIVITIES: None.

IV. ADMINISTRATIVE ACTIVITIES:

A. Medical School Admissions Committee, member, 1988-1989.
B. Veterans Administration Technical Advisory Group on Cancer, VA District #14, member.
C. Chief, Microbiology Laboratory, Ann Arbor Veterans Administration Medical Center.
D. Ad hoc editorial reviewer for Archives of Pathology and Laboratory Medicine, Kidney International, and Laboratory Investigation.
E. Narcotics Investigative Board, Chairperson, Ann Arbor Veterans Administration Medical Center.

V. OTHER RELEVANT ACTIVITIES:

A. Continuing Medical Education:
   1. National Institute on Health Care Leadership and Managment; Physicians in Management (PIM III). Amer. Col. Phys. Exec., 1988.
   2. National Conference on Health Care Leadership and Management. Amer. Col. Phys. Exec., 1989.

INVITED LECTURES AND SEMINARS:

1. Lecturer, Use of percutaneous needle biopsy in diagnosis of renal disease. Visiting Professor, Maricopa County Medical Center, Phoenix, Arizona, 1989.

VI. PUBLICATIONS: None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Director, Clinical Laboratories, Veterans Administration Medical Center.
B. Hematology/Coagulation, Veterans Administration Medical Center.
C. Surgical/Autopsy Pathology, Veterans Administration Medical Center.
D. Transfusion Review Committee, Veterans Administration Medical Center.
E. Special Chemistry/Immunology, Veterans Administration Medical Center.

II. TEACHING ACTIVITIES:

A. Medical Students, Pathology 600 laboratory course.
B. Pathology House Officers, Surgical Pathology/Autopsy supervision and instruction.
C. Technologists/technicians, Ongoing inservice lectures on clinical laboratory topics.
D. Physicians, educational lectures regarding aspects of the clinical laboratories.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator: Production and regulation of granuloma macrophage mediators, VAMC Merit Review ($49,800 annual), 1987-1990.
B. Principal Investigator: VAMC Research Advisory Group ($20,700 annual), 1987-1988.
C. Consultant on NIH-HL-RO1-31237, Macrophage Function in Pulmonary Inflammation, Dr. S. Kunkel, Principal Investigator.

PROJECTS UNDER STUDY:

A. Role of monokines and lymphokines in granulomatous inflammation.
B. Dynamics of monokine production during the peritoneal exudative response.
C. Immunolocalization of cytokines in mouse and human inflammatory and stromal cells.
D. Regulation and orchestration of cytokine production during granulomatous inflammation.
E. In situ hybridization to demonstrate local cytokine induction and synthesis of monokine mRNA in cultured cells and tissue sections.
F. Regulation of monokine production by arachidonic acid metabolites.
G. Regulation of interleukins 2 and 4 during spontaneous modulation of the schistosome egg granuloma.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL: None.

MEDICAL SCHOOL/HOSPITAL:

A. Blood Utilization (Transfusion) Review Committee, VAMC, Chairman.
B. Research and Development Committee, VAMC, voting member.
C. Personnel employment and evaluation.
D. Clinical laboratory equipment evaluation.
E. Editor, "VALABS Interface Laboratory News", Laboratory Newsletter.

REGIONAL AND NATIONAL:

A. Editorial, American Journal of Pathology.
B. Editorial, Clinical Immunology and Immunopathology.
C. Editorial, American Journal of Respiratory Cell and Molecular Biology.
D. Editorial, Agents and Actions.

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.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Chensue, S.W., Remick, D.G., Shmyr-Forsch, C., Beals, T.F. and Kunkel, S.L.: Immunohistochemical demonstration of cytoplasmic and membrane-associated tumor necrosis factor in murine macrophages. Am. J. Pathol. 1988;133:564.
2. Chensue, S.W., Otterness, I.G., Higashi, G.I., Shmyr-Forsch, C. and Kunkel, S.L. Monokine production by hypersensitivity (*Schistosoma mansoni* egg) and foreign body (Sephadex bead)-type granuloma macrophages: Evidence for sequential production of interleukin 1 and tumor necrosis factor. J. Immunol. 1989;142:1281.
3. Scales, W.E., Chensue, S.W., Otterness, I., and Kunkel, S.L. Regulation of monokine gene expression: Prostaglandin E_2 suppresses TNF but not IL-1α, β, mRNA and cell-associated bioactivity. J. Leuk. Biol. 1989;45:416.
4. Chensue, S.W., Shmyr-Forsch,C., Otterness, I.G. and Kunkel, S.L. The beta form is the dominant interleukin released by murine peritoneal macrophages. Biochem. Biophys. Res. Comm. 1989;160:404.
5. Chensue, S.W., Shmyr-Forsch, Weng, A., Otterness, I.G. and Kunkel, S.L. Biologic and immunohistochemical analysis of macrophage interleukin-1α,β and tumor necrosis factor production during the peritoneal exudative response. J. Leuk. Biol. 1989.

SUBMITTED ARTICLES

1. Chensue, S.W., Shmyr-Forsch, Otterness, I.G. and Kunkel, S.L. Immunohistochemical detection of IL-α and β murine macrophages. 1989. Lab. Invest
2. Strieter, R.M., Wiggins, R., Phan, S.H., Wharram, B.L., Showell, H.J. Remick, D.G., Chensue, S.W., and Kunkel, S.L. Monocyte chemotactic protein gene expression by cytokine treated human fibroblasts and endothelial cells. 1989. Biochem. Biophys. Res. Comm.
3. Warren, J.S., Yabroff, K.R., Remick, D.G., Kunkel, S.L., Chensue, S.W., Kunkel, R.G., Johnson, K.J., and Ward, P.A. Tumor necrosis factor participates in the pathogenesis of acute immune complex alveolitis in the rat. 1989. J. Clin. Invest.

BOOKS AND CHAPTERS IN BOOKS:

1. Chensue, S.W. and Kunkel, S.L. Monokine production and orchestration in hypersensitivity (*Schistosoma mansoni* egg) and foreign body-type granuloma formation. In, Boros, D.L. and Yoshida, T. (eds)., Symposium on Basic Mechanisms of Granulomatous Inflammation, Elsevier, North Holland, Amsterdam, in press. 1989.
2. Kunkel, S.L., Scales, W.E., STrieter, R., Chensue, S.W., Spengler, R.N. and Remick, D.G. Modulation of tumor necrosis factor-alpha and interleukin-1 gene expression, in, Otterness I.G. and Ross, A (eds)., The Therapeutic Control of Inflammatory Diseases, Elsevier, North Holland, Amsterdam, p. 219, 1989.
3. Kunkel, S.L., Strieter, R.M., Chensue, S.W., and Remick, D.G. Regulation of Tumour Necrosis Factor-alpha and Neutrophil Activating protein-1 Gene Expression: Potential Role of Cytokine Directed Cell Communication During Multiple Organ Injury. In, Brigham, K. and Stalhman, M. (eds)., Respiratory Distress Syndrome: Molecules to Man. Vanderbilt Press, Nashville, TN, in press.

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

1. Shmyr-Forsch, C., Chensue, S.W., Remick, D.G., and Kunkel, S.L. Immunohistochemical demonstration of interleukin 1 α, β and tumor necrosis factor α synthesis in cultured murine macrophages. Fed. Proc. 1989. 3:A825.
2. Chensue, S.W., Otterness, I., and Kunkel, S.L. Dynamics of interleukin 1 α, β and tumor necrosis factor production during the chronic peritoneal exudative response. 19891. Fed. Proc. 3:A1102.
3. Spengler, R.N., Chensue, S.W., and Kunkel, S.L. Alpha andrenergic receptor stimulation and the regulation of macrophage-derived tumor necrosis factor. Proc. Am. Assoc. Cancer Res. 1989. 30:410 (A1628).

RICHARD MITCHELL COURTNEY, D.D.S.
PROFESSOR OF DENTISTRY
DEPARTMENT OF ORAL PATHOLOGY
ASSISTANT PROFESSOR OF ORAL PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Oral Pathology Biopsy Service, Dental School.
B. Consultant in Oral Pathology for Veterans Administration Hospital.
C. Consultant in Dentistry for patients with head and neck malignancies, The University of Michigan Hospitals.

II. TEACHING ACTIVITIES:

GRADUATE DENTISTRY:

A. Oral Pathology 690--Seminar on current cases stressing clinical-microscopic characteristics (fall and winter terms) (one credit hour each term).
B. Oral Pathology 691--Seminar on diseases which affect the dental pulp and periapical tissues (fall term--two sections) (one hour credit).
C. Oral Pathology 694--Lectures on head and neck pathology (fall term) (two hours credit).
D. Oral Pathology 695--Laboratory (winter term) (two hours credit).
E. Oral Pathology 697--Seminar on diseases which involve the periodontium (fall term) (one hour credit).
F. Oral Pathology 698--Advanced seminar for graduate students in oral pathology (fall and winter terms) (two hours each term).

DDS PROGRAM:

A. Oral Pathology 816 and 818--Lectures and discussions on oral pathology for senior dental students (fall and winter terms) (one hour each term).
B. Oral Pathology 624--Basic oral pathology lectures for sophmore dental students (winter term) (3 credit hours).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT: None.

PROJECTS UNDER STUDY:

A. Odontogenic tumors and oral malignancies.

IV. ADMINISTRATIVE ACTIVITIES:

DENTAL SCHOOL:

A. Director of Oral Pathology Biopsy Service.
B. Program Director, Oral Pathology Graduate Program.
C. Graduate Studies Committee.
D. Member of several Master's degree thesis committees.

MEDICAL SCHOOL/HOSPITAL:

A. Hospital Dentistry Department.
B. Consultant, VA Hospital, Ann Arbor, Michigan.

REGIONAL AND NATIONAL:

A. Vice President, American Board of Oral Pathology.
B. Consultant to the Canadian Dental Association for the Evaluation of Oral Pathology Programs.
C. Consultant to the American Dental Association on Graduate Oral Pathology programs.
D. Consultant to the American Dental Association on Hospital Dentistry programs.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

A. Great Lakes Society of Oral and Maxillo-facial Surgeons Annual Meeting. Seminarist for Clinical Pathologic Conferences. Detroit, Michigan. May 7, 1988.
B. Lakeland Valley Dental Society, "An Update on Oral Cancer". St. Joseph, Michigan. October 17, 1988.
C. University of Toronto Faculty of Dentistry, "Forensic Dentistry", Toronto, Ontario. March 24, 1988.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Regezi, J.A., Zarbo, R.J., McClatchey, K.D., Courtney, R.M. and Crissman, J.D.: Osteosarcomas and chondrosarcomas of the jaws: Immunohistochemical correlations. Oral Surg. 1987;64:302-307.
2. Regezi, J.A., Zarbo, R.J., Tomich, C.E., Lloyd, R., Courtney, R.M. and Crissman, J.D.: Immunoprofile of benign and malignant fibrohistiocytic tumors. J Oral Path. 1987;16:260-265.
3. Regezi, J.A., Zarbo, R.J., Courtney, R.M., and Crissman J.D.: Immunoreactivity of granular cell lesions of skin, mucosa and jaw. Cancer (in press).

BOOKS AND CHAPTERS IN BOOKS:

1. Han, S.S., Courtney, R.M., and Morawa, A.P.: Aging of Oral Tissues. In Avery, J.K., ed. Oral Development and Histology. Williams and Wilkins, Baltimore, 1987, pages 64-78.

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

1. Regezi, J.A., Zarbo, R.J., Courtney, R.M., and Crissman, J.D.: Immunoreactivity of granular cell lesions of skin, mucosa, and jaw. I.A.D.R. Abstract. March, 1989. Annual meeting, San Francisco, California.
2. Courtney, R.M.: An Approach to the Diagnosis and Management of Oral Mucosal Abnormalities. Dental Journal of Malaysia 1986;8:15-20.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Work daily with house officers and staff in Pathology and other departments in their gross and microscopic examination and diagnosis of brains at the autopsy and from autopsies at University Hospital.

B. Attend and participate in the removal of brains from all autopsies at University Hospital.

C. Work in a similar way with the people in "A" on autopsy brain material sent for consultative study from University-associated hospitals, other hospitals, and institutions.

D. Plan and conduct weekly Brain Cutting Conference with house officers, students and staff, for diagnosis and demonstrations of diagnostic methods, and teaching, using selected cases in A and B.

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, 13 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 and brain cutting sessions of the course with other instructors.

B. Neuropathology for Pathology house officers. This exercise is integrated with Clinical Activities A,C,D, and E.

C. Neuropathology 858. Intensive laboratory-lecture course for house officers in Pathology, and in the several clinical services concerned with the nervous system, graduate students, and faculty; implement general plan of course. Annual, 18 hours. One credit hour elective.

D. Neuropathology for house officers from the several clinical services concerned with the nervous system, and senior 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:

A. Role of Glutamate in Alzheimer's Disease. Anne Young, M.D., (P.I.) C. D'Amato (5% effort).
NIH: 5-R01-AG06155-03 (current),
5-R01-AG06155-04 (8-1-89 to 7-31-92)

B. Rat Model of CNS AIDS Using HSV::HIV Mediated Gene Transfer. Joseph Glorioso, Ph.D. and David Fink, M.D., (P.I.'s). C. D'Amato (15% effort). NIH application submitted March, 1989.

PROJECTS UNDER STUDY:

A. This research with Samuel Hicks has centered principally on the early development of the nervous system in experimental mammals: mechanisms by which embryos are malformed by, or are able to recover from, effects of radiation, mutant, genes and other injuries. We have also studied the pathologic aspects of diseases associated with later developmental periods and aging in humans, the dementias such as Alzheimer's Disease. We are working on 1) the roles of basement membranes in the morphogenesis of a mutant rat which develops prenatal aqueduct stenosis and hydrocephalus, and 2) the possible beneficial versus harmful role that macrophages might play in the morphogenesis of brain malformations caused by prenatal irradiation of fetal rats. Macrophages can do harm as well as good in reactions to injury in some tissues, but their functions in fetuses, besides phagocytosis, are unknown. In these experiments we have been dependent on collaboration with Drs. K. Sue O'Shea, Department of Anatomy and Cell Biology, James Varani, and Ricardo V. Lloyd, Department of Pathology, and Kenneth S. Weeks, Department of Radiation Oncology.

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, 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., (Neurosurgery Section).

D. Pathologic examination of brains from rat model of CNS AIDS using HSV::HIV mediated gene transfer in collaboration with Joseph Glorioso, Ph.D. and David Fink, 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. Preprofessional Counselor, premedical and health-related students

REGIONAL AND NATIONAL:

A. Reviewer of research grant applications for National Science Foundation Neurobiology Program.
B. Reviewer of journal manuscripts, Teratology, Experimental Neurology, and Science.

V. OTHER RELEVANT ACTIVITIES:

A. Presentation: Alzheimer's Disease and other dementias, at the Alzheimer Disease and Related Disorders Association Regional Meeting in Adrian, Michigan 1988.
B. Presentation: Neuropathology of Aging and Dementia, at the 16th Annual Michigan Society of Histotechnologists Symposium/Convention, Ann Arbor, Michigan 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. O'Shea, K.S., Rheinheimer, J.S.T., D'Amato, C.J. and Hicks, S.P.: Alterations in the neuroepithelial basal lamina in a neurological mutant with prenatal hydrocephalus. J. Neuropath. Exper. Neur. 47:507-515, 1988.
2. Young, A.B., Greenamyre, J.T., Hollingsworth, Z., Albin, R., D'Amato, C.J., Shoulson I., and Penney, J.B. NMDA receptor losses in putamen from patients with Huntington's disease. Science 241:981-983, 1988.
3. Reiner, A., Albin, R.L., Anderson, K.D., D'Amato, C.J., Penney, J.B. and Young, A.B.: Differential loss of striatal projection neurons in Huntington's Disease. Natl. Acad. Sci. Proc. 85:5733-5737, 1988.
4. Papodopoulos, S.M., Gilbert, L., Webb, R.C., D'Amato, C.J. Characterization of contractile responses to endothelin in human cerebral arteries - implication for cerebral vasospasm (Submitted for publication).

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

1. Young, A.B., Greenamyre, J.T., Hollingsworth, Z., Albin, R., D'Amato, C.J., Shoulson, I., Penney, J.B.: NMDA receptor losses in Huntington's Disease putamen support a neurotoxic hypothesis. Society for Neuroscience Abstracts 14:419, 1988.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. **CLINICAL ACTIVITIES:** None.

II. **TEACHING ACTIVITIES:**

A. Supervised the following undergraduate students: Mark Burt, Kara Reynolds, Dave Berg
B. Supervised the following graduate students: Carol Laherty, B.S., Tony Opipari, B.S., Mary East, M.D.
C. Supervised the following postdoctoral fellows: Rachel Yabkowitz, Ph.D., Terry Bacon-Baguely, Ph.D., Vidya Sarma, Ph.D., Larry Holzman, M.D.

III. **RESEARCH ACTIVITIES:**

SPONSORED SUPPORT:

A. American Heart Association (AHA) Grant-in-Aid (#871329), "Role of Thrombospondin in Platelet and Vascular Biology". Period 07/01/87 - 06/30/90. Budget - $90,000 (3 years), Principal Investigator, 10% effort.
B. NIH-R01-39037-01 - "Structure and Regulation of Human Platelet Thrombospondin". Period 07/01/87 - 06/30/92. Budget - $99,788, Principal Investigator, 40% effort.
C. NHLBI-39415 - "Role of Endothelial Cell Proteins in Developmental Hemostasis". Period 06/01/87 - 05/31/90. Budget - $85,610, Principal Investigator, 20% effort.
D. NIH-R01-HD23867 - "Role of Thrombospondin in CNS Development". period 02/01/88 - 01/31/91. Budget - $103, 745, first year direct costs. Co-Investigator, 10% effort.
E. American Heart Association Established Investigatorship Award, #890217 - "Structure and Function of Thrombospondin", Period 07/01/89 - 06/31/94, Budget $35,000 annually, Principal Investigator.

PENDING GRANTS:

A. NCI - "Novel Thrombospondin Receptors on Squamous Carcinoma Cells", period 04/01/90-03/31/95, Budget $167,743, first year direct costs, Principal Investigator.
B. DK39255-03 - "Mechanisms of Glomerular and Tubular Injury (Roger C. Wiggins, Project Director) (Dr. Dixit's involvement begins 08/01/89). Period 09/01/87-07/31/92, first year direct costs $42,876.
C. Grant-in-Aid, American Heart Association, "Thrombospondin Heparin Binding Domain and Platelet Function", Period 07/01/90-06/30/93, $35,000 per year, Principal Investigator.

PROJECTS UNDER STUDY:

A. Structure/function relationships in thrombospondin.
B. Mechanisms of action of tumor necrosis factor.
C. Articles submitted for publication:

1. Wolf, F.W., and Dixit, V.M.: Structure of the thrombospondin gene provides evidence for exon shuffling. J. Biol. Chem., submitted.
2. Castle, V.P., Varani, J., Fligiel, S., Prochownik, E.V., Dixit, V.M.: Antisense-mediated reduction in thrombospondin reverses the malignant phenotype of a human squamous carcinoma. J. Cell Biol., submitted.
3. Yabkowitz, R. and Dixit, V.M.: Two distinct thrombospondin receptors specific for different functional domains in human carcinoma cells. J. Biol. Chem., submitted.
4. Suchard, S.J., Boxer, L.A. and Dixit, V.M.: Human neutrophils express two distinct thrombospondin receptors. J. Biol. Chem., submitted.
5. 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. Cell Biol., submitted.

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. Lecture, University of Michigan, Department of Hematology, 1988.
2. Invited Speaker, American Heart Association, Washington, D.C., 1988.
3. Invited Speaker, Case Western Reserve University, Cleveland, Ohio, 1988.
4. Invited Speaker, Oakland University, Rochester Hills, Michigan, 1988.
5. Invited Speaker, University of Minnesota, Minneapolis, Minnesota, 1989.
6. lecture, University of Michigan, Department of Nephrology, 1989.
7. Invited Speaker, Glycomed, Alameda, California, 1989.
8. Invited Speaker, Cytogen, Princeton, New Jersey, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Varani, J., Nickoloff, B.J., Riser, B.L., O'Rourke, K. and Dixit, V.M.: Role of thrombospondin in keratinocyte attachment and differentiation. J. Clin. Invest., 1988;81:1537-1545.
2. Nickoloff, B.J., Mitra, R.S., Riser, B.L., Dixit, V.M., and Varani, J.: Modulation of keratinocyte motility; Correlation with production of extracellular matrix molecules in response to growth promoting and antiproliferative factors. Am. J. Path. 1988;132(3):543-551.
3. Nickoloff, B.J., Riser, B.L., Mitra, R.S., Dixit, V.M. and Varani, J.: Inhibitory effect of Gamma Interferon on cultured human keratinocytes. Thrombospondin production distribution and biological activities. J. Invest. Dermatol., 1988;91:213-218.
4. O'Shea, K.S., Dixit, V.M.: Unique distribution of the extracellular matrix component thrombospondin in the developing mouse embryo. J. Cell Biol., 1988; 107:2737-2748.
5. McClenic, B., Mitra, R.S., Riser, B.L., Nickoloff, B.J., Dixit, V.M., Varani, J.: Production and utilization of extracellular matrix molecules by human melanocytes. Exp. Cell Res., 1989; 180:314-325.
6. Laherty, C., Gierman, T., and Dixit, V.: Characterization of the promoter region of the human thrombospondin gene. DNA sequences within the first intron increase transcription. J. Biol. Chem., 1989;264:11222-11227.
7. Yabkowitz, R., Lowe, J.B., Dixit, V.M.: Expression and initial characterization of a recombinant human thrombospondin heparin binding domain. J. Biol. Chem., 1989;264:10888-10896.
8. Varani, J., Riser, B.L., Hughes, L.A., Carey, T.E., Fligiel, S.G., Dixit, V.M.: Characterization of thrombospondin synthesis, secretion and cell surface expression by human tumor cells. Clin. Exp. Metastasis, 1989;7:265-276.
9. Varani, J., Mitra, R.S., McClenic, B.J., Fligiel, S.E.G., Inman, D.R., Dixit, V.M., and Nickoloff, B.J.: Modulation of fibronectin production in normal human melanocytes and malignant melanoma cells by interferon-γ and tumor necrosis factor-α. Amer. J. Pathol., 1989;134:827-836.
10. Prochownik, E.V., O'Rourke, K. and Dixit, V.M.: Expression and analysis of c-terminal deletions of the human thrombospondin molecule. J. Cell Biol., 1989;109:843-852.
11. Dixit, V.M., Marks, R.M., Sarma, V., and Prochownik, E.V.: Tumor necrosis factor induces proto-oncogene AP-1/C-JUN transcription in endothelial cells in the absence of concurrent c-fos induction. J. Biol. Chem., in press.
12. Long, M.W., Dixit, V.M.: Thrombospondin functions as a cytoadhesion molecule for human hematopoeitic progenitor cells. Mol. Cell. Biol., in press.

VICTOR M. ELNER, M.D., PH.D.
ASSISTANT PROFESSOR OF OPTHALMOLOGY AND PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Ophthalmic Surgical Pathology

II. TEACHING ACTIVITIES:

A. Instruction of Opthalmology residents in Ocular Pathology
B. Ophthalmic Pathology lecture series
C. Preceptor: Pre-residency fellow
D. Preceptor: Opthalmology resident research

III. RESEARCH ACTIVITIES:

A. Retinal Pigment Epithelial Cell Biology
B. Anatomic and Pathologic Correlations in Ophthalmic Plastic and Orbital Surgery
C. Sponsored Research - Co-investigator: Ultrastructural and Immunohistochemical Analysis of Mechanically-Induced Retinal Pigment Epithelial Fibrous Metaplasia (SG Elner; Principal Investigator - Michigan Eye Bank 1989-1990)

IV. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Elner SG, Elner VM, Diaz-Rohena R, Freeman HM, Tolentino FL, Albert DM: Anterior proliferative viteroretinopathy: Clinicopathologic, light microscopic, and ultrastructural findings. Opthalmology 1989; 95:1349-1357.
2. Elner SG, Elner VM, Freeman HM, Tolentino FL, Albert DM: The pathology of anterior peripheral proliferative viteroretinopathy (APVR). Trans Am Opthalmol Soc 1988; 86:330-353.
3. Freedman SF, Elner VM, Donev I, Gunta R, Albert DM: Intraocular neurilemmoma arising from the posterior ciliary nerve in neurofibromatosis. Pathologic findings. Opthalmology 1988; 95:1559-1564.
4. Yue BYJT, Kurosawa A, Alvart JL, Elner VM, Tso MOM: Monkey trabecular meshwork cells in culture: Growth, morphologic, and biochemical characteristics. Graefes Arch Clin Exp Opthalmol 1988; 226:262-268.

BOOKS AND CHAPTERS IN BOOKS:

1. Elner VM: The histologic anatomy of the medial canthal ligament and surrounding structures. American Society of Ophthalmic Plastic and Reconstructive Surgery 1989; thesis.
2. Freeman HM, Elner SG, Tolentino FL, Schepens CL, Elner VM, Albert DM: Anterior proliferative vitreoretinopathy. I. Clinical findings and management. In: Proliferative Viteroretinopathy. Freeman HM, Tolentino FL, eds. New York Springer-Verlag, 1988.

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

1. Elner VM, Nielsen JC, Elner SG, Franklin WA: Immunophenotypic modulation of cultured human retinal pigment epithelial cells by gamma-interferon and phytohemagglutinin-stimulated human T-lymphocytes. Invest Opthalmol Vis Sci 1989; 30 (suppl): 118.
2. Elner SG, Elner VM, Albert DM, Arnall M. Ocular associated systemic findings in suspected child abuse: A necropsy study. Invest Opthalmol Vis Sci 1989; 30 (suppl): 223.
3. Cajita VN, Tolentino FL, Refojo MF, Elner VM, Albert DM: Carmustine (BCNU)-silicone oil in proliferative vitreoretinopathy: Antiproliferative and toxicity drug studies. Invest Opthalmol Vis Sci 1989; 30 (suppl): 511.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988- 30 JUNE 1989

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Presented workshop on radioimmunoassay techniques for ovarian steroids and gonadotropins. Utah State University, April 27 & 28, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Henson, M.C., Piper, E.L., Perkins, J.L. and England, B.G.: Changes in Pelvic Conformation and Peripheral Estrone Levels in Pre- and Postpartum Beef Cows. Domestic Animal Endocrinology 1988, 6:95-99.
2. Grenman, S.E., Roberts, J.A., England, B.G., Gronroos, M., and Carey, T.E.: In vitro growth regulation of endometrial carcinoma cells by tamoxifen and medroxyprogesterone acetate. Gynecol Oncol 1988, 30:239-250.
3. Grenman, S.E., Van Dyke, D.L., Worsham, M.J., England, B.G., Hopkins, M., McClatchey, K.D., Grenman, R., and Carey, T.E.: UM-SCV-1A and UM-SCV-1B, Two new tamoxifen-sensitive hypotetraploid cell lines derived from primary and metastatic tumors in a patient with squamous cell carcinoma of the vulva. Gynecol Concol. Accepted for publication.
4. Jenei, S.R., Lusser, B.A., Bajpai, P.K., and England, B.G.: Delivery of polypeptides (inhibin) by implantable ceramic capsules. Proceedings of the Fourteenth Annual Northeast Bioengineering Conference, 1988 14:92-95.
5. Sonnenborn, A.A., Chiego, D.J Jr., England, B.G., and Johnson,R.A.: The effects of estradiol-17B on rat molar root development. J Dental Research. Accepted for publication.

BOOKS AND CHAPTERS IN BOOKS:

1. Carey, J.L. and England, B.G.: Leukocyte Antigens and Monoclonal Reagents: Production and Characterization, in Flow Cytometry in Clinical Diagnosis, D.F. Keren (ed), ASCP Press, 1989.

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

1. Vinik, A.I., McCleod, England, B.G. and Eckhauser, F.: Substance P - The putative neurohumor behind flushing and diarrhea of neuroendocrine tumors? Abs. 71st Annual Meeting of th Endocrine Society, Seattle, Washington, 1989.
2. Song, J., Jim, L., Lloyd, R., Chandler, W., England, B.G., and Smart, J.: Analysis of clinically nonfunctional pituitary adenomas by hybridization studies. Abs. 71st Annaul Meeting of the Endocrine Society, Seattle, Washington, 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Autopsy Service.
B. Occasional Surgical Pathology Interpretation.

II. TEACHING ACTIVITIES:

A. Course Director - Pathology 600.
B. Laboratory Instructor - Pathology 600.
C. Coordinator - Senior Medical Student Clerkships.
D. Sequence Coordinator and Lecturer - Sophomore Medical Students (ICS-600) Immunopathology.
E. Pulmonary Pathology Conference (monthly to Pulmonary Division - Internal Medicine).
F. Lecturer - Microbiology and Immunology 624.
G. Lecturer - Pathology 580.
H. Preceptor - Undergraduate and Medical Student Research.
I. Graduate Student Ph.D. Thesis Committee.
J. Preceptor for one Postdoctoral Fellow.

III. RESEARCH ACTIVITIES:

A. Regulation of phagocytic cell-mediated tissue injury.
B. Mechanisms of oxygen metabolite-mediated tissue injury.

SPONSORED SUPPORT:

A. Principal Investigator: Modulation of Immune Complex Lung Injury (NIH-R01-HL-32024).
B. Principal Investigator: Phagocytic Cell and Glomerular Injury. Section IV of Renal Center Grant (NIH-P50-DK39255).
C. Co-Investigator: Mechanisms and Genetic Regulation of Pulmonary Fibrosis. (S.H. Phan; Principal Investigator) (NIH-5-R01-HL-28737).
D. 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. Departmental ACAPT Committee
D. Resident Applicant Selection Committee.
E. Advisory Committee for Residency Training.

F. Graduate Program Committee (Chairman).
G. Research Space Advisory Committee
H. Department Computer Committee

MEDICAL SCHOOL/HOSPITAL:

A. Medical Student Advisor (3rd and 4th year).
B. ICS - Executive Committee.
C. Associate Director - Sophomore Medical Student ICS Course (ICS 600/601).
D. Basic Science Phase Committee (Chairman).
E. Clinical Phase Committee.
F. Medical Student Basic Science Academic Review Board.
G. Medical Student Clinical Phase Academic Review Board.
H. Academic Affairs Committee.
I. Grading Policies Committee.
J. External Review Committee (Chairman), Department of Post-Graduate Medicine and Health Professions Education.
K. Interphase Review Committee (Chairman)
L. LCME Review: Subcommittee for Educational Programs.
M. Medical School Retreat on Medical Education.

REGIONAL AND NATIONAL:

A. NIH Site Visit, Co-Chairman, Program Project: Biology of Acute Renal Tissue Injury, Vanderbilt University, 1989.
B. Editorial Board, Laboratory Investigation.
C. Reviewer, Veteran's Administration Research Grants.
D. Reviewer for: J. Clin. Invest., J. Immunol., Science, Am. J. Pathol., Lab. Invest., Prostaglandins, J. Biol. Chem., Clin. Immunol., Immunopathol., Am. Rev. Respir. Dis., J. Leuk. Biol., Circ. Res., Biochem. Pharm., Lung.

V. INVITED LECTURES AND SEMINARS:

1. Invited Speaker, Clinical Ischemic Syndromes. Mechanisms and Consequences of Tissue Injury, The University of Michigan Medical School, Program of Continuing Medical Education, 1988.
2. Invited Speaker, Mechanisms of Free Radical Formation and Tissue Injury, XII Meeting of the International Society of Oxygen Transport of Tissue, Ottawa, Ontario, Canada, 1988.
3. Co-Chairman, Symposium, Receptor Biology and the Immune Response, American Thoracic Society, Cincinnati, Ohio, 1989.
4. Invited Participant, Symposium on Inflammation and Healing of Sports-Induced Soft Tissue Injury, Bethesda, Maryland, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Mitsos, S.E., Kim, D., Lucchesi, B.R., and Fantone, J.C.: Modulation of myoglobin-H_2O_2 mediated peroxidation reactions by sulfhydryl compounds. Lab. Invest. 59:824-830, 1988.

2. Simpson, P.J., Fantone, J.C., Mickelson, J.K., Gallagher, K.P., and Lucchesi, B.R.: Identification of a time window for therapy to reduce experimental canine myocardial injury: Suppression of neutrophil activity during 72 hours of reperfusion. Cir. Res. 63:1070-1079, 1988.
3. Vissers, M.C.M., Fantone, J.C., Wiggins, R., and Kunkel, S.L.: Glomerular basement membrane-containing immune complexes stimulate tumor necrosis factor and interleukin-1 production by human monocytes. Am. J. Pathol. 134:1-6, 1989.
4. Brieland, J.K., Balazovich, K., and Fantone, J.C.: The effect of acute inflammatory lung injury on the respiratory burst and protein kinase C activity of rat pulmonary alveolar macrophages. Am. Rev. Respir. Dis. 139:378-381, 1989.
5. Fantone, J.C., Duque, R.E., Davis, B.H., and Phan, S.H.: 3-Deaza-adenosine inhibition of stimulus-response coupling in human polymorphonuclear leukocytes. J. Leuk. Biol. 45:121-128, 1989.
6. Brieland, J.K., Vissers, M.C.M., Phan, S.H., and Fantone, J.C.: Human platelets mediate iron release from transferrin by adenine nucleotide dependent and independent mechanisms. Biochem. Biophys. Acta, 978:191-196, 1989.
7. Vissers, M.C.M., Wiggins, R., and Fantone, J.C.: Comparative ability of human monocytes and neutrophils to degrade glomerular basement membrane *in vitro*. Lab. Invest. 60:831-838, 1989.
8. Fantone, J.C., Jester, S., and Loomis, T.: Metmyoglobin promotes arachidonic acid peroxidation at acid pH. J. Biol. Chem. 264:9408-9411, 1989.

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

1. Simpson, P.J., Todd, R.F., Mickelson, J.K., Fantone, J.C., Gallagher, K.P., Tamura, K.A., Lee, J.M., Kitzen, M., and Lucchesi, B.R.: Sustained limitation of myocardial reperfusion injury by a monoclonal antibody that inhibits leukocyte adhesion. FASEB J., 2:A1237, 1988.
2. Campbell, D.A., Jr., Tagge, E.P., Merion, R.M., Reichle, R., Turcotte, J.G., Juni, J.E., and Fantone, J.C.: Contribution of oxygen free radicals to hepatic preservation injury in a large animal model. American Society of Transplant Surgeons, Chicago, Illinois, 1988.
3. Fantone, J., Vissers, M.C.M., Jones, M.L., and Kunkel, S.L.: Inactivation of tumor necrosis factor by hypochlorous acid. FASEB J. 3:A636, 1989.
4. Homeister, J.W., Hoff, P.T., Fantone, J.C., Fletcher, D.D., and Lucchesi, B.R.: Adenosine and lidocaine in combination limit myocardial reperfusion injury in a canine model. FASEB J. 3:A742, 1989.
5. Brieland, J. and Fantone, J.C.: Human polymorphonuclear leukocyte-derived superoxide anion promotes the reductive release of iron from iron-tranferrrin·bicarbonate. FASEB J. 3:A1250, 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Rotations, July (2/4), August (2/4), Septem ber (2/4), October (2/4), November (2/4), December (2/4), March (2/4), April (2/4), June (2/4).

II. TEACHING ACTIVITIES:

A. Pathology 600 Lectures:
   1. Pulmonary Pathology I - January 18, 1989
   2. Pulmonary Pathology II - January 19, 1989
   3. Pulmonary Pathology III - January 20, 1989
   4. Pulmonary Pathology IV - January 23, 1989
   5. Gyn Pathology I - March 23, 1989
   6. Gyn Pathology II - March 24, 1989
   7. Gyn Pathology III - March 27, 1989
   8. Gyn Pathology IV - March 28, 1989

B. Pathology 630:
   1. Respiratory Disease I - October 24, 1988
   2. Respiratory Disease II - October 26, 1988

C. Residency Training:
   1. Diseases of the Chest I - January 24, 1989
   2. Diseases of the Chest II - January 31, 1989
   3. Diseases of the Chest III - February 7, 1989
   4. Diseases of the Chest IV - February 14, 1989

D. Other educational activities:
   1. M4 student elective mentor, August, 1988.
   2. Clinicopathologic Conference, Department of Internal Medicine, February, 1989.
   3. Clinicopathologic Conference, Department of Internal Medicine, May, 1989.
   4. Clinicopathologic Conference, Department of Internal Medicine, June, 1989.
   5. Department of Internal Medicine Seminar, "Pathology of Pulmonary Infections", August 19, 1988.
   6. Department of Internal Medicine Seminar, "Pathology of Allergic Lung Disease", October 28, 1988.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Pathology Consultant, Morphologic Studies of Diffuse Intersti tial Lung Diseases, A Multi-Institution Project, Reuben M. Cherniak, M.D., National Jewish Hospital, Program Director.
B. Pathology Consultant, Prospective Investigation of Pulmonary Embolism Diagnosis, John G. Weg, M.D., Principal Investigator.
C. Monoclonal Antibodies to Bladder Tumor Antigens, H. Barton Grossman, M.D. (Principal Investigator), Andrew Flint, M.D. (Co-Investigator), July 1, 1987 June 30, 1990.
D. Intensive Continuous Infusion High Dose Cisplatin, 5-Fluorour acil, and Mitoguazone (MGBG) Induction Chemotherapy for Ad vanced Head and Neck Cancer, Arlene A. Forastiere, M.D. (Study Coordinator), Andrew Flint, M.D. (Co-Investigator).

PROJECT UNDER STUDY:

A. Wegener's Granulomatosis: Morphologic and Immunohistochemical analysis.
B. Malignant lymphomas presenting in the Lung: Morphologic, Immunochemical and Clinical features.
C. Tall Cell Papillary Carcinoma of the Thyroid: DNA analysis and comparison to other forms of thyroid carcinoma.
D. Methotrexate - induced Hepatic Disease: An analysis of sequen tial Liver biopsy samples from 130 patients. Paper Submitted: Barnett J.L., Flint A., Moseley R.H., Nostrant T.T., Lucey M.R., Fleckenstein J.K., Appelman H.D.: Hepatotoxicity of Methotrexate Therapy in Psoriasis.
E. Pathologic Manifestations of Nasal Involvement by Wegener's Granulomatosis Paper Submitted: Del Buono E.A., Flint A.: The Diagnostic Utility of Nasal Biopsy in Wegener's Granulomatosis.
F. Papillary Adenoma of the Lung: Morphologic and Immunochemical Analysis.
G. Morphometric analysis and quantitation of peroxidase staining intensity of cultured urinary bladder carcinoma cells.
H. DNA measurement and morphometric analysis of ovarian neoplasms of borderline and outspoken malignancy. PAPER SUBMITTED: Drescher C., Flint A., Schmidt R.W.: Ovarian neoplasms of borderline malignancy: Morphometric and DNA analysis.
I. The pathologic manifestations of small airways disease.
J. The diagnosis of interstitial lung disease by open biopsy: does biopsy site selection influence diagnostic considerations?

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Educational Coordinator, Residency Training Program.
B. Chairman, Residency Candidates Selection Committee.
C. Coordinator, Senior Staff Service Rotation.
D. Member, Anatomic Pathology Director Search Committee.
E. Chairman, Pathology Residency Advisory Committee.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "DNA Analysis and the Practice of Surgical Pathology", Clinical Applications of Cytometry, Charleston, South Carolina, Septem ber, 1988.
2. "Pathology of Interstitial Lung Disease", Michigan Thoracic Society, Novi, Michigan, April, 1989.
3. Tri-State Thoracic Society, Guest Pathologist, Biloxi, Missis sippi, January, 1989.
4. Program Chairman, Section on Head and Neck Pathology, Interna tional Academy of Pathology, March, 1989.
5. "Pathology of Pulmonary Infections", Department of Internal Medicine, August, 1988.
6. "Pathology of Allergic Lung Disease", Department of Internal Medicine, October, 1988.
7. Editorial Review: Annals of Thoracic Surgery, American Review of Respiratory Diseases, Archives of Pathology, Acta Cytologica.
8. "Wegener's Granulomatosis", Department of Pathology, Allen Park VA Medical Center, February, 1989.

VI PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Flint, A.: DNA analysis and the practice of Surgical Pathology. Cytometry (in press).
2. Flint, A., Lloyd R.V.: Hurthle Cell Neoplasms of the Thyroid Gland. Pathology annual (in press).
3. Flint, A., Appelman, H.D., Beckwith, A.L.: DNA analysis of gastric stromal neoplasms: Correlation with pathologic fea tures. Surgical Pathology (in press).
4. Liebert, M., Wedemeyer, G.A., Stein, J.A., Washington, R.W., Flint, A., Ren, L., Grossman, H.B.: Identification by mono clonal antibodies of an antigen shed by bladder cancer cells. Cancer Research (in press).
5. McCoy, J.P., Flint, A., Schade, W.J., Grekin, R.C., Zachary, C., Swanson, N.A.: DNA content of Human Basal Cell Carcinoma. J. Am. Acad. Dermatology (in press).

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

1. Flint, A.: Flow Cytometry: General principles and Applica tions to Diagnostic Cytopathology. The Cytotechnologist's Bulletin 26:27-29, 1989.ia
2. Mazzara, P.F., Flint, A., Naylor, B.: Adenoma of the Nipple: Cytopathologic Features. American Society of Cytology, Novem ber, 1988.
3. Del Buono, E.A., Flint, A.: The diagnostic Utility of Nasal Biopsy in Wegener's Granulomatosis. International Academy of Pathology, U.S.-Canadian Division, San Francisco, March, 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Director, Pathology Data Systems.
B. Director, Phlebotomy Services and Central Distribution.
C. Staff supervision of the Autopsy Service (12 weeks).

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Co-Director of a laboratory section for Pathology 600.
B. Program Director of the Seventh Annual Clinical Laboratory Computer Symposium at the Towsley Center for Continuing Medical Education, June 7-9, 1988. The Symposium attracted 160 registrants and 16 system vendors/laboratory consultants.

III. RESEARCH PROJECTS UNDER STUDY:

A. The integration of heterogenenous hospital information systems with relational data base software.
B. Organizational structures at the hospital and departmental levels to support information processing

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Development of the Self-Study Report for the Liaision Committee on Medical Education (LCME).
A. Computer Advisory Committee (Chairman).
B. Quality Assurance Committee.
C. Editor of Pathology Electronic News (PEN) and Spectrum.
D. Clinical Pathology Faculty Committee.

HOSPITAL COMMITTEES:

A. Task Force for the Integration of Hospital Information Systems (Chairman).
B. Physicians' Computer Advisory Committee (Chairman).
C. Steering Commitee for ISIHS (Information Systems Integration for the Health Sciences).
D. Physicians' Liaison Committee.

REGIONAL AND NATIONAL:

A. Appointed to the Council on Medical Informatics of the American Society of Clinical Pathologists for a three-year term of office.
B. Professional Advisory Board of the Cerner Corporation
C. Committee on Medical Informatics of the Michigan Society of Pathologists (Chairman)

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1.. The use of computers in the hospital blood bank. A lecture delivered to the Toledo Chapter of the American Red Cross on October 4, 1988, in Toledo, Ohio.
2. Who should direct the development of medical information systems? A lecture delivered as part of a workshop sponsored by the College of American Pathologists in Las Vegas, Nevada, on October 24, 1988, and in Chicago, Illinois, on March 14, 1989.
3. Forces in the evolution of information systems in hospitals. A lecture delivered at the Center for Medical Informatics, Columbia-Presbyterian Hospital, New York, New York, on January 23, 1988.
4. Empowering the stakeholders of hospital information systems. A lecture delivered to the Annual Meeting of the Hospital Information Systems Sharing Group (HISSG) at La Jolla, California, on March 21, 1989.
5. The path toward medical system integration. A lecture delivered as part of a Symposium on Nursing Information Systems. Sponsored by the Hospital Information System Association (HISA) of Michigan on May 24, 1989, in Troy, Michigan.
6. The laboratory information system as a tool for automating hospital quality assurance activities. A lecture delivered to the Annual Meeting of the Cerner Users' Group on April 19, 1989, In Kansas City, Missouri.
7. Automating quality assurance activities with an LIS. A lecture delivered to the seventh annual Clinical Laboratory Computer Symposium at the Towsley Center, Ann Arbor, Michigan, on June 8, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATON IN REFEREED JOURNALS:

1. Friedman B A, Martin J B: The physician as a locus of authority, responsiblity, and operational control of medical systems. J Med Sys 1988;12:389-396.
2. Friedman B A: The impact of new features of laboratory information systems on quality assurance in anatomic pathology [Editorial]. Arch Pathol Lab Med 1988;112:1189-1191.
3. Friedman B A: The laboratory information system as a tool for implementing a strategic plan. Amer J Clin Pathol (in press).
4. Friedman BA: The potential role of physicians in the management of hospital information systems. Clin Lab Med (In Press).

ABSTRACTS, BOOK REVIEWS, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Friedman B A: Laboratory information systems and the competency trap. Proceedings of the Twelfth Annual Symposium on Computer Applications in Medical Care, IEEE Computer Society, 1988, pp. 659-662.
2. Friedman B A: Handbook of Phlebotomy (Book Review). Arch Pathol Lab Med 1989;113:102.
3. Friedman B A: Selection of Methods and Instruments for Blood Banks (Book Review). Arch Pathol Lab Med 1989;113:701.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

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. Chairman, Replacement Instrumentation Selection Committee, Biochemistry Section.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Medical Students
    1. Lecturer, Path 600.
B. Pathology House Officers
    1. Lecturer, Clinical Pathology Rounds.
    2. Lecturer, Clinical Pathology Didactic Lecture Series.
    3. Coordinator, Pathology House Officer rotation through General Chemistry Lab.
    4. Review daily sign-out and interpretation of electrophoresis results.
    5. Review of selected topics in Clinical Chemistry.
C. Medical Technologists
    1. Program Director, Continuing Education Series for Medical Technologists.

III. RESEARCH ACTIVITIES:

A. Comparison of Apolipoprotein A-I and B concentrations with lipoprotein fractions in heart transplant patients.
B. Development of colorimetric and HPLC assays for homovanillic acid (HVA) in patients with neuroblastoma.
C. Development of an assay for plasma oxalate.
D. Development of electrophoretic methods to quantitate amylase isoenzymes in patients with pancreatic pseudocyst.
E. Evaluation of automated electrophoresis and luminescent immunoassay techniques for the measurement of the MB isoenzyme of creatine kinase.
F. Measurement of intracellular magnesium concentrations in patients with congestive heart failure.
G. Serum enzymes as indicators of ischemia reperfusion injury of the liver.
H. Catecholamine levels in LPS stimulated macrophages.

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".

REGIONAL AND NATIONAL:

A. Coordinator, College of American Pathologists Clinical Chemistry Standards Assay Laboratory.
B. Education Committee, Michigan Section, AACC.
C. Program and Education Committees, Program Committee Chairman, Michigan Section, AACC.
D. Lipids and Lipoproteins Subgroup, AACC.

V. INVITED LECTURES:

1.. American Society for Medical Technology, Region IV Annual Meeting, Detroit, Michigan.
   a. "Cholesterol Measurement: Fact vs Fiction".
   b. "Lipid Metabolism and the Role of Lipoproteins in Atherosclerosis".

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Judd, W.J., Steiner, E.A., Oberman, H.A. and Giacherio, D.A.: False-positive results with chemically modified anti-D do not indicate a need to use a separate immunologically inert Rh control reagent. Transfusion, 1988; 28:339-341.
2. Nicklas, J.M., Giacherio, D.A., Moskowitz, D., Lemmer, J.H., Kirsh, M.J. and Grekin, R.J.: Natriuresis associated with elevated plasma atrial natiuretic hormone during supraventricular tachycardia. Am Heart J 198;117:377-381.
3. Yuzbasian-Gurkan, V., Brewer, J.G., Abrams, G.D., Main,B., and Giacherio, D.A.: Treatment of Wilson's disease with zinc: Changes in serum levels of lipase, amylase, and alkaline phosphatase in Wilson's disease patients. J Lab Clin Med 1989 (accepted for publication).

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

1. Spengler, R.N., Spengler, M.L., Giacherio, D.A., Strieter, R.M., and Kunkel, S.L.: Alpha adrenergic receptor mediation of LPS stimulated tumor necrosis factor production from macrophages. Fed Proc 1989;3:A634.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Surgical Pathology - twenty-two weeks
B. Diagnostic EM - 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 with Dr. K. Johnson
F. Autopsy and Frozen Section "on call" Rotation.

II. TEACHING ACTIVITIES:

A. Lectures to sophomore Pathology 600 students:
   1. Death certification and forensic pathology
   2. Pathogenesis of highway injuries
   3. Renal tubulo-interstitial disease
   4. Diseases of prostate and external genitalia
   5. Testicular disease
B. Lab instructor for Pathology 600
C. Lecture on Urologic Pathology to Dental Pathology 630 students.
D. Monitor for M-4 clerks during Elective Pathology Rotation, October 24-November 9.
E. Pathology Resident Teaching:
   1. Attending staff for 22 weeks on Surgical Pathology Diagnostic Services with Residents
   2. Two lectures on Urologic Pathology
   3. One lecture on Pathogenesis of Highway Injury
   4. Journal Club on Prostatic Glandular Dysplasia
F. Lecture on Highway Trauma to University Hospital Operating Room Nurses.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Collaborate with Urology Staff and Radiology Staff on projects.
B. Radiological Diagnostic Oncology Group Prostate Study.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

MEDICAL SCHOOL/HOSPITAL:

A. Hospital Claims Control Committee.

UNIVERSITY:

A. Faculty Representative to Big Ten Intercollegiate Conference and National Collegiate Athletic Association (NCAA). Term ended December 31, 1988.
B. Board in Control of Intercollegiate Athletics. Term ended December 31, 1988.

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. National Task Force on Anabolic Androgenic Steroid Abuse (NCAA, U.S. Olympic Committee, National Federation of State High School Associations and Amateur Athletic Foundation).
E. Board of Directors, Physicians for Automotive Safety through 1988.
F. Board of Directors, Public Citizen, Inc. (Ralph Nader, initial Chairman and Founder)
G. Deputy Medical Examiner, County of Washtenaw
H. Chairman, Big Ten Awareness Committee on Alcohol and Drug Abuse

V. OTHER RELEVANT ACTIVITIES: None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Quint LE, Glazer GM, Chenevert TL, Klaus PF, Gikas PW, Shireman PK, Grossman BH and King CL.: In Vivo and in Vitro MR Imaging of Renal Tumors: Histopathologic Correlation and Pulse Sequence Optimization. Radiology 169: 359-362, 1988.

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 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES: None.

II. TEACHING ACTIVITIES:

D.D.S. LEVEL:

A. Oral Pathology 625. 30 Lab Hours.
B. General & Oral Pathology 293 (Dental Hygiene). 30 Lab Hours.
C. Student Research Advisement:
Joanne Hartrick - Summer Research, 6 Months
Graduate Level: Student Research Advisement:
John Wataha - Ph.D. Program (Biomaterials)
Janice Wilmont - Orthodontics Masters Program

DENTAL HYGIENE:

A. Oral Pathology 293. General and Oral Pathology Lectures (two credits), Course director and principal lecturer - 38 lectures, (Winter term, junior year).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. National Institute of Dent. Res., Grant No. 1-R01-DE07987-02, "In Vitro Biocompatibility: Composite Resins and Bacteria, ", C.T. Hanks, (P.I.), 5/1/87-4/30/90.

PENDING:

A. National Institute for Dental Research (in answer to RFA 88-DE-6). "Specialized materials science research center." R.G. Craig (P.I. and Center Director), C.T. Hanks (Co-director and co-P.I.), W.J. O'Brien, T.-Y. Tien, W.C. Wagner, C.L. Groh, A. Koran, A.F. Yee, E.R. Dootz, F.E. Filisko, R.E. Robertson, D.J. Chiego, C.A. Edwards, P.-L. Makinen, R.M. Nassiri, S.A. Syed. (Submitted March 7, 1989) 9/1/89-8/31/94.
B. National Institute of Dental Research. "Dental-Scientist Award - Institutional (K16).: D.S. Carlson (P.I.), C.T. Hanks (Co-invesigator and mentor) (Submitted 10/12/88). 7/1/89-6/30/94.
C. National Institute of Dental Research (completing renewal of NIDR grant no. R01-DE0798). "Diffusion Systems in Cytotoxicity Testing," C.T. Hanks (P.I.), 5/1/90-4/30/95. (Submitted July 1, 1989).

IV. ADMINISTRATIVE ACTIVITIES:

SCHOOL OF DENTISTRY AND DEPARTMENT OF ORAL PATHOLOGY:

A. Admissions Committee, School of Dentistry, 1985-1989
B. Nominations and Elections Committee, School of Dentistry, 1987-1990.
C. Hazardous Waste Committee, School of Dentistry, 1987-1990 (Chairman).
D. Dental School Reorganization Task Force of Bylaws and Promotions and Tenure Documents.
E. Director of Research of newly organized Dental School Department (Department of Oral Medicine, Pathology and Surgery, "OMPS").
F. Table Clinics Committee (188-1991)

REGIONAL AND NATIONAL:

A. Committee on Standardization of Biocompatibility Testing for Pulp Biology Group of International Association for Dental Research, Chiar, 1987.
B. ADA Subcommittee on Biological Evaluation of Dental Materials.
C. President-Elect (and Program Chairman, Annual AADR/IADR Meeting), Pulp Biology Research Group of the International Association for Dental Research.

V. OTHER RELEVANT ACTIVITIES:

A. Consultant: With Grace Co.
B. Consultant: Ken Manufacturing Co.

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 BOARDS:

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

INVITED LECTURES/SEMINARS:

1. C.T. Hanks, "Galvanotaxis and Ca^{++} flux in cultured osteoblasts in electormagnetic fields". Presentation at Fifth International Congress on Bone Morphometry, July 24-29, 1988, Niigata, Japan.
2. C.T. Hanks, "The use of "in vitro pulp chamber" in the testing of dental restorative materials". Seminar to faculty and students of the University of Nagasaki Dental School, Japan, August 1988.
3. C.T. Hanks, "Tissue culture methods for testing of toxic substances used in tooth restoration and in implants". Seminar to faculty and students of The University of Kagoshima Dental School, Japan, Aug. 1988.

4. C.T. Hanks, "The influence of electromagnetic fields on cells in culture". Paper given at Multipurpose Arthritis Center (U/M) Symposium, Oct. 1988.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hanks, C.T., Craig, R.G., Diehl, M.L. and Pashley, D.H.: Cytotoxicity of dental composites and other materials in a new in vitro device. J. Oral Pathology 17:396-403, 1988.
2. Parkinson, W.C., C.T. Hanks: Experiments on the interaction of electromagnetic fields with mammollian systems. The Biological Bulletin, Supplement 32:(? pages), 1989.
3. Craig, R.G., C.T. Hanks: Reaction of fibroblasts to various dental casting alloys. J. Oral Pathology 17:341-347, 1988.
4. Parkinson, W.C., C.T. Hanks, Search for cyclotron resonance in cells in vitro. Bioelectromagnetics 10:129-145, 1989.
5. Hanks, C.T., M.L. Diehl, R.G. Craig, P.-L. Makinen, D.H. Pashley: Characterization of the "in vitro pulp chamber" using the cytotoxicity of phenol. J. Oral Pathology 18(2) 97-107, 1989.

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

1. Hartrick, J., C.T. Hanks, S. Syed, M. Diehl. Direct cytotoxicity of bacterial fractions on cultured mammalian cells. J. Dent Res. 68(spec. iss.):243, 1989.
2. Craig, R.G., C.T. Hanks. Cytotoxicity of experimental casting alloys by cell culture testing. J. Dent. Res. 68(spec. iss.):322, 1989.
3. Wataha, J.C., R.G. Craig, C.T. Hanks. Analysis of culture medium for elements dissolved form casting alloys. J. Dent. Res. 68(spec. iss.):322, 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Clinical Flow Cytometry Laboratory
B. Clinical Hematology Laboratory
C. Diagnostic Surgical Pathology, Hematopathology
D. Consultant for Hematopathology cases.
E. Review of Southwest Oncology Group (SWOG) leukemia cases

II. TEACHING ACTIVITIES:

A. Medical Students and Graduate Students.
   1. M4 Clerkship, Hematology portion of Clinical Pathology Rotation
   2. Dental students, Lecture on Hematologic Disorders.
   3. 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.
C. Hematopathology teaching.
   1. Hematopathology Lectures/Monthly.
   2. Hematopathology unknown conferences/biweekly.
D. Clinical Pathology Grand Rounds (three lectures).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT: None

PROJECTS UNDER STUDY:

A. S100 Positive Chronic Lymphoproliferative Disorders.
B. CD11c Positive Chronic Lymphoproliferative Disorders - Role of Adhesion Molecules and Homing Receptors.
C. Oncogene Expression in Malignant Lymphoma.
D. Expression and Regulation of *ets* and other Oncogenes in Translocations Involving Chromosome 11q23.
E. Genotypic Analysis of Adult Acute Lymphocytic Leukemia.
F. Platelet-Associated and Serum Anti-platelet Immunoglobulin Detection by Flow Cytometry: Comparison with Staph Protein A and Radioimmunoassays.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Clinical Flow Cytometry Laboratory
B. Associate Director, Clinical Hematology Laboratory
C. Leukemia Conference, biweekly

REGIONAL AND NATIONAL:

A. Associate Editor of Pathology Patterns (American Journal of Clinical Pathology, Suplement).
B. Council for New Scientific Technology in Clinical Pathology, American Society of Clinical Pathologists.
C. Reviewer of articles for Blood, American Journal of Pathology, American Journal of Clinical Pathology, Laboratory Medicine and Clinical Immunology and Immunopathology.
D. 1989 Pathology Resident ASCP In-service Examination; Hematology section test questions.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Acute Lymphoproliferative Diseases, Course presented at American Society of Clinical Pathologists (ASCP), October, 1988.
2. Flow Cytometry and Southern Blotting in the Diagnosis of Leukemia and Lymphoma, Course presented at American Society of Clinical Pathologists (ASCP), October, 1988.
3. Acute Lymphoproliferative Diseases, Course presented at American Society of Clinical Pathologists, March, 1989.
4. Acute Myelogenous Leukemia and the Myelodysplastic Syndromes, Invited lecture at the Michigan Society of Pathologists, June, 1989.
5. Molecular and Immunologic Analysis of Adult Acute Lymphoblastic Leukemia, Invited Lecture at the University of Minnesota, June, 1989.
6. Director, Clinical Applications of Flow Cytometry in Diagnostic Pathology, American Society of Clinical Pathologists, June 27-30, 1989.
7. Flow Cytometric Detection of Anti-Platelet and Anti-Neutrophil Antibodies; Lecture given at Clinical Applications of Flow Cytometry in Diagnostic Pathology, American Society of Clinical Pathologists, June 30, 1989.
8. Establishing a Clinical Flow Cytometry Laboratory; Lecture given at Clinical Applications of Flow Cytometry in Diagnostic Pathology, American Society of Clinical Pathologists, June 30, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hanson, C.A. and Kersey, J.H.: A modified method of DNA extraction from blood and bone marrow specimens. Am. J. Hematol. 1988;28:176-180.
2. Hanson, C.A., Bolling, S.F., Stoolman, L.M., Schlegelmilch, J.A., Abrams, G.D., Miska, P.T. and Deeb, G.M.: Cytoimmunologic monitoring and cardiac transplantation. J. Heart Transplant. 1988;7:424-429.

3. Hanson, C.A. and Schnitzer, B.: Flow cytometric analysis of cytologic specimens in hematologic disease. J. Clin. Lab. Anal. 1989;3:2-7.
4. Hanson, C.A.: Applications of flow cytometry in diagnostic pathology. Am. J. Clin. Pathol. (Pathology Patterns) 1989;91:S27-S31.
5. Hanash, S.M., Kuick, R., Strahler, J., Richardson, B., Reaman, G., Stoolman, L., Hanson, C., Nichols, D. and Tuesche, J.: Identification of a cellular polypeptide that distinguishes between acute lymphoblastic leukemia in infants and in older children. Blood 1989;73:527-532.
6. Kueck, B.D., Hanson, C.A., Weissman, D.E. and Bayliss, K.: Primary lymph node presentation of angiocentric lymphoma associated with features of a hemophagocytic syndrome. Am. J. Hematol. 1989;30:104-111.
7. Nickoloff, B.J., Griffiths, C.E.M., Baadsgaard, O., Voorhees, J.J., Hanson, C.A. and Cooper, K.D.: Markedly diminished epidermal keratinocyte expression of intercellular adhesion molecule-1 (ICAM-1) in Sezary syndrome. J. Am. Med. Assoc. 1989;261:2217-2221.
8. Hanson, C.A., Ward, P.C.J. and Schnitzer, B.: A multilobular variant of hairy cell leukemia with morphologic similarities to T-cell lymphoma. Am. J. Surg. Pathol. (In Press).
9. Hanson, C.A., Jaszcz, W., Swanson, P.D., Wick, M.R., Peterson, B.A., Gajl-Peczalska, K.J., Kersey, J.H. and Frizzera, G.: True histiocytic lymphoma: histopathologic, immunophenotypic and genotypic analysis. Br. J. Haematol. (In Press).
10. 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. Pathol. (In Press).
11. Hanson, C.A., Levine, E.G., Frizzera, G. and Peterson, B.A.: True histiocytic lymphoma: a review of clinical and pathologic findings. Semin. Oncol. (In Press).
12. 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. Am. J. Ped. Hem. Onc. (In Press).
13. Gribbin, T.E., Stein, C.K., Glover, T.W., Hanson, C.A., Cody, R.L. and Mitchell, B.S.: Association of a hairy cell leukemia variant with a 4p+ chromosomal abnormality: derivation and characterization of a cell line. Leukemia (In Press).
14. Bayliss, K.M., Hanson, C.A., Matthaeus, W.G., Almagro, U.A. and Kueck, B.K.: Richter's syndrome presenting as primary CNS lymphoma transformation of an identical clone. Am. J. Clin. Pathol. (In Press).
15. Savage, P.D., Jones, C., Silver, J., Geurts von Kessel, A.H.M., Gonzalez-Sarmiento, R., Palm, L., Hanson, C.A., Kersey, J.H.: Mapping studies and expression of genes located on human chromosome 11 band q23. Cancer Genet. Cytogenet. (In Press).
16. Ho, V.C., Hansen, E., Elder, J.T., Baadsgaard, O., Wantzin, G., Hanson, C. and Cooper, K.D.: T-cell receptor beta chain gene rearrangement without gamma chain gene rearrangement: a novel finding. Clin. Immuno. Immunopath. (In Press).
17. Stahler, J.R., Kuick, R., Eckerskorn, C., Lottspeich, F., Reaman, G., Richardson, B.C., 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. (In Press).

18. Ho, V.C., Baadsgaard, O., Elder, J.T., Hansen, E., Hanson, C., Wantzin, G., 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. Dermatopath. (In Press).
19. Remick, D.R., Hanson, C.A. and Kunkel, S.L.: Polymerase chain reaction: theory and application. Am. J. Clin. Pathol. (Pathology Patterns) (In Press).

BOOKS AND CHAPTERS IN BOOKS:

1. Brunning, R.D., Parkin, J.L. and Hanson, C.A.: Hematopoietic and lymphoreticular neoplasms, in, Azar, H.A. (ed) Pathology of Human Neoplasms: An Atlas of Diagnostic Electron Microscopy and Immunohistochemistry, Raven Press, New York, NY, 1988, pp 221-304.
2. Hanson, C.A.: Non-traditional applications of flow cytometry, in, Keren, D.F. (ed) Flow Cytometry in Clinical Diagnosis. ASCP Press, Chicago, IL, 1989, pp 280-309.
3. Hanson, C.A.: The acute leukemias and myelodysplastic syndromes, in McClatchey, K.D. (ed) Clinical Laboratory Medicine. Williams & Wilkins, Baltimore, MD, (In Progress).
4. Hanson, C.A.: Clinical applications of molecular biology: Hematopoietic disorders, in McClatchey, K.D. (ed) Clinical Laboratory Medicine. Williams & Wilkins, Baltimore, MD (In Progress).

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

1. Gribbin, T.E., Mahoney, J.F., Hanson, C.A., and Mitchell, B.S.: 2-Deoxyadenosine (dAdo) and an inhibitor of adenosine deaminase are highly toxic to activated B cells and induce B5 surface antigen expression. Presented at The American Society of Hematology; San Antonio, Texas, December, 1988. Blood 1988;72:162A.
2. Hanson, C.A., Thamilarasan, M., Ross, C.W., Patel, M.J., Stoolman, L.M. and Schnitzer, B.: Immunoglobulin, T-cell receptor and bcr gene rearrangements in adult acute lymphoblastic leukemia (ALL). Presented at The American Society of Hematology; San Antonio, Texas, December, 1988. Blood 1988;72:203A.
3. Grossman, D.M., Hanson, C.A., Kueck, B.D., Hanson, G.A., Schnitzer, B.: Red pulp splenic infiltrates by B-cell immunoblastic lymphomas. Presented at International Academy of Pathology; San Francisco, California, March, 1989. Lab. Invest. 1989;60:36A.
4. Grossman, M.D., Hanson, C.A. and Schnitzer, B.: Simulataneous lymphocyte predominant Hodgkin's disease (LPHD) and large cell lymphoma (LCL). Presented at International Academy of Pathology; San Francisco, California, March, 1989. Lab. Invest. 1989;60:36A.
5. Hanson, C.A., Remick, D.G., Fox, D.A., Bockenstedt, P.L. and Schnitzer, B.: S100-positive chronic lymphoproliferative disease: association with natural killer (NK) cell expression and function. Presented at International Academy of Pathology; San Francisco, California, March, 1989. Lab. Invest. 1989;60:37A.
6. Hanson, C.A., Ward, P.C.J. and Schnitzer, B.: A multilobular variant of hairy cell leukemia with morphologic similarities to T-cell lymphoma. Presented at International Academy of Pathology; San Francisco, California, March, 1989. Lab. Invest. 1989;60:38A.
7. Ross, C.W., Schnitzer, B., Stoolman, L.M. and Hanson, C.A.: Aberrant antigen expression in adult acute lymphoblastic leukemia. Presented at International Academy of Pathology; San Francisco, California, March, 1989. Lab. Invest. 1989;60:80A.

8. Hanson, C.A., Schlegelmilch, J.A., Anselm, S.F., Dabich, L. and Stoolman, L.M.: Flow cytometry and radioimmunoassay detection of platelet-associated antibodies. Presented at American Society of Clinical Pathologists; Chicago, Illinois, March, 1989. Am. J. Clin. Pathol. 1989;91:370.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Clinical Dermatology.
B. Dermatopathology, private consultations.
C. Dermatopathology, M-Labs.
D. Dermatopathology, UMH.
E. Dermatopathology, tutorials.

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. The incidence of LaFora bodies in skin biopsies in patients with known LaFora body disease.
B. Long term effects of topical retinoic acid on photoaged skin.
C. Expression of ICAM-1 in hair bulbs in patients with alopecia areata.
D. Factor XIIIa-positive dendritic cells in perifollicular adventitia in health and disease.
E. The possible role of an unidentified fusobactenium in the etiology of perioral dermatitis.
F. A clinical and immunohistochemical study of dermal eccrine mixed tumors.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Pigmented Lesion Clinic.

MEDICAL SCHOOL/HOSPITAL:

A. Dermatopathology Unit.
B. Co-Director, Clinical Microbiology Laboratory.

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 Committe For Dermatopathology.
D. Member, Council on Clinical and Laboratory Services, American Academy of Dermatology.
E. Invited participant. Scientific Advisory Meeting on Hair and Alopecia. National Institute of Health. Bethesda, Maryland, April, 1989.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Scarring Alopecias. New Concepts of Telogen Effluvium. Guest speaker. Texas Dermatological Society, Galveston, Texas, October, 1988.
2. Howard Fox Lecturer. The Diversity of Cutaneous T-cell Lymphoma. New York University. New York. November, 1988.
3. The Diagnosis of Alopecia in Horizontal Section. Advanced Course in Dermatopathology. American Academy of Dermatology. Washington, D.C. December, 1988.
4. Moles and Melanoma. Munson Medical Center, Traverse City. January, 1989.
5. The Dermal Dendrocyte. American Dermatologic Society. Tucson, March, 1989.
6. Tumors of the Hair Follicle. Royal College of Pathologists. London, March 1989.
7. The Diagnosis of Pigmented Skin Lesions. Hurley Medical Center. Flint, April 1989.
8. The Diagnosis and Management of Alopecia. Columbia Hospital. Milwaukee. April 1989.
9. Moles and Melanoma. Mercy Hospital. Port Huron. May, 1989.
10. Pleomorphic Large Cell Lymphoma of Skin. International Society of Dermatopathology. Charleston, S.C. June, 1989.
11. The Scarring Alopecias. Clinicopathologic Correlates of Two New Topical Agents: Topical Retinoic Acid and Topical Minoxidil. Puerto Rico Dermatological Society. San Juan. June, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wiss K., Solomon A.R., Rainer S.S., Lobe T.E., Gourley W. and Headington J.T.: Rhabdomyosarcoma Presenting as a Cutaneous Nodule. Arch Dermatol. 124:1687-1690, 1988.
2. Solomon, A.R., Comite, S.L., Headington, J.T.: Epidermal and Follicular Calciphylaxis. J Cut Pathol. J. Cutan pathol 15:282-285, 1988.
3. Auletta, M.J. and Headington J.T.: Purpura fulminans: A cutaneous manifestation of severe protein C deficiency. Arch Dermatol. Arch Dermatol 124:1387-1391, 1988.
4. Headington, J.T., Gupta, A.K.,Goldfarb, M.T., et al: A Morphologic and Histologic Study of the Scalp in Psoriasis. Arch Dermatol 125:639-642, 1989.
5. Hernandez R.J., Headington, J.T., Kaifan R,A, Mortel, W.: Fibroblastic rheumatism. Skeletal Radial 18:43-45, 1989.
6. Headington, J.T.: Androgenetic alopecia, Trichotrophic Substances and Histologic Studies of the Human Scalp. Clin Dermatol. 6:188-190, 1988.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Maxon, B.M., Scott, R.F. and Headington, J.T.: Management of oral squamous cell carcinoma in situ with topical 5-FU and laser surgery. J Oral Med, Oral Surg, Oral Path.
2. Fast, P.E., Riva, M.C., Blane, C.E., Headington, J.T., Roth, M. and Sullivan, D.B.: Multisystem inflammatory disease in an infant. J. Ped.
3. Solomon, A.R., Brown, M., Swanson, N.A., and Headington, J.T.: Centrofacial Fibrohistocytic Neoplasms with Borderline Microscopic Features. J.A.A.D.
4. Santa Cruz, D.J., Barr, R.J., and Headington, J.T.: Desmoplastic lymphoepithelial tumor of the skin. J. Cutan Pathol.
5. Logan R.L., and Headington, J.T.: Alopecia Mucinosa. Arch Dermatol.

BOOKS AND CHAPTERS IN BOOKS:

1. Headington, J.T.: Neoplasms of hair follicle differentiation. Chapter in, Dermatopathology, Farmer, E. and Hood, T.F., (eds), Appelton-Lange.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

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.)
I. Bone consultation cases, backup for Lee Weatherbee.

II. TEACHING ACTIVITIES:

A. M2: Pathology 600, four 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 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. CPC/General Death Conference, quarterly.

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. Histologic studies of myocardium in hypoplastic left heart syndrome.
B. Participant in 14 institution study of associated lethal defects in hypoplastic left heart syndrome.
C. Review of the effects of pulmonary artery banding on the lung biopsy findings in young children with complete atrioventricular septal defect with pediatric cardiologists and thoracic surgeons.
D. Study of aneurysm formation of repaired coarctation with pediatric cardiologists.
E. Autopsy study of aluminum breakdown products of ECMO heat exchanger.
F. Review of congenital lymphangiomas of bone in children.
G. Study of newborn alveolar proteinosis
H. Diagnosed cardiomyopathy in association with resistant arrhythmias with pediatric cardiologists.
I. Chemotherapy associated myocardial infarcts with Hem/Onc Fellow.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Departmental ACAPT.
B. Interviewing House Officer candidates.

MEDICAL SCHOOL/HOSPITAL:

A. Executive Committee for Mott/Women's/Holden Unit.
B. Executive Committee of the Medical School, 1987-.

REGIONAL AND NATIONAL:

A. Member, American Board of Pathology Test Committee for Pediatric Pathology.
B. Member of the Education Committee of the Society for Pediatric Pathology, Subcommittee I, charged with the documentation and position preparation for subspecialty qualification.

V. OTHER RELEVANT ACTIVITIES: None.

VI. PUBLICATONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Schumacher, R.E., Marrogi, A.J. and Heidelberger, K.P.: Newborn Pulmonary Alveolar Proteinosis (In Press, Pediatric Pulmonology).
2. Bromberg, B., Beekman, R.A., Banks, E., Rocchini, A.P., Snider, A.R. and Heidelberger, K.P.: Aneurysms following patch aortoplasty for coarctation in childhood: An anlysis of screening, prevalence and risks. (In Press, J. Am. Coll. Cardiology).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Keim, D., Ragsdale, C., Heidelberger, K.P., Sullivan, D.B.: Hepatic fibrosis with use of methotrexate for juvenile rheumatoid arthritis.
2. Evans, D., Baugh, R., Gilsdorf, J., Heidelberger, K.P. and Niparko, J.K.: Lymphangiomatosis of skull manifesting with recurrent menigitis and cerebrospinal fluid otorrhea.

ABSTRACTS:

1. Evans, D., Baugh, R., Gilsdorf, J., Heidelberger, K.P. and Niparko, J.K.: Lymphangiomatosis of skull manifesting with recurrent menigitis and cerebrospinal fluid otorrhea. The American Academy of Otolaryngology, Head and Neck Surgery Annual Meeting. Scientific Poster Session. Washington D.C., September 1988.
2. Bromberg, B., Dick, M., Snider, A.R., Scott, W.A., Serwer, G., Bove, E. and Heidelberger, K.P: Tachycardia related cardiomyopathy in children: Response to control of the arrhythmia. 37th Annual Scientific Sessions, American College of Cardiology, Atlanta, 1988.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. With C.J. D'Amato collaborate to prepare gross and microscopic descriptions of virtually all UM autopsy brains and other brains referred for consultation. These are given to the house officer-prosectors to compare with their own findings, and to facilitate completion of autopsy reports; in consultations they become the report.

II. TEACHING ACTIVITIES:

A. Review autopsy brains as above with Pathology house officers and sometimes with other house officers, students, or staff.
B. Neural and Behavioral Sciences 600 for second year medical students: three lectures.
C. Neuropathology 858 for house officers in Pathology, clinical neurological sciences, others, and graduate students: 18 hours including three lectures.

III. RESEARCH ACTIVITIES:

With C.J. D'Amato in two areas: experimental mammalian developmental neurobiology and neuropathology of human dementias and aging.

A. Role of basement membranes in the morphogenisis of prenatal aqueduct stenosis and hydrocephalus in a mutant rat.
B. The possible role of fetal brain macrophages in aggravating brain malformations initiated by prenatal X-irradiation in rats vs the possibility that macrophages have an ameliorating effect on the malformative processes. We have been dependent on the collaboration of K. Sue O'Shea, J. Varani, R.V. Lloyd, K.S. Weeks and Paul Killen in these projects.
C. Neuropathologic support in examining human autopsy brains from subjects with Alzheimer's, Huntington's and other dementing diseases for A.B. Young and J.B. Penny who examine the brains biochemically.

IV. SERVICE ACTIVITIES:

A. Neural and Behavioral Sciences 500,600
Curriculum Committee (Medical School)

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. O'Shea, K.S., Rheinhiemer, J.S.T., D'Amato, C.J. and Hicks, S.P.: Alterations in the neuroepithelial basal lamina in a neurological mutant with prenatal hydrocephalus. J. Neuropath. Exp. Neur. 47:507-515, 1988.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVTIES:

SPONSORED SUPPORT:

A. Lung injury Produced by Oxygen Metabolites. National Institutes of Health, $507,078 for four years. Co-investigator with Peter A. Ward.
B. Immune Complex Injury of Lung and Oxygen Metabolites. National Institutes of Health, $245,304 for three years. Co-investigator with Peter A. Ward.
C. Mediators in IgA and IgG Lung Injury. National Institutes of Health, Principal Investigator $466,791 for five years.
D. Pathogenesis of Pancreatitis Induced Pulmonary Injury. National Institues of Health, $285,558 for three years. Co-investigator with Karen Guice.
E. Renal Center Grant. National Institutes of Health. Principal Investigator, Section V and Core II. $444,520 for five years.
F. Oxidant and protease interaction in Acute Lung Injury. National Institutes of Health. Principal Investigator. $621,275 for five years.

PENDING SUPPORT:

A. Anesthetic and Viral Pulmonary Immunopathology. National Institutes of Health. Co-investigator with Paul Knight (Anesthiology) and Daniel Remick. $1,052,949.00 for five years. (Submitted February 1, 1989).

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.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Immunopathology Fellowship Program.
B. Renal Pathology Conference - Biweekly.
C. Departmental Appointment and Promotions Committee.
D. Space Utilization Committee.
E. Stobbe Funds Committee.
F. 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. OTHER RELEVANT ACTIVITIES:

A. Consultant on Dermatology and Nephrology training grants.

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Warren, J.S., Kunkel, S.L., Cunningham, T.W., Johnson, K.J. and Ward, P.A.: Macrophage-derived cytokines amplify immune complex-triggered O_2^- responses by rat alveolar macrophages. Amer. J. Pathol. 1988;130(3):489-495.
2. Ward, P.A., Cunningham, T.W., McCulloch, K.K., Phan, S.H., Powel, J., and Johnson, K.J.: Platelet Enhancement of O_2^- responses in stimulated human neutrophils: Identification of platelet factor as adenine nucleotide. Lab. Invest. 1988;58:37-47.
3. Cohen, R., Johnson, K.J. and Humes, H.D.: Potentiation of aminoglycoside nephrotoxicity by vitamin-D induced hypercalcemia. Amer. J. Nephrol. (Min and Elec. Metab.), 1988;14:121-128.
4. Oldham, K.T., Guice, K.S., Ward, P.A. and Johnson, K.J.: The role of oxygen radicals in immune complex injury. Free Rad. Bio. and Med., 1988;4:387-397.
5. Guice, K.S., Oldham, K.T., Johnson, K.J., Kunkel, R.G., Morganroth, M.L. and Ward, P.A.: Pancreatitis induced lung injury: An ARDS model. Ann. Surg., 1988;208:71-78.

6. Ward, P.A., Cunningham, T.W., McCulloch, K.K. and Johnson, K.J.: Regulatory effects of adenosine and adenine neucleotides on oxygen radical responses of rat and human neutrophils. Lab. Invest., 1988;58:438-447.

ARTICLES ACCEPTED FOR PUBLICATION:

1. Carpenter, L.J., Johnson, K.J., Kunkel, R.G., and Roth, R.A.: Phorbol myristate acetate produces injury to isolated rat lung in the presence and absence of perfused neutrophils. J. Tox. App. Pharm., In Press.
2. Guice, K.S., Oldham, K.T., Johnson, K.J. and Ward, P.A.: Mechanisms of capillary endothelial cell injury in acute pancreatitis. Surgical Forum, In press, 1987.
3. Ward, P.A. and Johnson, K.J.: Lung inflammatory mechanisms. J. of Human Path., In Press.
4. Ward, P.A., Warren, J.S., Remick, D., Varani, J., Gannon, D., Johnson, K.J.: Cytokines and oxygen radical mediated tissue injury. J. Crit. Care Med., In Press.
5. Guice, K.S., Oldham, K.T., Johnson, K.J.: Anti-oxidant therapy (PEG-catalase) in acute pancreatitis. Annal Surg., In Press.
6. Guice, K.S., Oldham, K.T., Kunkel, R.G., Morganroth, M.L. Ward, P.A.: pancreatitis induced acute lung injury. An ARDS model. International Synopses, in press.
7. Warren, J.S., Kunkel, R.G., Simon, R.H., Johnson, K.J., and Ward, P.A.: Ultrastructural cytochemical analysis of IgA immune complex induced lung injury in the rat. Labv. Invest., in press.
8. Schuger, L., Varani, J., Marks, R.M., Kunkel, S.L., Johnson, K.J., and Ward, P.A.: Cytotoxicity of TNF-a for human umbilical vein endothelial cells. 1989 Lab. Invest. in press.
9. Warren, J.S., Johnson, K.J., and Ward, P.A.: PAF and immune complex induced injury. J. Lipid Mediators, in press.
10. Weinburg, J.M., Johnson, K.J., Dela, Iglesia, F.A. and Allen, E.D.: Acute alterations of tissue Ca^{++} and lethal tubular cell injury during $HgCL_2$ nephrotoxicity in the rat. J.Toxicol., in press.
11. Ward, P.A., Johnson, K.J., Till, G.O.: Mechanisms of lung injury. Prax. Klin. Pneumonol., in press.
12. Ginsburg, I., Schuger, L., Gibbs, F., Johnson, K.J., Ryan, U.S., Ward, P.A., Varani, J.: Endothelial cell killing by polymorphonuclear leukocytes: Independent and synergistic roles for oxygen radicals and proteases. Amer. J. Pathol., in press.
13. Kennedy, T.P., Johnson, K.J., Ward, P.A., Knight, P.R., Finch, J.S.: Biphasic pathogenesis of acute acid aspiration pneumonitis. Amer. J. Anest., in press.
14. Walker, B.A.M., Cunningham, T.W., Freyer, D.R., Todd III, R.F., Johnson, K.J. and Ward, P.A.: Regulation of superoxide responses of human neutrophils by adenine compounds: Independence of requirement for cytoplasmic granules.

ARTICLES SUBMITTED FOR PUBLICATION:

1. 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.
2. Fligiel, S.E.G., Johnson, K.J., Johnson, R.D., Bendilaw, M.J., He, X. and Varani, J.: The effect of oxygen metabolites on elastin degradation by purified enzymes and human neutrophils. Submitted for publication.
3. Warren, J.S., Yabroff, K.R., Remick, D.G., Kunkel, S.L., Kunkel, R.G., Johnson, K.J., Ward, P.A.: Tumor necrosis factor participates in the pathogenesis of acute immune complex alveolitis in the rat. J. Clin. Invest., Submitted for publication.
4. Schuger, L., Varani, J., Marks, R., Kunkel, S.L., Johnson, K.J., Ward, P.A.: Cytotoxicity of TNF-alpha for human umbilical vein endothelial cells. Submitted for publication.
5. Schuger, L., Varani, J., Johnson, K.J., Ryan, U.S., Gannon, D., Ward, P.A.: Neutrophil-dependent oxygen radical mediated lung injury associated with acute pancreatitis. Annals. Surg. In Press.
6. Penna, A.M., Johnson, K.J., Camilleri, Knight, P.R.: Alterations in influenza A, virus specific immune injury in mice anesthetized with Halothine of Ketamine. Submitted for publication.

BOOKS AND CHAPTERS IN BOOKS

1. 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, MA, In press.
2. Johnson, K.J., Chensue, S.W., Kunkel, S.L. and Ward, P.A.: Immunopathology, in, Rubin, E. and Farber, J.L. (eds.), Textbook of Pathology, Lippincott Inc., New York, NY 1988.
3. Ward, P.A., Johnson, K.J., Till, G.O. and Warren, J.S.: Activated phagocytes, oxygen radicals and tissue injury, in Chow, C. (ed.) Cellular Anti-oxidant Defense Mechanism, CRC press, Marcell Deckker, Inc., New York, NY, In press.
4. Ward, P.A., Johnson, K.J. and Till, G.O.: Tissue injury as a consequence of oxygen radicals produced by phagocytic cells, in Preceedings of a Symposium by the Comparative Respiratory Society, Anaheim, CA, 1986, In press.
5. 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 Sumposium, given at the Graduate Hospital, Philadelphia, PA, 1986, In press.
6. 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, 1987, In press.
7. Ward, P.A., Till, G.O., Gannon, D.E., Varani, J.A. and Johnson K.J.: The role of iron injury of endothelial cells in vitro and in vivo. Oxyten Radicals in Biology and Medicine. Fourth International Congress On Oxygen Radicals, 1987, In press.
8. Ward, P.A., Warren, J.S., Till, G.O., Varani, J., Johnson, K.J.: Modification of disease by preventing free radical formation. A new concept in pharmacologic intervention. In: Bailliere's Clinical Hematology: International Practive and Research, Ed. by C. Hershko, London, W.B. Saunders CO., In press.
9. Warren, J.S., Ward, P.A., Johnson, K.J.: The inflammatory response, Chapter 8 In: W.J. Williams (ed.), Hematology, 4th Edition, In press.
10. Warren, J.S., Ward, P.A., Johnson, K.J.: Oxygen radicals as 'Mediators of inflammation', Volume 6 in Henson, P.S. (ed.) The Handbook of Inflammation, Vol. 6, Elsevier Biomedical Division, Amsterdam, The Netherlands, In press.
11. 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, NY, in press.

12. Till, G.O., Warren, J.S., Gannon, D.E., Chensue, S.W., Kunkel, S.L., Varani, J., Johnson, K.J. and Ward, P.A.: Effects of pentoxifylline on phagocytic responses in-vitro and acute and chronic inflammatory reactions in-vivo, In Novick, W. (ed.), Pentoxifylline and Leukocyte Function Symposium, Hoechst-Roussell Pharm., Somerville, NJ, 124-137, 1988.
13. Ward, P.A., Warren, J.S>, Johnson, K.J., and Varani, J.: Cytokines and oxygen radical responses, in, Maier, R. (ed.), Proceedings of the 1st International Congress on The Immune Consequences of Trauma, Shock, and Sepsis: Mechanisms and Therapeutic Approaches, in press.
14. Ward, P.A., Warren, J.S., and Johnson, K.J.: Leukocytes, Oxidants and Tissue injuty, in Cerra, F. (ed.), Perspectives in Critical Care, Quality Medical Publishing, St. Louis, MO, 1988, pp. 69-81.
15. Ward, P.A., Macconi, D., Sulavik, M.C., Till, G.O., Warren, J.S., Johnson, K.J. and Powell, J.: Rat neutrophil-platelet interactions in oxygen radical-mediated lung injury. UCLA Sym. Molec. and Cell Biol., in Oxy-Radicals in Molecular Biology and Pathology, Edited by P. Cerutti, I. fridovich, J.M. McCord, Alan R. Liss, Inc., New York, NY pp. 83-98, 1988.
16. Ward, P.A., Warren, J.S., Remick, D., Varani, J., Gannon, D., and Johnson, K.J.: Cytokines and oxyten-radical-mediated tissue injury, in Shoemaker, W.C. (ed.) New Horizons III, Critical Care Medicine, (in press).
17. Ward, P.A., Johnson, K.J., Till, G.O.: Aminal models for oxidant lung injury. In Proceedings of Stressa Symposium in Zambon, Italy, In press.
18. Ward, P.A., Warren, J.S., Johnson, K.J.: Oxygen radicals, inflammation and tissue injury, In Pryor, W. and Godber, S.L. (eds.) Free Radical Biology and Medicine , In press.
19. 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 colloquim. London, England, in press.
20. Warren, J.S., Johnson, K.J., Till, G.O., and Ward, P.A.: Mechanism of oxygen radical-mediated acute tissue injury: In vivo studies. Proceedings of Enzyme Meeting, July, 1986, In press.

ABSTRACTS, PRELIMINARY COMMUNICATIONS, PANEL DISCUSSIONS

1. Guice, K.S., Oldham, K.T., Johnson, K.J.: Anti-oxidant therapy (PEG-catalase) in acute pnacreatitis. SSAT. 1988.
2. Oldham, K.T., Schmeling, D.J., Guice, K.S., Johnson, K.J.: Obliterative cholangitis: A model of biliary inflammation. ACS, 1988.
3. Guice, K.S., Oldham, K.T., Johnson, K.J., Ward, P.A.: Pacreatitis induced acute lung injury: Mechamisms of injury. ACS, 1988.
4. Mandel, D.M., Warren, J.S., Johnson, K.J., and Ward, P.A.: Specific interactions between platelet-activating factor (PAF) and neutrophils in a rat model of immune complex vasculitis. Fed. Proc. 1988;2:A414.
5. Yabroff, K.R., Warren, J.S., Johnson, K.J., and Ward, P.A.: Desparate patterns of susceptibility of pulmonary and dermal vascular beds to phagocyte-derived oxidant injury. Fed. Proc. 1988;2:A1175.
6. Kunkel, R.G., Warren, J.S., Johnson, K.J. and Ward, P.A.: Demonstration of the complement membrane attack complex (MAC) in IgA-immune complex induced acute lung injury. Fed. Proc. 1988;2:A1176.
7. Schmeling, D.J., Oldham, K.T., Guice, K.S., Johnson, K.J.: Noninfectious obliterative cholangitis: A model of bilinary inflammation. Fed. Proc. 1988;2:A1177.

8. Kennedy, T.P., Johnson, K.J., Ward, P.A., FInch, J.S.: Conditions associated with maximal lung injury in an experimental model of aspiration pneumonitis. Fed. Proc. 1988;2:A1608.
9. Guice, K.S., Oldham, K.T., Johnson, K.J., Ward, P.A.: Pulmonary capillary endothelial injury in acute pancreatitis: protection by oxygen radical scavengers. Fed. Proc. 1988;2:A1608.
10. Warren, J.S., Robert, M., Kunkel, S.L., Johnson, K.J., and Ward, P.A.: Modulation of interleukin I (IL-1) and tumor necrosis factor (TNF) production by monocytes and alveolar macrophages: Implications for immune complex-mediated lung injury. Fed. Proc. 1988;2:A1822.
11. Kennedy, T.P., Johnson, K.J., Ward, P.A., Knight, P.R., Finch, J.S.: Biphasic pathogenesis of acute acid aspiration pneumonitis. Amer. Soc. Anesth. Natl. Meeting, 1988.
12. Ward, P.A., Maccone, D., Sulavik, M.C., Till, G.O., Warren, J.S., Johnson, K.J. and Powell, J.: Rat neutrophil-platelet interactions in oxygen radical mediated lung injury. UCLA Symposium on Molecular and Cellular Biology, January, 1988.
13. Ward, P.A., Warren, J.S., Gannon, D., Johnson, K.J., Phan, S.H., Varani, J.: Cytokines and oxygen radical mediated injury. oxy. Radicals in Molecular Biology and Pathology. B025, 1988.
14. Ward, P.A., Varani, J., Ryan, U.S., Warren, J.S., Johnson, K.J.: Cytokines and oxygen radical mediated lung injury. Sixth Annual Aspen Basic/Clinical Science Conference on "Oxygen Radicals", The University of Colorado, Aspen, CO, August, 1988, submitted (abstract).
15. Barton, P.A., Warren, J.S., Johnson, K.J., Ward, P.A.: Rat alveolar macrophages express cell membrane-associated IL-1 activity. FASEB J. 1989;3(3):535.
16. Warren, J.S., Yabroff, K.R., Remick, D.G., Kunkel, S.L., Kunkel, R.G., Johnson, K.J., and Ward, P.A.: Intrapulmonary IL-1 and TNF in acute immune complex lung injury in the rat. FASEB J. 1989;3(3):2230.
17. Penna, A.M., Johnson, K.J., Kennedy, T.P., Knight, P.R.: Time course of sublethal lung injury in mice exposed to PR-8 influenza virus: a new model. FASEB J. 1989;3(3):2271.
18. Schuger, L., Varani, J., Marks, R., Kunkel, S.L., Johnson, K.J., and Ward, P.A.: Cytotoxicity of TNF-a for human umbilical vein endothelial cells. FASEB J. 1989;3(3):2391.
19. Kennedy, T.P., Johnson, K.J., Ward, P.A., Knight, P.R., Finch, J.S.: Isoflurane increases alveolar-capillary leak in acid aspiration in rat. FASEB J. 1989;3(3):4001.
20. Yabroff, K.R., Warren, J.S., Mandel, D.M., Johnson, K.J., and Ward, P.A.: Xanthine oxidase inhibitors reduce neutrophil influx into sites of immune complex-induced dermal vasculitis in the rat. FASEB J. 1989:3(3):4009.
21. Guice, K.J., Oldham, K.T., Caty, M.G., Bagnasco, J.M., Johnson, K.J.: Pancreatic capillary endothelial injury in acute pancreatitis: the hydroxyl radical and iron. FASEB J. 1989;3(3):5850.
22. Knight, P.R., Penna, A., Kennedy, T.P., Johnson, K.J.: Effects of volatile anesthetics on viral pathogenesis. Proceeding of the Dr. Fred Rapp honorary symposium. Hershey Medical School Pennsylvania State University, May 1989.
23. Ward, P.A., Warren, J.S., Varani, J., Johnson, K.J.: Cytokines, oxygen radicals and tissue injury. Am. Assoc. Lab. Animal Med., Detroit, MI 1988 (abstract).
24. Ward, P.A., Warren, J.S., Johnson, K.J.: PAF, ctyokines and immune complex induced injury. Satellite meeting of the International Conference on Tumor Necrosis Factor. UCLA - Institute Henri Beafour, Napa, CA January 1989 (abstract).
25. Ward, P.A., Till, G.O., McCulloch, K.D., Johnson, K.J.: Peptides and complement in lung microvascular injury.

26. Schmeling, D.J., Oldham, K.T., Guice, K.S., Johnson, K.J.: Noninfectious obliterative cholangitis: A model of Biliary inflammation. 1st annual Dept of Surgery Research Conf. 1989 (abstract).
27. Kunkel, R.G., Johnson, K.J., Ward, P.A., Marks, R.M.: Morphology of complement mediated neutrophil adhesion and migration through vascular endothelium. Fed. Amer. Soc. for Exper. Bio. 1989.
28. Penna, A., Johnson, K.J., Knight, P.R.: Pathophysiologic effects of volatile anesthetics on influenza A infected mice. Amer. Soc. Anest. 1989.

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

ANNUAL DEPARTMENT REPORT
1 JULY, 1988 - 30 JUNE, 1989

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Directed 1988-89 Clinical Pathology Grand Rounds.
B. Coordinated 1988-89 Anatomical Pathology Conferences.
C. Coordinated Core-Lecture Series 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. Biochemistry of the ABO, Se, Le, P and I Blood Group Systems.
   2. Special Methods in Immunohematology.
F. Trained Pathology and Pediatric Hematology Residents in Immunohematology.
G. Provided instruction to Pathology Residents during their Blood Bank Rotation.
H. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
   1. Course Director.
   2. Presented Direct Antiglobulin Testing Workshop.
   3. Presented talk entitled: Testing, Testing, Testing: What to Use and When.
I. Visiting Lecturer, Specialist in Blood Banking Program, Wayne State University.

III. RESEARCH ACTIVITIES:

A. Knafl P, Horan M, Judd WJ, Oberman HA. Is autologous blood over-utilized? Submitted for presentation at the 1989 Annual Meeting of the American Association of Blood Banks, New Orleans, October, 1989.
B. Judd WJ, Steiner EA, Oberman HA. Can the 37 C reading be eliminated from antibody detection tests? Submitted for presentation at the 1989 Annual Meeting of the American Association of Blood Banks, New Orleans, October, 1989.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Blood Bank Technical Committee.
B. Clinical Pathology Committee.

REGIONAL/NATIONAL:

A. National Committee for Clinical Laboratory Standards: Chairman, Subcommittee on Lectins.
B. Michigan Association of Blood Banks:
   1. Nominating Committee.
   2. Program Committee.
C. American Association of Blood Banks:
   1. Nominating Committee.
   2. Associate Editor, AABB Technical Manual, ed 10 (to be published late 1989):
      a. revised pretransfusion testing chapter.
      b. revised antibody identification chapter.
      c. revised direct antiglobulin testing chapter.
      d. edited and compiled special methods section.
   3. Scientific Section Coordinating Committee:
      a. Communications Group Leader.
      b. Chairman, Subcommittee on Prenatal Testing.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES

1. XXVI Congress of the International College of Surgeons, Milan, Italy, July, 1988: Blood Usage During Surgery.
2. 26th Anniversary Seminar, Blood Bank of Alaska, Anchorage, Alaska, September, 1988:
   a. Compatibility Testing - Where Have We Been and Where Are We Going?
   b. Red Cell Elution - How, What and Why?
   c. Cases I Have Known and Loved.
   d. Antibody Identification - How Much is Enough?
   e. Special Methods in Immunohematology.
3. Hoxworth Blood Center, University of Cincinnati, Cincinnati, Ohio, October, 1988: Compatibility Testing - Where Have We Been and Where Are We Going?
4. Annual Meeting of the Michigan Association of Blood Banks, Troy, Michigan, November, 1988: Compatibility Testing - Where Have We Been and Where Are We Going?
5. Duke University Medical Center, Durham, North Carolina, January, 1989:
   a. Compatibility Testing - Where Have We Been and Where Are We Going?
   b. The MN Blood Group System.
6.. Current Topics in Blood Banking Seminar, Broward Community Blood Center, Fort Lauderhill, Florida, January, 1989:
   a. Compatibility Testing - Where Have We Been and Where Are We Going?
   b. Red Cell Elution - How, What and Why?
   c. Cases I Have Known and Loved.
   d. Antibody Identification - How Much is Enough?
   e. Special Methods in Immunohematology.
7. Mt Sinai Medical Center, Miami Beach, Florida, January, 1989: Compatibility Testing - Where Have We Been and Where Are We Going?
8. University of Utah Medical Center, Salt Lake City, Utah, February, 1989: Prenatal Testing.

9. Current Topics in Blood Bank Seminar, Billings, Montana, March, 1989:
    a. Compatibility Testing - Where Have We Been and Where Are We going?
    b. Red Cell Elution - How, What and Why?
    c. Cases I Have Known and Loved.
    d. Antibody Identification - How Much is Enough?
    e. Special Methods in Immunohematology.
10. California Blood Bank Society Annual Meeting, San Diego, California: Compatibility testing - Where Have We Been and Where Are We Going?
11. Mid-Atlantic Association of Blood Banks Annual Meeting, McLean, Virginia, May, 1989: Antibody Identification - How Much is Enough?

WORKSHOPS/PANEL DISCUSSION

1. Ask the Experts. American Association of Blood Banks Annual Meeting, Kansas City, Missouri, October, 1988.
2. Investigation and management of immune hemolysis: autoantibodies and drugs. American Association of Blood Banks Annual Meeting, Kansas City, Missouri, October, 1988.

VI. PUBLICATIONS:

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

1. Judd WJ, Steiner EA, O'Donnell DB, Oberman HA. Discrepancies in ABO typing due to prozone: how safe is the immediate-spin crossmatch? Transfusion 1988;28:334-338.
2. Judd WJ, Steiner EA, Oberman HA, Giacherio D. False-positive results with chemically modified anti-D do not indicate the need for a separate immunologically inert Rh control reagent. Transfusion 1988;28: 339-341.
3. Daniels GL, Reid ME, Anstee DJ, Beattie KM, Judd WJ. Transient reduction in erythrocyte membrane sialoglycoprotein ß associated with the presence of elliptocytosis in a patient with severe anemia. Blood 1988;70:477-81.
4. Annesley TD, Judd WJ. LISS, bleach and their admixture: a potential hazard. Med Lab Sci 1989;46:83-85.
5. McCoy-Pardington D, Judd WJ, Knafl P, Abruzzo LV, Coombes KR, Butch SH, Oberman HA. Blood utilization during extracorporeal membrane oxygenation. Transfusion, 1989: In press.
6. Steiner EA, Judd WJ, Oberman HA, Hayashi RH, Nugent CE. Percutaneous umbilical blood sampling and umbilical vein transfusions: new roles for the blood bank. Transfusion, 1989: In press.
7. Judd WJ, Stroup-Walters M, Luban, NLC, Ness PM, Silberstein LE, Widmann FK. Prenatal and perinatal immunohematology. Transfusion, 1989: In press.

CHAPTERS IN BOOKS:

1. Judd WJ. Investigation and management of immune hemolysis: autoantibodies and drugs. *In*: Wallace ME, Levitt JS, eds. Current applications and interpretation of the direct antiglobulin test. Arlington, VA, American Association of Blood Banks, 1988:47-103.
2. Judd WJ. Lectins and polyagglutination. *In*: Petz LD, Swisher SN. Clinical practice of blood transfusion, ed 2. Churchill-Livingstone, 1989:137-51.

ABSTRACTS/LETTERS:

1. Gilsdorf J, Cinat MA, Judd WJ. Relationship of *H. influenzae* type b (Hib) pili and adherence to human red blood cells. Proceedings of the Interscience Conference on Antimicrobial Agents and Chemotherapeutics, 1988.
2. Should hospitals draw donors? A cost appraisal. Proceedings of the XX Congress of the International Society of Blood Transfusion. London, UK, 1988:125.
3. Judd WJ, Prozones due to potent hemolytic anti-A(α) and anti-B(ß): how safe is the immediate-spin crossmatch? Proceedings of the XX Congress of the International Society of Blood Transfusion. London, 1988:151.
4. Steiner EA, Hayashi RH, Nugent CE, Oberman HA, Judd WJ. PUBS: A new role for the blood bank. Proceedings of the XX Congress of the International Society of Blood Transfusion. London, 1988:270
5. Steiner EA, Hayashi RH, Nugent CE, Oberman HA, Judd WJ. PUBS: A new role for the blood bank. 41st Annual Meeting of the American Association of Blood Banks, Kansas City, Missouri. Transfusion 1988;28(supplement):28.
6. McCoy-Pardington D, Knafl P, Butch SH, Oberman HA, Judd WJ. ECMO: Minimal impact on the blood bank. 41st Annual Meeting of the American Association of Blood Banks, Kansas City, Missouri. Transfusion 1988;28(supplement):6.

DAVID F. KEREN, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Head, Biochemistry Section.
B. Director, Clinical Immunopathology Laboratory.
C. Surgical Pathology, Consultant on Immunopathology and Gastrointestinal Pathology, on-call duties.
D. Autopsy Pathology, staff coverage and on-call duties.

II. TEACHING ACTIVITIES:

A. Medical Students and Graduate Students.
   1. Biology 414, Lecture on Mucosal Immunity.
   2. Pathology 600, Lectures on myeloma, autoimmunity, clinical pathology.
   3. Pathology Course, Laboratory Director.
B. House Officers:
   1. Coordinator, Weekly Clinical Pathology Rounds.
   2. Participant, Clinical Pathology Grand Rounds.
   3. Clinical Immunopathology, Daily sign-out.
   4. Immunology Journal Club, Weekly.
   5. Graduate Student Conference, Monthly.
C. Medical Student Teaching Award.

III. RESEARCH ACTIVITIES:

A. Studies on kinetics of the mucosal immune response to bacterial antigens.
B. Creation of carcinogen-protein conjugates to study systemic and mucosal immune response to carcinogens.
C. Cell Differentiation within the liver.

SPONSORED SUPPORT:

A. United States Army Research and Development Command, "An Investigation of the Memory Response of the Local Immune System to Shigella Antigens", $367,694. April 6, 1987-July 3, 1990, Principal Investigator.
B. Smokeless Tobacco Research Council, Inc. "Significance of Immune Responses to Mucosal Carcinogens", $553,805. January 1, 1984-July 31, 1989, Principal Investigator.
C. National Cancer Institute, "The Mucosal Immune Response to Aflatoxin B1", $893,625. April 1, 1989-March 31, 1993, Principal Investigator.

STUDENT AND FELLOW RESEARCH PROJECTS:

A. Larry Silbart - "The detection of AAF adducts in rat hepatocytes by RIA".
B. Joseph Wassef - "Uptake of Shigella by M cells in the pathogenesis of dysentery".

C. Lori Armstrong - "The cellular basis for enhanced mucosal IgA memory responses."
D. Mark Sukow - "Secretory IgA response to Shiga toxin".

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Clinical Pathology Committee.
B. Biochemistry Section Committee.
C. Resident Counselor.
D. Stobbe Fund Committee.
E. Department Executive Committee.
F. Graduate Program Committee.
G. Chairman's Advisory Council.

REGIONAL AND NATIONAL:

A. Editorial Board - Clinical Laboratory Update.
B. Council on Continuing Education, (ASCP).
C. Chairman, Immunopathology Rounds (ASCP).
D. Reviewer, Clinical Chemistry, The Journal of Nutrition, Gastroenterology, Infection and Immunity.
E. Editorial Board: Clinical Immunology Newsletter

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Strategies to Diagnose Monoclonal Gammopathies", Rush Medical School, Chicago, Illinois, August, 1988.
2. "High Resolution Electrophoresis and Immunofixation", American Society of Clinical Pathologists, Pathology Update, Cherry Hill, New Jersey, September, 1988.
3. "Strategic Approach to Monoclonal Gammopathies", Montreal General Hospital, Toronto, Ontario, Canada, October, 1988.
4. "Whipple's Disease at Medical Grand Rounds" and "Secretory IgA Responses to Small Carcinogenic Molecules", University of Washington in Seattle, Seattle, Washington, October, 1988.
5. "Electrophoresis and Immunofixation: Techniques and Use in Interpretive Reporting", American Society of Clinical Pathologists and College of American Pathologists, Las Vegas, Nevada, October, 1988.
6. "Secretory IgA Response to Shiga Toxin", 24th U.S.-Japan Joint Conference on Cholera and Related Diarrheal Diseases, Tokyo, Japan, November, 1988.
7. "Strategies to Diagnose Monoclonal Gammopathies", Anderson Hospital in Houston, Houston, Texas, December 1988.
8. Strategies to Diagnose Monoclonal Gammopathies", Ochsner Clinic, New Orleans, Louisiana, December, 1988.
9. "New ANA testing in Autoimmune Disease", St. John's Hospital, Detroit, Michigan, February, 1989.
10. Board Meeting, United States and Canadian Academy of Pathology, Gastrointestinal Pathology Society, San Francisco, California, March, 1989.
11. Course Director, Immunopathology Rounds, American Society of Clinical Pathologists National Meeting, Chicago, Illinois, March, 1989.

12. "High-Resolution Electrophoresis in Clinical Diagnosis", Beckman Instruments, Incorporated, Jacksonville, Florida, March, 1989.
13. Workshop on Protein Chemistry, Canadian Clinical Chemists Meeting, Hamilton, Ontario, Canada, May 1989.
14. "New Concepts of Monoclonal Gammopathies", Methodist Hospital of Indiana, Inc., Indianapolis, Indiana, May, 1989.
15. Immunopathology Case Conference, American Medical Laboratory Immunologists, Albany, New York, June, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Keren, D.F., Kumar, N.B. and Appelman, H.D.: Quantification of IgG-containing plasma cells as an adjunct to histopathology in distinguishing acute self-limited colitis from active idiopathic inflammatory bowel disease. Pathol. Immunopathol. Res. 1987;6:435-441.
2. Davenport, R.D. and Keren, D.F.: Oligoclonal bands in cerebrospinal fluid: significance of corresponding bands in serum for diagnosis of multiple sclerosis. Clin. Chem., 1988;34:764-765.
3. Wojcik, E., Dvorak, C., Chianale, J., Traber, P., Keren, D.F. and Gumucio, J.J.: Demonstration by in situ hybridization of the zonal modulation of rat liver cytochrome P450b and P450e gene expression after phenobarbital. J. Clin. Invest. 1988;82:658-666.
4. Keren, D.F., Warren, J.S. and Lowe, J.B.: Strategy to diagnose monoclonal gammopathies in serum: high resolution electrophoresis, immunofixation and K/L quantification. Clin. Chem., 1988;56:910-915..
5. Latov, N., Hays, A.P., Donofrio, P.D., Liao, J., Ito, H., McGinnis, S., Manoussos, K., Freddo, L., Shy, M.E., Sherman, W.H., Chang, H.W., Greenberg, H.S., Albers, J.W., Alessi, A.G., Keren, D.F., Yu, R.K., Rowland, L.P. and Kabat, E.A.: Monoclonal IgM with unique specificity to gangliosides GM_1 and CD_{1b} and to lacto-N-tetraose associated with human motor neuron disease. Neurol. 1988;38:763-768.
6. Keren, D.F.: Mucosal IgA elaboration. CRC Crit. Rev. in Clin. Lab. Sci. 1989;27:159-177.
7. Silbart, L.K. and Keren, D.F.: Reduction of intestinal carcinogen absorption by carcinogen-specific secretory immunity. Science 1989;243:1462-1464.
8. Wassef, J.S., Keren, D.F. and Mailloux, J.L.: The role of M cells in both initial antigen uptake and in ulcer formation in the rabbit intestinal loop model of Shigellosis. Infect. Immun. 1989;57:858-863.
9. Keren, D.F., McDonald, R.A., Wassef, J.S., Armstrong, L.R. and Brown, J.E.: The enteric immune response to shigella antigens. Curr. Top. Microbiol. Immunol. 1989;146:213-223.
10. Keren, D.F.: High-Resolution Electrophoresis aids Detection of Gammopathies. Clin. Chem. News 1989;15:11-16.
11. Wassef, J.S. and Keren, D.F.: Uptake of Shigella flexneri by follicle-associated epithelium: role in immunogenic stimulation and pathogenicity. J. Microbiol. (In Press).

12. Maganto, P., Traber, P.G., Wojcik, E., Rusnell, C., Keren, D., Gumucio, J.J.: Intrasplenically transplanted hepatocytes: an expression system for liver cytochrome P450b and P450e genes. Hepatology (In Press).
13. Levenson, S.S., Keren, D.F.: Immunoglobulins from the sera of immunologically activated persons with pairs of electrophoretic restricted bands show greater tendency to aggregate than normal. J. Clin. Invest. (In Press).
14. Register, L.J. and Keren, D.F.: Hazard of commercial antiserum cross-reactivity in monoclonal gammopathy evaluation. Clin. Chem. (In Press).

BOOKS AND CHAPTERS IN BOOKS:

1. Keren, D.F. (Editor): Flow cytometry, surface marker assays, and DNA studies in diagnostic pathology. ASCP Press, 1989..
2. Keren, D.F.: Chapter 1: Introduction - History and evolution of surface marker assays, in, Keren, D.F.(Editor) Flow Cytometry, Surface Marker Assays, and DNA Studies in Diagnostic Pathology, ASCP Press, Chicago, pp. 1-11, 1989.
3. Keren, D.F.: Chapter 7: Surface marker assays in the evolution of immune deficiency diseases, in, Keren, D.F.(Editor) Flow Cytometry, Surface Marker Assays, and DNA Studies in Diagnostic Pathology, ASCP Press, Chicago, pp. 213-247, 1989.
4. Keren, D.F.: Chapter V: Structure and function of the immunologic system of the gastrointestinal tract, in, Ming, S.(Editor) The Pathology of the Gastrointestinal Tract, W.B. Saunders, Co., New York, (In Press).

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

1. Keren, D.F., Brown, J.E. and McDonald, R.A.: Functional significance of secretory immunoglobulin A against shiga toxin. ASM Abstracts, 1988;38.
2. Armstrong, L.A. and Keren, D.F.: Cellular events surrounding oral stimulation of the mucosal immune response to Shigella flexneri. FASEB, 1988;5605
3. Levinson, S.S., Keren, D.F. and Goldman, J.O.: Immunoglobulins from immunologically activated persons show greater tendency to aggregate than normal. Clin. Chem. 1988.
4. Bush D.M. and Keren, D.F.: Quantification of kappa- and lambda-containing immunoglobulins by rate nephelometry: comparison of two commercial reagent antisera. AACC, 1989
5. Richardson, B. and Keren, D.F.: Antigen specific CD4+ cells kill the macrophage that activates them. FASEB, 1989.
6. Del Buono, D.A. and Keren, D.F.: Comparison of high-resolution electrophoresis of concentrated urine with immunoelectrophoresis as a screen for Bence Jones proteinuria. ASCP/CAP (In Press).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES: NONE

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. Resident Teaching Conference

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIH- P01-HL31963, Principal Investigator, Project VI "Molecular Biology of Alveolar Wall Injury", (40%) $109,105/year, ($602,508/5 years) 3/1/89 - 2/28/94.
B. NIH-DC39225 Principal Investigator, Project XI "Monokine-Mediated Matrix Biosynthesis by Mesangical Cells." (10%) $45,784/year.
C. NIH-1R01-CA51806-01, Principal Investigator, Regulation of Collagen IV Gene Transcription (25%) $85,340/year $407,036/5 years (pending).
D. AHA-GIA, Principal Investigator, Mesangial Cell, Expression of Collagen IV Genes. (5%) $24,500/year $49,000/2 years.
E. MDRTC-Pilot and Feasibility - "Collagen IV Metabilism by Human Retinal Pigment Epithelial Cells in Vitro". (5%) $18,600/year.

PROJECTS UNDER STUDY:

A. Basement membrane gene expression by alveolar wall cells.
B. Regulation of collagen IV gene expression during development.
C Expression of mutant alpha 1(IV) genes by eukaryotic cells in vitro.
D. Regulation of basement membrane gene expression by glomerular cells in culture.
E. Molecular cloning of α3(IV) and α4(IV) collagen chains.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL: NONE

MEDICAL SCHOOL/HOSPITAL:

A. Interviewed candidates for faculty positions.
B. Interviewed candidates for research fellowships.

REGIONAL AND NATIONAL:

A. Ad hoc reviewer, Division of Extramural Activities, NIDDK, NIH.
B. Reviewer, Laboratory Investigation, American Journal of Pathology
C. Ad hoc Reviewer, Juvenile Diabetes Foundation.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. American Society of Cell Biology, Collagen IV Workshop, San Francisco, Califoria, February, 1988.
2. MDRTC Workshop, Diabeties on Complications of Diabetes Mellitus.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ebihara, I., Killen, P.D., Laruie, G.W., Huang, T., Yamada, Y., Martin, G.R., and Brown, K.S.: Altered mRNA expression of basement membrane components in a murine model of polycystic kidney disease. Lab. Invest., 1988;58(3):262-269.
2. Killen, P.D., Burbelo, P.D., Martin, G.R., Yamada, Y.: Structures of the amino-terminal portion of the murine α1(IV) collagen chain and the corresponding region of the gene. J.Biol. Chem., 1988, 263 (18):8706-8709.
3. Killen, P.D., Burbelo, P.D., Martin, G.R., Yamada, Y.: Characterization of the promoter for the α1(IV) collagen gene: DNA sequences within the first intron enhance transcription. J. Biol. Chem., 1988, 263:12310-12314.
4. Cutting, G.R., Kazazian, H.H., Antonarakis, S.E., Killen, P.D., Yamada, Y., Francomano, C.A.: Macrorestriction mapping of COL4A1 and COL4A2 collagen genes on chromosome 13q34. Genomics 1988;3:256-263.
5. McGuire, P.G., Brocks, D., Killen, P.D., and Orkin, R.W.: Increased deposition of basement membrane macromolecules in specific vessels of the spontaneously hypertensive rat. Amer. J. Pathol. 1989, in press.
6. Laurie, G.W., Killen, P.D., Sequi-Real, B., Yamada, Y., Martin, G.R.: In situ hybridization reveals temporal and spatial changes in cellular expression of mRNA for a laminin receptor, Laminin and basement membrane (Type IV) collagen in the development kidney. J. Cell Biol., 1989, in press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Killen, P.D., Yamada, Y., and Francomano, C.A.: TaqI and BclI polymorphisms in the COL4A1 gene. Nucl. Acid Res., 1989, submitted.
2. Francomano, C.A., Yamada, Y. and Killen, P.D.: MspI ;and EcoRV polymorphisms in the COL4A2 gene. Nucl. Acid Res., 1989, submitted.
3. Killen, P.D., Yamada, Y. and Francomano, C.A.: High frequency HpaI polymorphism in the LAMB1 laminin gene. Nucl. Acid Res., 1989, submitted.
4. Francomano, C.A., Yamada, Y., and Killen, P.D.: MspI restriction fragment length polymorphism in the LAMB2 laminin gene. Nucl. Acid Res., 1989, submitted.

5. Weiser, M.M., Sykes, D.E., Killen, P.D.: Rat intestinal basement membrane synthesis epithelial vs. non-epithelial contributions. Lab. Invest. 1989. submitted.
6. Merritt, S., Killen, P., Phan, S., Downer, G., Wiggins: Intraglomerular inflammation is associated with extraglomerular collagen synthetic activity early in a crescentic model of antiGBM disease in the rabbit. Evidence from measurement of alpha 1(IV) collagen and beta-actin mRNA from glomeruli and renal cortex. J. Clin. Invest., 1989, submitted.

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

1. Wiggins, R., Merritt, S., Phan, S., Killen, P.: Increased glomerular mRNA for types I and IV collagen prior to cellular crescent formation in rabbit anti-GBM disease. Amer. Soc. Neph., 1988 submitted.
2. Briggs, J.P., Todd, K.M., Schnermann, J., and Killen, P.D.: Feasibility studies of mRNA quantification in single dissected nephron segments by PCR amplification of cDNA. Amer. Soc. Neph. submitted, 1989.
3. Killen, P.D., Long, R., DeMeester, C.A., O'Brein, E.: Transcriptional regulation of collagen IV genes. Amer. Soc. Neph., 1989, submitted.
4. Weiser M.M., Killen, P.D.: Rat intestinal basement membrane synthesis: the relative contributions of villus vs crypt epithelial cells and non-epithelial cells. Intl. Conf. Gast. Bio., 1988, submitted.
5. Hansch, G.M., Schonermark, M., Berger, B., Jahn, B., Killen, P., Rother, K.: Proline analogous inhibit the extracellular deposits of collagen type IV by human glomerular epithelial cells., 1989, submitted.
6. Wiggins, C., Merritt, S., Killen, P., Downer, G., Phan, S.: Cortical before glomerular collagen synthesis early in rabbit model of crescentic glomerulo nephritis., J. Clin. Invest., 1988, submitted.
7. Killen, P.D., DeMeester, C.A.: An enhancer in the first intron of the α1(IV) collagen gene regulates expression during differentation of F9 teratocarcinoma cells in vitro., J. Clin. Invest., 1988, submitted.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES: None.

II. TEACHING ACTIVITIES:

A. Inflammation/Immunopathology Series ICS-600.
B. Pathology 580.
C. Epidemiology 570.
D. Teaching/Research Seminars in various departments.
E. Supervised the following and postdoctoral fellows, residents, and students: Dr. Robert Strieter, Dr. Robert Spengler, Dr. Amanda Thornton, Dr. Lynn Abruzzo, and Michael Genord.
F. Doctoral Committee Member/Oral Presentation Committee for the following graduate students: Sandra Reynolds, Nancy Long, Marjorie Minkoff, Lin LeMay, Ron Allen and Dale Selby.
G. Development of Molecular-Immunopathology Course (with Dr. Jeffrey Bonadio)

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIH - Macrophage/Monocyte Signals in Lung Granuloma Formation; HL-R01-35276; Principal Investigator.
B. NIH - Macrophage Function in Pulmonary Inflammation; 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. American Heart Association Established Investigator - Regulation of Pulmonary Granuloma Formation by Macrophages; Principal Investigator.
E. NIH - Crescentic Nephritis; Program Project P01-DK38149; Principal Investigator - Section II.
F. NIH - Modulation of Immune Complex Lung Injury by Prostaglandins; Co-investigator.
G. NIH - Fibroblast Heterogeneity in Pulmonary Fibrosis; HL-39925; Co-investigator.

PROJECTS UNDER STUDY:

A. Regulation of macrophage signals that dictate immune responsiveness.
   1. Tumor necrosis factor production.
   2. Interleukin-1 production.
   3. Chemotactic cytokines.
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. Space Utilization and Research committee (Chairman).
B. Graduate Program Committee.
C. Conduct Research Seminar Series.
D. Interview Candidates for Residency Program.

MEDICAL SCHOOL/HOSPITAL:

A. Medical School Financial Aid Committee.
B. Committee on Medical Student Research.
C. Medical School Admission Committee.
D. Medical Scientist Training Program Admission Committee.
E. Reviewer for Biomedical Research Council Grants.
F. Reviewer for Diabetes Research and Training Center Grants.
G. Member, Michigan Cancer Center.

REGIONAL AND NATIONAL:

A. Associate Editor, Journal of Immunology.
B. Associate Editor, American Journal of Respiratory Cell and Molecular Biology.
C. Organizing Committee, Second International Workshop on Non-lymphocytic Cytokines.
D. 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 ofRespiratory Cell and Molecular Biology.
E. American Heart Association Undergraduate Research Committee.
F. Research Peer Review Committee of the American Heart Association (Michigan).
G. Grant Reviewer, United States Department of Agriculture.
H. Grant Reviewer, The Arthritis Society.
I. Grant Reviewer, Veterans' Administration
J. Session Chair, FASEB, Symposium on Cell-to-Cell Interactions.
K Session Chair, ATS, Symposium on Tumor Necrosis Factor.
L. Session Chair, ATS, Symposium on Pulmonary Cell Biology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Workshop on Islet Hormones and Diabetes, July, 1988; Invited Speaker
2. Concordia College, Ann Arbor, Michigan, September, 1988; Invited Lecturer.
3. Fourth International Conference of Inflammation Research Association, Therapeutic Control of Inflammatory Diseases, White Haven, Pennsylvania, November, 1988; Invited Speaker.
4. Fukuoka International Symposium on Granulomatous Inflammation. Fukuoka, Japan, December, 1988; Invited Speaker
5 Kitasata Institute, Tokyo, Japan, December, 1988; Lecturer.
6. Pfizer Nagoya, Nagoya, Japan, December, 1988; Lecturer.

7. International Symposium on Novel Neutrophil Stimulating Peptides: Source, Structure, and Role in Inflammation. London, United Kingdom, December, 1988; Invited Speaker.
8. Wayne State University, Department of Physiology, Detroit, Michigan, January 1989; Invited Speaker.
9. Sandoz Research Forum, Basel Switzerland, February, 1989; Invited Lecturer.
10. Molecular Biology Institute Sandoz, Vienna, Austria, February, 1989; Invited Lecturer.
11. Symposium on Respiratory Distress Syndrome: Molecule to Man. Vanderbilt University, Nashville, Tennessee, March 1989; Invited Speaker.
12. Harvard University, Department of Nephrology, April, 1989; Visiting Professor.
13. Symposium on Progressive Renal Injury, Airlie, Virginia, April, 1989; Invited Speaker.
14. American Thoracic Society, Symposium on Cytokines and Cytokine Networks in the Lung. Cincinnati, Ohio, May, 1989; Invited Speaker.
15. Case Western Reserve University, Cleveland Ohio, May, 1989; Visiting Professor.
16. Shock Society, Tumor Necrosis Factor and Chemotactic Cytokines, Marco Island, Florida, June, 1989; Invited Speaker.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Chensue, S.W., Remick, D.G., Shmyr-Forsch, C., Beals, T.F., and Kunkel, S.L.: Immunochemical demonstration of cytoplasmic and membrane associated tumor necrosis factor in murine macrophages. Am. J. Pathol. 133:564-572, 1988.
2. Strieter, R.M., Remick, D.G., Lynch, J.P., Spengler, R.N., and Kunkel, S.L.: Interleukin-2 induced tumor necrosis factor-alpha (TNF-α) gene expression in human alveolar macrophages and blood monocytes. Am. Rev. Respir. Dis. 139:335-342, 1989.
3. Chensue, S.W., Otterness, I.G., Higashi, G.I., Shmyr-Forsch, C.S., and Kunkel, S.L.: Monokine production by hypersensitivity (*Schistosoma mansoni* egg) and foreign body (Sephadex bead)-type granuloma macrophages: Evidence for sequential production of interleukin-1 and tumor necrosis factor. J. Immunol. 142:1281-1286, 1989.
4. Scales, W.E., Chensue, S.W., Otterness, I., and Kunkel, S.L.: Regulation of monokine gene expression: Prostaglandin E_2 suppresses TNF but not IL-1α or β mRNA and cell-associated bioactivity. J. Leuk. Biol. 45:416-421, 1989.
5. 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-1β. Science, 243:1467-1469, 1989.
6. Vissers, M.C.M., Fantone, J.C., Wiggins, R., Kunkel, S.L.: Glomerular basement membrane-containing immune complexes stimulate tumor necrosis factor and interleukin-1 production by human monocytes. Am. J. Pathol., 134:1-6, 1989.
7. Remick, D.G. and Kunkel, S.L.: Toxic effects of cytokines *in vitro*. Lab. Invest. 60:317-319, 1989.
8. Eskandari, M.K., Kunkel, S.L., and Remick, D.G.: Failure of arachidonic acid metabolite to suppress the CTLL assay for IL-2. J. Immunol. Meth. 118:85-89, 1989.
9. Osborn, L., Kunkel, S.L., and Nabel, G.J.: Tumor necrosis factor-α and interleukin-1 stimulated HIV enhancer by activation of the NF kB transcriptional factor. Proc. Natl. Acad. Sci. USA, 86:2336-2340, 1989.

10. Chensue, S.W., Shmyr-Forsch, C., Otterness, I., and Kunkel, S.L.: The beta form is the dominant interleukin-1 released by murine peritoneal macrophages. Biochem. Biophys. Res. Commun. 160:404-408, 1989.
11. Strieter, R.M., Phan, S.H., Showell, H.J., Remick, D.G., Lynch, J.P., Genord, M., Raiford, C., Eskandari, M., Marks, R.M., and Kunkel, S.L.: Monokine-induced neutrophil chemotactic factor gene expression in human fibroblasts. J. Biol. Chem. 264:10621-10626, 1989.
12. Griffin, G.E., Leung, K., Folks, T.M., Kunkel, S.L., and Nabel, G.J.: Activation of HIV gene expression during monocyte differentiation by induction of NF-kB. Nature, 339:70-73, 1989.
13. Strieter, R.M., Remick, D.G., Lynch, J.P. III, Genord, M., Raiford, C., Spengler, R., and Kunkel, S.L.: Differential regulation of tumor necrosis factor-alpha in human alveolar macrophages and peripheral blood monocytes: A cellular and molecular analysis. Am. J. Respir. Cell Molec. Biol.1:57-63, 1989.
14. Bradley, S.F., Vighagool, S., Kunkel, S.L., and Kauffman, C.A.: Monokine secretion in aging and protein malnutrition. J. Leuk. Biol. 45:510-514, 1989.
15. Remick, D.G., Nguyen, D.T., Eskandari, M.K., Strieter, R.M., and Kunkel, S.L.: Cyclosporine A inhibits TNF production without decreasing mRNA. Biochem. Biophys. Res. Commun. 161:551-555, 1989.
16. Spengler, R.N., Spengler, M.L., Strieter, R.M., Remick, D.G., Larrick, J.W., and Kunkel, S.L.: Modulation of tumor necrosis factor alpha gene expression: Desensitization of prostaglandin E_2-induced suppression. J. Immunol. 142:4346-4350, 1989.
17. Remick, D.G., Strieter, R.M., Lynch, J.P., Nguyen, D., Eskandari, M., and Kunkel, S.L.: *In vivo* dynamics of murine tumor necrosis factor-α gene expression: Kinetics of dexamethasone-induced suppression. Lab. Invest. 60:766-771, 1989.
18. Kunkel, S.L., Chensue, S.W., Strieter, R.M., Lynch, J.P., and Remick, D.G.: Cellular and molecular aspects of granuloma formation. Am. J. Respir. Cell Molec. Biol. (in press)
19. Baggiolini, M., Walz, A., and Kunkel, S.L.: NAP-1/IL-8, a novel cytokine that activates neutrophils. J. Clin. Invest. (in press)
20. Strieter, R.M., Wiggins, R., Phan, S.H., Wharram, B.L., Showell, H.J., Remick, D.G., Chensue, S.W., and Kunkel, S.L.: Monocyte chemotactic protein gene expression by cytokine-treated human fibroblasts and endothelial cells. Biochem. Biophys. Res. Commun. (in press)
21. Spengler, R.N., Spengler, M.L., Lincoln, P., Remick, D.G., Strieter, R.M., and Kunkel, S.L.: Dynamics of dibutyryl cyclic AMP and prostaglandin E_2-mediated suppression of lipopolysaccharide-induced tumor necrosis factor alpha gene expression. Infect. Immun. (in press)
22. Colletti, L.M., Burtch, G.D., Remick, D.G., Kunkel, S.L., Strieter, R.M., Guice, K.S., Oldham, K.T., and Campbell, D.A., Jr.: Production of tumor necrosis factor alpha and the development of a pulmonary capillary injury following hepatic ischemia/reperfusion. Transplantation (in press)

BOOKS AND CHAPTERS IN BOOKS:

1. Scales, W.E., and Kunkel, S.L.: Regulatory interactions between IL-1, TNF, and other inflammatory Mediators, in, Bomford, R.H.R., and Henderson, B. (Eds.) Interleukin 1, Inflammation, and Diseases, Research Monograph in Cell and Tissue Physiology, Elsevier, North Holland, 1989.
2. Remick, D.G., Scales, W.E., Chensue, S.W., and Kunkel, S.L.: The pathophysiology of interleukins and tumor necrosis factor, in, Sayeed, M., (Ed.) Focus on Cellular Pathophysiology, CRC Press, Boca Raton, Florida, 1989.

3. Kunkel, S.L., Scales, W.E., Strieter, R.M., Chensue, S.W., Spengler, R.N., and Remick, D.G.: Modulation of tumor necrosis factor-alpha and interleukin-1 gene expression, in, Otterness I., (Ed.) The Therapeutic Control of Inflammatory Diseases, Elsevier, New York, New York, 1989.
4. Kunkel, S.L., Remick, D.G., Strieter, R.M., and Larrick, J.W., Mechanisms that regulate the production and effects of tumor necrosis factor-alpha, in, Critical Reviews of Immunology, CRC Press, Boca Raton, Florida, 1989.
5. Chensue, S.W., and Kunkel, S.L.: Monokine production and orchestration in hypersensitivity (*Schistosoma mansoni* egg) and foreign body-type granuloma formation, in, Yoshida, T., and Boros, D. (Eds.) Symposium on Basic Mechanisms of Granulomatous Inflammation, Elsevier, Amsterdam, 1989.
6. Kunkel, S.L., Strieter, R.M., Chensue, S.W., and Remick, D.G.: Regulation of tumor necrosis factor and neutrophil activating protein-1 gene expression: Potential role of cytokine-directed cell communication during multiple organ injury, in, Brigham, K., and Stalhman, M. (Eds.) Respiratory Distress Syndrome: Molecules to Man, Vanderbilt Press, Nashville, Tennessee, 1989.

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

1. Strieter, R.M., Remick, D.G., Lynch. J.P., and Kunkel, S.L.: Interleukin-2-induced tumor necrosis factor-alpha gene expression by human alveolar macrophages and blood monocytes. Am. Thoracic. Soc., Las Vegas, Nevada, 1988.
2. Bradley, S.F., Kunkel, S.L., and Kauffman, C.A.: Age and senescence; role of cachectin/tumor necrosis factor (TNF). Soc. Leuk. Biol., Washington, D.C., 1988.
3. Wharram, B., Fitting, S., Remick, D., Fantone, J., and Wiggins, R.: Immune complex-induced monocyte-dependent endothelial cell tissue factor synthesis is mediated by interleukin-1. Eighteenth Annual Michigan Cardiovascular Research Forum, Ann Arbor, Michigan, 1988.
4. Warren, J.S., Yabroff, K.R., Remick, D.G., Kunkel, S.L., Kunkel, R.G., Johnson, K.J., and Ward, P.A.: Intrapulmonary IL-1 and TNF in acute immune complex lung injury in the rat. FASEB, 1989.
5. Shmyr-Forsch, C., Chensue, S.W., Remick, D.G., and Kunkel, S.L.: Immunohistochemical demonstration of interleukin-1α,β, and tumor necrosis factor-α synthesis in cultured murine macrophages. FASEB, 1989.
6. Nguyen, D., Eskandari, J., Kunkel, S., and Remick, D.: Inhibition of tumor necrosis factor-α (TNF) by cyclorsporine A (CsA). FASEB, 1989.
7. Strieter, R.M., Showell, H.J., Phan, S.H., Remick, D.G., Lynch, J.P., Marks, R.M., and Kunkel, S.L.: Cytokine-induced gene expression of a neutrophil chemotactic factor from cellular constituents of the alveolar capillary membrane. FASEB, 1989.
8. Eskandari, M., Raiford, C., Nguyen, D., Strieter, R., Kunkel, S., and Remick, D.: Differential regulation of tumor necrosis factor (TNF) production in primary cultures and cell lines. FASEB, 1989.
9. Remick, D., Strieter, R., Eskandari, M., Nguyen, D., and Kunkel, S.: *In vivo* stimulation of tumor necrosis factor-α (TNF) production by interleukin-2 (IL-2). FASEB, 1989.
10. Raiford, C., Spengler, R.N., Spengler, M.L., Allen, R., Remick, D.G., Strieter, R.M., and Kunkel, S.L.: The heat shock response regulates macrophage (MO) derived tumor necrosis factor-α (TNF) gene expression. FASEB, 1989.
11. Genord, M., Strieter, R., Raiford C., Remick, D., Lynch, J., and Kunkel, S.: Assessment of TNF gene expression in whole blood: An *ex vivo* kinetic analysis. FASEB, 1989.

12. Remick, D., Strieter, R., Nguyen, D., Eskandari, M., Genord, M., Lynch, J. III, and Kunkel, S.: Comparison of pathophysiologic effects of exogenous and endogenous tumor necrosis factor. AFIP, 1989.
13. Spengler, R.N., Spengler, M.L., Giacherio, D.A., Evanoff, H., Strieter, R.M., and Kunkel, S.L.: Alpha-adrenergic receptor mediation of LPS-stimulated TNF production from macrophages. FASEB, 1989.
14. Fantone, J., Vissers, M.C.M., Jones, M.L., and Kunkel, S.L.: Inactivation of TNF by hypochlorous acid. FASEB, 1989.
15. Schuger, L., Varani, J., Marks, R., Kunkel, S.L., Johnson, K.J., and Ward, P.A.: Cytotoxicity of TNF-α for human umbilical vein endothelial cells. FASEB, 1989.
16. Chensue, S.W., Otterness, I.G., and Kunkel, S.L.: Dynamics of IL-1α,β and TNF production during chronic peritoneal exudative response, FASEB, 1989.
17. Long, N.C., Kunkel, S.L., Vander, A.M., and Kluger, M.J.: Antiserum against TNF blocks early phase of LPS fever, enhances later phase. FASEB, 1989.
18. Dixit, V.M., Kunkel, S.L., Sarma, V., Strieter, R.M., Showell, H.J., Ward, P.A., and Marks, R.M.: Molecular cloning of an endothelial-derived neutrophil chemotatic factor: Identify with monocyte-derived factor. FASEB, 1989.
19. Colletti, L.M., Burtch, G.D., Guice, K.S., Oldham, K.T., Remick, D.G., Kunkel, S.L., and Campbell, D.A., Jr.: Increased pulmonary microvascular permeability following hepatic ischemia/reperfusion injury with protection by antibody to tumor necrosis factor. Am. Soc. Transplant Surgeons, Chicago, Illinois, 1989.
20. Spengler, R.N., Chensue, S.W., and Kunkel, S.L.: Alpha adrenergic receptor stimulation and the regulation of macrophage-derived tumor necrosis factor. Proceedings of the American Association for Cancer Research, 30:410, 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Surgical Pathology - 12 weeks.
B. Consultant for soft tissue lesions.
C. Consultant for endocrine lesions.
D. Consultant to Veterans Administration Medical Center, Ann Arbor, Michigan.

II. TEACHING ACTIVITIES:

A. Lectures to sophomore medical students - Pathology 600.
B. Laboratory session for medical students - Pathology 600.
C. Fourth Year medical student rotation in Pathology - 1 month.
D. Lectures to dental students - Pathology 630.
E. Lectures to pathology house officers.
F. Immunoperoxidase Rounds - twice monthly.
G. Supervision of three postdoctoral fellows in research laboratory.

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 - 6/91, (PI - R. Lloyd).
B. Analysis of Rat Pituitary Neoplasms with Monoclonal Antibodies. CTR Grant 1850, 1/1/85 - 12/31/88, (PI - R. Lloyd).
C. Studies of Normal and Neoplastic Human Pituitary Tissues. NIH Grant CA 42951, 7/86 - 6/90 (PI - R. Lloyd).

PROJECTS UNDER STUDY:

A. Regulation of human and rat pituitary growth and differentiation.
B. Applications of molecular biological techniques to diagnostic pathology.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director of Immunoperoxidase Service.
B. Coordinator of Anatomic Pathology Journal Club.
C. Resident Selection Committee.
D. Residency Advisory Committee.
E. Pathology Graduate Training Program Committee.
F. Space Utilization Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Thyroid Therapy Conference.
B. Pituitary Study Group.
C. Medical School Admissions Committee - August 1983 to June 1988.
D. Pathology presentations at General Endocrine Conference.

REGIONAL AND NATIONAL:

A. Editorial Board - American Journal of Pathology
B. Editorial Board - Endocrine Pathology
C. Editorial Board - American Journal of Surgical Pathology.
D. Reviewer of articles for Laboratory Investigation, The American Journal of Pathology, Journal of the American Medical Association, Journal of Histochemistry and Cytochemistry, the American Journal of Medical Sciences and others.
E. Review Committee for International Academy of Pathology Abstracts.
F. Pathology B Study Section, National Cancer Institute, Member 1987-1991.
G. College of Pathology - Cell Markers Committee.

V. OTHER RELEVANT ACTIVITIES:

Sabbatical leave, July 1, 1988 - December 31, 1988.
National Institute of Health - 4 months.
Armed Forces Institute of Pathology - 2 weeks.

INVITED LECTURES AND SEMINARS:

1. Memorial Sloan Kettering Cancer Center - Immunochemistry of Soft tissue Tumors. September 15, 1988.
2. Michigan Society of Technologist Lecture on In Situ Hybridization, May 12, 1989.
3. Arthur Purdy Stout Society Lecture at the International Academy of Pathology on Molecular Probes and Endocrine Diseases. San Francisco, California - March 5, 1989.
4. Endocrinology Research Seminars. Studies of rat and human pituitary tumors. December 15, 1988.
5. Warner Lambert - Regulation of Rat Pituitary Tumor Development, June 7, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOU RNALS

1. Johnson, T.L., Lloyd, R.V., Thompson, N.W., Beierwaltes, W.H., Sisson, J.C.: Prognostic implications of the tall cell variant of papillary thyroid carcinoma. J. Surg. Pathol. Am. J. Surg. Pathol. 1988; 12:22-27.
2. Pike, A.M., Lloyd, R.V., Appelman, H.D.: Cell markers in gastrointestinal stromal tumors. Human Pathology 1988; 19: 830-834.

3. Barkan, A.L., Lloyd, R.V., Chandler, W.F., Hatfield, M.K., Gebarski, S.S., Kelch, R.P., Beitins, I.: Preoperative treatment of acromegaly with long-acting somatostatin analog SMS201-995: Shrinkage of invasive pituitary macroadenomas and improved surgical remission rate. J Clin Endocrinol Metab 1989; 67: 1040-1048.
4. Johnson, T.L., Zarbo, R.J., Lloyd, R.V., Crissman, J.D.: Paragangliomas of the head and neck: immunohistochemical neuroendocrine and intermediate filament typing. Modern Pathol. 1988 1:216-223, 223, 1988.
5. Lloyd, R.V.: Analysis of mammosomatotropic cells in normal and neoplastic human pituitaries. Pathol. Res. and Prac. 1988; 183: 577-579.
6. Lloyd, R.V.: Analysis of human pituitary tumors by in situ hybrid ization. Pathol. Res. and Prac. 1988; 183: 558-560.
7. Wolber, R.A., Beals, T.F., Lloyd, R.V., Massab, H.F.: Ultrastruc tural localization of viral nuclei acid by in situ hybridization. Lab. Invest. 1988; 59: 144-151.
8. Wolber, R.A., Lloyd, R.V.: Cytomegalovirus detection by in situ DNA hybridization and capsid antigen immunostaining using a 2-color technique. Human Pathol. 1988; 19: 736-741.
9. Lloyd, R.V., Mailloux, J.: Analysis of S-100 protein positive folliculo-stellate cells in rat pituitary tissues. Am. J. Pathol. 1988; 133: 338-346.
10. Eckhauser, F.G., Lloyd, R.V., Thompson, N.W., Roper, S.E., Vinik, A.I.: Antrectomy for multicentric argyrophil gastric carcinoids: A preliminary report. Surgery 1988; 104: pp 1046-1053.
11. Buchsbaum, D., Lloyd R.V., Juni, J., Wollner, I., Brubaker, P., Hanna D., Spicker, J., Burns, F., Steplewski, Z., Colcher, D., Scholm, J., Buchegger, F., Mach, J.P.: Localization and imaging of tumor bearing nude mice. Cancer Res 1988; 48: 4324-4333.
12. McLeod, M.K., Thompson, N.W., Hudson, J.L., Gaglio, J.A., Lloyd, R.V., Harness, J.K., Nishiyama, R., Polley, C.Y.: Flow cytometric measurements of nuclear DNA and poloidy analysis in Hurthle cell neoplasms of the thyroid. Arch of Surgery 1988; 123: (7), pp 849-854.
13. Lloyd, R.V., Cano, M., Landefeld, T.D.: The effects of estrogens in tumor growth and on prolactin and growth hormone mRNA expression in rat pituitary tissues. Am J. Pathol 1988; 133: 397-406.
14. Kovacs, K., Lloyd, R.V., Horvath, E., Asa, S.L., Stafaneanu, L., Killinger, D.W., Smyth, H.S. Silent somatotroph adenomas of the human pituitary. A morphologic study of three cases including immunocytochemistry, electron microscopy, in vitro examination and in situ hybridization. Am J Surg Pathol 1989; 134: 345-353.
15. Lloyd, R.V., Cano, M., Chandler, W.F., Barkan, A.L., Horvath, E., Kovacs, K.: Human growth hormone and prolactin secreting pituitary adenomas analyzed by in situ hybridization. Am J Pathol 1989; 134: 605-613.
16. Song, J., Jin, L., Lloyd, R.V.: Effects of estradiol on prolactin and growth hormone messenger RNA in cultured normal and neoplastic (MtT/W15 and GH_3) rat pituitary cells. Cancer Res. 1989; 49: 1247-1253.
17. Lloyd, R.V., Iacangelo, A., Eiden, L.E., Cano, M., Jin, L., Grimes, M.: Chromogranin A and B messenger ribonucleic acids in pituitary and other normal and neoplastic human endocrine tissues. Lab Invest 1989; 60: 548-556.
18. Hankin, R.C., Lloyd, R.V.: Detection of messenger RNA in routinely processed tissue sections with biotinylated oligonucleotide probes. Am J. Clin Pathol (In Press).

19. Lloyd, R.V., Dafoe, D.C., Campell, D.A., Jr., Merion, R.M., Tur cotte, J.G., Vinik, A.I.: Pancreas transplantation: An immunohistochemical analysis of pancreatic hormones and HLA-DR expression. Modern Pathol (1989) (In Press)
20. Hawkins, K.L., Lloyd, R.V., Toy, K.A.: Immunohistochemical local ization of chromogranin A in normal tissues from laboratory animals. Vet Pathol (In Press).
21. Jin, L., Song, J., Lloyd, R.V.: Estrogen stimulates both prolactin and growth hormone mRNAs expression in the MtT/F4 transplantable tumor. Proc Soc Expt Biol Med (In Press).
22. Flint, A., Lloyd, R.V.: Hurthle cell neoplasms of the thyroid gland. Pathol Ann (In Press).
23. Lloyd, R.V.: Molecular probes and endocrine diseases. Am J Surg Pathol (In Press).
24. Lloyd,R.V., Jin, L., Fields, K.: Detection of chromogranins A and B in endocrine tissues with radioactive and biotinylated oligonucleo tide probes. Am J Surg Pathol (In Press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. 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.
2. Song J, Jin L, England B, Smart J, Lloyd RV. Regulation of gonadotropin hormone secretion and mRNAs and of chromogranin A and B mRNAs in cultured human pituitary cells.
3. Jin L, Song J, Lloyd RV. Hybridization analysis of prolactin and growth hormone in cultured human pituitary cells. Regulation by releasing hormones and phorbol esters.
4. Lloyd RV, Jin L, Horvath E, Kovacs K. Functional and silent corticotropic pituitary adenomas analyzed by in situ hybridizaiton.
5. Lloyd RV, Jin L, Song J. Ultrastructural localization of chromogranin and prolactin mRNAs with colloidal gold in cultured human pituitary tumor cells.

BOOKS/CHAPTERS IN BOOKS

1. Lloyd, R.V.: Immunohistochemical localization of catecholamine, catecholamine synthesizing enzymes and chromogranins in neuroendo crine cells and tumors. R.A. DeLellis (ed.), Advances in Immuno histochemistry, Raven Press, New York, 1988, pp 317-340.
2. Lloyd, R.V.: Neuroendocrine and Paracrine Systems in Sternberg S. (ed) Chapter 12, Diagnostic Surgical Pathology. Raven Press, New York 1988, pp 435-445.
3. Lloyd, R.V.: Immunohistochemical localization of chromogranin in polypeptide hormone producing cells and tumors in J. Lechago and T. Kameya (eds.) (In Press), Endocrine Pathology Update. Field and Wood Publishers, PA. 1989. (In Press).
4. Lloyd, R.V.: Tumors of the pituitary gland in V.S. Turusov (ed.). Pathology of Tumors in Laboratory Animals. International Agency for Research on Cancer. World Health Organization, 1989. (In Press).
5. Lloyd, R.V.: Tumors of the pituitary, In Stinson, S.F., Schuller, H.M. and Reznik, G. (Eds), Atlas of Tumor Pathology of the Fischer Rat, CRC Press, Boca Raton, Florida 1989. (In Press).

6. Lloyd, R.V.: Analysis of chromogranin A and B proteins and messenger ribonucleic acids in neuroendocrine tissues. In: CM Fenoglio and M Wolfe (eds) Progress in Surgical Pathology (1989) (In Press).
7. Lloyd, R.V.: Morphologic Methods, In Kovacs and Asa S. (eds) Functional Endocrine Pathology. Blackwell Scientific Publishers, Boston, MA 1990 (In Press).

BOOKS:

1. Endocrine Pathology. Springer Verlag,New York (1990)

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

1. Lloyd RV, Jin L, Fields K: Detection of chromogranin A and B mRNAs in neuroendocrine neoplasms with biotinylated oligonucleotide probes. Lab Invest 1989; 60: 54A (Abstract 321).
2. Lloyd RV, Hawkins KL, Jin L. Analysis of spontaneous pituitary tumors in aged female rats by in situ hybridization and immunohisto chemistry. Lab Invest 1989; 60: 54A (Abstract 322).
3. Horvath E, Lloyd RV, Kovacs K. Emergence of bihormonal cells produc ing growth hormone and thyrotropin in the pituitary of the hypothy roid rat. 8th International Congress of Endocrinology, Kyoto Japan, July 17-23, 1988. P 236, Abstract No. 09-18-022.
4. Lloyd RV, Jin L, Horvath E, Kovacs K. In situ hybridization analysis of the human pituitary. Lab Invest 1989; 60: 55A (Abstract 323).
5. Hankin RC, Lloyd RV. Detection of messenger RNA in routinely processed tissue sections with biotinylated oligonucleotide probes. Lab Invest 1989; 60: 37A (Abstract 218).
6. Song J, Jin L, Lloyd RV, Chandler WF, England B, Smart J. Analysis of clinically nonfunctional pituitary adenomas by hybridization studies. 71st Ann Meeting of the Endocrine Society. Seattle, WA June 21-24, 1989 (Abstract 1226).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

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 two postdoctoral fellows (Robert Larsen, Ph.D., and Jolanta Kukowska-Latallo, Ph.D.)
B. Lecturer- Graduate School - Pathology 630 (2 lectures: The Atherosclerotic Process I and II).
C. Clinical Pathology Grand Rounds - Clinical use of the TdT assay.
D. Clinical Pathology Grand Rounds - In search of the H gene.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. 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.
B. Co-investigator, "Fatty acid binding proteins - ligand specificity", NIH DK-41402 (F. Schroeder, University of Cincinnati Medical Center, Principal Investigator). (5% effort) $10,672/year direct cost ($53,360/five years), 4/1/89-3/31/94.

PROJECTS UNDER STUDY:

A. 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.
B. Structure and function of intracellular lipid transport proteins; liver and enterocyte fatty acid binding proteins.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL: None.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

A. Howard Hughes Medical Institute, Assistant Investigator.

INVITED LECTURES AND SEMINARS:

1. Genetic approaches to the isolation of cloned cDNAs encoding mammalian glycosyltransferases. 1989 Gordon Conference on Glycoproteins and Glycolipids, February, 1989.
2. Isolation of mammalian glycosyltransferase genes by gene transfer. Hospital for Sick Children and Mt. Sinai Hospital, Toronto, Canada, February, 1989.
3. Molecular cloning of mammalian glycosyltransferase genes. Cellular and Molecular Biology Department, Roswell Park Memorial Institute, Buffalo, N.Y., March, 1989.
4. Isolation of human fucosyltransferase genes by gene transfer, Department of Research and Development; Smith, Kline and French Laboratories, King of Prussia, PA, March, 1989.
5. Molecular cloning of mammalian glycosyltransferase genes by gene transfer, Glycomed, Inc., San Francisco, CA, May, 1989.
6. Isolation of mammalian glycosyltransferase genes by gene transfer, The Biomembrane Institute, Seattle, WA, June, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Keren, D.F., Warren, J.S., and Lowe, J.B.: Strategy to diagnose monoclonal gammopathies in serum: High resolution electrophoresis, immunofixation and L/K quantification. Clin Chem 1988;34:2196-2201.
2. Ernst, L., Rajan, V.P., Larsen, R., Ruff, M., and Lowe, J.B.: Stable expression of blood group H determinants and GDP-L-fucose: β-D-Galactoside 2-α-L-fucosyltransferase in mouse cells after transfection with human DNA. J Biol Chem 1989;264:3436-3447.
3. Yabkowitz, R., Lowe, J.B., and Dixit, V.M.: Expression and initial characterization of a recombinant human thrombospondin heparin binding domain. J Biol Chem 1989;264:10888-10896.
4. Schroeder, F., Butko, P., Nemecz, G., Jefferson, J.R., Powell, D., Rymaszewski, Z., Dempsey, M.E., Kukowska-Latallo, J., and Lowe, J.B.: Sterol carrier protein; ubiquitous protein in search of a function. In: Bioengineered Molecules: Basic and Clinical Aspects (R. Verna, ed.) Serono symposia, In Press, 1988.
5. Rajan, V.P., Larsen, R.D., Ajmera, S., Ernst, L.K. and Lowe, J.B.: A cloned human dna restriction fragment determines expression of a GDP-L-fucose: β-D-galactoside 2-α-L-fucosyltransferase in transfected cells. Evidence for isolation and transfer of the human H blood group locus. J Biol Chem 1989;264:11158-11167.
6. Zhu, X.X., Kozarsky, K., Trahler, J.R., Eckerskorn,C., Lottspeich, F., Melhem, R., Lowe, J.B., Fox, D.A., Hanash, S.M., and Atweh, G.F.: Molecular cloning of a novel human leukemia associated gene: evidence of conservation in animal species. J Biol Chem 1989; (in press).
7. Larsen, R.D., Rajan, V.P., Ruff, M.M, Kukowska-Lattallo, J., Cummings, R.D., and Lowe, J.B.: Isolation of a cDNA encoding a murine UDP-Gal:β-D-Gal(1,4)-D-GlcNac α(1,3)-Galactosyltransferase; expression cloning by gene transfer. Proc Natl Acad Sci USA, 1989 (in press).

ARTICLES SUBMITTED OR IN PREPARATION:

1. 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 fucosyltransferse (in preparation).
2. Larsen, R.D., Ernst, LK., and Lowe, J.B.: Molecular cloning of cDNAs encoding the human H blood group α1,2 fucosyltransferase (in preparation).
3. Lowe, J.B., Ernst, L.K., Larsen, R.D, and Rajan, V.P.: Molecular organization of the human H blood group α1,2 fucosyltransferase gene (in preparation).
4. Ernst, L.K., Larsen, R.D., and Lowe, J.B.: Molecular basis of the Bombay blood group: A nonsense mutation creates an enzymatically inactive α1,2 fucosyltransferase (in preparation).
5. Larsen, R.D., Ernst, L.K., Rajan, V.P., and Lowe, J.B.: Structure and function of multiple transcripts derived from the human H blood group α1,2 fucosyltransferase gene (in preparation).

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

1. Ernst, L.K., Larsen, R.D., Rajan, V.P., and Lowe, J.B.: Gene transfer and molecular cloning of DNA sequences that determine expression of blood group H structures and an (α1,2)-L-fucosyltransferase. UCLA Glycobiology Symposium, 1989.
2. Kukowska-Latallo, J.F., Larsen, R.D., Rajan, V.P. and Lowe, J.B.: Molecular cloning of a cDNA that directs expression of SSEA-1 determinants and an (α1,3)-L-Fucosyltransferase. UCLA Glycobiology Symposium, 1989.
3. Lowe, J.B., Larsen, R.D., Ruff, M.M. and Cummings, R.D.: Isolation of cloned cDNAs that direct expression of oligosaccharides recognized by Griffonia Simplicifolia isolectin B4. UCLA Glycobiology Symposium, 1989.

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

ANNUAL DEPARTMENTAL REPORT
July 1, 1988 -- June 30, 1989

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.
H. Consulting Staff, Chelsea Community Hospital, Chelsea, Michigan.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Pathology 630/631; Course Director
   1) Five hours credit (M,W,F 1-4 pm).
   2) 100 Dental students, 20 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, Richard L. Wahl, M.D., Department of Internal Medicine, The University of Michigan. Radioimmunodiagnosis of Squamous Cell Carcinoma, Department of Health and Human Services; $608,579, 1985-1988.
B. Consultant, Principal Investigator, Thomas E. Carey, Ph.D., Deparment of Otorhinolaryngology, The University of Michigan, Human Squamous Cell Carcinoma: Culture and Serology, NIH R01-CA28564-06, $139,388/year, $815,326/project period, 1985-1990.
C. Consultant, Principal Investigator, Thomas E. Carey, Ph.D., Department of Otorhinolaryngology, The University of Michigan. Monoclonal Antibodies to Human Squamous Cell Carcinoma: Culture and Serology, NIH, $382,843, 1987-1988.

PROJECTS UNDER STUDY:

A. 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.

B. See laboratories under my direction.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Medical Service Plan Executive Committee, Department of Pathology, 1979.
B. Director, Residency Program, Department of Pathology, 1982.
C. Chairman/Member, Resident Selection Committee, Department of Pathology, 1982-present.

MEDICAL SCHOOL/HOSPITAL:

A. Ambulatory Care Committee, The University of Michigan Hospitals, 1980-present.
B. Multi-Organ Transplant Program: Planning Group, Alternate, The University of Michigan Hospitals, 1985-present.
C. Advisor, Medical and Biological Illustration Program, The Univesity of Michigan Medical School, 1986-present.
D. Infection Control Committee, The University of Michigan Hospi tals, 1978-present.
E. Chairman, Laboratories Committee of the Medical Staff, University Hospitals, 1987-present.
F. Transition Committee, The University of Michigan School of Dentistry, 1987-
    1) Chairman, Operational Analysis Task Force
    2) Chairman, Computer Committee
    3) Member, Dean Search Committee, 1988-1989

REGIONAL AND NATIONAL:

A. College of American Pathologists, Fellow, 1975-
    1) Board of Governors, 1986-
    2) Budget Planning and Review Committee, 1986-
    3) Credentials Committee, 1986-
    4) Liaison, Standards Committee, 1986-
    5) Chairman, Commission on Anatomic Pathology, 1986-
    6) Micro-Fellowship Committee, 1987-1988
    7) Building Committee, 1987-
    8) Subcommittee on National Institute of Drug Abuse (NIDA), 1987-88
    9) Council on Government Relations, 1987-
B. National Committee for Clinical Laboratory Standards - Corresponding Membership, 1987.
    1) Council of the National Reference System for the Clinical Laboratory, 1987-
    2) Subcommittee on Cost Accounting, member, 1986-
    3) Chairman, Area Committee on General Laboratory Practice, 1986-.
        a) Chairman, Subcommittee on Standardization of the PAP technique, 1988.
    4) Subcommittee on Cost-Effective Quality Control, 1986-88.
    5) Flow Cytometry Committee, member, 1987-88
    6) International Relations Committee, member, 1988-
C. American Society of Clinical Pathologists, 1975.

1) ASCP Advisory Council, 1984-
2) ASCP Advisory Council, State Councilor, 1987-

D. Michigan Society of Pathologists, 1982-
1) President, 1988.
2) Board of Directors, 1987-
3) Chairman of Program Committee, 1988-
4) Newsletter Editor, 1988-

E. Technical Advisory Committee, State of Michigan Department of Health, Bureau of Laboratory and Epidemiological Services, 1987-

F. American Society for Testing Materials (ASTM)
1) Committee F31 on Health Care Services, member, 1988-

INTERNATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Present Schemes and Further Development in Quality Assurance in Medical Laboratories in the U.S.A. Guest Speaker, XV World Congress of Anatomic and Clinical Pathology, Firenze, Italy, May, 1989.
2. Consequences of the WHO Recommendations in the U.S.A. Guest Speaker, XV World Congress of Anatomic and Clinical Pathology, Firenze, Italy, May, 1989.
3. Variables in the Laboratory and in the Patient Population. CAP Consensus Conference, Chicago, Illinois, March, 1989.
4. Quality Assurance Program in Cytopathology. CAP Conference on Cytopathology, Chicago, Illinois, March, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Rubinstein, M.I., Drake, A.F., and McClatchey, K.D.: Alveolar Soft Part Sarcoma of the Nasal Cavity: Report of a Case and a Review of the Literature. Laryngoscope, 1988.
2. McClatchey, K.D., Sullivan, M.J., and Paugh, D.R.: Peripheral Ameloblastic Carcinoma: Case Report of a Rare Neoplasm. The Journal of Otolaryngol., February, 1988.
3. Bradford, C.R., Hoffman, H.T., Wolf, G.T., Carey, T.E., and McClatchey, K.D.: Squamous Carcinoma of the Head and Neck in Organ Transplant Recipients: Possible Role of Oncogenic Virus es. Laryngoscope, 1989.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Wolf, G.T., Hudson, J., Peterson, K.A., Poore, J.A., and McClatchey, K.D.: Interleukin-2 Receptor Expression in Pa tients With Head and Neck Squamous Carcinoma: Effects of Thymosin Alpha$_1$ In Vitro. Archives of Otolaryngol. Head and Neck Surgery, September, 1988.
2. Grenman, S.E., Worsham, M.J., Van Dyke, D.L., England, B., McClatchey, K.D., Babu, R., Roberts, J.A., Maenpaa, J., and Carey, T.E.: Establishment and

Characterization of UM-EC-2, A Tamoxifen Sensitive Estrogen Receptor Negative Human Endome trial Carcinoma Cell Line. Gynecologic Oncology, 1989.

3. 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.: UM-SCV-1A and UM-SCV-1B, Two New Tamoxifen-Sensi tive Hypotetraploid Cell Lines Derived From a Primary and Metastatic Tumor in a Patient With Squamous Cell Carcinoma of the Vulva. Cancer Research, 1989.
4. Wells, M.D., Hoffman, H.T., and McClatchey, K.D.: An Interest ing Case of Parotid Sialolithiasis. Oral Surgery, Oral Medi cine, Oral Pathology, 1989.

BOOKS AND CHAPTERS IN BOOKS:

1. McClatchey, K.D.: Diseases of the Jaws, in, Diagnosis in Surgical Pathology, Drs. Sternberg, Antonioli, Carter, Eggle ston, Oberman and Mills (eds), Raven Press, New York, New York, 1987 (published).
2. McClatchey, K.D. and McMahon, Jr., L.F.: Laboratory Medicine, in, Textbook of Internal Medicine, William N. Kelley, Editor, J.B. Lippincott, Philadelphia, Pennsylvania, 1988 (published).

CHAPTERS IN PREPARATION:

1. McClatchey, K.D. and McMahon, Jr., L.F.: Revision - Title of Chapter Laboratory Medicine, in, Textbook of Internal Medicine, J.B. Lippincott, Philadelphia, Pennsylvania, 1989.
2. McClatchey, K.D.: Oral Cavity, Sinuses, Tongue, and Minor Salivary Gland, in, Histology for Pathologists, Raven Press, 1989.

BOOKS OR JOURNALS EDITED:

1. Laboratory Medicine, Williams & Wilkins (in preparation), 1989-90.

PAMPHLETS:

1. McClatchey, K.D.: NCCLS Papanicolaou Technique Proposed Guidelines, NCCLS Publication GP15, Villanova, Pennslyvania, 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Gross and microscopic examination of autopsy neuropathologic material with House Officers and Faculty. The cases shared with other faculty members were from University Hospital, University Associated Hospitals, and State Institutions. Medical Examiner Cases.
B. Daily supervision of House Officer or Staff participation in diagnostic neuropathology and electron microscopic neuropathology. Responsible for final report and diagnosis in each category.
C. Consultations on diagnostic neuropathology from other hospitals and medical centers.
D. Ceroid Service, buffy coat division.
E. Primary substitute for nerve and muscle biopsy diagnostician.
F. Weekly adult Brain Tumor Board Review of Neurosurgery, Nuclear Medicine, Neuroradiology, and Neuropathology in clinical research setting of brain tumor cases by staff. Responsible for neuropathology segment of tumor review and clinical-pathologic correlation.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Neural and Behavioral Sciences 600, Neuropathology for Second Year Medical Students. Lectures and laboratories. Twenty hours shared with other faculty.
B. Neuropathology 858. Intensive laboratory-lecture course for all beginning House Officers in Pathology, and in several clinical services concerned with the nervous system, Graduate Students and Faculty. Annual, 16 hours shared with other Faculty. One credit hour elective.
C. House Officers:
    1. Review of microscopic neuropathological postmortem material with Pathology House Officers, shared with other Faculty Members.
    2. Weekly brain cutting with Pathology House Officers.
    3. Review all neurosurgically removed material in this hospital in CME-approved biweekly conference for Pathology, Neurology and Neurosurgery House Officers and Staff.
    4. Shared consultations with Pathology House Officers.
    5. Invited presentations of neuropathologic observations at joint Pathology-Neurology-Neurosurgery and clinical conferences.
    6. Direct teaching of one Pathology and two Neurology House Officers who took electives in Neuropathology. One month or longer rotation with teaching shared with other Pathology Faculty and with Neurohistologists.

7. Rotation on Dr. Flint's Wednesday seminar series.
8. Wednesday lectures to Neurologist on brain tumors.

D. Teach laboratory techniques to our Laboratory Technologists.

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 Institutes of Health Grant NIH CA43863, "Brain Tumor Imaging with Benzodiazepine Analogs", Co-investigator. 1/1/87 - 1/1/90.

D. National Institutes of Health Grant NIH CA-33768, "Intra-arterial BUdR Radiosensitization of Malignant Gliomas", Co-investigator, 5/1/86 - 4/30/89.

E. 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. 12/1/84-11/30/89.

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. Robertson Davenport, Curtis Hanson, William Ensminger, William Chandler, and James Varani.

C. Production of monoclonal antibodies to human brain tumors for diagnosis and therapy, with Drs. James A. Taren, Julian T. Hoff, and Richard L. Wahl.

D. Extracellular matrix products of gliomas with Drs. James Varani and Suzanne Fligiel.

E. Distribution of microspheres in tumor and normal tissues with Dr. William Ensminger.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Chief, Section of Neuropathology.

MEDICAL SCHOOL/HOSPITAL:

A. Organization and scheduling of Pathology, Neurology and Neurosurgery House Officer Neuropathology teaching conferences, individual instruction and consultation review.
B. Organization of call logistics of 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 neuropathology.

REGIONAL AND NATIONAL:

A. Reviewer for Pathology, Neuropathology, Oncology and Neurooncology journals and texts.
B. M-Lab Neuropathology Services.
C. Reviewer of NCI Program Project Grant applications.
D. International Editorial Board for Cellular and Molecular Biology.
E. Primary Review Pathologist, Children's Cancer Study Group CCG 9002 nation wide study of childhood low grade astrocytomas.

V. OTHER RELEVANT ACTIVITIES:

A. Faculty of Graduate Program of Department of Pathology.
B. Member of the University of Michigan Cancer Center.
C. Participant in Michigan Cancer Research Institute Gull Lake Conference, Gull Lake, Michigan, 1988.
D. Pathology Committee, Children's Cancer Study Group, Columbus, Ohio.

INVITED LECTURES AND SEMINARS

1. "Antigen Expression and Tumor Progression of Human Gliomas", University of Tokyo meeeting on immunology of brain tumors, Tokyo, Japan, 1989.
2. "Applications of Flow Cytometry to brain tumors", Children's Cancer Study Group National Meeting, Pathology Work shop, Los Angeles, California, 1989.
3. "Characteristics of Human Gliomas", Veteran's Administration Hospital, Allen Park, Michigan, 1989.
4. "Brain Tumors", series of 3 lectures, Department of Neurology, University of Michigan, 1989.
5. "Hybridoma Supernatant Reactivities for Human Gliomas", Tumor Immunology Program, University of Michigan Cancer Center, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. McKeever, P.E., Letica, L.H., Shakui, P., Averill, D.R.: A multiple-well method for immunohistochemical testing of many reagents on a single microscopic slide. Lab. Invest. 1988; 59:409-413.
2. Greenberg, H.S., Chandler, W.F., Diaz, R.F., Ensminger W.D., Junck, L., Page, M.A., Gebarski, S.S., McKeever, P.E., Hood, T.W., Stetson, P.L., Lichter, A.S., Tankanow, R.: Intra-arterial bromodeoxyuridine radio sensitization and radiation in treatment of malignant astrocytomas. J. Neurosurg. 1988; 69:500-505.
3. Richfield, E.K., Ciliax, B.J., Starosta-Rubinstein, S.R., McKeever, P.E., Penney, J.B. and Young, A.B.: Comparison of ^{14}C-deoxyglucose metabolism and peripheral benzodiazepine receptor binding in rat C6 glioma. Neurol. 1988; 38:1255-1262.
4. Feldenzer, J.A., McKeever, P.E., Schaberg, D.R., Campbell, J.A., and Hoff, J.T.: The pathogenesis of spinal epidural abscess: micro-angiographic studies in an experimental model. J Neurosurg 69: 110-114, 1988.
5. Mountz, J.M., Stafford-Schuck, K., McKeever, P.E., Taren, J.A. and Beierwaltes, W.H.: The tumor/cardiac ratio: A new method to estimate residual high grade astrocytoma using thallium-201 radionuclide imaging. J. Neurosurg. 1988;68:705-709.
6. Hood, T.W., McKeever, P.E.: Sterotaxic management of cystic brainstem gliomas. Neurosurg. 1989, 24:373-378.
7. 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. Anticancer Ther. (In Press).
8. Junck, L., Olson, J.M., Ciliax B.J., Koeppe, R.A., Watkins, L.G., Jewett, D.M., McKeever, P.E., Wieland, D.M., Kilbourn, M.R., Starosta-Rubinstein, S., Mancini, W.R., Kuhl, D.E., Greenberg, H.S., Young, A.B.: PET imaging of human gliomas with ligands for the peripheral benzodiazepine binding site. Neurology (In Press).
9. Sackellares, C.J., Abou-Khalil, B.W., Siegel, G.J., Hood, T.W., Gilman, S., McKeever, P.E., Hichwa, R.D., Hutchins, G.D.: Differences between lateral and mesial temporal metabolism interictally in epilepsy of mesial temporal origin. Neurology (In Press).
10. Mountz, J.M., Raymond, P.A., Modell, J.G., Barthel, L.K., McKeever, P.E., Hood, T.W. and Stafford-Schuck, K.A.: Specific localization of thalium-201 in human high-grade astrocytoma by microautoradiography. J Neurosurg. (In Press).
11. Feldenzer, J.A., McKeever, P.E., Hoff, J.T.,: the Effect of Steroid Therapy on Postlaminectomy Epidural Fibrosis in the Rabbit. Spine (In Press).
12. McKeever, P.E., Feldenzer, J.A., McCoy, J.P., D'Amato, C.J., Laug, M., Chandler, W.F., Varani, J.: Nuclear parameters as prognostic indicators in glioblastoma patients. J. Neuropathol. Exp. Neurol. (In Press).
13. McKeever, P.E., Fligiel, S.E.G., Varani, J., Castle, R.L. and Hood, T.W.: Products of cells cultured from gliomas: VII, Extracellular matrix proteins of gliomas wich contain Glial fibrillary acidic protein positive gliomas. Lab. Invest. 1989; 60:286-293.

BOOKS AND CHAPTERS IN BOOKS:

1. McKeever, P.E., Blaivas, M.: Surgical pathology of the brain, spinal cord and meninges. Eds. Sternberg, S., Antonioli, D., Kempson, D., Carter, D., Eggleston, J., Oberman, H.A.: Diagnostic Surgical Pathology, vol. 1, Raven, New York, New York, pp. 315-370.
2. Greenberg, H.S., Chandler, W.F., Ensminger, W.D., Junck, L., Page, M.A., Gebarski, S.S., Hood, T.W., Stetson, P.L., Diaz, R.F., Hegarty, T., Thornton, A., Lichter, A.S., McKeever, P.E., Tankanow, R.: Radiosensitization with constant intra-arterial infusion of bromodeoxyuridine (BUdR) and focal external beam radiation in the treatment of malignant astrocytomas. Infusion Systems in Medicine.
3. McKeever, P.E., Davenport, R.D.: Patterns of antigenic expression in cultured glioma cells. Ed. Nelson, J.S.: Critical Reviews in Neurobiology, CRC Press, Boca Raton, Florida. (Chapter in preparation).

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

1. McKeever, P.E., Feldenzer, J.A., D'Amato, C.J., Castle, R.L., Chandler, W.F., Varani, J.: Flow cytometry and morphometry of glioblastoma multiforme nuclear DNA. J. Neuropathol. Exp. Neurol 1988; 47:351.
2. D'Amato, C.J., Hood, T.W., McKeever, P.E.: Serial Transplantation of frozen ethylnitrosourea-induced glioma and neurinoma tissue in rats. J. Neuropathol. Exp. Neurol 1988; 47:376.
3. McKeever, P.E., Shakui, P., Letica, L.H., Averill, D.R.: A multiple-well method for immunohistochemical testing of many reagents on a single microscopic slide. 8th Int. Congr. Histochem. and Cytochem. J. Histochem. Cytochem. 1988; 36:931.
4. Olson, J.M.M., Junck, L., Young, A.B., Penney J.B., McKeever, P.E., Mancini, W.R.: Human glial tumors have high affinity for isoquinoline derivatives but not benzodiazepines. Soc. Neurosci. Abstr. 1988; 14:344.
5. McKeever, P., Wahl, R., Shakui, P, Jackson, G., Letica, L., Liebert, M., Taren, J., Laug, M., Beierwaltes, W., Hoff, J.: Immunoreactivity of primary hybridoma supernatants with human glioma tissue and cultured glioma cells. Lab. Invest. 1989; 80:61A.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

Note: This year was spent on a 50% Leave of Absence for work at BioQuant, Inc.

I. **CLINICAL ACTIVITIES**: None.

II. **TEACHING ACTIVITIES:**

A. Taught major portion of Physiology 581, "Mammalian Reproductive Endocrinology", plus occasional other lectures.
B. Primary Supervision of five graduate students:
   1. Mahmoud Ghazzi, Bioengineering.
   2. Jane Wiesen, CMB.
   3. Hal Cantor, Bioengineering.
   4. Craig Halberstadt, Bioengineering.
   5. Rhonda Brand, Bioengineering.
C. Served on several other dissertation committees.
D. Provided guidance to visiting professor, Dr. Sang Ho Baik, former Dean of Medicine, Gyeongsang National University; currently Professor of Anatomy, Seoul National University.

III. **RESEARCH ACTIVITIES:**

SPONSORED SUPPORT:

A. NIH-P30-HD 18258. "Center for the Study of Reproduction", $326,483 TDC year #5, 3/1/84-2/20/89, Principal Investigator, 10% effort (5% as director of Administrative Core; 5% as Director, Standards and Reagents Core; renewed for five years (3/1/89-2/28/94)).
B. NIH, R01 HD 18018, "Gonadotropin Control of the Ovary", renewed, $101,894 TDC current year, Principal Investigator, 10% effort, (3/1/88-11/30/91).
C. NIH, T32 HD-07048, "Training Program in Reproductive Endocrinology", $186,439 direct and stipends year #04, 7/1/85-6/30/90, Principal Investigator, 5% effort.
D. Mellon Foundation "Mellon Young Investigator Program in Reproductive Endocrinology", $300,000 total for four years, 7/1/85-6/30/89, 5% effort.
E. W.K. Kellogg Foundation, Presidential Initiatives Fund, "Cellular Bioengineering: Positioning The University of Michigan for the 1990s and Beyond", 7/1/87-6/30/90, $270,000 total for three years, $83,500 second year TDC, 8% effort, PI: M. Savageau, Department of Microbiology.
F. NSF EET-871256, Cluster Research Proposal for Molecular Biosensing, "Efficient Monoclonal Antibody Production", 9/15/87-2/28/89, $518,772 total direct costs, $193,129 2nd year TDC, 10% effort, PI: B. Palsson, Department of Chemical Engineering.

G. NSF-BNS-8608024. "Hormones and Psychosocial Development in Early Adolescence", a multidepartmental, interdisciplinary project, 7/1/87-7/14/88, $146,949 (total), PI: Jacquelyn Eccles, (Co-Investigator), 5% effort.
H. NIH K11 HD00828, "Nutritional influence on hypothalamic control of reproduction", $62,258 TDC year #2, 9/30/87-8/31/92, 5% effort (sponsor), PI: mahmound Ghazzi (Physician Scientist Award).

SUBMITTED:

A. NSF 89-2655, "Site-Directed Bioreagent Immobilization for Development of Microbiosensor Arrays", 9/1/89-8/31/92, $383,050 requested TDC for total period, PI: R.B. Brown (Electrical Engineering).
B. NIH, "Biotechnology Training Program at Michigan", 12/1/89-11/30/94, $1,534,704 requested TDC for total period, PI: M. Savageau (Microbiology and Chemical Engineering).
C. NIH, T32 HD-07048, "Training Program in Reproductive Endocrinology", 7/1/90-6/30/95, $1,405,659 requested TDC for total period, PI: D. Foster (Repro. Sci Prog. & Obstetrics & Gynecology).

PROJECTS UNDER STUDY:

A. Development of a computer-controlled perifusion system for on-line analysis of cellular responses to pulsatile and other controlled signalling.
B. Analysis of dynamic control of ovarian function by gonadotropins: 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.
E. Development of novel biosensors, especially immunosensors.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Director, Reproductive Sciences Program.
B. Director, Center for Study of Reproduction.
C. Director, Mellon New Investigator Grant.
D. Director, NIH Training Grant.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. August 1-4, 21st Annual Meeting of the Society for the Study of Reproduction, University of Washington, Seattle.
2. October 4-6, 1988, Symposium on Microminiature Actuators and Sensing Systems, Case Western Reserve University, Cleveland.
3. November 3-4, 1988, NICHD Population Reserve Committee Meeting, Bethesda.
4. December 19, 1988, Project Site Visit, National Pituitary and Hormone Distribution Program, Baltimore.
5. March 2, 1989, Meeting of NICHD Population Research Committee, Bethesda.
6. June 3, 1989, Meeting of NIDDK Endocrinology Research Program Advisory Committee and NIDDK Hormone Distribution Program Subcommittee, Bethesda.
7. June 19-20, 1989, Meeting of NICHD Population Research Committee, Seattle.
8. June 21-22, 1989, Meeting of Endocrine Society, Seattle.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Bagavandoss, P. and Midgley, A.R., Jr. Biphasic action of retinoids on gonadotropin receptor induction in rat granulosa cell in vitro. Life Sciences 43:1607-1614, 1988.
2. Ozturk, S.S., Palsson B.O., Midgley, A.R., Halberstadt, C.R. Transtubular bioreactor: A perfusion device for mammalian cell cultivation. Biotechnology Tech 3:55-60, 1989.

ARTICLES SUBMITTED:

1. Miyauchi, F. and Midgley, A.R., Jr.: Morphologically and functionally distinct subpopulations of rat luteal cells. Submitted.

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

1. Brand, R.M., Curl, R.L. and Midgley, A.R. Understanding the dynamics of perifusion systems: A generalized computer model, 2nd Annual Meeting, Society for the Study of Reproduction, 1989.
2. Canton, H.C., and Midgley, A.R. Development of an active biosensor for use in studying the ovarian/pituitary axis, 22nd Annual Meeting, Society for the Study of Reproduction, 1989.
3. Midgley, A.R., Jr., Cantor, H.C., Ghazzi, M.N., Brand, R.M., and Prohaska, O.J., Approaches to continuous monitoring of biological activities in situ. Symposium on microminiature actuators and sensing systems, Case WEstern Reserve University, Celeveland, 1988.
4. Halberstadt, C.r., Ozturk, S.S., Smith, R.H., Palsson, B.O. and Midgley, A.R. Novel mammalian bioreactor with transtubular convective flow. Meeting of the American Chemical Society, 1987.
5. Ozturk, S.S., Halberstadt, C.r., Midgley,A.R. and Palsson, B.O. Transtubular bioreactor: Characterization and potential use for mammalian cell cultivation. Meeting of the American Inst. Chemical Engineering, 1987.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Cytopathology - 13 weeks (sabbatical leave January 1 - June 30, 1989).
B. Director, Cytopathology Laboratory - full time.
C. Consultation Service, Department of Pathology: Cytopathology, pulmonary pathology and gynecologic pathology - 6 months.
D. Necropsy service - on call coverage.
E. Consultant, Breast Care Center - 6 months.

II. TEACHING ACTIVITIES:

A. Pathology residents - supervision and teaching during cytopathology rotation and when covering necropsies.
B. Pathology residents - biweekly cytopathology conferences.
C. Gynecology - Pathology - Radiation Oncology Conference-backup coverage.
D. Senior medical students during pathology electives.

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 rheumatoid disease in serous fluids.
C. Cytologic manifestation of systemic lupus erythematosus.
D. The use of stained wet films in cytologic diagnosis.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. 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. Editorial Advisory Board and American Review Board, Acta Cytologica.
C. Editorial Board, The Cytotechnologist's Bulletin.
D. Chairman, Editorial and Publications Committee, International Academy of Cytology.

E. Membership Committee, International Academy of Cytology.
F. Scientific Program Committee, International Academy of Cytology.
G. Participant, workshop on "The 1988 Bethesda System for Reporting Cervical/Vaginal Cytology", National Cancer Institute, Bethesda, Maryland.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Naylor, B.: Fine needle aspiration cytology of the breast: What it shows and is it worth it? Lecture, Symposium on Breast Disease: Diagnostic Imaging and Current Management, The University of Michigan, Mackinac Island, Michigan, July, 1988.
2. Naylor, B.: a) Non-neoplastic entities seen in routine cytologic specimens (workshop), and b) Perspectives in cytology: From Battle Creek to Atlanta, Georgia (lecture). Southern Association of Cytotechnologists, Atlanta, Georgia, August, 1988.
3. Francis, J.R., Glazer, G.M., Gross, M.D. Naylor, B., and Kucharski, A.J.: Adrenal metastases: MRI/histopathological correlation. Poster presentation, Annual Meeting of the Society of Magnetic Resonance in Medicine, San Francisco, California, August, 1988.
4. Naylor, B.: Some aspects of quality control in gynecologic cytology. Lecture, Grand Rounds, Department of Obstetrics and Gynecology, The University of Michigan, Ann Arbor, Michigan, August, 1988.
5. Naylor, B.: Non-neoplastic entities manifested in routine cytologic specimens. Workshop, Maine Society of Cytology, Cape Elizabeth, Maine, September, 1988.
6. Kini, S.R., Johnson, T.L., and Naylor, B.: Cytomorphology of neuroendocrine tumors other than small cell carcinoma of lung. Poster presentation, Annual Scientific Meeting of the American Society of Cytology, Kansas City, Missouri, November, 1988.
7. Mazzara, P.F., Flint, A., and Naylor, B: Adenoma of the nipple: Cytopathologic features. Poster presentation, Annual Scientific Meeting of the American Society of Cytology, Kansas City, Missouri, November, 1988.
8. Naylor, B.: Some aspects of quality control in gynecologic cytology. Lecture, Department of Family Practice, The University of Michigan, Chelsea, Michigan, November, 1988.
9. Francis, J.R., Glazer, G.M., Gross, M.D., Naylor, B., and Kucharski, A.J.: Adrenal metastases: MRI/histopathological correlation. Paper, Scientific Assembly and Annual Meeting of the Radiological Society of North America, Chicago, Illinois, November, 1988.
10. Naylor, B.: Some aspects of the biological effects of asbestos. Lecture, Division of Pulmonary Medicine, Ann Arbor, Michigan, December, 1988.
11 Helvie, M.A., Baker, D.E., Adler, D.D., Anderson, I., Naylor, B., and Buckwalter, K.: Mammographic guided fine needle aspiration biopsy of non-palpable breast lesions. Paper, Annual Meeting of the American Roentgen Ray Society, New Orleans, Louisiana, March, 1989.
12. Naylor, B.: The pathognomonic cytologic picture of rheumatoid pleuritis. Lecture, International Congress of Cytology, Buenos Aires, Argentina, May, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN RERereED JOURNALS:

1. Naylor, B.: Perspectives in Cytology: From Battle Creek to New Orleans. Acta Cytol, 1988;32:613-621.
2. Mazzara, P.F., Flint, A., and Naylor, B: Adenoma of the nipple: Cytopathologic features. Acta Cytol., 1989;33:188-190.
3. Smith-Purslow, M.J., Kini, S.R., and Naylor, B.: Cells of squamous cell carcinoma in pleural, peritoneal and pericardial fluids: Origin and morphology. Acta Cytol., 1988;33:245-253.

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

1. Naylor, B.: In Memoriam: Emmerich von Haam, M.D., F.I.A.C. --1903-1988. Cytotechnol. Bull., 1988;25:49.

HONORS

1. Maurice Goldblatt Cytology Award of the International Academy of Cytology for 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

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. 5 Week Medical Student (Year 2) Research Elective.
D. Year 1 Medical Student Dermatopathology Lecture Series.
E. Dermatology Grand Rounds - Dermatopathology Presentations.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIH First Award (50% effort: $90,000 Direct Costs; Aug 1989 - Aug 1990): Interaction of Gamma Interferon with Keratinocytes.
B. NIH RO-1 (40% effort: $147,702 Direct Costs; June 1989-July 1990). Role of Adhesion Molecules in Psoriasis.
C. NIH RCDA (50% effort: $40,000 Direct Costs; July 1989-June 1990). Role of Adhesion Molecules in Skin Diseases.

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. Influence of retinoids on keratinocyte, melanocyte, and fibroblast function in-vitro and in-vivo.
K. Characterization of effect of Cyclosporin A on Phorbol ester induced cutaneous inflammation and hyperplasia.
L. Immunophenotypic analysis of response of psoriasis and 22 other dermatological conditions to Cyclosporin A.

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

A. Editorial Board - American Journal of Dermatopathology.
B. Reviewer of articles for: Journal of Investigative Dermatology, Journal of Cutaneous 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 (Review approximately 3-4 manuscripts per month).
C. Ad-hoc Review Committee - NIH Study Section - Skin Disease Research Center Grant Applications.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Whats New in Dermatopathology; Invited Speaker. Annual Meeting of Michigan Dermatological Society. July 23, 1988, Traverse City, Michigan.
2. The Role of Gamma Interferon in Trafficking of Cells and Monocytes into the Epidermis. Visiting Professor, Department of Dermatology, University of Aarhus, Marselisborg Hospital, August 25, 2988, Aarhus, Denmark.
3. Pathomechanisms of Psoriasis-Regulation of Trafficking of T Lymphocytes and Monocytes. Invited Speaker. Workshop on Psoriasis. Treatment with Cyclosporin A. Sandoz Sponsored. Hotel Marselis, August 27, 1988, Aarhus, Denmark.
4. Role of Adhesion Molecules in the Pathophysiology of Inflammatory Skin Diseases. Invited Speaker. Immunodermatology Workshop. 2nd Annual Conference on Clinical Immunology-Clinical Immunology Society. November 4, 1988, San Francisco, California.
5. Intraepidermal Lymphocytes Correlate with Keratinocyte Intercellular Adhesion Molecule-1 (ICAM-1) Expression in Skin Diseases, Plenary Scientific Session, Annual Meeting of American Society of Dermatopathology. December 2, 1988, Washington D.C.
6. Role of Adhesion Molecules in Cutaneous T Cell Lymphoma; Faculty Participant-CPC-Annual Meeting of American Academy of Dermatology. December 5, 1988, Washington, D.C.
7. Role of Adhesion Molecules and their Modulation in Psoriasis. Invited Speaker-Psoriasis Mini Symposium. Annual Meeting of American Academy of Dermatology. December 5, 1988. Washington, D.C.
8. Role of Gamma Interferon in Cutaneous Trafficking of Lymphocytes, Invited Lecturer, University of Toledo, College of Pharmacy Seminar Series, February 7, 1989, Toledo, Ohio.
9. Adhesion Molecules in Inflammatory Skin Diseases, Invited Speaker, Upjohn Company, March 3, 1989, Kalamazoo, Michigan.

10. Characterization of a Novel Adhesion Assay Using Frozen Sections of Gamma Interferon Treated Skin. FASEB Meeting, March 23, 1989, New Orleans, LO.
11. Molecular Basis for Lymphocyte Trafficking in the Skin, Invited Speaker, Michigan Dermatological Society. March 29, 1989, Ann Arbor, Michigan.
12. Epidermis as Immune Target. Invited Speaker, 1 hour lecture at opening of the Tricontinetal Annual Meeting of the SID, ESDR, JSID Societies. April 26, 1989, Washington, D.C.
13. Molecular Phenotype of Cultured Psoriatic Keratinocytes, Society of Investigative Dermatology National Meeting, April 27, 1989, Washington, D.C.
14. Factor XIIIa Expressing Dermal Dendrocytes are Increased in AIDS-Associated and Non-AIDS Associated Kaposi's Sarcomas, American Federation for Clinical Research, April 28, 1989, Washington, D.C.
15. Epithelial Cells in Immunity, Organizing Co-Chairman, American Society of Microbiology Annual Meeting - Session #46, May 15, 1989, New Orleans, LO.
16. IFN-γ Affects Cutaneous Trafficking of Lymphocytes Through Induction of Intercellular Adhesion Molecules on Keratinocytes, Invited Speaker, American Society of Microbiology, May 15, 1989, New Orleans, LO.
17. Usefulness of Novel Skin Frozen Section Adherence Assay for Understanding the Molecular Basis of Lymphocyte Trafficking, Invited Speaker, Genentech, Inc, Cardiovascular Research Group, June 14, 1989, San Francisco, CA.
18. Dermatopathological Pattern Recognition Explained by Differential Adhesion Molecule Expression, Department of Dermatology-USCF, June 17, 1989, San Francisco, CA.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Nickoloff, BJ: The light microscopic assessment of 100 patients with patch/plaque stage mycosis fungoides. Am. J. Dermatopath. 1988;10:469-480.
2. Reusch MK, Fullerton SH, Nickoloff BJ, Glinski W, Karasek MA: Leukotriene B4 enhances adherence of human polymorphonuclear leukocytes to dermal microvascular endothelial cells in-vitro. Arch Dermatol Res 1988;280:194-197.
3. Nickoloff BJ, Mitra RS: Phorbol treatment enhances binding of mononuclear leukocytes to autologous and allogeneic gamma interferon treated keatinocytes which is blocked by anti-LFA-1 monoclonal antibody. J Invest Dermatol. 1988;90:684-689.
4. Nickoloff BJ, Fisher GS, Mitra RS, Voorhees JJ: Additive and synergistic antiproliferative effects of cyclosporine A and gamma interferon on cultured human keratinocytes. Am J Pathol 1988;131:12-18.
5. Nickoloff BJ, Riser BL, Mitra RS, Dixit VM, Varani J: Inhibitory effect of gamma interferon on cultured keratinocyte thrombospondin production, distribution and biological activity. J Invest Dermatol, 1988;91:213-218.
6. Lewinsohn DM, Nickoloff BJ, Butcher EC: A fluorometric approach to the quantitation of cell number with application to cell adhesion assay. J Immunol Meth 1988;110:93-100.
7. Fisher GJ, Duell EA, Nickoloff BJ, Annesley TM, Kowalke JK, Voorhees JJ: Levels of Cyclosporin in epidermis of treated psoriasis patients inhibit growth of keratinocytes cultured in serum-free but not serum containing media. J Invest Dermatol 1988;91:142-146.
8. Gupta AK, Fisher GJ, Elder JT, Nickoloff BJ, Voorhees JJ: Sphingosine inhibits phorbol ester induced inflammation ornithine decarboxylase activity, activation of protein kinase C in mouse skin. J Invest Dermatol 1988;91:486-491.

9. Shiohara T. Nickoloff BJ, Moriya N, Gotoh C, Nagashima M: In-vivo effects of interferon-γ and interferon-γ antibody on the experimentally induced lichenoid tissue reaction. Br J Dermatol 1988;119:199-206.
10. Nickoloff BJ, Fusher GJ, Mitra RS, Voorhees JJ: Direct Cytopathic effects of Cyclosporine A on rapidly proliferating cultured keratinocytes and dermal fibroblasts. Trans Proc 1988;XX:85-90.
11. Nickoloff BJ, Mitra RS, Riser BL, Varani J: Modulation of keratinocyte motility: Correlation with production of extracellular matrix molecules by growth promoting and antiproliferative factors. Am J Pathol 1988;132:543-551.
12. Nickolff BJ: The role of gamma interferon in epidermal trafficking of lymphocytes with emphasis on molecular and cellular adhesion events. Arch Dermatol 1988;124:1835-1843.
13. Reusch MK, Karasek MA, Nickoloff BJ: The effect of neuropeptides present in skin on the proliferation of human peripheral blood mononuclear cells and T cells. Arch Dermatol REs 1988;280:279-284.
14. Griffiths CEM, Nickoloff BJ: The use of interferon in psoriasis. Interferon -Today and Tomorrow. 9:34-35, 1988.
15. Varani J, Mitra RS, McClenic BJ, Dixit VM, Nickoloff BJ: Modulation of fibronectin production in normal human melanocytes and malignant melanoma cells by interferon-γ and tumor necrosis factor. Am J Path 1989;134:827-836.
16. Griffiths CEM, Voorhees JJ, Nickoloff BJ: Characterization of intercellular adhesion molecule-1 and HLA-DR expression in normal and inflamed skin: Modulation by recombinant gamma interferon and tumor necrosis factor. J Am Acad Dermatol 1989;20:617-629.
17. Griffiths CEM, Voorhees JJ, Nickolff BJ: Gamma interferon induced different keratinocyte cellular patterns of expression of HLA-DR and DQ and intercellular adhesion molecule-1 (ICAM-1) antigens. Br J Dermatol 1989;120:1-8.
18. Nickoloff BJ, Griffiths CEM, Voorhees JJ, Baadsgard O, Hanson K, Cooper KD: Markedly diminished epidermal keratinocyte expression of intercellular adherence molecule-1 (ICAM-1) in Sezary Syndrome. JAMA 1989;261:1-5.
19. Nickoloff BJ, Griffiths CEM: T lymphocytes and monocytes bind to keratinocytes in frozen sections of normal skin biopsies maintained in organ culture in the presence of gamma interferon via lymphocyte function associated antigen-1 (LFA-1) and intercellular adhesion molecule-1 (ICAM-1) interaction. J Am Acad Dermatol 1989;20:736-743.
20. Nickoloff BJ, Griffiths CEM: Factor XIIIa expressing dermal dendrocytes are increased in AIDS-associated Kaposi's sarcoma. Science 1989;243:1736-1737.
21. Naukkarinen A, Nickoloff BJ, Farber EM: Quantification of cutaneous sensory nerves and their substance P content in psoriasis. J Invest Dermatol 1989;92:126-129.
22. Nickoloff BJ: Keratinocytes produce a lymphocyte inhibitory factor which is partially reversible by an antibody to transforming growth factor-beta. Ann N.Y. Acad Sci 1989;548:312-320.
23. Headington JT, Gupta AK, Goldfarb MT, Nickoloff BJ, Hamilton TA, Ellis CN, Voorhees JJ: A morphometric and histologic study of the scalp in psoriasis: Paradoxical sebaceous gland atrophy and decreased hair shaft diameters without alopecia. Arch Dermatol 1989;125:639-642.
24. Ho VC, Gupta AK, Ellis CN, Cooper KD, Nickoloff BJ, Voorhees JJ: Cyclosporine in lamellar icthyosis. Arch Dermatol 1989;125:511-514.
25. Reusch MK, Morhenn VB, Nickoloff BJ: Immunophenotyping of skin during healing of suction blister injury. Arch Dermatol Res. (In Press).
26. McClenic BD, Mitra RS, Riser BL, Nickoloff BJ, Dixit VM, Varani J: Production and utilization of extracellular matrix components by human melanocytes and malignant melanoma cells. Exp Cell Res (In Press).

27. Ho VC, Gupta AK, Ellis CN, Nickoloff BJ, Voorhees JJ: Treatment of Severe lichen planus with cyclosporine A. J Amer Acad Dermatol (In Press).
28. Gupta AK, Ellis CN, Cooper KD, Nickoloff BJ, Ho VC, Chan LS, Tellner BC, Voorhees JJ: Cyclosporine A for the treatment of alopecia areata. J Am Acad Dermatol (In Press).
29. Riser BL, Varani J, Nickoloff BJ, Mitra RS, Dixit VM: Thrombospondin binding by keratinocytes: Modulation under conditions which alter thrombopondin biosynthesis. Dermatologica (In Press, 1989).
30. Nickoloff BJ, Mitra RS, Elder JT, Fisher GJ, Voorhees JJ: Decreased growth inhibition by recombinant gamma interferon is associated with increased production of transforming growth factor alpha in keratinocytes cultured from psoriatic lesions. Br J Dermatol (In Press, 1989).
31. Ho VC, Griffiths CEM, Gupta AK, McCuaig CC, Nickoloff BJ, Cooper KD, Voorhees JJ: Intralesional Cyclosporine-A in the treatment of psoriasis: A clinical, immunologic and pharmacokinetic study. J Am Acad Dermatol (In Press, 1988).
32. Shiohara T, Nickoloff BJ, Moriya N, Nagashima M: Expression of intercellular adhesion molecule-1 (ICAM-1) in fixed drug eruptions. Arch Dermatol (In Press, 1989).
33. Cerio R, Griffiths CEM, Cooper KD, Nickoloff BJ, Headington JT: Characterization of dermal dendritic cells with Factor FXIIIa in normal and inflamed skin. Br J Dermatol (In Press, 1989).
34. Whittemore AS, Holley E, Lee IM, Abel EA, Adams R, Nickoloff BJ, Bley L, Peters J, Gibney C: Mycosis fungoides in relation to evniromental exposures and immune response: A case control study. JNCI (In Press, 1989).
35. Nickoloff BJ, Griffiths CEM: The spindle-shaped cell in cutaneous Kaposi's sarcoma and simulators is the factor XIIIa positive dermal dendrocyte. Am J Path (In Press, 1989).

BOOKS/CHAPTERS IN BOOKS:

1. Nickoloff BJ: Interferons and Cutaneous Metabolism. In: Biochemistry and Physiology of the Skin, Oxford University Press, New York. (In Press, 1988).
2. Nickoloff BJ: Leukocyte Adhesion Molecules and Inflammatory Cell Migration Pathways in the Skin: Skin Immune System, CRC Press Inc, Boca Raton, Florida. (In Press, 1988).

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

1. Griffiths CEM, Voorhees JJ, Nickoloff BJ: Lymphocytes bind to the epidermis of frozen sections of normal skin treated with gamma interferon. Br J Dermatol. 1988;119:463.
2. Griffiths CEM, Voorhees JJ, Nickoloff BJ. Differential modulation of cultured keratinocyte HLA-DR and intercellular adhesion molecule-1 (ICAM-1) expression by gamma interferon. Clin Res 1988;36:906.
3. Nickoloff BJ, Mitra RS: Pretreatment of keratinocytes with gamma interferon dramatically reduces binding by epidermal growth factor. Clin Res 1988;36:908.
4. Nickoloff BJ, Griffiths CEM: Intra-epidermal lymphocytes correlate with keratinocyte intercellular adhesion molecule-1 (ICAM-1) in skin diseases. J Cut Path 1988;15:331.
5. Riser B, Mitra RS, Nickoloff BJ, Varani J: Modulation of fibronectin production in melanocytic cells by interferon-γ and tumor necorsis factor. J Cell Biochem Supp 12A, 1988;215.

6. Nickoloff BJ, Voorhees JJ, Griffiths CEM: Characterization of a novel adhesion assay using frozen sections of gamma interferon treated skin. FASEB 1989;3:6356.
7. Abel EA, Whittemore AS, Holly C, Adams RM, Nickoloff BJ: Mycosis fungoides in relation to enviormental exposures and immune response: A case control study. Clin REs 1989;37:228A.
8. Esmann J, Fisher GJ, Talwar HS, Nickoloff BJ, Voorhees JJ: Inflammatory mediators activate protein kinase C in adult human keratinocytes. J Invest Dermatol 1989;92:425.
9. Ho VC, Griffiths CEM, Ellis CN, Gupta AK, Nickoloff BJ, Cooper KD, Voorhees JJ: Intralesional cyclospoine A in the treatment of psoriasis: A clinical, immunologic and pharmacokenetic study. J Invest Dermatol 1989;92:445.
10. Nickoloff BJ, Reusch MA, Karasek MA: Characterization of adherent mononuclear leukocytes to interferon-gamma treated skin endothelial cells and keratinocytes. Clin Res 1987;35:389A.
11. Morhenn VB, Nickoloff BJ: Gamma Interferon treated human keratinocytes can stimulate allogeneic, resting T lymphocytes in the presence of interleuken-2. J Invest Derm 1987;88:508.
12. Wastek GJ, Reusch MK, Karesek MA, Nickoloff BJ: Characterization of ^{3}H-Substance P binding to a mouse monoclonal mast cell line. Clin Res 1987;35:724A.
13. Nickoloff BJ, Mitra RS: Activation of resting T lymphocytes by phorbol esters enhances binding to autologous gamma interferon treated cultured keratinocytes. J Cut Path 1987;14:363.
14. Nickoloff BJ, Fisher GJ, Mitra RS, Voorhees JJ: Additive antiproliferative effect of cyclosporine A and gamma interferon on cultured keratinocytes. J Cut Path 1987;14:363.
15. Riser B, Varani J, Nickoloff BJ, Dixit V: Gamma interferon and tumor necorsis factor modulate thrombospondin production by human blood monocytes. J Cell Biochem Supp 1988; 12A:208.
16. Nickoloff BJ, Fisher GJ, Mitra RS, Voorhees JJ: Direct antiproliferative effects of cyclosporines A and H on rapidly proliferating keratinocytes grown in low calcium, serum-free media. Transp Proceed (In Press, 1987).
17. Varani J, Riser B, Nickoloff BJ: Effect of γ–Interferon on keratinocyte biosynthecis and expression of thrombospondin. J Cell Biochem, Supp 1988;12A:218.
18. Fisher GJ, Gupta AK, Elder JT, Talwar H, Nickoloff BJ, Voorhees, JJ: Sphingosine inhibits phorbol ester-induced inflammation, ornithine decarboxylase activity and activation of protein kinase C in mouse skin. J Invest Dermatol 1988;90:559.
19. Nickoloff BJ, Griffiths C: Gamma interferon induces different keratinocyte expression of HLA-DR, DQ and Intercellular Adhesion Molecule-1 antigens. J Invest Dermatol 1988;90:592.
20. Nickoloff BJ, Mitra RS, Fusher GS, Voorhees JJ: Altered responsivness of psoriatic keratinocytes to gamma interferon. J Invest Dermatol 1988;90:592.
21. Nickoloff BJ, mitra RS: Transforming growth factor-beta is a keratinocyte-derived lymphocyte inhibitory factor. J Invest Dermatol. 1988;90:592.
22. Cerio R, Griffiths CEM, Cooper KD, Nickoloff BJ, Headington JT, Wilson-Jones E: The immunophenotype of FXIIIa dendritic cells in normal and inflamed human skin. J Invest Dermatol. 1989;92:437.
23. Nickoloff BJ, Mitra RS, Fisher GJ, Elder JT, Griffiths CEM, Voorhees JJ: Molecular phenotype of cultured psoriatic keratinocytes: Decreased growth inhibiton by gamma interferon and increased production of transforming growth factor-alpha. J Invest Dermatol 1989;92:490.
24. Mitra RS, Voorhees JJ, Nickoloff BJ: Modulation of ^{125}I-EGF ligand binding to cultured keratinocytes. J Invest Dermatol 1989;92:482.

25. Taylor RS, Griffiths CEM, Brown MD, Swanson NS, Nickoloff BJ: Constitutive absene of cytokine induced expression of adhesive molecules in basal cell carcinoma. J Invest Dermatol. 1989;92:530.
26. Griffiths CEM, Fisher GJ, Esman J, Voorhees JJ, Nickoloff BJ: Adhesion molecules and cutaneous inflammation: Modulation by gamma interferon and protein kinase C. J Invest Dermatol 1989;92:437.
27. Varani J, Mitra RS, Gibbs D, Dixit V, Mitra RS, Wang T, Nickoloff BJ: All-trans retinoic acid modulated keratinocyte and fibroblast growth, adhesion and extracellular matrix production. J Invest Dermatol. 1989;92:537.
28. Esman J, Griffiths CEM, Talwar HS, Hammerberg C, Nickoloff BJ, Fisher GJ, Cooper KD, Voorhees JJ: Biochemical and immunological characterization of the :retinoid reaction", in normal human skin. Clin Res. 1989;37:349.
29. Nickoloff BJ, Griffiths CEM: Factor XIIIa expressing dermal dendrocytes are increased in AIDS-associated and non-AIDS Kaposi's sarcomas.
30. Nickoloff BJ: Role of gamma interferon in epidermal trafficking of T lymphocytes and monocytes: A possible ciclosporin A sensitive pathway. Act Sandoz Sponsored Symposium. Aarrhus, 1988.
31. Fligiel SEG, Inman D, Mitra RS, Nickoloff BJ, Varani J: Modulation of normal and malignant extracellular matrix by interferon-gamma and tumor necrosis factor. FASEB J 3, A1052, 1989.
32. Nickoloff BJ, Sigel MM: Epithelial Cells in Immunity. Session 46. American Society of Microbiology. 1989.
33. Nickoloff BJ: Epidermis as an Immune Target. Dialogues in Dermatology. Monthly Audiojournal of the American Academy of Dermatology. 1989.
34. Nickoloff BJ: Whats New in Interferon-Related Research. Dermatology Quarterly XIV, 1-5, 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

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 (four) to sophomore class.
B. Instruction of sophomore (M-2) pathology laboratory, Pathology 600.
C. Postgraduate course, "Current Topics in Blood Banking", Planning Committee.
D. Course on Transfusion Medicine presented to Pathology and Hematology/Oncology House Officers.
E. Seminars and lectures on Pathology of Breast to Pathology House Officers.
F. Responsible for senior student (M-4) elective in pathology (Nov-Dec, 1988).
G. Lecture to Department of Surgery, Section of General Surgery: Blood Component Therapy. August 18, 1988.
H. Presentation to Section of Orthopedic Surgery, Department of Surgery, Grand Rounds: "Infectious and non-infectious complications of blood transfusion". October 29, 1988.
I. Lecture to Department of Anesthesiology: "Complications of Blood Transfusion". November 3, 1988.
J. Section of Clinical Pathology Grand Rounds: "Medical-Legal Problems in Blood Banking". January 6,1989.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Transfusional requirements in extracorporeal membrane oxygenator treatment.
B. Detection of source of blood in percutaneous umbilical blood sampling procedures.
C. Significance of intraductal carcinoma and lobular carcinoma in-situ presenting in adenofibromas or in sclerosing adenosis.

D. Adenomyoepithelial neoplasms of breast.
E. Pleomorphic adenomas of breast.

IV. ADMINISTRATIVE ACTIVITIES:

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. Transfusion 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

REGIONAL AND NATIONAL:

A. American Association of Blood Banks:
   1. Awards Committee, Chairman.
   2. Publications Committee.
B. American Society of Clinical Pathologists:
   1. Council on Anatomical Pathology.
   2. Chairman, Check Sample Program, Anatomical Pathology.
   3. Expert Review Panel in Anatomic Pathology.
C. Michigan Society of Pathologists:
   1. Medical Legislation Committee.
   2. Medical Care Insurance Committee.
D. Southeastern Michigan Red Cross Blood Program:
   1. Blood Operations Committee.
   2. Medical Advisory Committee.
E. Consultant, Veterans Administration Hospital, Ann Arbor.
F. Test Committee on Blood Banking/Transfusion Medicine, American Board of Pathology.
G. Breast Cancer Task Force, Michigan Department of Public Health.

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. Editor, Anatomical Pathology Check Sample Program, American Society of Clinical Pathologists.
G. Reviewer, Cancer.
H. Reviewer, Journal of the American Medical Association.

INVITED LECTURES/SEMINARS:

1. Lecture, "Legal Aspects of Blood Banking". Course on Hematology and Blood Banking, Flint Osteopathic Hospital. July 13, 1988.
2. Platform presentation: Prozones due to potent hemolytic anti-A and anti-B: How safe is the immediate spin crossmatch? (with Judd WJ, Steiner EA) Int. Soc. Blood Trans. London. July, 1988.
3. Poster presentation: Should hospitals draw donors? A cost appraisal. (with Butch SH, Judd WJ) Int. Soc. Blood Trans. London. July, 1988.
4. Poster presentation: Blood use by DRG in a U.S. tertiary care hospital (with Butch SH, Dieterle RA). Int. Soc. Blood Trans. London. July, 1989.
5. Platform presentation: PUBS: A new role for the blood bank (with Steiner EA, Hayashi RH, Judd WJ) Int. Soc. Blood Trans. London. July, 1988.
6. Lecture to Grand Rounds of Department of Obstetrics and Gynecology, Henry Ford Hospital, "Complications of Blood Transfusion". September 22, 1988.
7. Lecture to Department of Surgery, St. Joseph Mercy Hospital, Pontiac, Michigan, "Diagnosis and Management of Non-invasive Breast Cancer". October 19, 1988.
8. Poster presentation: ECMO: Minimal impact on the blood bank (with McCoy-Pardington D, Knafl P, Butch SH, Judd WJ). Annual Mtg, Am Assoc Blood Banks. Kansas City, MO. October, 1988.
9. Platform presentation: PUBS: A new role for the Blood Bank (with Steiner EA, Hayashi RH, Nugent CE, Judd WJ) Annual Meeting, Am Assoc Blood Banks. Kansas City, MO. October, 1988.
10. Poster presentation: Computer-assisted utilization review (with Butch SH, Dieterle RC). Annual Meeting, Am Assoc Blood Banks. Kansas City, MO. October, 1988.
11. Lecture, "Diagnostic Problems in Surgical Pathology". Annual Meeting, American Society of Clinical Pathologists. Las Vegas, NV. October 26, 1988.
12. Seminar, "Diagnostic Problems in Surgical Pathology of the Breast". Annual Meeting, American Society of Clinical Pathologists. Las Vegas, NV. October 27, 1988.
13. Microscopic Tutorial, "Problems in Surgical Pathology of Breast Disease". Annual Meeting, American Society of Clinical Pathologists. Las Vegas, NV. October 26, 1988.
14. Course (three days), "Problems in the Diagnosis and Management of Breast Cancer". American Society of Clinical Pathologists, Tucson, AZ. December 7-9, 1988.
15. Lecture, "Informed Consent for Blood Transfusion". American Association of Blood Banks. Miami, FL. February 24, 1989.
16. Platform presentation, "Mammary Hamartomas: A unifying Concept" Annual Meeting, International Academy of Pathology. San Francisco, CA. March 6, 1989.
17. Presentation of seminar to New York Society of Pathologists, "Problems in Diagnostic Pathology of Breast Disease". New York, NY. April 28, 1989.
18. Annual lectureship, "History of Blood Transfusion". Massachusetts Association of Blood Banks. Boston, MA. May 10, 1989.
19. Workshop, "Problem-solving in the Blood Bank". Annual Course, "Current Topics in Blood Banking". Department of Postgraduate Medicine, University of Michigan. May 31, 1989.

20. Lecture, "Legal Issues Related to Blood Transfusion". Annual Course, "Current Topics in Blood Banking", Department of Postgraduate Medicine, University of Michigan, June 1, 1989.
21. Visiting Professor, William Beaumont Army Hospital, El Paso, Texas. June 7-9, 1989.
22. Lecture, "Benign Breast Lesions Simulating Carcinoma". El Paso Society of Pathologists. El Paso, Texas. June 8, 1989.

HONORS AND AWARDS:

1. Commissioner's Medal, American Society of Clinical Pathologists.
2. Commission on Education Distinguished Service Award, American Society of Clinical Pathologists.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Judd WJ, Steiner EA, O'Donnell DB, Oberman HA: Discrepancies in ABO typing due to prozone: How safe is the immediate spin crossmatch? Transfusion 28:334-338, 1988.
2. Flint A, Oberman HA, Davenport RD: Cytophotometric measurements of metaplastic carcinoma of the breast: Correlation with pathologic features and clinical behavior. Mod. Path. 1:193-197, 1988.
3. Judd WJ, Steiner EA, Oberman HA, Giacherio D: False positive results with clinically modified anti-D do not indicate a need to use a separate, immunologically inert Rh control reagent. Transfusion 28:339-341, 1989.
4. Oberman HA: Strategies for blood transfusion. Mayo Clin. Proc. 63:950-951, 1988.
5. Helvie MA, Rebner M, Sickles EA, Oberman HA: Calcifications in metastatic breast carcinoma in axillary lymph nodes. J. Radiol. 151:921-922, 1988.
6. Helvie MA, Adler DD, Rebner M, Oberman HA: Breast hamartomas: variable mammographic appearance. Radiology 170:417-421, 1989.
7. Oberman HA: Hamartomas and hamartoma variants of the breast. Semin. Diag. Path. 6:135-145, 1989.

BOOKS/CHAPTERS IN BOOKS:

1. Oberman HA: Complications of blood transfusion. In: Greenfield, L. (ed.) Complications in Surgery and Trauma. J.B. Lippincott, Philadelphia, PA (in press).
2. Sternberg S, Antonioli D, Carter D, Eggleston J, Mills S, Oberman HA: Diagnostic Surgical Pathology. Raven Press, New York 1988 (2 vols, 1776 pages).
3. Oberman HA: The history of Blood Transfusion. In: "Clinical Practice of Blood Transfusion, ed. 2. Swisher SN and Petz LD, eds. New York, Churchill Livingstone, 1989. p. 9-30.
4. Oberman HA: Surgical Blood Ordering, Blood Shortage Situations, and Emergency Transfusion. In: "Clinical Practice of Blood Transfusion", ed. 2. Swisher SN and Petz LD, eds. New York, Churchill Livingstone, 1989. pp 213-222.

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

1. Blood review: Blood, Textbook of Hematology (Jandl). Arch Pathol Lab Med 112:857, 1988.

2. Letter to the Editor: Appropriateness of autologous transfusion. J Am Med Assoc 260:181-2, 1988.
3. Blood review: Soft Tissue Tumors (Enzinger and Weiss). Arch Pathol Lab Med 113:702, 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1987 - 30 JUNE 1988

I. CLINICAL ACTIVITIES:

A. Serum Angiotensin Converting Enzyme Assay.

II. TEACHING ACTIVITIES:

A. Lecturer - Pathology 630 (Dental Course).
B. Lecturer - Pathology 580 (Graduate Course).
C. Elizabeth Denholm, Ph.D. - Postdoctoral Fellow.
D. Barbara Markey, M.D. - Postdoctoral Fellows/Resident

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Mechanisms and Genetic Regulation of Pulmonary Fibrosis, R01-HL28737-04. Principal Investigator, S.H. Phan, Ph.D., M.D.
B. Macrophage Function in Lung Injury and Fibrosis. P01-HL31963, Section IV. Principal Investigator, S.H. Phan, Ph.D., M.D.
C. Fibroblast Regulatory Factors in Pulmonary Fibrosis 84-136. Established Investigator Award (American Heart Association).
D. Fibroblast Heterogeneity in Pulmonary Fibrosis, R01-HL39925. Principal Investigator, S.H. Phan, Ph.D., M.D.
E. Crescentic Nephritis. P01DK38149, Section IV, P.I. S.H. Phan, Ph.D., M.D.

PROJECTS UNDER STUDY:

A. Lung macrophage/monocyte, recruitment and activation during lung injury and fibrosis.
B. Fibroblast function - in terms of chemotaxis, collagen metabolism and proliferation during lung injury, and their regulation of connective tissue cells by inflammatory and immune mediators and cytokines.
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 diseases renal tissue.
E. Production of fibrogenic mediators and cytokines by endothelial cells.
F. Analysis of bleomycin receptors on alveolar macrophages and fibroblasts.
G. Production of monocyte chemotactic factors by alveolar macrophages and its regulation by bleomycin and cytokines.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Member, Ann Arbor VA Hospital Research & Development Committee

REGIONAL AND NATIONAL:

A. Reviewer for the following journals: Journal of Immunology, Laboratory Investigation, Journal of Clinical Investigation, American Review of Respiratory Diseases, Experimental Lung Research, Infection and Immunity, American Journal of Pathology, Chest.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. NATO Advanced Studies Institute - "Vascular Endothelium: Receptors and Transduction Mechanism", June 18-29, 1988, Halkidiki, Greece.
2. Fifth International Colloquium on Pulmonary Fibrosis, October 4-6, 1988, Lyon, France.
3. NIH/NHLBI Workshop - "Cellular and Molecular Mechanisms of Lung Fibrosis", June 26-27, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Strieter, R.M., Phan, S.H., Showell, H.J., Remick, D.G., Lynch, J.P. III, Genord, M., Raiford, C., Eskandari, M., Marks, R.M., and Kunkel, S.L.: Monokine-induced neutrophil chemotactic factor gene expression in human fibroblasts. J. Biol. Chem. 1989, in press.
2. Denholm, E.M., Wolber, F.M., and Phan, S.H.: Secretion of monocyte chemotactic activity by alveolar macrophages. Am. J. Pathol. 1989; in press.
3. Strieter, R.M., Wiggins, R., Phan, S.H., Wharram, B.L., Showell, H.J., Remick, D.G., Chensue, S.W., and Kunkel, S.L.: Monocyte chemotactic protein gene expression by cytokine-treated human fibroblasts and endothelial cells. Biochem. Biophys. Res. Commun. 1989; in press.
4. Phan, S.H. and Kunkel, S.L.: Effects of muramyldipeptide and indomethacin on schistosome egg-induced granulomatous inflammation in the lung, In, Grassi, C., Rizzato, G., and Pozzi, E. (Eds.) Sarcoidosis and Other Lung Granulomatous Disorders, Excerpta Medica, Amsterdam, 1988.
5. Wiggins, R.C., Fantone, J.C., Phan, S.H.: Mechanisms of vascular injury, In, Tisher, C.C., and Brenner, B.M. (Eds.) Renal Pathology, Chapter 30, J.B. Lippincott, Co., Philadelphia, 1989; pp. 965-993.
6. Phan, S.H.: Diffuse interstitial fibrosis, In, Massaro, D., (Ed.) Lung Cell Biology, Marcel Dekker, New York, 1989; Chapter 19, pp. 907-979.

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

1. Solsky, M., Phan, S.H., and Cantor, W.: Collagen synthesis by human chondrocytes in monolayer culture differs from fibroblasts. American Gerontology Society Meeting, 1988.
2. Denholm, E.M., Wolber, F., and Phan, S.H.: Alveolar macrophage production of monocyte chemoattractants in pulmonary fibrosis. 4th International Congress of Cell Biology, August, 1988.
3. Wiggins, R., Merritt, S., and Phan, S.H.: Increased glomerular mRNA for types I and IV collagen prior to cellular crescent formation in rabbit anti-GBM disease. 21st Annual Meeting of the American Society of Nephrology, December 11-14, San Antonio, Texas, 1988.
4. Phan, S.H., McGarry, B., and Wiggins, R.: Regulation of mesangial cell proliferation and collagen synthesis by renal glomerular and cortical conditioned media. Fed. Proc. 3:A446, 1989.
5. Denholm, E.M., and Phan, S.H.: Bleomycin binding sites on alveolar macrophages. Fed. Proc. 3:A905, 1989.
6. Wiggins, R.C., Merritt, S., Killen, P., Downer, G., Phan, S: Cortical before glomerular collagen synthesis early in rabbit model of crescentic glomerulonephritis. Fed. Proc. 3:A933, 1989.
7. Strieter, R.M., Showell, H.J., Phan, S.H., Remick, D.G., Lynch, J.P., Marks, R.M., and Kunkel, S.L.: Cytokine-induced gene expression of a neutrophil chemotactic factor from cellular constituents of the alveolar capillary membrane. Fed. Proc. 3:A1048, 1989.
8. Strieter, R.M., Showell, H.J., Phan, S.H., Remick D.G., Lynch J.P., Staats, P.S., Raiford, C., Marks, R.M., and Kunkel, S.L.: Neutrophil chemotactic factor gene expression from cellular constituents of the alveolar capillary membrane. Am. Rev. Respir. Dis. 139:253, 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Lecturer, Pathology 600
B. Lecturer, Pathology 630
C. Coordinator, Pathology House Officer Microbiology Laboratory rotation.
D. Lecturer, Clinical Pathology Grand Rounds.
E. Lecturer, Clinical Pathology Core Lecture Series.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "A National Survey of the In Vitro Susceptibility of Aerobic and Anaerobic Pathogenetic Bacteria to Piperacillin", American Cyanamid Co.
B. "National Survey of the Susceptibility of the Bacteroides fragilis group," Merck, Sharp and Dohme and Beecham Labortories.
C. "Unasyn Comparative Susceptibility Study," Pfizer, Inc.

PROJECTS UNDER STUDY:

A. Alternatives for direct specimen Chlamydia testing.
B. Evaluation of DNA probes for direct specimen testing and culture confirmation.
C. Frequency and sequelae of contaminated vascular procedures - with Surgery (Drs. Wakefield and Stanley).
D. Application of gas-liquid chromatography for bacterial identification.
E. PEN Team Catheter contamination study-with Pediatric Surgery and Infectious Disease.
F. Evaluation of gamma interferon to correct bactericidal defects in CGD patient granulocytes-with Pediatric Hematology/Oncology.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Clinical Pathology Laboratory Director's Committee.
B. M-Labs Technical Advisory Committee (Chairperson).
C. Coordinator, Clinical Microbiology Senior Staff Meeting.
D. Coordinator, Clinical Microbiology Inservice Education Program.

MEDICAL SCHOOL/HOSPITAL:

A. Hospital Infection Control Committee.
B. Ad hoc Committee for Body Substance Precautions.
C. Alternate, Task Force on AIDS

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. College of American Pathologists site inspection team member at U. of Cincinnati.
D. Coordinator, Clinical Microbiology Laboratory Directors of Michigan Group meetings.

V. OTHER RELEVANT ACTIVITIES:

A. Reviewer, Journal of Clinical Microbiology.
B. Editorial Consultant, Bozell, Jacobs, Kenyon and Eckhardt Healthcare, Inc., New York, New York.
C. Lecturer, Roche Pharmaceutical Training series.

INVITED LECTURES/SEMINARS:

1. Region IV American Society for Medical technologists: "Detecting Mycobacterium tumberculosis with DNA Probes" and "Impact of Transplants on the Microbiology Laboratory".

IV. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lockwood, W., Friedman, C., Bus, N., Pierson, C.L. and Gaynes, R.: An outbreak of Mycobacterium terrae in clinical specimens associated with potable water. American Review of Respiratory Diseases, in press.
2. 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. of Vascular Surgery, in press.

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

1. Pierson, C.L., and Baker, R.W.: "Clinical Evaluatin of a Chemiluminescent-labeled DNA Probe for Direct Detection of Chlamydia trachomatis Urogenital Infection: Abstracts, Interscience Conference on Antimicrobial Agents and Chemotherapy, 1989: In press.

JOSEPH A. REGEZI, D.D.S., M.S.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Oral Pathology biopsy service: four months/year (5,000 biopsies /year.).
B. Patient consultations: Oral Pathology/Dermatology Referral Service--Friday mornings.

II. TEACHING ACTIVITIES:

A. Course Director and Lecturer in Senior Oral Pathology 816 and 818.
B. Laboratory section director for General Pathology for Dental Students 631.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Histologic and immunohistologic study of mucoepidermoid carcinomas.
B. Immunohistochemical differentiation of adenocystic carcinoma from terminal duct carcinoma.
C. Immunohistochemical study of oral lymphoid lesions.
D. Develoment of vehicles for delivery of topical drugs to oral mucous membranes.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Thesis Committee Chairman for Dr. D.E. Turunen, Department of Periodontics.
B. Coordinator of oral pathology clinical consultative services.

DENTAL SCHOOL:

A. Member of Transition Committee, 1987-1989.
B. Interim Director of Graduate Studies.

REGIONAL AND NATIONAL:

A Member of Editorial Board for Oral Surgery, Oral Medicine and Oral Pathology.
B. Member of the Task Force to Plan the Future of Oral Pathology.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATIONS IN REFEREED JOURNALS:

1. Zarbo, R., Regezi, J., Hatfield, J., Maisel, H., Trojanowski, J., Batasakis, J. and Crissman, J: Immunoreactive glial fibrillary acidic protein in normal and neoplastic salivary gland: a combined immunohistochemical and immunoblot study. Surg. Pathol. 1988;1:55-63.
2. Chan, Il, Regezi, J., Cooper, K.: Linear IgA disease. J. Am. Acad. Dermatol. (in press).
3. Regezi, J., Zarbo, R., and Crissman, J.: Immunoreactivity of granular cell lesions of skin, mucosa and jaw. Cancer (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Weiss, J., Gupta, A., Regezi, J., Rasmussen, J.: Oral ulcers and cobblestone plaques. J. Am. Acad. Dermatol.
2. Batsakis, J., Regezi, J., Luna, M., El-Naggar, A.: Histogenesis of salivary gland neoplasms: a postulate with prognostic implications. J. Larying. Oto.

BOOKS/CHAPTERS IN BOOKS:

1. Regezi, J. and Sciubba, J. Oral Pathology: Clinical Pathologic Correlations, Saunders Pub., Philadelphia, 1989.

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

1. Regezi, J., Smith, F., Smith, R.: Langerhans cell immunoreactivity in chemically fixed gingival tissue. Abstract #347, A.A.D.R., Montreal, Canada, March, 1988.
2. Regezi, J., Zarbo, R., Courtney, R., Crissman, J.: Immunoreactivity of granular cell lesions of skin, mucosa, and jaw. Abstract #884, A.A.D.R., San Francisco, California, March, 1989.
3. Turunen, D., Regezi, J., Lopatin, D., Caffessee, R., Smith, B.: Immunologic identification of sulcular epithelial differentiation antigens in cytology preparations. Abstract #1429 A.A.D.R., San Francisco, California, March, 1989.
4. Zarbo, R., Raju, U., Regezi, J., Krutchkoff, D., Perrin, E.: Melanotic neuroectrodermal tumors (MNT) in Infancy: intermediate filament, neuroendocrine and melanoma associated antigen profile. U.S. and Canadian Acad. of Pathol., San Francisco, California, March, 1989, in Lab. Invest. 60:109A, 1989, #650.

DANIEL G. REMICK, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Director of Autopsy Service.
B. Supervision of Autopsies (4.5 months)
C. Coordinator of Senior Staff Call Schedule
D. Pediatric Pathology

II. TEACHING ACTIVITIES:

A. Monthly Urology Conference.
B. Course Director - Pathology 631.
C. Mentor - Fourth Year Medical Student Clerkship Rotation.
D. Coordinator - Pathology Gross Conference.
E. Lectures to Pathology House Officers.

III. RESEARCH ACTIVITIES:

A. Regulation of Soluble Mediators of Inflammation.
B. Toxic Effects of Immunomodulators.

SPONSORED SUPPORT:

Current:

A. National Institutes of Health - Granulomatous Inflammation and Interleukin-2 - Principal Investigator, 5 years, $350,000
B. American Heart Association of Michigan - Role of TNF and PAF in Septic Shock, $24,500.

Pending:

A. National Institutes of Health - Regulation of the Production and Effects of Tumor Necrosis Factor - Principal Investigator.
B. National Institutes of Health - Liver Transplantation and TNF-Induced Organ Injury - Principal Investigator
C. National Institutes of Health - Monokine Gene Expression/Regulation in Lung Injury - Co-Investigator

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director - Autopsy Service.
B. Member - Post-Sophomore Pathology Fellowship Committee.
C. Member - Quality Assurance Committee
D. Member - Microcomputer Advisory Committee

MEDICAL SCHOOL/HOSPITAL:

A. Medical School Admissions Committee

REGIONAL AND NATIONAL:

A. Member - Dementia Subcommittee, Other Chronic Disease. Advisory Committee to the Michigan Department of Public Health.
B. NIH - Site Visitor, Burn and Trauma Center Program Project, Louisiana State University.
C. Deputy Medical Examiner for Washtenaw County (16 cases).
D. Reviewer, American Review of Respiratory Diseases.
E. Reviewer, Laboratory Investigation.
F. Reviewer, Journal of Immunology.
G. Reviewer, American Journal of Applied Physiology.
H. Reviewer, Journal Immunopharmacology
I. Reviewer, Journal Leukocyte Biology

INVITED LECTURES/SEMINARS:

1. Invited Speaker - UpJohn Corporation, Sterile Motrin I.V. Sepsis Study Group, Chicago, Illinois, October, 1988.
2. Invited Lecturer, Rusch Science Seminar, Concordia College, Ann Arbor, Michigan, October, 1988..

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Strieter, R.M., Remick, D.G., Ward, P.A., Spengler, R.N., Lynch, J.P., III, Larrick, J., and Kunkel, S.L.: Cellular and molecular regulation of tumor necrosis factor-alpha production by pentoxifylline. Biochem. Biophys. Res. Commun. 155:1230-1236, 1988.
2. Remick, D.G., Scales, W.E., May, M.A., Spengler, M., Nguyen, D., and Kunkel, S.L.: *In situ* hybridization analysis of macrophage-derived tumor necrosis factor and interleukin-2 mRNA. Lab. Invest. 59:809-816, 1988.
3. Chensue, S.W., Remick, D.G., Shmyr-Forsch, C., Beals, T., and Kunkel, S.L.: Immunohistochemical demonstration of cytoplasmic and membrane-associated tumor necrosis factor in murine macrophages. Am. J. Pathol. 133:564-572, 1988.
4. Strieter, R.M., Remick, D.G., Lynch, J.P., Spengler, R.N., and Kunkel, S.L.: Interleukin-2-induced tumor necrosis factor-alpha (TNF) gene expression in human alveolar macrophages and blood monocytes. Am. Rev. Respir. Dis. 139:335-342, 1989.

5. Kunkel, S.L., and Remick, D.G.: Toxic effects of cytokines *in vivo*. Lab. Invest. 60:317-319, 1989.
6. 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-1β. Science 243:1467-1469, 1989.
7. Eskandari, M.K., Kunkel, S.L., and Remick, D.G.: Effects of arachidonic acid metabolites and other compounds on the CTLL assay for interleukin-2. J. Immunol. Meth. 118:85-89, 1989.
8. Remick, D.G., Nguyen, D.T., Eskandari, M.K., Strieter, R.M., and Kunkel, S.L.: Cyclorsporine A inhibits TNF production without decreasing TNF mRNA levels. Biochem. Biophys. Res. Commun. 161:551-555, 1989.
9. Spengler, R.N., Spengler, M.L., Strieter, R.M., Remick, D.G., Larrick, J.W., and Kunkel S.L.: Modulation of tumor necrosis factor alpha gene expression: Desensitization of prostaglandin E_2-induced suppression. J. Immunol. 142:4346-4350, 1989.
10. Strieter, R.M., Remick, D.G., Lynch, J.P., III, Genord, M., Raiford, C., Spengler, R., and Kunkel, S.L.: Differential regulation of tumor necrosis factor-alpha in human alveolar macrophages and peripheral blood monocytes: A cellular and molecular analysis. Respir. Cell and Molec. Biol. 1:57-63, 1989.
11. Remick, D.G., Strieter, R.M., Lynch, J.P., III, Nguyen, D., Eskandari, M., and Kunkel, S.L.: *In vivo* dynamics of murine tumor necrosis factor-α gene expression: Kinetics of dexamethasone-induced suppression. Lab. Invest. 60:766-771, 1989.
12. Strieter, R.M., Phan, S.H., Showell, H.J., Remick, D.G., Lynch, J.P., Genord, M., Raiford, C., Eskandari, M., Marks, R.M., and Kunkel, S.L.: Monokine-induced neutrophil chemotactic factor gene expression in human fibroblasts. J. Biol. Chem. (in press)
13. Podrazik, R.M., Obedian, R.S., Remick, D.G., Zelenock, G.B., and D'Lacey, L.G.: Attenuation of structural and functional damage from acute renal ischemia by the 21-amino steroid U74006F in rats. (in press)
14. Kunkel, S.L., Chensue, S.W., Strieter, R.M., Lynch, J.P., and Remick, D.G.: Cellular and molecular aspects of granuloma formation. Am. J. Respir. Cell. Molec. Biol. (in press)
15. Strieter, R.M., Wiggins, R., Phan, S.H., Wharram, B.L., Showell, H.J., Remick, D.G., Chensue, S.W., and Kunkel, S.L.: Monocyte chemotactic protein gene expression by cytokine-treated human fibroblasts and endothelial cells. Biochem. Biophys. Res. Commun. (in press)
16. Spengler, R.N., Spengler, M., Lincoln, P., Remick, D.G., Strieter, R.M., and Kunkel, S.L.: Dynamics of dibutyryl cyclic AMP and prostaglandin E_2-mediated suppression of lipopolysaccharide-induced tumor necrosis factor-α gene expression. Infect. Immun. (in press)
17. Colletti, L.M., Burtch, G.D., Remick, D.G., Kunkel, S.L., Strieter, R.M., Guice, K.S., Oldham, K.T., and Campell, D.A., Jr.: Production of tumor necrosis factor-α and the development of capillary injury following hepatic ischemia/reperfusion. Transplantation Proc. (in press)
18. Davis, P.K., Remick, D.G., Parascandola, S.A., Spangler, S., Wise, R.K., and Martin, L.F.: Intravascular plastic catheters potentiate tumor necrosis factor release and cardiac dysfunction secondary to infection. Current Surgery (in press)

BOOKS/CHAPTERS IN BOOKS:

1. Kunkel, S.L., Scales, W.E., Strieter, R.M., Chensue, S.W., Spengler, R.N., and Remick, D.G>: Modulation of tumor necrosis factor-α and interleukin-1 gene expression. *In*, Otterness, I. (Ed.) The Therapeutic Control of Inflammatory Diseases, Elsevier, New York, New York, 1989.
2. Kunkel, S.L., Strieter, R.M., Chensue, S.W., and Remick, D.G.: Regulation of tumor necrosis factor and neutrophil activating protein-1 gene expression: Potential role of cytokine-directed cell communication during multiple organ injury. In, Brigham, K., and Stahlman, M. (Eds.) Respiratory Distress Syndrome: Molecules to Man, Vanderbilt Press, Nashville, Tennessee, 1989.

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

1. Wharram, B., Fitting, K., Kunkel, S., Remick, D., Fantone, J., and Wiggins, R.: Immune complex-induced monocyte-dependent endothelial cell tissue factor synthesis is mediated by interleukin-1. Eighteenth Annual Michigan Cardiovascular Research Forum, Ann Arbor, Michigan, 1988.
2. Warren, J.S., Yabroff, K.R., Remick, D.G., Kunkel, S.L., Kunkel, R.G., Johnson, K.J., and Ward, P.A.: Intrapulmonary IL-1 and TNF in acute immune complex lung injury in the rat. FASEB, 1989.
3. Shmyr-Forsch, C., Chensue, S.W., Remick, D.G., and Kunkel, S.L.: Immunohistochemical demonstration of interleukin-1α,β and tumor necrosis factor-α synthesis in cultured murine macrophages. FASEB, 1989.
4. Nguyen, D., Eskandari, M., Kunkel, S., and Remick, D.: Inhibition of tumor necrosis factor-α (TNF) by cyclosporin A (CsA). FASEB, 1989.
5. Strieter, R.M., Showell, H.J., Phan, S.H., Remick, D.G., Lynch, J.P., Marks, R.M., and Kunkel, S.L.: Cytokine-induced gene expression of a neutrophil chemotactic factor from cellular and constituents of the alveolar capillary membrane. FASEB, 1989.
6. Eskandari, M., Raiford, C., Nguyen, D., Strieter, R., Kunkel, S., and Remick, D.: Differential regulation of tumor necrosis factor (TNF) production in primary cultures and cell lines. FASEB, 1989.
7. Remick, D., Strieter, R.M., Eskandari, M., Nguyen, D., and Kunkel, S.: *In vivo* stimulation of tumor necrosis factor-1α (TNF) production by interleukin-2 (IL-2). FASEB, 1989.
8. Raiford, C., Spengler, R.N., Spengler, M.L., Allen, R., Remick, D.G., Strieter, R.M., and Kunkel, S.L.: The heat shock response regulates macrophage (MO) derived tumor necrosis factor-α (TNF) gene expression. FASEB, 1989.
9. Genord, M., Strieter, R., Raiford, C., Remick, D., Lynch, J., and Kunkel, S.: Assessment of TNF gene expression in whole blood: An *ex vivo* kinetic analysis. FASEB, 1989.
10. Hanson, C.A., Remick, D.G., Fox, D.A., Bockenstedt, P.L., and Schnitzer, B.: S100-positive chronic lymphoproliferative disease: Association with natural killer (NK) cell expression and function AFIP, 1989.
11. Remick D.G., Strieter, M., Nguyen, D., Eskandari, M., Genord, M., Lynch, J. III, Kunkel, S.L.: Comparison of pathophysiologic effects of exogenous and endogenous tumor necrosis factor. AFIP, 1989.
12. Caty, M.G., Remick, D.G., Schmeling, D.J., Kunkel, S., Guice, K.S., and Oldham, K.T.: Evidence for endotoxin related tumor necrosis factor (TNF) release in intestinal ischemia-reperfusion injury. Natl. Conference on Pediatric Trauma, Ann Arbor, Michigan, 1989.

13. Caty, M.G., Remick, D.G., Schmeling, D.J., Kunkel, S., Guice, K.S., and Oldham, K.T.: Evidence for endotoxin related tumor necrosis factor (TNF) release in intestinal ischemia-reperfusion injury. Twelfth Annual Conference on Shock, Marco Island, Florida, 1989.
14. Caty, M.G. Schmeling, D.J., Guice, K.S., Oldham, K.T., Kunkel, S.L., and Remick, D.G.: Anti-tumor necrosis factor (TNF) antibody attenuates acute lung injury induced by intestinal ischemia and reperfusion. First Annual Department of SUrgery Research Conference, Ann Arbor, Michigan, 1989.
15. Strieter, R.M., Showell, H.J., Phan, S.H., Remick, D.G., Lynch, J.P., Staats, P.S., Raiford, C., Marks, R.M., and Kunkel, S.L.: Neutrophil chemotatic factor gene expression from cellular constituents of the alveolar capillary membrane. American Thoracic Society, 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Responsible for biopsy service four months/year.
B. Responsible for clinical patient diagnostic problems, both in house and state-wide referral, and management thereof on an as needed basis eleven months per year.
C. Responsible for staffing the Oral Diagnosis Clinic in the mornings four months/year.

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. Oral Pathology, Course 624, to Sophomore Dental Students.
D. Oral Pathology Elective, course 818, to Senior Dental Students.
E. Dental Hygiene, Course 220, to Freshmen Students.
F. Dental Hygiene, Course 321, Senior Seminar.
G. Graduate Oral Pathology, Course 694.
H. Graduate Operative Dentistry, Course 691.
I. Graduate Pediatric Dentistry, Course 596.

III. RESEARCH ACTIVITIES:

SPONSORED RESEARCH:

A. Tolerance and efficacy study comparing 15% 5-IODO-2'-deoxyuridine (IDU) in 80% dimethyl sulfoxide (DMSO) and 5% H_20 to control groups of 80% DMSO and 2% DMSO for the treatment of herpes simplex labialis. Principal Investigator. Sponsor: Research Medical, Inc. July, 1985 - October, 1988. Total Direct Costs: $68,696.00

UNDER CURRENT NEGOTIATION:

A. Prevention of Ultraviolet-Induced Recurretn Herpetic Labialis. Squibb Co. 5% Effort. Project Director. (Amount approximately $100,000.00, 2 years).
B. Oral Zovirax in the Treatment of Recurrent Herpes Labialis. Burroughs WEllcome Company. 3% Effort. Project Director. (Amount approximately $50,000.00, 1 year).

IV. ADMINISTRATIVE ACTIVITIES:

A. Director of Diagnostic Laboratory and Consultative Services, Department of Oral Medicine, Pathology, Surgery. Activities include:
   1. Plan and supervise all activities of the various laboratories and consultative services. These include: Research Services, C.T. Hanks, Director, Patient Consultative Services, J.A. Regezi, Director, Anatomic Pathology Services, R.M. Courtney, Director, and Clinical Pathology Services, N.H. Rowe and J.C.B. Stewart, Co-Directors.

B. 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 program.
   2. Provide infection control monitoring services for the School of Dentistry.
   3. Provide, on a fee-for-service basis, infection control monitoring servies for dental health care practitioners in the State of Michigan.

C. Associate Director of the Dental Research Institute. Activities include:
   1. Participant in deliberation of various other committees such as the Scientific Advisory Committee, the Policy Committee, Executive Committe and the Operating Committee of the Institute during its final phase out year.

D. School of Dentistry Committees include:
   1. Department of Oral Medicine/Pathology/Surgery Advisory Committee.
   2. Guest Relations Task Force Committee, Chairman.
   3. Infection Control Committee, School of Dentistry.

REGIONAL AND NATIONAL:

STATE OF MICHIGAN

A. Member, Governor's AIDS and Risk Reduction Polyic Commission.
B. Member, Governor's Task Force on AIDS: Michigan State Medical Society. Physicians Reference Manual.
C. Member, AIDS Speaker's Bureau, Michigan State Medical Society.
D. State of Michigan, Department of Health, Tobacco Use Reduction. Associate Co-Chairman, Committee on Legislation.
E. Member, Executive Committee, American Cancer Society, Michigan Division.
F. Member, Board of Directors, American Cancer Society, Michigan Division.
G. Area Delegate Director, American Cancer Society, Michigan Division.
H. Co-Chairman, Public Issues Committee, American Cancer Society, Michigan Division.
I. Consultant, Committee on Cancer and Infection Control, Michigan Dental Association.
J. Member, Research Screening Committee, Delta Dental Fund.
K. Member, Michigan Coalition on Smoking or Health.

NATIONAL

A. Civilian Professor and Consultant, Office of the Surgeon General, United States Army.
B. National Board of Directors, American Cancer Society, Medical Deligate.
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, Appeals Board, Commission on Dental Accreditation, American Dental Association.
G. Consultant, 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.

2. INTERDEPARTMENTAL:

a. Oral Pathology, clinical consultations on an as needed basis, The University of Michigan Medical School of Dentistry Clinics.
b. Consultant to VA Hospital, Ann Arbor.

B. CONTINUING EDUCATION:

1. UNIVERSITY

a. President, Science Research Club, The University of Michigan.

2. OTHER: LECTURER TO VARIOUS GROUPS INCLUDING:

a. Washtenaw Disterict Dental Hygienists' Society, Ann Arbor, speaker, "Public School Educational Needs Regarding Smokeless Tobacco", September 7, 1988.
b. Trident Continuing Dental Education Seminars, Canada, speaker, "Practical Management of Oral Diseases", September 20-27, 1988.
c. Ninth Dental District Society, Mt. Pleasant, speaker, "Infection Risks in the Dental Operatory", January 4, 1989.
d. Midland County Dental Society, speaker, "Oral Pathology of Interest ot the Dental Practitioner", January 26, 1989.
e. Michigan Dental Association, Annual Meeting, Detroit, speaker, "Oral Pathology of Interest to the Dental Practitioner", April 16, 1989.
f. Nippon Dental Universities, Niigata and Tokyo, Japan, July 30 - August 16, 1988.
g. University of Louisville, Kentucky, speaker, "Oral Cancer", November 17, 1989.

h. Flemish Scientific Dental Congres, Onstend, Belgium, speaker, (Biannual meeting), "Viral Infections Related to Dental Practice", May 5, 1989.
i. Onstend, Belgium, speaker, (Biannual meeting), "Dental Hygiene in the Dental Operatory of Importance for Practitioners", May 6, 1989.
j. University of Ghent, Belgium, "Principles of Infection Pertinent to Disinfection and Sterilization of the Dental Operatory", May 8, 1989.

C. MANUSCRIPT CONSULTANT AND REVIEWER:

1. BARRIER, Infection Control in Dental Practice (Consulting Editor)
2. Journal of the American Medical Association
3. Journal of Oral Pathology
4. Journal of the American Dental Association
5. CANCER
6. Journal of the Academy of General Dentistry

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Jordan, B., McDowell, G. and Rowe, N.H.: An allergic reaction to polysulfide dental impression material. J. Mich. Dent. Assoc. 71:79, Feb. 1989.
2. Rowe, N.H.: Counterpoint: Treating the Patient with AIDS. J. Mich. Dent. Assoc. 71:221, April - May, 1989.
3. Rowe, N.H.: Universal Precautions to Prevent Transmission of Human Immunodeficiency Virus. BARRIER 3 (1):3, 1988.
4. Spruance, S.L., Stewart, J.C.B., Freeman, D.J., Brightman, V.J., Cox, J.L., Wenerstrom, G., McKeough, M.B, and Rowe, N.H.: A multicenter trial of 15% idoxuridine in dimethyl sulfoxide for the treatment of herpes simplex labialis. J. Am. Med. Assoc.
5. Spruance, S.L., Stewart, J.C.B., Rowe, N.H., McKeough, M., Wenerstrom, G., and Freeman, D.: Treatment of recurrent herpes simplex labialis with oral acyclovir. J. Infec. Dis.

BOOKS AND CHAPTERS IN BOOKS:

1. Rowe, N.H.: Dental Caries, Chapter 17. In: Regezi, J.A. and Sciubba, J.J.: Oral Pathology, 1st ed., W.B. Saunders Company. Philadelphia, 1989.
2. Rowe, N.H.: "Viral Infections Related to Dental Practic", In: Proceedings of the Flemish Scientific Dental Congres, (Biannual meeting), Flemish Scientific Dental Congres, Onstend, Belgium, May 5, 1989.

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

1. Steward, J.C.B., Rowe, N.H. and Spruance, S.L.: Treatment of recurrent herpes labialis with idoxuridine in dimethyl sulfoxide. Abstracts of Am. Assoc. ent. Res., 1989.

ROBERT W. SCHMIDT, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Find needle aspiration of superficial tumors, bedside or in clinic, full time (39 weeks) and backup (13 weeks).
B. Gynecologic pathology - consultation service, 12 months.
C. Surgical Pathology - backup coverage. Most outside (transfer) gynecologic pathology cases.
D. Cytopathology, full time (39 weeks) and backup coverage (13 weeks).

II. TEACHING ACTIVITIES:

A. Gynecologic tumor conference, twice weekly.
B. Pathology Residents - Supervision and teaching during cytopathology rotation, for gynecologic surgical pathology cases, and when covering necropsies.
C. Pathology Residents - Gynecologic pathology lecture (4) and parasitology lectures (2).
D. Dental Students - Gynecologic pathology lectures (2).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Radioimmunodiagnosis and Radiotherapy of Ovarian Carcinoma, Richard L. Wahl, M.D., Principal Investigator. NIH-sponsored.

PROJECTS UNDER STUDY:

A. Coexistent endocervical adenocarcinoma and mucinous adenocarcinoma of the ovary: A clinicopathologic study of two cases.
B. Endometrial adenocarcinoma and endometrioid adenocarcinoma of ovaries in a 27-year-old.
C. Glassy cell carcinoma of the cervix.
D. Squamous cell carcinoma of ovary arising in endometriosis: case report.
E. Grandlosa cell tumor of broad ligament: case report.
F. Uterine myxoid leiomyosarcoma: case report and review.

IV. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hopkins, M.P., Roberts, J.A. and Schmidt, R.W.: Cervical adenocarcinoma in situ. Obstetrics and Gynecology. 1988;71:842-844.
2. Hopkins, M.P., Schmidt, R.W., Roberts, J.A. and Morley, G.W.: the prognosis and treatment of stage I adenocarcinoma of the cervix. Obstetrics an Gynecology. 1988;72:915-921.
3. Terada, K.Y., Schmidt, R.W. adn Roberts, J.A.: Malignatn schwannoma of the vulva. The Journal of Reproductive Medicine. 1988;33:969-972.
4. Reid, Gary C., Morley, G.W., Schmidt, R.W. and Hopkins, M.P.: The role of pelvic exenteration for sarcomatous malignancies. Obstetrics and Gynecology. 1989;74:80-84.
5. Reid, G.C., Schmidt, R.W. and Morley, G.W.: Primary melanoma of the vagina (In Press).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

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 Hematopathlogy cases.
G. Review of Southwest Oncology Group (SWOG) cases (circa 200/year).
H. Review of lymphoma cases entered into Children's Cancer Study Group protocols.
I. Diagnostic electron microscopy of lymphoreticular and hematopathology cases.
J. Acting Director, Immunohistochemistry Laboratory July - November 1988 (during Dr. R.V. Lloyd's sabbatical).

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.

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 study 8515 and 8516.

SERVICE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITALS:

A. Hematology Laboratory.
   1. During the past fiscal year, there was an overall increase in the total number of tests from 427,000 to 463,000.
   2. The increase in labor-intensive tests included: a) a 10 per cent increase in differential white blood cell counts; b) and 8 per cent increase in reticulocyte counts; and c) an increase of 30 per cent of microscopic examinations of bloods and fluids by hematopathologists.
   3. New procedures: Labor-intensive procedures related to the autologous bone marrow transplant program (see Clinical Hematology Laboratory report).
   4. Daily in-house, transfer cases, cases from UM clients, and outside consultation are reviewed and signed out with house officers and fellows. When immunologic data (flow cytometry and/or immunohistochemistry) are generated, they are correlated with morphologic findings.
B. University of Michigan Health Service Laboratories.

REGIONAL AND NATIONAL:

A. President Elect, 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 Pathologist of lymphoma cases.
E. Regional Center Review Pathologist, Southwest Oncology Group.
F. Member, Executive Committee, National Panel for Lymphoma Clinical Studies.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARD:

A. American Journal of Clinical Pathology.
B. Human Pathology.
C. Hematologic Pathology. Designated reviewer.

INVITED LECTURES/SEMINARS:

1. "A Practical Approach to Diagnostic Hematological Problems", ASCP Educational Course, San Diego, California, November, 1988. 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; e) Immunologic Classification of Acute Lymphoblastic Leukemias.
2. ASCP Workshop. October, 1988. Acute Lymphoproliferative Disorders. Las Vegas, Nevada.
3. New Horizons in Laboratory Medicine. Non-Hodgkin's Lymphomas and Hodgkin's Disease. Lake Tahoe, Nevada, February 1989.
4. ASCP Workshop. April, 1989. Acute Lymphoproliferative Disorders, Chicago, Illinois.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hanson, C.A., and Schnitzer, B.: Flow cytometric analysis of cytologic specimens in hematologic disease. J. Clin. Lab. Anal. 3:2-7, 1989.
2. Hanson, C.A., Ward, P.C.J., and Schnitzer, B.: A multilobular variant of hairy cell leukemia. Am. J. Surg. Pathol. 1989 (accepted).

BOOKS AND CHAPTERS IN BOOKS:

1. Hyder, D.M., and Schnitzer, B.: Analysis of Hematopoietic Malignancies. In: Use of Surface Markers and DNA Studies in Diagnostic Pathology. D. Keren, (Ed), ASCP Press. 1989.

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

1. Hanson, C.A., Thamilarasan, M., Ross, C.W., Patel, M.J., Stoolman, L.M., Schnitzer, B.: Immunoglobulin, T-cell receptor and BCR gene rearrangements in adult acute lymphoblastic leukemia. Blood 72 (suppl): 203a, 1988.
2. Grossman, D.M., Hanson, C.A., Schnitzer, B.: Simultaneous lymphocyte predominant Hodgkin's disease (LPHD) and large cell lymphoma (LCL). Lab Invest 60:36A, 1989.
3. Grossman, D.M., Hanson, C.A., Klueck, B.D., Hanson,G.A., Schnitzer, B.: Red pulp splenic infiltrates by B-cell immunoblastic lymphomas. Lab Invest 50:36A, 1989.
4. Hanson, C.A., Remick, D.G., Fox, D.A., Bockenstedt, P.L., Schnitzer, B.: S-100 positive chronic lymphoproliferative disease: Association with natural killer (NK) cell expression and function. Lab Invest 60:37A, 1989.
5. Hanson, C.A., Ward, P.C.J., Schnitzer, B.: A multilobular variant of hairy cell leukemia with morphologic similarities to T-cell lymphoma. Lab Invest 60:38A, 1989.
6. Ross, C.W., Schnitzer, B., Stoolman, L.M., Hanson, C.A.: Aberrant antigen expression in adult acute lymphoblastic leukemia. Lab Invest 60:80A, 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

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, "Generation of Therapeutic T Cells from Tumor-Bearing Hosts", American Cancer Society, IM-494 (20%), $135,000/year (270,000/2 years), 1/1/88 - 12/31/90.
B. Principal Investigator, "Adoptive T Cell Immunotherapy of Nonimmunogenic Tumors", NIH Grant 1 R01 CA47285 (50%), $151,921/year ($796,763/5 years), 6/1/88 - 5/31/93.

PENDING:

A. Co-Principal Investigator, "T Cell Therapy of Human Cancer with IVS Lymphocytes", NIH, R01 (15%), $197,601/year ($1,083,756/5 years), 12/1/89 - 11/30/94.
B. Co-Investigator, "Multidisciplinary Treatment of Esophageal Cancer", NIH, R01 (5%), $204,999/year ($718,984/3 years), 12/1/89 - 11/30/92.
C. Co-Principal Investigator, "Adoptive Cellular Therapy of Cancer with Vaccine-Primed Lymphocytes Secondarily sensitized to Autologous Tumor and Expanded in INterleukin-2 In Vitro", American Cancer Society (20%) ($626,531/3 years), 1/1/90 - 12/31/93.

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 and Journal of Biological Response Modifiers.

V. OTHER RELEVANT ACTIVITIES:

A. Member, Experimental Therapeutics II Study Section, NCI, NIH, 1989-.
B. Special reviewer, Small Business Innovation Research (SBIR) Study Section, NIH, July 26, 1988 and April 4, 1989.

INVITED LECTURES AND SEMINARS:

A. Department of Pathology, University of Kansas, "Therapy of Cancer with Sensitized Lymphocytes", November 30, 1988.
B. Department of Microbiology, Medical College of Ohio, "Principles and Potential for Cancer Therapy with Immune T Lymphocytes", June 7, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ward, B.A., Shu, S., Chou, T., Perry-Lalley, D.M. and Chang, A.E.: Cellular basis of immunologic interactions in adoptive T cell therapy of established metastases from a syngeneic murine sarcoma. J. Immunol. 141:1047-1053, 1988.
2. Chou, T., Bertera, S., Chang, A.E., and Shu, S.: Adoptive immunotherpay of microscopic and advanced visceral metastases with in vitro sensitized lymphoid cells from mice bearing progressive tumors. J. Immunol. 141:1775-1781, 1988.
3. Stephenson, K.R., Perry-Lalley, D.M., Griffith, K.D., Shu, S., and Chang, A.E.: Development of antitumor reactivity in regional draining lymph nodes from tumor-immunized and tumor-bearing murine hosts. Surgery 105:523-528, 1989.
4. Chang, A.E., Perry-Lalley, D.M., and Shu, S.: Distinct Immunologic Specificity of Tumor Regression Mediated by Effector Cells Isolated from Immunized and Tumor-Bearing Mice. Cell. Immunol. 120:419-429, 1989.
5. Shu, S., Chou, T., Sakai, K: Lymphocytes generated by in vivo priming and in vitro sensitization demonstrate therapeutic efficacy against a murine tumor that lacks apparent immunogenicity. J. Immunol. 143 (in press), 1989.

BOOKS/CHAPTERS IN BOOKS:

1. Shu, S., Chou, T., Saki, K., and Chang, A.E.: Development of adoptive immunotherapy with in vitro sensitized T lymphocytes from mice bearing progressively growing tumors. In: Role of Interleukin-2 Activated Killer Cells in Cancer. Ed. E. Lotzova. Published by CRC Press, Inc. Boca Ration, FL., 1988.

ABSTRACTS, BOOK REVIEWS, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Shu, S., Chou, T., and Sakai, K.: Generation of T lymphocytes with therapeutic efficacy against a nonimmunogenic murine tumor. American Association for Cancer Research (Annual Meeting), 1989.
2. Logan, T.F., Shu, S.,, Bahnson, R.R., Leong, S.P.L., Banner, B.B.: Generation of specific cytolytic cells from patients with melanoma and renal cell carcinoma by in vitro sensitization. American Association for Cancer Research (Annual Meeting), 1989.
3. Chang, A.E., Perry-Lalley, D.M., and Shu, S.: Different immunologic specificity of tumor regression mediated by effector cells from immunized versus tumor-bearing mice. American Association for Cancer Research (Annual Meeting), 1989.
4. Sondak, V.K., Shu, S., and Chang, A.E.: Differences in the induction of antitumor reactive T cells by visceral versus subcutaneous tumor growth. Society of Surgical Oncology (Annual Meeting), 1989.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Coverage of M-Labs cases including all cases from:

1. Albion Community Hospital, Albion, Michigan.
2. Newman Laboratories, Dearborn, 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.
C. Clinical consultations and Hematology review at Chelsea Community Hospital, Chelsea, Michigan.
D. Rotation with other staff pathologists.
   1. Five weeks coverage at the University Hospital of evening frozen sections.
   2. 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 M-Labs 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 and Pharmacy and Therapeutics Committees, Albion Community Hospital.
F. Director of Laboratories, Chelsea Hospital, Chelsea, Michigan.

G. Tissue Committee, Chelsea Hospital, Chelsea, Michigan.
H. Laboratory Committee, Chelsea Hospital, Chelsea, Michigan.

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

VI. **PUBLICATIONS:**

1. Silverman, E.M., Reznick, H.A. and Wolf, B.A. Chronic Lymphocytic Leukemia Presenting in the Marrow of a Phalanx. The Journal of Foot Surgery. 28:151-153, 1989.

JAMES E. SMOLEN, PH.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENTS OF PEDIATRICS AND PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. **CLINICAL ACTIVITIES**: None.

II. **TEACHING ACTIVITIES**: None.

III. **RESEARCH ACTIVITIES**:

SPONSORED SUPPORT

A. NIH grant DK32471, "The Initiation of Granulocyte Responses". James Smolen, Principal Investigator (75% effort). $166,455 from 12/1/87 to 11/30/92.
B. NIH grant NHLBI-HL31963-05, "Inflammatory Cells and Lung Injury". Peter Ward, Principal Investigator (20% effort). $17,000 from 4/1/84 to 3/11/88.
C. Children's Leukemia Foundation of Michigan. "Purine Nucleotides as Mediator of Neutrophil Secretion and Oxygen Radical Production". Richard A. Axtell, Principal Investigator (5% effort). $25,000 from 7/1/89 to 6/30/89.

IV. **ADMINISTRATIVE ACTIVITIES:**

DEPARTMENTAL: None.

MEDICAL SCHOOL/HOSPITAL:

University of Michigan, Medical School Admissions Committee, 1988 - present.

REGIONAL AND NATIONAL:

A. NIH, special study section for neutrophil program projects, 1989.
B. NIH, special study section for individual proposal, 1989.
C. Review of individual proposals for National Science Foundation, 1984-1989.

V. **OTHER RELEVANT ACTIVITIES:**

INVITED LECTURES AND SEMINARS: None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Stoehr, S.J., and Smolen, J.E.: Osmotic forces are not critical for Ca^{2+}-induced secretion from permeabilized human neutrophils. J Cell Physiol 135:169-178, 1988.
2. Sandborg, R.R. and Smolen, J.E.: The effects of heavy metal cations and sulfhydryl reagents on degranulation from digitonin-permeabilized neutrophils. Biochim Biophys Acta 1010:330-337, 1989.
3. Smolen, J.E., Stoehr, S.J., and Bartone, D.: Protein kinase C is not involved in secretion by permeabilized human neutrophils. Cell Signal (in press), 1989.

BOOKS AND CHAPTERS IN BOOKS:

1. Boxer, L.A., and Smolen, J.E.: Neutrophil granule constituents and their release in health disease, in: Hematology/Oncology Clinics. Phagocytic Defects I, ed. J.T. Curnette, III, W.B. Saunders Co., pp. 101-134, 1988.
2. Sandborg, R.R, and Smolen, J.E.: Early events in leukocyte activation, in Lab Invest 59:300-320, 1988.
3. Smolen, J.E.: Characteristics and mechanisms of secretion by neutrophils, in The Neutrophil: Cellular Biochemistry and Physiology, ed M.B. Hallett, CRC Press Inc., Boca Raton, FL, pp. 23-61, 1989.
4. Smolen, J.E., and Boxer, L.A.: Functions of Neutrophils, in, Hematology 4th edition, eds, W.J. Williams, E. Beutler, A.J. Ersley and M.A. Lichtman, McGraw-Hill (in press).

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

1. Stoehr, S.J., Balazovich, K.J. and Smolen, J.E.: Protein Kinase C of Human Neutrophils Utilizes GTP as an Alternate Phosphate Donor, Clin. Res., 1988;36:420A.
2. Sandborg, R. and Smolen, J.E.: Heavy Metals Induce Granule Secretion from Permeabilized Neutrophils, FASEB J., 1988;2:1584A.
3. Axtell, R.A. Smolen, J.E., and Boxer, L.A.: Human Neutrophils Require Adenine Nucleotides for Full Activity of the Soluble Component of the NADPH Oxidase, Clin. Res., 1988;36:839A.
4. Axtell, R.A., Smolen, J.E. Boxer, L.A.: Human Neutrophils (PMN) Require Adenine Nucleotides for Full Activity of the Soluble Component of the NADPH Oxidase, Blood 1988;72:141A.
5. Stoehr, S.J., Suchard, S.J. and Smolen, J.E.: Lipocortin I and II are the Major Substrates fo Neutrophil Protein Kinase C in Extracts from Human Neutrophils, Blood 1988;72:153A.
6. Stoehr, S.J., Smolen, J.E., and Suchard, S.J.: Lipocortins I and II are Major Substrates of Neutrophil Protein Kinase C in vitro, FASEB. J. 1989;3:A962.
7. Smolen, J.E. and Balazovich, K.J.: Characteristics of Ca^{2+}-induced Section by Electropermeabilized Human Neutrophils, FASEB J. 1989;3:A1087.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

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 post-doctoral 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. Tai-Ling Wang, M.D. Chairwomen, Department of Pathology, Japanese-Chinese Friendship Hospital, Bejing, China-visiting scholar studying the expression of receptors for the extracellular matrix in cultured human T-lymphoblastic leukemias.
3. Zhiwei Song, M.S., Graduate student, University of Michigan, School of Medicine, Department of Biochemistry - (1) distribution and functional significance of leukocytic glycoconjugates containing terminal mannose residues recognized by the Snow Drop lectin and (2) characterization of the endogenous carbohydrate ligand for the peripheral lymph node homing receptor of normal and malignant lymphoid cells.
4. Praveen Reidy, Undergraduate student, University of Michigan, School of Arts and Sciences, Departments of Archeology and Psychology- co-investigator with Dr. Jim Grober in the study of adhesive interactions between leukocytes and endothelium in rheumatoid synovium.

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

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

D. Lecturer, Hematopathology, Medical School.

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

F. Lecturer, Clinical Applications of Flow Cytometry, Pathology Residents Core Lecture Series.

G. Pediatric/Adult Leukemia Conferences.

H. Adult Lymphoma Conferences.

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

III. RESEARCH ACTIVITIES:

SPONSORED RESEARCH:

FUNDED:

A. NIH, R01 ($425,000; 3 years; 30 September 1989 through 31 August 1992): Endothelial Binding Lectins of Lymphoid Malignancies.
B. NIH, NCI Physician Investigator Award, competitive renewal ($136,000; 2 years; 1 April 1988 through 31 May 1990): Lymphocyte migration and the metastatic process.
C. NIH, Multipurpose Arthritis Center, Development and Feasability Grant ($143,469; 3 years; 1 February 1988 through 31 January 1991): The role of lymphocyte migration in chronic inflammatory arthritis.

IN PREPARATION:

A. NIH, R01: Leukocyte-endothelial interactions in chronic rheumatoid synovitis.

PROJECTS UNDER STUDY:

A. Transmembrane signalling and the control of endothelial adhesion receptors during lymphocytic migration and activation. Specifically, the detection of transmembrane signals initiated by the organ-selective attachment of lymphocytes to the high endothelial venules of lymph nodes.
B. Characterization of the endogenous carbohydrate ligand for the lymph node homing receptor of normal and malignant lymphocytes. Recently purified lectins specific for sialic acid in the 2,3 and 2,6 linkages will be used to confirm the role of endothelial sialic acid in the lymphocyte-endothelial adhesive interaction, establish the linkage of the endogenous carbohydrate ligand and attempt purification.

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. Coordinator, Pathology Services (clinical) in The University of Michigan Cancer Center.
B. Member, The University of Michigan Cancer Center Clinical and Basic Research Implementation Committees.

INVITED LECTURES AND SEMINARS:

1. Miles Pharmaceuticals, Inc. Research Laboratories, invited speaker, 1988
2. Genentech, Inc., invited speaker, 1989
3. University of Wisconsin Department of Pathology, invited speaker 1989
4. University of California at San Francisco Department of Laboratory Medicine, invited speaker, 1989

5. Federation of American Societies for Experimental Biology, workshop, chairman, 1989
6. Federation of American Societies for Experimental Biology, minisymposium speaker, 1989
7. American Thoracic Society Annual Meeting, invited speaker, 1989
8. American Society of Clinical Pathologists, workshop, invited speaker, 1989
9. Biogen Inc., invited speaker, 1989
10. FASEB Summer Symposium Series, invited speaker, 1989

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.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Stoolman, I.M. 1989. Adhesion molecules controlling lymphocyte recirculation. Cell. 56: 907.
2. Stoolman, L.M and H. Ebling. 1989. Adhesion molecules of cultured hematopoetic malignancies: a calcium-dependent lectin is the principle mediator of binding to the high endothelial venule of lymph nodes. J. Clin. Invest. (in press).
3. Strahler, J.R., Kuick, R., Eckerskorn, Lottspeich, F., Richardson, B.C., Fox, D.A., Stoolman, L.M., Hanson, C.A., Nichols, D., Tueche, H.J. and S.M. Hanash. 1989. Identification of two related markers for common acute lymphoblastic leukemia as heat shock proteins. J. Clin. Invest. (in press).
4. Hanson, C.A., Thamilarasan, M., Ross, C.W., Stoolman, L.M. and Schnitzer, B. 1989. Kappa light-chain gene rearrangement in T-cell acute lymphoblastic leukemia. Am. J. Clin. Path. (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Ross, C.W., Stoolman, L.M., Schnitzer, B., Schlegelmilch, J.A. and Hanson, C.A. 1989. Immunophenotypic aberrancy in adult acute lymphoblastic leukemia.
2. Stoolman, L.M., Wang, L. and J. Varani. 1989. Regulation of fibronectin and laminin binding activity in human T-lymphoblastic cell lines.

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

1. Hanson, C.A., Thamilarasan, M., Ross, C.W., Patel, M.J., Schnitzer, B. and Stoolman, L.M. 1989. Immunoglobulin, T-cell receptor and BCR gene rearrangements in adult acute lymphoblastic leukemia (ALL). International Academy of Pathology Annual Meeting.

2. Ross, C.W., Schnitzer, B., Stoolman, L.M. and C.A. Hanson. 1989. Aberrant antigen expression in adult acute lymphoblastic leukemia. International Academy of Pathology Annual Meeting.
3. Stoolman, L.M., Wang, L., Ebling, H. and J. Varani. 1989. The Regulation of intercellular, matrix and HEV adhesion during phorbol activation of human lymphoblastic cell lines. FASEB Journal. 3(4): A1319.
4. Stoolman, L.M. and H. Ebling. 1989. Rapid up and down regulation of the human lymphocyte-nodal HEV interaction by phorbol esters. J. Cellular Biochem. 13A(Supplement): 146.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Neutrophil function assays

II. TEACHING ACTIVITIES:

A. Medical students (ICS-Immunopathology)
B. Dental students (Dental Course 630)
C. Postdoctoral fellows, residents, undergraduate students

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Thermal Injury, ATP Depletion and Oxygen Radicals (GM-39397). Principal Investigator.
B. Thermal Injury, "Complement and Leukocyte Dysfunction (GM-28499). Co-Principal Investigator with Dr. P.A. Ward.
C. Lung Injury Produced by Oxygen Metabolites (GM-29507). Co-Principal Investigator with Dr. P.A. Ward.

PROJECTS UNDER STUDY:

A. Pathophysiology of oxygen radical-mediated acute inflammatory tissue injury: Role of complement, neutrophils, histamine, and xanthine oxidase.
B. Experimental thermal injury: Role of complement, leukocytes, mast cells, and xanthine oxidase.
C. Mechanisms of ischemia-reperfusion injury of the liver
D. Pathophysiology of edema formation in thermally injured skin

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. Reviewer for the following scientific journals: American Journal of Pathology, American Journal of Physiology, American Review of Respiratory Disease, Immunobiology, Infection and Immunity, Journal of Clinical Investigation, Laboratory Investigation, Transfusion.

V. OTHER RELEVANT ACTIVITIES:

A. Member, Editorial Advisory Board, Immunobiology.

VI. PUBLICATIONS:ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Morgan, R.A., Manning, P.B., Coran, A.G., Drongowski, R.A., Till, G.O., Ward, P.A., Oldham, K.T.: Oxygen free radical activity during live E. coli septic shock in the dog. Circ. Shock 1988;25:319-323.
2. Rao, N.A., Fernandez, M.A., Sevanian, A., Romero, J.L., Till, G.O., Marak, G.E.: Treatment of experimental lens-induced uveitis by dimethylthiourea. Ophthalmic. Res. 1988;20:106-111.
3. Teng, C.-L.C., Kim, J.-S., Port, F.K., Wakefield, T.W., Till, G.O., Yang, V.C.: A protamine filter for extracorporeal blood heparin removal. ASAIO. Trans. 1988;34:743-746.
4. Brothers, T.E., Graham, L.M., Till, G.O.: Systemic effects of prosthetic vascular graft implantation. Surgery 1988;104:375-382.
5. Marak, G.E., de Kozak, Y., Faure, J.P., Rao, N.A., Romero, J.L., Ward, P.A., Till, G.O.: Pharmacologic modulation of acute ocular inflammation. I. Adenosine. Ophthalmic Res. 1988;20:220-226.
6. Oldham, K.T., Guice, K.S., Till, G.O., Ward, P.A.: Activation of complement by hydroxyl radical in thermal injury. Surgery 1988;104:272-279.
7. Wakefield, T.W., Till, G.O., Lindblad, B., Saenz, N., Stanley, J.C.: Complement depletion and persistent hemodynamic-hematologic responses in protamine-heparin reactions. J. Surg. Res. 1988;45:320-326.
8. Wolter, J.R., Till, G.O.: Protein deposition and leukocyte accumulation on lens implants: following exposure to whole blood in vitro. Implants Ophthalmol. 1988;2:159-163.
9. Oldham, K.T., Guice, K.S., Till, G.O., Ward, P.A.: Evidence of local complement activation in cutaneous thermal injury in rats. Prog.Clin.Biol.Res. 264:421- 424, 1988
10. Till, G.O., Guilds, L.S., Mahrougui, M. Friedl, H.P., Trentz, O., Ward, P.A.: Role of xanthine oxidase in thermal injury of skin. Amer J. Pathol. (in press).
11. Friedl, H.P., Till, G.O., Trentz, O., Ward, P.A.: Roles of histamine, complement and xanthine oxidase in thermal injury of skin. Amer. J. Pathol. (in press).
12. Wolter, J.R., Till, G.O.: Multinucleated giant cells on Bruch's membrane in recurrent retinal and subretinal hemorrhaging. Ophthalmologica (in press).
13. Wolter, J.R., Till, G.O.: Granulocyte invasion related to detachment and degeneration of corneal endothelium in acute kerato-uveitis. Cornea (in press).
14. Lawton, J.W.M., Robinson, J.P., Till, G.O.: The effect of intravenous immunoglobulin on the in vitro function of human neutrophils. Immunopharmacol. (in press).
15. Sullivan, J.L., Till, G.O., Ward, P.A., Newton, R.B.: Nutritional iron restriction diminishes acute complement-dependent lung injury. Nutrition Res. (in press).
16. Friedl, H.P,. Cramer, T., Guerra, E.E, Till, G.O., Toledo-Pereyra, L.H.: Role of histamine and xanthine oxidase in experimental ischemia-reperfusion injury of the liver. Transplant. Proc. (in press).

17. Friedl, H.P., Smith, D.J., Thomson, P.D., Louis, D.S., Till, G.O., Ward, P.A.: Histamine and xanthine oxidase activity in a human model of ischemia-reperfusion injury. Surg. Forum (in press).
18. Friedl,. H.P., Caty, M.G., Guice, K.S., Oldham, K.T., Till, G.O.: Oxygen radical-mediated acute pancreatitis: a role for histamine. Surg. Forum (in press).
19. Morganroth, M.L., Schoeneich, S.O., Till, G.O., Pickett, W., and Ward, P.A.: Complement and neutrophil-mediated lung injury is attenuated in rats raised on an essential fatty acid deficient diet. Amer. J. Physiol. (in press).
20. Morganroth, M.L., Schoeneich, S.O., Till, G.O., Ward, P.A., Glovsky, M.M.: C3a 57-77, a C-terminal peptide of C3a causes thromboxane-dependent pulmonary vascular constriction in isolated perfused rat lungs. Am. J. Pathol. (in press).
21. Thomson, P.D., Till, G.O., Woolliscroft, J.O., Prasad, J.K., Smith, D.J.: Superoxide dismutase prevents lipid peroxidation in burn patients. J. Trauma (in press).
22. Friedl, H.P., Till, G.O., Ryan, U.S., Ward, P.A.: Mediator-induced activation ofxanthine oxidase in endothelial cells. FASEB J. (in press).
23. Winn, W.C., Davis, G.S., Durda, J.P., Till, G.O.: The effect of neutropenia on experimental Legionella pneumonia. Infec. Immun. (in press).
24. Caty, M.G., Schmeling, D.J., Friedl, H.P., Oldham, K.T., Guice, K.S., Till, G.O.: Histamine: a promoter of xanthine oxidase activity in intestinal ischemia-reperfusion. J.Ped.Surg. (in press).
25. Marak, G.E., Till, G.O., Ward, P.A.: Xanthine oxidase generation of toxic oxygen metabolites in acute uveitis. Internat..Ophthalmol. (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Till, G.O., Friedl, H.P., Morganroth, M.L., Phan, S.H., Schuger, L.A., Grum, C.M., Varani, J., Ryan, U.S., Ward, P.A.: Neutrophil-mediated injury of endothelial cells and lung: Evidence for role of xanthine oxidase and histamine. Am. J. Pathol. (submitted).
2. Sannomiya, P., Craig, R.A., Clewell, D.B., Suzuki, A., Fujino, M. Till, G.O., Marasco, W.A.: Characterization of a new class of bacteria-derived neutrophil chemotactic peptides, the sex pheromones. Proc. Natl. Acad. Sci. (submitted).
3. Woolliscroft, J.V., Prasad, J.K., Thomson, P., Till, G.O., Fox, I.H.: Evidence for adenosine triphosphate breakdown and lipid peroxidation in burned patients. J. Trauma (submitted).
4. Yang, V.C., Port, F.K., Teng, C.-L.C., Kim, J.-S., Till, G.O., Wakefield, T.W.: Pr evention of heparin-induced hemorrhage and protamine-induced complications in animals during an extracorporeal blood circulation procedure. J. Clin. Invest. (submitted).
5. Friedl, H.P., Smith, D.J., Till, G.O., Thomson, P.D., Louis, D.J., Ward, P.A.: Ischemia-reperfusion in humans: Appearance of xanthine oxidase activity. J.Clin.Invest. (submitted).

BOOKS AND CHAPTERS IN BOOKS:

1. Ward, P.A., Johnson, K.J., Till, G.O., Warren, J.S.: Activated phagocytes, oxygen radicals, and tissue injury; In: Chow, C.K., (ed), Cellular Antioxidant Defense Mechanisms, 1st Edition, Chapter 10, pp. 151-157, CRC Press, Inc., Boca Raton, 1988.
2. Ward, P.A., Macconi, D., Sulavik, M.C., Till, G.O., Warren, J.S., Johnson, K.J., Powell, J.: Rat neutrophil-platelet interactions in oxygen radical-mediated lung injury; In: Cerutti, P.A., Fridovich, I., McCord, J.M. (eds.), Oxy-Radicals In Molecular Biology and Pathology, pp. 83-98, Alan R. Liss, Inc., New York, 1988.

3. Till, G.O., Warren, J.S., Gannon, D.E., Chensue, S.W., Kunkel, S.L., Varani, J., Johnson, K.J., Ward, P.A.: Effects of pentoxifylline on phagocyte responses in vitro and acute and chronic inflammatory reactions in vivo; In: Mandell, G.L., and Novick, W.J. (eds.) Pentoxifylline and Leukocyte Function; Hoechst-Roussel Pharmaceuticals Inc., Sommerville, New Jersey, pp. 124-137, 1988.
4. Friedl, H.P., Till, G.O., Ward,P.A., Trentz, O.: Bedeutung der Xanthinoxidase am mikrovaskulaeren Permeabilitaetsschaden nach Verbrennungstrauma II.o; In: Chirurgisches Forum 1989 f.experim. u. klinische Forschung, pp 59-62; H. Hamelmann (Hrsg.); Springer-Verlag, Berlin Heidelberg, 1989.
5. Marak, G.E., Rao, N.A., Gannon, D.E., Varani, J., Ward, P.A., Till, G.O.: Antiphlogistic mechanisms of benzoic derivatives in experimental uveitis. In: Modern Trends in Immunology and Immunopathology of the Eye, pp 137-139; Eds: Secchi, A.G., Fregona, I.A., Masson, Milano, 1989.
6. Till, G.O., Friedl, H.P., Ward, P.A., Trentz, O.: Komplementsystem und Xanthinoxidase-vermittelter mikrovaskulaerer Permeabilitaetsschaden nach Verbrennungstrauma II.o In: Chirurgisches Forum 1989 f. experim. u. klinische Forschung, pp55-58; H. Hamelmann (Hrsg.); Springer-Verlag, Berlin Heidelberg, 1989.
7. Ward, P.A., Warren, J.S., Till, G.O., Varani, J., Johnson, K.J.: Modification of disease by preventing free radical formation: a new concept in pharmacologic intervention, in: Hershko, C. (ed.) Bailliere's Clinical Hematology: International Practice and Research; Vol.2, No 2 Iron Chelating Therapy, pp. 391-402. W.B. Saunders, London, UK , 1989.
8. Ward, P.A., Till, G.O., Gannon, D.E., Varani, J., Johnson, K.J.: The role of iron in injury of endothelial cells in vitro and in vivo. In: Oxygen Radicals in Biology and Medicine, pp 969-974; Eds.: Simic, M.G., Taylor, K.A., Ward, J.F., von Sonntag, C.; Plenum Publishing Corp., London, 1989.
9. Ward, P.A., Warren, J.S., Till, G.O., Varani, J., Johnson, K.J.: Free radicals in lung disease. In: Proceedings on Free Radicals, Diseases States and Anti-Radical Interventions (in press).
10. Till, G.O., Friedl, H.P., Ward, P.A.: Phagocytic cell-mediated injury: relationship to ischemic injury. In: Clinical Ischemic Syndromes: Mechanisms and Consequences of Tissue Injury. Mosby Co., St. Louis (in press).
11. Till, G.O., Ward, P.A.: Complement-induced lung injury. In: Said,S.I. (ed), The Pulmonary Circulation and Acute Lung Injury, 2nd edition; Mount Kisco, N.Y., Futura Publishing Co. (in press).
12. Ward, P.A., Till, G.O., Johnson, K.J.: Oxygen-derived free radicals and inflammation; Proc.Am.Orthopaed. Soc. (in press).
13. Till, G.O., Friedl, H.P., Ward, P.A.: Antioxidant treatment in experimental thermal injury. In: Emerit, I., Auclair, C., Packer, L. (eds.) Antioxidants in Therapy and Preventive Medicine. Plenum Publishing Co.,London, (in press).

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

1. Friedl, H.P., Till, G.O., Guilds, L.S., Mahrougui, M., Ward, P.A.: Thermal injury of rats. Enhancement of xanthine oxidase activity by histamine. FASEB J. 3:A1320, 1989.
2. Till, G.O., Friedl, H.P., Guilds, L.S., Mahrougui, M., Ward, P.A.: Role of histamine in oxygen radical-mediated acute lung injury. FASEB J. 3:A1049, 1989.
3. Caty, M.G., Friedl, H.P., Oldham, K.T., Guice, K.S., Till, G.O.: A role for histamine in the pathogenesis of intestinal ischemia-reperfusion injury. FASEB J. 3:A625, 1989.
4. Bagnasco, J.M., Friedl, H.P., Guice, K.S., Oldham, K.T., Till, G.O.: Measurement of xanthine oxidase activity in rat plasma. FASEB J. 3:A628, 1989.

5. Guilds, L.S., Till, G.O., Mahrougui, M., Friedl, H.P., Ward, P.A.: Protection against complement-mediated acute lung injury by diclofenac sodium. FASEB J. 3:A289, 1989.
6. Mahrougui, M., Till, G.O., Guilds, L.S., Friedl, H.P., Ward, P.A.: Evidence for in vivo and in vitro scavenging of hydroxyl radical by cimetidine. FASEB J. 3:A1233, 1989.
7. Till, G.O., Friedl, H.P., Ward, P.A., Trentz, O.: Role of complement, histamine and xanthine oxidase in oxygen radical-mediated microvascular injury post burn. Circ.Shock 27:335, 1989.
8. Friedl, H.P., Till, G.O., Ward, P.A., Trentz, O.: Oxygen radical-mediated acute lung injury: enhancement of xanthine oxidase activity by histamine. Circ.Shock 27:366, 1989
9. Till, G.O., Friedl, H.P., Guilds, L.S., Ward, P.A.: Antioxidant treatment in experimental thermal injury. International Meeting Soc. Free Radic. Res., Paris, December 9-10,1989.
10. Wakefield, T.W., Brothers, T.E., Hantler, C.B., Till, G.O., Stanley, J.C., Kirsh, M.M.: Complement activation: absent role in adverse protamine responses. Annual Meeting Assoc. Acad. Surg. Salt Lake City, November 16-19, 1988.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. TEACHING ACTIVITIES:

A. Three postdoctoral fellows, two visiting scientists, one graduate student and several undergraduate students worked in my laboratory.
B. Participated in the graduate student/dental student pathology course.
C. Participated in the Tissue Culture Methods Course offered by the Department of Epidemiology; School of Public Health.

II. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Inhibition of Tumor Cell Chemotactic Responses by Prostaglandins. BC-512, Principal Investigator, 25% effort, $55,512 current annual direct cost, American Cancer Society.
B. Laminin/Laminin Receptors in NK/NC Cell Function. IM-432. Principal Investigator, 25% effort, $72,000 current direct cost, American Cancer Society.
C. Thrombospondin and Squamous Carcinoma Cell Behavior. PDT-324, Co-Principal Investigator, 25% effort, $70,000 current annual direct costs, American Cancer Society.
D. Biochemical Control of Microcarrier Culture. CA3352. Principal investigator on subcontract, 10% effort, $22,200. Current annual direct costs. National Institutes of Health.
E. Mechanisms of neutrophil-mediated and monocyte-mediated killing of endothelial cells.

PROJECTS UNDER STUDY:

A. Regulation of chemotactic responses in tumor cells by prostaglandins produced by the tumor cells and by other cells.
B. The development of substrates for optimum growth of cells in large-scale culture.
C. The role of laminin and laminin receptors in mediating NK/NC-tumor cell interactions.
D. The role of thrombospondin in the biology of human squamous carcinoma cells.

III. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Member, Departmental Advisory Committee on Appointments, Promotion and Tenure.
B. Member, Departmental Review Committee.
C. Member, Departmental Advisory Committee on Space Allocation.

MEDICAL SCHOOL/HOSPITAL:

A. Director, Cancer Center Program on Tumor Cell Metastasis and the Extracellular Matrix.
B. Member, Kellogg Research Internship Program.

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. Chairman of NIH special study section 006.

IV. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Speaker, FASEB Conference on "Biology of Tumor Metastasis", Saxon River, Vermont, July 26-31, 1987.
2. Invited Speaker, Second International Conference on Squamous Carcinoma, Alexandria, Virginia, September 9-13, 1987.
3. Session Moderator, Second International Conference on Squamous Carcinoma, Alexandria, Virginia, September 9-13, 1987.
4. Invited Speaker, Pathology Seminar Series VAMC-Wayne State University, Allen Park, Michigan, May 9, 1987.
5. Invited Participant, Second Annual Recent Advances in Biotechnology Symposium, Lansing, Michigan, June 17-18, 1987.
6. Invited Speaker, Pathology Seminar Series VAMC-Wayne State University, Allen Park, Michigan, May 9, 1987.
7. Invited Speaker, Department of Pharmacology, Baylor College of Medicine, Houston, Texas, November 20, 1987.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Varani, J., McKeever, P.E., Fligiel, S.E.G., Sitrin, R.G.: Plasminogen activator production by human tumor cells: Effect on tumor cell - extracellular matrix interactions. Int.J. Cancer, 40:772-777, 1987.

2. Riser, B.L., Varani, J., O'Rourke, K., Dixit, V.M.: Thrombospondin binding by human squamous carcinoma and melanoma cells. Exp. Cell Res., 74:319-329, 1988.
3. Gannon, D.E., Varani, J., Phan, S.H., Ward, J.H., Kaplan, J., Till, G.O., Simon, R.G., Ryan, U.S., Ward, P.A.: Source of iron in neutrophil-mediated killing of endothelial cells. Lab. Invest., 57:37-44, 1987.
4. Chakrabarty, S., Brattain, M.G., Ochs, R.L., Varani, J.: Modulation of fibronectin, laminin and cell adhesion in the transformation and differentialtion of murine AKR fibroblasts. J. Cell Physiol., 133:415-425, 1987.
5. McKeever, P.E., Hood, T.W., Varani, J., Taren, J.A., Beierwaltes, W.H., Wahl, R., Liebert, M. and Nguyen, P.K.: Products of cells cultured from gliomas: IV. Cytology and morphometry of two cell types cultured from gliomas, J. Nat. Cancer Inst., 78:75-84, 1987.
6. Varani, J., Bendelow, M.J., Sealey, D., Gannon, D., Ryan, U., Kunkel, S.L., Ward, P.A.: TNF-induced susceptibility of endothelial cells to neutrophil-mediated killing. Lab. Invest. (in press).
7. Ginsburg, I., Fligiel, S.E.G., Kunkel, R., Varani, J.,: Phagocytosis of Candida Albicans enhances malignant behavior of murine tumor cells. Science, 238:1573-1575, 1988.
8. Varani, J., Nickoloff, B., Mitra, R.S., Riser, B., O'Rourke, K., Dixit, V.M.: Thrombospondin induced adhesion of human keratinocytes. J. Clin. Invest. 88:1537-1544, 1988.
9. Ginsburg, I., Ward, P.A., Varani, J.: Lysophosphatides enhance superoxide responses of stimulated human neutrophils. Inflammation (in press).
10. Ginsburg, I., Fligiel, S.E.G., Ward, P.A., Varani, J.: Lipoteichoic acid-anti-lipoteichoic acid complexes induce superoxide generation by human neutrophils. Inflammation (in press).
11. Chakrabarty, S., Tobon, A., Varani, J., Brattain, M.G.: Transforming growth factor-beta induces carcinoembryonic antigen secretion, modulates protein secretion/expression and fibronectin/laminin expression in human colon carcinoma cells. Cancer Res. (in press).
12. Frenette, G.P., Carey, T.E., Varani, J., Schwartz, D.R., Fligiel, S.E.G., Ruddon, R.W., Peters, B.P.: Biosynthesis and secretion of laminin and laminin-associated glycoproteins by nonmalignant and malignant human keratinocytes: A comparison of cell lines from primary and secondary tumors in the same patient. Cancer Res. (in press).
13. Grimstad, I.A., Thorsrud, A.K., Varani, J., Ward, P.A., Jellum, E.: Marker polypeptide differences between spontaneously strongly and weakly metastatic cancer cells identified by 2-dimensional gel electrophoresis. Int. J. Cancer 41:567-572, 1988.
14. Varani, J., Fligiel, S.E.G., Inman, D.R., Helmreich, D.L., Bendelow, M.J., Hillegas, W.J.: Substrate-dependent differences in production of extracellular matrix molecules by squamous carcinoma cells and diploid fibroblasts. Biotech. Bioengineer. (in press).
15. Varani, J., Bendelow, M.J., Hillegas, W.J.: Effect of substrate on production of infectious virus by cells in culture. J. Biol. Stand. (in press).
16. Riser, B.L., Laybourn, K.A., Varani, J.: Treatment of mice with anti-asialor-GM_1 antibody or poly I:C.: Effects on metastasis dissociable from modulation of macrophage anti-tumor activity. Nat. Immun. Cell Growth Regul. (in press).
17. Varani, J., Riser, B.L., Hughes, L.A., Carey, T.E., Fligiel, S.E.G., Dixit, V.M.: Characterization of thrombospondin synthesis, secretion and cell surface expression by human tumor cells. Clin. Exp. Metastasis (in press).
18. Nickoloff, B.J., Riser, B.L., Mitra, R.S., Dixit, V.M., Varani, J.: Inhibitory effect of gamma interferon on cultured human keratinocyte thrombospondin production, distribution and biological activities. J. Invest. Dermatol. (in press).

19. Nickoloff, B.J., Mitra, R.S., Riser, B.L., Dixit, V.M., Varani, J.: Modulation of keratinocyte motility; correlation with production of extracellular matrix molecules in response to growth promoting and anti-proliferative factors. Am. J. Path. (in press).

BOOKS AND CHAPTERS IN BOOKS:

1. Varani, J., McCoy, J.P., Ward, P.A.: Attraction of wandering metastatic tumor cells. In: Progressive Stages of Malignant Neoplastic Growth, Volume II. Clinical Aspects of Neoplastic Progression: Host-tumor interactions and Its Modification by Therapy. H.E. Kaiser, (ed.), Martinus Nijhoff, Publishers, Norwell, MA, 1988 (in press).
2. Varani, J.: Interaction of Tumor Cells with the Extracellular Matrix. Revisions Sobre Biologia Celular. E. Barbera-Guillem (ed.) Leioa-Viscaya, Spain. 12:1-122, 1987.
3. Varani, J.: Arachidonic acid metabolism in malignant tumor cells: Relationship to adhesion, motility and invasion. In: Carcinogenesis and Dietary Fat. S. Abraham (ed.). Martinus Nijhoff Publishing; Boston, MA, 1988 (in press).
4. Varani, J., Riser, B.L.: Squamous carcinoma cells synthesize thrombospondin and use it as an adhesion factor. In: Proceed. International Head and Neck Oncology Research Conference. G.T. Wolf (ed.)., Martinus Nijhoff Publishing; Boston, MA, 1988 (in press).
5. Gannon, D.E., Varani, J., Ward, P.A.: Endothelial cell injury by neutrophils, In Endothelial Cells, Volume II. Ryan US, (ed.) CRC Press, Inc., 1988.
6. Ward, P.A., Till, G.O., Gannon, D.E., Varani, J., Johnson, K.J.: The role of iron in injury of endothelial cells in vitro and in vivo. In Oxygen Radicals in Biology and Medicine. Simic, M.G., Ward, J.F., Taylor, K.A., (ed.) Plenum Publishing Co., (in press).
7. Till, G.O., Warren, J.S., Gannon, D.E., Chensue, S.W., Kunkel, S.L., Varani, J., Johnson, K.J., Ward. P.A.: Effects of pentoxiphylline on phagocyte responses in vitro and acute and chronic inflammatory reactions in vivo, In Symposium on Pentoxiphylline and Leukocyte Function. Mandell, G. and Novick, W., (ed.) Haber, Flora, Inc., (in press).

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

1. Gannon, D.E., Phan, S.H., Varani, J., Ryan, U.S., Ward, P.A.: Alterations of xanthine oxidase activity in endothelial cells undergoing neutrophil-mediated injury. Am. Rev. Respir. Dis. 1988;137(4):82.

2. Wencel, M.L., Morganroth, M.L., Gannon, D.E., Todd, R.F. III, Varani, J., Boxer, L.A.: Plasma and LPS preincubation of intact neutrophils deficient in Mol expression increase injury to endothelial cell monolayers and isolated lungs. Am. Rev. Respir. Dis. 1988;137(4):363.
3. Schuger, L., Varani, J., Ward, P.A., Gannon, D.E., Ryan, U.S.: Neutrophil-mediated killing of endothelial cells; comparison of rat pulmonary artery and microvascular cells. FASEB J. 2 1988;(5):A1169.
4. Ward, P.A., Warren, J.E., Gannon, D.E., Johnson, K.J., Phan, S.H., Varani, J.: Cytokine and oxygen radical-mediated injury. J. Cell. Biochem. Suppl. 1988;12A:41.
5. Riser, B.L., Varani, J., Nickoloff, B.J., Dixit, V.M.: Gamma-interferon and tumor necrosis factor modulate thrombospondin production by human blood monocytes. J. Cell Biochem. Suppl. 1988;12A:208.
6. Varani, J., Riser, B.L., Nickoloff, B.J.: Effect of gamma-interferon on keratinocyte biosynthesis and expression of thrombospondin. J. Cell Biochem. Suppl. 1988;12A:218.
7. Varani, J., Nickoloff, B.J., Riser, B.L., Mitra, R.S., Dixit, V.M.: Regulation of keratinocyte motility by extracellular matrix components and cytokines. FASEB J. 1988;2:A1821.
8. Riser, B.L., Varani, J., Nickoloff, B.J., Mitra, R.S., Dixit, V.M.: Receptor-mediated binding of thrombospondin (TSP) to human keratinocytes; Effect of gamma-interferon and relationship to biological activity. FASEB J. 1988;2:A1608.
9. Ginsburg, I., Fligiel, S.E.G., Ward, P.A., Varani, J.: Lipoteichoic acid-anti-lipoteichoic acid complexes trigger superoxide generation by human neutrophils. FASEB J. 1988;2:A825.
10. Chakrabarty, S., Daniels, Y.J., Levine, A., McClenic, B., Varani, J.: Differences in aberrant growth control mechanisms in HA-RAS oncogene-transformed and epidermal growth factor (EGF) - transformed. FR3T3 cells. FASEB J. 1988;2:A806.
11. Fligiel, S.E.G., Varani, J.: The effect of EGF on the production of matrix components by human neoplastic cells. FASEB J. 1988;2:A401.
12. Varani, J., Mitra, R.S., Riser, R.L., Dixit, V.M., Nickoloff, B.J.: Modulation of keratinocyte behavior and extracellular matrix production by growth regulating factors. J. Invest. Dermatol. (in press).

PETER A WARD, M.D.
PROFESSOR AND CHAIRMAN
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. These have been chiefly related to administrative responsibility for all clinical service functions of the Department.

II. TEACHING ACTIVITIES:

A. Medical Students:

1. Lecture annually to medical students at the Medical College of Pennsylvania and Hospital (two four hour sessions).

B. Graduate students:

1. Responsible during the current academic year for teaching activities for the following:
   a. Blair A.Walker, M.D. , Postdoctoral Fellow
   b. Rory A. Marks, M.D. , Postdoctoral Fellow
   c. Cheryl Swenson, D.V.M., Ph.D. Postdoctoral Fellow
   d. Michael M. Mandell, 3rd Year Medical School
   e. Vonda Douglas, 2nd Year Medical School
2. Indirect supervision of four Research Scientists.
3. Lecture to faculty and students at the Hospital of the University of Pennsylvania.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Thermal Injury, Complement, and Leukocyte Dysfunction", NIH GM-28499 (10%), $110,950/year ($577,063/five years), 1/1/86-12/31/90.
B. Principal Investigator, "Lung Immunopathology", NHLBI HL-07517 (5%), $257,166/year ($1,291,531/five years), 7/1/86-6/30/91.
C. Principal Investigator, "Leukocyte Chemotaxis", NIH HL-28442 (10%), $93,628/year ($505,936/five years), 7/1/86-6/30/91.
D. Principal Investigator, "Lung Injury Produced by Oxygen Metabolites", NIH GM-29507 (20%), $116,376/year ($507,078/five years), 7/1/82-6/30/87
E. Principal Investigator, "Inflammatory Cells and Lung Injury", NHLBI HL-31963 (35%), $653,281/year ($3,876,003/five years), 3/1/84-2/28/94.
F. Co-Investigator, "Mechanisms of Glomerular and Tubular Injury", NIH-DK39255 (5%), $44,185 (Project V only), 9/1/87-8/31/92.

PENDING:

None

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chief, Section of General Pathology.
B. MSP Executive Committee.
C. Pathology Associates.

MEDICAL SCHOOL/HOSPITAL:

A. Dean's Council of Clinical Chairmen, 1985--.
B. Michigan Eye Bank Research Review Committee, 1980--.
C. Michigan Diabetes Research and Training Center Policy Committee, 1981--.
D. National Task Force on Organ Transplantation, 1985--.
E. Professional Fee Policy Committee, 1984--.
F. Interdepartmental Coordinating Committee, 1984--.
G. Dean's Advisory Council, 1985--.
H. Dean's Advisory Committee on Clinical Affairs, May, 1985--.
I. Advisory Committee for the Howard Hughes Medical Institute, 1984--.
J. Internal Advisory Board Committee of the Michigan Gastrointestinal Peptide Research Center, 1985--.
K. Council of Operations and Quality Assurance, 1986--.
L. Board of Directors, M-Care, 1986--.
M. Member, Neuromuscular Program Policy Committee, The University of Michigan Medical School, 1987--.
N. Member, Center Advisory Committee for The University of Michigan Multipurpose Arthritis Center, 1987--.
O. Member, Medical Service Plan Advisory Committee, 1987--
P. Member, Medical Service Plan Executive Committee, 1987--.
Q. Member, Gilford Upjohn Endowed Chair in Internal Medicine and Oncology, Department of Internal Medicine, Hematology and Oncology Unit, The University of Michigan, February, 1987--.
R. Member, Presidential Initiatives Fund, The University of Michigan, March, 1987--.
S. Member, Hospitals Advisory Group, 1988--
T. Member, Southeastern Michigan American Red Cross Scientific Council Meeting, 1987--
U. Member, University of Michigan Multipurpose Arthritis and Musculoskeletal Diseases Center, 1989--
V. Member, Committee to Review VA FTE's, The University of Michigan Medical School, October, 1988--

REGIONAL AND NATIONAL:

A. American Society for Clinical Investigation.
B. American Association of Pathologists.
    1. Member, 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.

C. Trustee, American Board of Pathology, effective January 1, 1988.
D. Member, Advisory Committee, Health Policy Agenda for the American People.
E. Member, American Association for Advancement of Science.
F. Member, American Association of Immunologists.
G. Member, American Pathology Foundation.
H. Member, Association of Pathology Chairmen.
I. Charter Member, A. James French Society of Pathologists, 1988--.
J. Member, Michigan Society of Pathologists.
K. Member, Center for Alternatives to Animal Testing, Johns Hopkins University.
L. Member, International Academy of Pathology.
   1. Council Member, April 1, 1986-1989.
   2. Member, Finance Committee, April 1, 1986-1990.
M. Member, The New York Academy of Sciences.
N. Member, Society of Medical Consultants to the Armed Forces.
O. Member, Michigan Thoracic Society, 1988--.
Q. Member, The Oxygen Society, 1988--
   1. President, 1988
R. Ann Arbor Veterans Administration Medical Center, Consultant, 1980--.
S. Board of Directors, Universities Associated for Research and Education in Pathology, Inc.
T. Phi Rho Sigma, President, The University of Michigan Chapter, September, 1988
U. Cytogen, 1983--.
V. Mallinckrodt, Inc., Advisory Board, 1984--.

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. Invited Speaker, "Oxyradicals in the Inflammatory Process", in the 4-ICOR 4th International Congress on Oxygen Radicals sponsored by the National Bureau of Standards, at the University of California, San Diego, LaJolla, California, June 27-July 3, 1987.
2. Consultant, NHLBI SCOR Research Review Committee A, "SCOR in Adult Respiratory Failure" by Dr. James E. Gadek, Ohio State University, Columbus, Ohio, February 8-10, 1988.
3. Invited Lecturer, "Oxygen Radicals and Lung Injury" and "Cytokines and Lung Injury", sponsored by the Lung Club at Stony Brook and Winthrop-University Hospital, Pulmonary and Clinical Care Medicine Division, Mineola, Long Island, New York, February 24-25, 1988.
4. Invited Lecturer, "Oxidants" and "Antioxidants" in New Horizons III: Cell Damage and Organ Failure, sponsored by the European Society of Intensive Care and the Society for Critical Care Medicine at the Hyatt Regency Hotel, Brussels, Belgium, March 19-21, 1988.
5. Invited Sommer Memorial Lecturer,"Oxygen Radicals and Lung Injury", "The Role of Cytokines in Lung Injury", and "Interaction Between Neutrophils and Platelets", sponsored by St. Vincent Hospital, Portland, Oregon, April 6-8, 1988.
6. Visiting Professor, "Acute Lung Injury", Advanced Respiratory Pathophysiology Course sponsored by the Pulmonary and Critical Care Medicine Section of the Department of Medicine, The University of Chicago, Chicago, Illinois, April 11-12, 1988.
7. Invited Participant, Scientific Advisory Board Sub-Committee - Research Review, Armed Forces Institute of Pathology, Washington, D.C., April 13-14, 1988.
8. Invited Lecturer, "Free Radicals and Lung Injury - Implication for Therapy", and moderate morning session in the International Conference on Oxygen-Free Radicals in Health and Disease, Marriott Hotel, London, England, April 16-20, 1988.
9. Invited Lecturer, "Cytokines and Oxygen Radical Mediated Injury", in the Symposium, Endothelial Cells: A Target and Source of Oxidant Injury, sponsored by the American Physiological Society, in Las Vegas, Nevada, May 5, 1988.
10. Invited Lecturer, Research Seminar, "Tissue Injury and Oxygen Radicals", Graduate Hospital, Philadelphia, Pennsylvania, May 31, 1988.
11. Invited Lecturer and Participant, "Molecular Mechanisms of Cytotoxicity in PMN Leukocyte-Endothelial Cell interactions", in the Gordon Research Conference, "Vascular Cell Biology", Meriden, New Hampshire, August 5, 1988.
12. Guest Speaker, "Cytokines and Oxygen Radical Mediated Lung Injury", Conference on Oxygen Radicals, Given Institute, Aspen, Colorado, August 16-19, 1988.
13. Invited Lecturer, Sophomore Course of Pathology, Medical College of Pennsylvania, Philadelphia, Pennsylvania, September 1-2, 1988.
14. Invited Pathology Grand Rounds Presentation, "Mechanisms of Injury in Inflammation", Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia, September 8-9, 1988.
15. Invited Faculty Member, Conference on Role of Macrophages in Wound Healing, sponsored by Marion Laboratories Grapevine, Texas, September 15-17, 1988.
16. Invited Lecturer and Participant, "Inflammation", Conference on Platelet Activating Factor:Role in Pulmonary Injury, sponsored by the National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland, September 18-21, 1988.

17. Invited Lecturer, "Cytokines, Oxygen Radicals and Tissue Injury", at the 39th Annual Meeting of the American Association for Laboratory Animal Science, in conjunction with the 27th Annual Meeting of the Canadian Association for Laboratory Animal Science, Detroit, Michigan, October 10, 1988.
18. Invited Lecturer, "Mechanisms of TNF-Induced Injury of Endothelial Cells", Cetus Corporation, "In-Depth Analysis of Endotoxin Mediated Sepsis", Emeryville, California, October 13-15, 1988.
19. Visiting Professor, "Phagocytic Cell Oxidants and Tissue Injury", Department of Pathology, Northwestern University, The McGaw Medical Center, Chicago, Illinois, OctOber 17, 1988.
20. Visiting Professor, "Leukocyte-Derived Oxygen Radicals in Tissue Injury", Department of Pathology, Duke University Medical Center, Durham, North Carolina, November 17, 1988.
21. Invited 6th Maranze Memorial Lecturer, "Oxygen Radicals and Tissue Injury", Pulmonary Division, Albert Einstein Medical Center, Northern Division, Philadelphia, Pennsylvania, December 6, 1988.
22. Invited Lecturer, "Mechanisms of Endothelial Cell Killing", "Blood Club", Division of Hematology, Department of Medicine, University of Minnesota, Minneapolis, Minnesota, December 13, 1988.
23. Visiting Professor, "Roles of Cytokines and Platelet Activity Factor in Lung Injury", Departments of Laboratory Medicine and Pathology and Medicine, University of Minnesota Medical School, Minneapolis, Minnesota, December 14, 1988.
24. Visiting Lecturer, "Free Radicals in Lung Disease", Specialty Colloquium on Free Radicals, Disease States and Anti-Radical Interventions, sponsored by the Biochemical Society, London, England, December 19, 1988.
25. Lecturer, "Immune Complexes, Oxygen Radicals and Tissue Injury", in Minisymposium, "Role of Oxygen Radicals in Health and Disease", sponsored by the Detroit Immunological Society, Wayne State University, Detroit, Michigan, March 14, 1989.
26. Chair Minisymposium for American Association of Pathologists, "Inflammatory Mediators", FASEB Meeting, New Orleans, Louisiana, March 21, 1989.
27. Chair Minisympoisum for American Association of Immunologists, "Leukocyte Stimulation: Receptor, Membrane and Metabolic Events", FASEB Meeting, New Orleans, Louisiana, March 22, 1989.
28. Moderator, NIH SCOR Workshop on Occupational and Immunologic Diseases, Rockville, Maryland, March 27-19, 1989.
29. Invited Lecturer, Japanese Society of Chest Dieases Meeting, "Lung Injury", Kyoto, Japan, April 3-7, 1989.
30. Invited Lecturer, "TNF, Oxygen Radicals and Tissue Injury", in Symposium I: Cytokines and Lymphokines Following Hemorrhage and Sepsis, Shock Society Meeting, Marco Island, Florida, June 9-10, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Till, G.O., Lutz, M.J., and Ward, P.A.: Hydroxyl radical as autotoxin in chemotactically activated neutrophils. Biomedicine & Pharmacotherapy. 1987; 41: 349-354.
2. Warren, J.S. , Johnson, K.J. and Ward P.A.: Oxygen radicals in cell injury and cell death. Pathol. Immunopathol. Res. 1987;6:301-315

3. Warren, J.S., Kunkel, R.G., Johnson, K.J. and Ward P.A.: Comparative 0^2- responses of lung and blood phagocytic cells in the rat: Possible relevance to IgA immune complex induced lung Injury. Lab. Invest. 1987;57:311-320.
4. Warren, J.S., Ward, P.A., Johnson, K.J. and Ginsburg, I.: Modulation of acute immune complex mediated tissue injury by presence of polyionic substances. Amer. J. Pathol. 1987;128:67-77.
5. Ginsburg, I., Fligiel, S.E.G., Ward, P.A. and Varani, J.: Lipoteichoic acid-antilipoteichoic acid complexes induce superoxide generation by human neutrophils. Inflammation 1988;12:525-548.
6. Grimstad, I.A., Thorsrud, A.K., Varani, J., Ward, P.A. and Jellum, E.: Marker polypeptide differences between spontaneous strongly and weakly metastatic cancer cells identified by 2-dimensional gel electrophoresis. Int. J. Cancer 1988;41:568-572.
7. Guice, K.S., Oldham, K.T., Johnson, K.J., Kunkel, R.G., Morganroth, M.L. and Ward, P.A.: Pancreatitis-induced acut lung injury: An ARDS model. Ann. Surg. 1988;208:71-77.
8. Marak, G.E., Jr., de Kozak, Y., Faure, J-P, Rao N.A., Romero, J.L., Ward, P.A. and Till, G.O.: Pharmacologic modulation of acute ocular inflammation: I. Adenosine. Ophthalmic Res., 1988:20;220-226.
9. Morgan, R.A., Manning, P.B., Coran, A.G., Drongowski, R.A., Till, G.O., Ward, P.A. and Oldham, K.T.: Oxygen free radical activity during live E. coli septic shock in the dog. Circulatory Shock 1988;25:319-323.
10. Morganroth, M.L., Till, G.O., Schoenich, S.O. and Ward, P.A.: Eicosanoids are involved in the permeability changes but not the pulmonary hypertension after systemic activation of complement. Lab. Invest. 1988;58:316-323.
11. Oldham, K.T., Guice, K.S., Till, G.O. and Ward, P.A.: Activation of complement by hydroxyl radical in thermal injury. Surgery 1988;25:319-323.
12. Oldham, K.T., Guice, K.S., Ward, P.A. and Johnson, K.J.: The role of oxygen radicals in immune complex injury. Adv. Free Rad. Biol. Med. 1988;4:387-397.
13. Rao, N.A., Romero,J.L., Sevanian, A., Fernandez, M.A., Wong, C., Ward, P.A. and Marak, G.E., Jr.: Anti-inflammatory effect of glutathione peroxidase on experimental lens-induced uveitis. Ophthalmic Res. 1988;20:213-219.
14. Robinson, J.P., Bruner, L.H., Bassoe, C.-F., Hudson, J.L., Ward, P.A. and Phan, S.H.: Measurement of Intracellular fluorescence of human monocytes relative to oxidative metabolism. J. Leukocyt. Biol., 1988;43:304-410.
15. Robinson, J.P., Duque, R.E., Boxer, L.A., Ward, P.A. and Hudson, J.L.: Measurement of antineutrophil antibodies by flow cytometry: Simultaneous detection of antibodies against monocytes and lymphocytes. Diagn. Clin. Immunol. 1988;5:163-170.
16. Strieter, R.M., Remick, D.G., Ward, P.A., Spengler, R.N., Lynch, J.P., III, Larrick, J. and Kunkel, S.L.: Cellular and molecular regulation of tumor necrosis factor - Alpha production by pentoxifylline. Biochem. Biophys. Res. Comm. 1988;155:1230-1236.
17. Varani, J., Bendelow, M.J., Sealey, D.E., Kunkel, S.L., Gannon, D.E., Ryan, U.S. and Ward, P.A.: Tumor necrosis factor enhances susceptibility of vascular endothelial cells to neutrophil-mediated killing (Brief Communication). Lab. Invest. 1988;59:292-295.
18. Ward, P.A., Cunningham, T.W., Walker, B.A.M. and Johnson, K.J.: Differing calcium requirements for regulatory effects of ATP, ATPgS and adenosine on 0_2- responses of human neutrophils. Biochem. Biophys. Res. Comm. 1988:154;746-751.
19. Ward, P.A., Warren, J.S. and Johnson, K.J.: Oxygen radicals, inflammation and tissue injury. Free Rad Biol Med 1988;5:403-408.
20. Ward, P.A., Warren, J.S. and Johnson, K.J.: Leukocytes, oxidants, and tissue injury. Perspec. Crit. Care 1988;1:69-81.

21. Warren, J.S., Ward, P.A. and Johnson, K.J.: Tumor necrosis factor: A plurifunctional mediator of acute inflammation. Review Article, Modern Pathology 1988;1:242-247.
22. Friedl, H.P., Till, G.O., Ward, P.A. and Trentz, O.: Role of xanthine oxidase in microvascular damage following thermal injury of skin. Chorurgisches Forum 1989:59-62.
23. Ginsburg, I., Ward, P.A. and Varani, J.: Lysophosphatides enhance superoxide responses of stimulated human neutriphils. Inflamm. 1989;13:163-174.
24. 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.
25. 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.
26. Schuger, L., Varani, J., Marks, R.M., Kunkel, S.L., Johnson, K.J. and Ward, P.A.: Cytotoxicity of tumor necrosis factor- for human umbilical vein endothelial cells. Lab. Invest. 1989;61:62-68.
26. 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- , LPS, and IL-1 . Science 1989;243:1467-1469.
27. Sullivan, J.L., Till, G.O., Ward, P.A. and Newton, R.B.: Nutritional iron restriction diminishes acute complement-dependent lung injury. Nutrition Res. 1989;9:625-634.
28. 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.
29. 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.
30. 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. Laboratory Investigation 1989;60:651-658.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Dixit, V.M., Green, S., Sarma, V., Holzman, L.B., Wolf, F.W., O'Rourke, K., Ward, P.A., Prochownik, E.V. and Marks, R.: Tumor necrosis factor-α induction of novel gene products in human endothelial cells including a macrophage specific chemotaxin. J. Cell Biol., In Press.
2. Friedl, H.P., Till, G.O., Ryan, U.S. and Ward, P.A.: Mediator-induced activation of xanthine oxidase in endothelial cells. FASEB J., In Press.
3. Friedl, H.P., Till, G.O., Trentz, O. and Ward, P.A.: Roles of histamine complement and xanthine oxidase in thermal injury of skin. Amer. J. Pathol., In Press.
4. Ginsburg, I., Gibbs, D.F., Schuger, L., Johnson, K.J., Ryan, U.S., Ward, P.A. and Varani, J.: Vascular endothelial cell killing by combinations of membrane-active agents and hydrogen peroxide. Free Radical Biology and Medicine, In Press.
5. 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. Annals Surg., In Press.
6. Guice, K.S., Oldham, K.T., Johnson, K.J. and Ward, P.A.: Mechanisms of capillary endothelial cell injury in acute pancreatitis. Surg. Forum, In Press.
7. Kennedy, T.P., Johnson, K.J., Kunkel, R.G., Ward, P.A., Knight, P.R. and Finch, J.S.: Acute acid aspiration lung injury in rat: Biphasic pathogenesis. Anesth. Analg., In Press.

8. 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.
9. 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.
10. 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.
11. Sullivan, J.L., Till, G.O., Ward, P.A. and Newton, R.B.: Nutritional iron restriction diminishes acute complement-dependent lung injury. Nutrition Research, In Press.
12. Till, G.O., Guilds, L.S., Mahrougui, M., Friedl, H.P., Trentz, O. and Ward, P.A.: Role of xanthine oxidase in thermal ijury of skin. Amer. J. Pathol., In Press.
13. Till, G.O. and Ward, P.A.: Immunologic and phagocytic cell defects in thermally injured patients. J. Crit. Care Med., In Press.
14. Ward, P.A.: The wound environment - Local and systemic perturbations: Inflammation and the burn wound. J. Burn Care & Rehab., In Press.
15. 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.
16. Ward, P.A., Johnson, K.J. and Till, G.O.: Mechanisms of lung injury. Prax. Klin. Pneumonol., In Press.

BOOKS/CHAPTERS IN BOOKS:

1. Gannon, D.E., Varani, J. and Ward, P.A.: Endothelial cell injury by neutrophils, Chapter 22, in, Ryan, U.S. (ed) Endothelial Cells, Volume II, CRC Press, Boca Raton, Florida, pp. 173-192, 1988.
2. Johnson, K.J. and Ward, P.A.: Mechanisms of acute and chronic immune inflammatory response in the lung, Chapter 11, in, Daniele, R.P. (ed) Immunology and Immunologic Diseases of the Lung, Blackwell Scientific Publications, Inc., Boston, Massachusetts, pp. 193-214, 1988.
3. Till, G.O., Warren, J.S., Gannon, D.E., Chensue, S.W., Kunkel, S.L., Varani, J., Johnson, K.J. and Ward, P.A.: Effects of pentoxifylline on phagocyte responses in vitro and acute and chronic inflammatory reactions *in vivo*, Mandell, G.L. and Novick, W.J., Jr. (eds) Pentoxifylline and Leukocyte Function, Key Biscayne, Florida, 30 November - 1 December 1987, Haber & Flora, Inc., pp. 124-127, July, 1988.
4. Fantone, J.C. and Ward, P.A.: Inflammation, in, Rubin, E. and Farber, J.L. (eds), Pathology, J.B. Lippincott, Inc., Philadelphia, 1988, pp. 34-64.
5. Johnson, K.J., Chensue, S.W., Kunkel, S.L. and Ward, P.A.: Immunopathology, in, Rubin, E. and Farber, J.L. (eds), Pathology, J.B. Lippincott, Inc., 1988, 96-139.
6. Johnson, K.J., Rehan, A. and Ward, P.A.: The role of oxygen radicals in kidney disease, in, Halliwell, B. (ed) Oxygen Radicals and Tissue Injury, Proceedings of an Upjohn Symposium, Upjohn Company, Federation of American Societies for Experimental Biology, Bethesda, Maryland, 1988, pp. 114-121.
7. Ward, P.A., Johnson, K.J., Till, G.O. and Warren, J.S.: Activated phagocytes, oxygen radicals and tissue injury, in, Chow, C.K. (ed) Cellular Antioxidant Defense Mechanism, Volume I, Chapter 10, CRC Press, Marcel Dekker, Inc., New York, New York, pp. 151-157.
8. Ward, P.A., Johnson, K.J., Warren, J.S. and Kunkel, R.G.: Immune complexes, oxygen radicals and lung injury, in, Halliwell, B. (ed) Oxygen Radicals and Tissue Injury, Proceedings of an Upjohn Symposium, Upjohn Company, Federation of American Societies for Experimental Biology, Bethesda, Maryland, pp. 107-114, 1988.

9. Ward, P.A., Macconi, D., Sulavik, M.C., Till, G.O., Warren, J.S., Johnson, K.J. and Powell, J.: Rat Neutrophil-platelet interactions in oxygen radical-mediated lung injury, in, Cerutti, P.A., Fridovich, I and McCord, J.M. (eds) Oxy-Radicals in Molecular Biology and Pathology, UCLA Symposia on Molecular and Cellular Biology, New Series, Volume 82, Alan R. Liss, Inc., New York, New York, pp 83-98, 1988.
10. Ward, P.A. and Remick, D.G.: Immune mechanisms in lung injury, Chapter 42, Volume 1, in, Fishman, A.P. (ed) Pulmonary Diseases and Disorders, McGraw-Hill Book Company, New York, New York, pp. 607-618, 1988.
11. Ward, P.A., Warren, J.S. and Johnson, K.J.: Leukocytes, oxidants and tissue injury, Volume 1, Number 2, in, Cerra, F.B. (ed) Perspectives in Critical Care, Quality Medical Publishing, Inc., St. Louis, Missouri, pp. 69-81, 1988.
12. Marak, G.E., Jr., Rao, A., Gannon, D.E., Varani, J., Ward, P.A. and Till, G.O.: Antiphlogistic mechanisms of benzoic derivatives in experimental uveitis, Secchi, A.G. and Fregona, I.A. (eds), Modern Trends in Immunology and Immunopathology of the Eye, Masson, Milano, Italy, pp. 137-139, 1989.
13. 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.
14. Ward, P.A., Till, G.O. and Johnson, K.J.: Oxygen-derived free radicals and inflammation. Chapter for Workshop on Inflammation and Healing of Sports Induced Soft Tissue Injury, held in Bethesda, Maryland, May 23, 1989.
15. Ward, P.A., Warren, J.S., Remick, D.G., Varani, J., Gannon, D. and Johnson, K.J.: Cytokines and oxygen-radical-mediated tissue injury, Chapter 6, in, Bihari, D.J. and Cerra, F.B. (eds) New Horizons: Multiple Organ Failure, Society of Critical Care Medicine, pp. 93-100, 1989.
16. 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 pharmacological intervention, Chapter 7, in, Hershko, C. (guest ed), Bailliere's Clinical Haematology, Volume 2, Number 2, Bailliere Tindall,London, England, pp. 391-402, 1989.
17. Fantone, J.C. and Ward, P.A.: Mechanisms of inflammation, in, Cohen, A.S. (ed), Rheumatology and Immunology, Grune and Stratton, In Press.

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

1. Barton, P.A., Warren, J.S., Johnson, K.J. and Ward, P.A.: Rat alveolar macrophages express cell membrane-associated interleukin-1 activity. FASEB J 1989;3:A318.
2. Dixit, V.M., Kunkel, S.L., Sarma, V., Strieter, R.M., Showell, H.J., Ward, P.A.and Marks, R.M.: Molecular cloning of an endothelial derived neutrophil chemotactic factor: Identity with monocyte derived factor. FASEB J 1989;2:A305.
3. Friedl, H.P., Till, G.O., Guilds, L.S., Mahrougui, M. and Ward, P.A.: Thermal injury of rats. Enhancement of xanthine oxidase activity by histamine. FASEB J 1989;3:A1320.
4. Guilds, L.S., Till, G.O., Mahrougui, M., Friedl, H.P. and Ward, P.A.: Protection against complement-mediated acute lung injury by diclofenac sodium. FASEB J 1989;3:A289.
5. Hagenlocker, B.E., Walker, B.A.M. and Ward, P.A.: Extracellular ATP induces a $[CA^{++}]i$ signal in rat alveolar macrophags but does not enhance 0_2-. FASEB J 1989;3:A911.
6. Kennedy, T.P., Johnson, K.J., Ward, P.A., Knight, P.R. and Finch, J.S.: Isoflurane increases alveolar-capillary leak in acid aspiration in rat. FASEB J 1989;3:A915.

7. Kunkel, R.G., Johson, K.J., Ward, P.A. and Marks, R.M.: Morphology of complement mediated neutrophil adhesion and migration througj vascular endothelium. FASEB J 1989;3:A304.
8. Mahrougui, M., Till, G.O., Guilds, L.S., Friedl, H.P. and Ward, P.A.: Evidence for *in vivo* and *in vitro* scavenging of hydroxyl radial by cimetidine. FASEB J 1989;3:A1233.
9. Marks, R.M., Todd, R.F., III, Boxer, L.A. and Ward, P.A.: A novel mechanism of neutrophil-endothelial adhesion induced by endothelial complement fixation. FASEB J 1989;3:A1319.
10. Schuger, L., Varani, J., Marks, R., Kunkel, S.L., Johnson, K.J. and Ward, P.A.: Cytotoxicity of TNF-α for human umbilical vein endothelial cells. FASEB J 1989;3:A637.
11. Shayvitz, J.R., Ward, P.A., Knight, P.R., Varani, J. and Ryan, U.S.: Halothame (H) enhances pulmonary artery endothelial cell (PaEC) susceptibility to oxidant-induced killing. FASEB J 1989;3:A1226.
12. Till, G.O., Friedl, H.P., Guilds, L.S., Mahrougui, M. and Ward, P.A.: Role of histamine in oxygen radical-mediated acute lung injury. FASEB J 1989;3:A1049.
13. Walker, B.A.M., Cunningham, T.W. and Ward, P.A.: Alteration of the superoxide response of human neutrophils by ATP, ATP γ S or adenosine is independent of specific granule fusion or upregulation of F-met-leu-[^{3}H]phe receptors. FASEB J 1989;3:A911.
14. Ward, P.A.: Lung injury. Japanese Journal of Thoracic Diseases. 1989;27:84-85.
15. Warren, J.S., Yabroff, K.R., Remick, D.G., Kunkel, S.L., Kunkel, R.G., Johnson, K.J. and Ward, P.A.: Intrapulmonary Il-1 and TNF in acute immune complex lung injury in the rat. FASEB J 1989;3:A610.
16. Yabroff, K.R., Warren, J.S., Mandel, D.M., Johnson, K.J. and Ward, P.A.: Xanthine oxidase inhibitors reduce neutrophil influx into sites of immune complex-induced dermal vasculitis in the rat. FASEB J 1989;3:A916.

JEFFREY S. WARREN, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Clinical Immunopathology Laboratory (25% effort)

II. TEACHING ACTIVITIES:

A. Pathology 630, 631 (3 Lectures; Laboratory instructor : 4 contact hours/week, Fall semester)
B. Clinical Pathology Grand Rounds (1 presentation)
C. Immunopathology Signout (daily, every third week with resident(s) on service)
D. Supervision of medical students in research laboratory
David M. Mandel, (M1); May - August (1988,1989)
Kevin Matrosic, (M1); May - August (1989)

III. RESEARCH ACTIVITIES:

A. Role of cytokines (tumor necrosis factor, interleukin 1) in immune complex lung injury.
B. Platelet-activating factor in immune alveolitis.

SPONSORED SUPPORT:

A. NIH (R29 - HL40526), Principal Investigator, "Monocyte macrophage cytokines in immune complex lung injury": 4/1/89 - 2/31/94 (350,000; direct costs).
B. American Heart Association of Michigan Grant-in-Aid, Principal Investigator, "Platelet-activating factor in immune alveolitis": 7/1/89 - 6/30/91 ($44,400; direct costs).

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

A. Medical School Admissions Committee

REGIONAL AND NATIONAL:

A. Independent grant reviewer for Merit Review Board (respiration category); U.S. Veterans Administration, Spring 1989.
B. Reviewer; American Journal of Pathology, Laboratory Investigation, Human Pathology, Journal of Applied Physiology, Lung, Blood, Journal of Laboratory and Clinical Medicine, Pediatric Research, Journal of Leukocyte Biology, American Review of Respiratory Disease, Chest, Journal of Pharmacology and Experimental Therapeutics, and Circulation.

V. INVITED LECTURES/SEMINARS:

A. PAF, cytokines and immune complex induced injury. Satellite Meeting of the International Conference on Tumor Necrosis Factor. UCLA-Institue Henri Beaufour, Napa, CA, January 14-15, 1989.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Warren, J.S., Kunkel, R.G., Simon, R.H., Johnson, K.J., and Ward, P.A.: Ultrastructural cytochemical analysis of IgA immune complex induced lung injury in the rat. Lab. Invest., 1989;60:651-658.
2. Warren, J.S., Mandel, D.M., Johnson, K.J., and Ward, P.A.: Evidence for the role of platelet-activating factor in a rat model of immune complex vasculitis. J. Clin. Invest., 1989;83:669-678.
3. Keren, D.F., Warren, J.S., and Lowe. J.B.: Strategy to diagnose monoclonal gammopathies in serum: high resolution electrophoresis, immunofixation and K/L quantification. Clin. Chem., 1988;34:2196-2201.
4. McNeeley, S.G., Elkins, T.E., Portz, D.M., Warren, J., DeLancey, J.O.L.: Comparison of copolymer staple versus chromic suture during hysterectomy: gross, histologic and microbiologic findings. Obstet and Gynecol, 1988;72:862-865.
5. Portz, D.M., Elkins, T.E., White, R., Warren, J., Adadevoh, P., 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. Fertility, in press.

BOOKS/CHAPTERS IN BOOKS:

1. Warren, J.S., Ward, P.A., Johnson, K.J.: The inflammatory response, in Williams, W.J., (ed.) Hematology, 4th Edition, (In press).
2. Ward, P.A., Warren, J.S., Till, G.O., Varani, J., Johnson K.J.: Modification of disease by preventing free radical formation: A new concept in pharmacologic intervention, in Hershko, C. (ed.) Bailliere's Clinical Hematology: International Practice and Research, W.B. Saunders, London, UK, pp. 391-402, 1989.
3. Ward, P.A., Warren, J.S., Johnson, K.J., and Varani, J.: Cytokines and oxygen radical responses, in Maier, R. (ed.), Proceedings of the 1st International Congress on The Immune Consequences of Trauma, Shock, and Sepsis: Mechanisms and Therapeutic Approaches, (In press).
4. Ward, P.A., Warren, J.S., and Johnson, K.J.: Leukocytes, oxidants and tissue injury, in Cerra, F. (ed.), Perspectives in Critical Care, Quality Medical Publishing, St. Louis, MO, pp. 69-81, 1988.
5. Ward, P.A., Macconi, D., Sulavik, M.C., TIll, G.O., Warren, J.S., Johnson, K.J. and Powell, J: Rat neutrophil-platelet interactions in oxygen radical-medicated lung injury. UCLA Symp. Molec. and Cell Biol., in Oxy-Radicals in Molecular Biology and Pathology, Alan R. Liss, Inc., New York, NY pp. 83-98, 1988.
6, 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).
7. Warren, J.S., Ward, P.A., Johnson, K.J.: Immune complex injury in Cantor, J.O. (ed.) Handbook of Animal Models of Pulmonary Disease, CRC Press Inc., Boca Raton, FL, (In press).

8. Warren, J.S., Ward, P.A., Johnson, K.J.: Oxygen radicals as 'mediators of inflammation', in Henson, P.M. (ed.) Mediators of the Inflammatory Process, Handbook of Inflammation, Vol. 6, Elsevier, Amsterdam, The Netherlands, (In press).

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

1. Ward, P.A., Warren, J.S., and Johnson, K.J.: Oxygen radicals, inflammation and tissue injury, Free Rad. in Biol. Med., in press.
2. Warren, J.S., Ward, P.A., and Johnson, K.J.: Tumor necrosis factor: A plurifuctional mediator of acute inflammation. Mod. Pathol., 1988;1(3):242-247.
3. Warren, J.S., Johnson, K.J., and Ward, P.A.: PAF and immune complex induced injury. J. Lipid Mediators, in press.
4. Warren, J.S., Yabroff, K.R., Remick, D.G., Kunkel, S.L., Kunkel, R.G., Johnson, K.J., and Ward, P.A.: Intrapulmonary IL-1 and TNF in acute immune complex lung injury in the rat. FASEB, 1989 (minisymposium).
5. Ward, P.A., Warren, J.S., Varani, J., and Johnson, K.J.: Cytokines, oxygen radicals and tissue injury. Am. Assoc. Lab. Animal Med., Detroit, MI, 1988 (abstract).
6. Ward, P.A., Warren, J.S., Gannon, D., Johnson, K.J., Phan, S.H., and Varani, J.: Cytokines and oxygen radical mediated injury. Upjohn-UCLA Symposium, Park City, UT, 1988 (abstract).
7. Ward, P.A., Varani, J., Ryan, U.S., Warren, J.S., and Johnson, K.J.: Cytokines and oxygen radical mediated lung injury. Sixth Annual Aspen Basic/Clinical Science Conference on "Oxygen Radicals", The University of Colorado, Aspen, CO, August, 1988 (abstract).
8. Barton, P.A., Warren, J.S., Johnson, K.J., and Ward, P.A.: Rat alveolar macrophages express cell membrane-associated interleukin 1 activity. FASEB, 1989 (abstract).
9. Yabroff, K.R., Warren, J.S., Mandel, D.M., Johnson, K.J., and Ward, P.A.: Xanthine oxidase inhibitors reduce neutrophil influx into sites of immune complex-induced dermal vasculitis in the rat. FASEB, 1989 (abstract).

LEE WEATHERBEE, M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1987 - 30 JUNE 1988

I. CLINICAL ACTIVITIES:

A. Chief, Laboratory Service, VA Medical Center, Ann Arbor, Michigan and VA Outpatient Clinic, Toledo, Ohio.
B. Consultant for referred orthopedic cases at University of Michigan.
C. Primary activities in surgical and autopsy pathology.
D. General overview of clinical pathology at VA Medical Center.
E. Consultant in surgical pathology for VAMC, Battle Creek.

II. TEACHING ACTIVITIES:

A. One to three days per week read out surgical cases with resident on one to one basis.
B. Readout and oversee review of all autopsies with residents.
C. Participate in VA autopsy conferences with residents.
D. Oversee weekly VA surgical pathology conference.
E. Coordinate surgical and autopsy diagnostic teaching of resident by staff pathologists at VA.
F. Maintain primary responsibility for Medicine and Surgical interdepartmental teaching conferences.
G. Gave two orthopedic pathology lectures for second year medical students and participate in the pathology laboratory teaching with other VA pathologists.
H. Informal resident teaching of bone and joint cases primarily at University of Michigan on a continuing basis.
I. Conduct a gross pathology seminar for pathology residents.
J. Coordinate the fourth year medical student elective rotation at the VA.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT: None.

IV. ADMINISTRATIVE ACTIVITIES:

A. Overall responsibility for VA Medical Center Laboratory Service and for Laboratory at VA 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. Major advisory board to the Director, VA Medical Center, regarding clinical affairs.
E. Dean's committee, VA representative.
F. Radiation Safety Committee, VA Medical Center.
G. Quality Assurance Board, Co-Chair, VA Medical Center.
H. Pharmacy and Therapeutics Committee, VA Medical Center.
I. Professional Standards Board, VA Medical Center.
J. Equipment Committee, VA Medical Center.

K. General responsibility for participation of VA pathology staff in other VAMC committees, including Blood Utilization Committee, Surgical Case Review Committee, Ambulatory Care Committee and Infection Control Committee.

REGIONAL AND NATIONAL:

A. Red Cross Medical Advisory Board, Southeastern Michigan Region.
B. Clinical and Programs Advisory Council to Chief Medical Director VA Central Office. 1987 to present.

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. Ellis, J.H., Seigel, C.L., Martel, W., Weatherbee, L., Dorfman, H. Radiologic Features of Well-differentiated Osteosarcoma. AJR, 1988 Oct; 151(4):739-42.

J. REIMER WOLTER, M.D.
PROFESSOR OF OPHTHALMOLOGY
DEPARTMENTS OF OPHTHALMOLOGY AND PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

I. CLINICAL ACTIVITIES:

A. Retirement Furlough 1989/90.
B. In charge of 1/2 Ophthalmic Pathology Service, Departments of Ophthalmology and Pathology, University of Michigan Medical Center.

II. TEACHING ACTIVITIES:

A. Taking part in the regular teaching efforts for students, residents and fellows as well as the postgraduate programs in Ophthalmology.
B. In charge of teaching and representation of Ophthalmic Pathology in the Departments of Ophthalmology and Pathology as well as at national and international Meetings. Ophthalmic Pathology is one of the basic subspecialties of Ophthalmology - and it is an important part of the written and oral examination of the American Board of Ophthalmology.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Research in Ophthalmic Pathology has had continuous support from the Research to Prevent Blindness, Inc., New York, New York for more than ten years.
B. Experts in both, the Ophthalmology and Pathology Departments, have continuously contributed the most valuable support and advice in the general research effort as well as in specific research projects in Ophthalmic Pathology. As a result of progressing integration of the Ophthalmic Pathology Service, the most modern technical facilities in both Departments have been available and have been utilized continuously with much success.

PROJECTS UNDER STUDY:

A. Reactions of the inner eye to lens implants.
B. Pathology of uveal melanoma, retinoblastoma, optic nerve glioma, expulsive hemorrhage.
C. Ocular granulomas in reaction to cotton, cardboard, displaced hair, oil, and old blood, as well as fungus and bacterial endophthalmitis occurring in eyes with lens implants.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Planning and organization of daily routine, teaching and research in Ophthalmic Pathology - including continuous publication and presentation of results on an international level.
B. Usual administrative function of a Professor in the Departments of Pathology and Ophthalmology.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Medical Student Research Committee.
B. Member, Tissue Committee.
C. Member, Medical Staff of University Hospital.

REGIONAL AND NATIONAL:

A. Member, AMA.
B. Member, American Ophthalmological Society.
C. Member, American Academy of Ophthalmology.
D. Member, German Ophthalmological Society.
E. Member, Association for Research in Ophthalmology.
F. Member, Detroit Ophthalmology Club.
G. Member, University of Michigan Ophthalmology Alumni Association.
H. Member, Contact Lens Association of America.
I. Member, Association of American Ophthalmic Pathologists.
J. Member, Theobald Society of Ophthalmic Pathology.
K. Member, Michigan Ophthalmological Society.
L. Honorary Member, Association of Pediatric Ophthalmology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Wolter, JR: Deposition of exudates on intraocular lens implants. German Ophthalmol Soc, Berlin Sept. 1988.
2. Wolter, JR and Vine, AK: Immediate tenonectomy added to enucleation for grossly observed extraocular melanoma extension. International Symposium on Tumors of the Eye. Essen, Germany Sept. 89.
3. Wolter, JR and Benz, SC: Melanophages in Tenon's capsule following tenonectomy for extraocular melanoma extension. International Symposium on tumors of the eye. Essen, Germany Sept. 89.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wolter, JR, Awan, KJ: Retinoschisis filled with condensed exudate. Pakistan J. Opthalmol 4:17-21, 1988.
2. Soong, KH, Meyer, RF, Wolter, JR: Fistula excision and peripheral grafts in the treatment of persistent limbal wound leaks. Ophthalmol. 95:31-36, 1988.
3. Wolter, JR: Neovascular glaucoma in pseudophacia. Fortschr. Ophthalmol. 85:105-112, 1988.
4. Wolter, JR: Ten years without orbital optic nerve: late clinical results after removal of retrobulbar gliomas with preservation of bind eyes. J. Ped. Ophthalmol. 25:55-59, 1988.
5. Wolter, JR, Garfinkel, RA: Ciliochoroidal effusion as precursor of suprachoroidal hemorrhage. Ophthalm. Surg. 19:344-349, 1988.
6. Wolter, JR, Anderson, CJ: Failed PC-IOL implantation in one eye and successful AC-IOL implantation in the other eye in a patient with pre-existing bilateral uveitis. Ophthalm. Surg. 19:475-479, 1988.
7. Wolter, JR: The corneal endothelium in eyes with lens implants. Proceedings XXV. Internat. Congress Ophthalmol. pp. 85-93, 1988.
8. Wolter, JR, Till, GO: Protein deposition and leucocyte accumulation on lens implants following exposure to whole blood in vitro. Implants in Ophthalmol., Singapore, 2:159-163, 1988.
9. Wolter, JR, Lindenmuth, KA: Surface reaction on glass anterior chamber foreign body removed 24 hours after injury. Ophthalm. Surg. 19:799-801, 1988.
10. Wolter, JR: Necrosis of choroidal melanoma in ciliary artery involvement with temporal arteritis. Brit, J. Ophthalmol. 73:216-219, 1989.
11. Wolter, JR, Sugar, A: Reactive membrane on a foldable Silicone lens implant in the posterior chamber of the human eye. Ophthalm. Surg. 20:17-20, 1989.
12. Wolter, JR: Regional uveal response to increased nutritional needs in the retinal zone of the developing eye in retinoblastoma. J. Ped. Ophthalmol. 26:120-123, 1989.
13. Johnson, MW, Skuta, GL, Kincaid, MC, Nelson, CC, Wolter, JR: Malignant melanoma of the iris in xeroderma pigmentosum. Arch. Opthth 107:402-407, 1989.
14. Wolter, JR: Morphology of exudate membranes on intraocular lens implants. Fortschritte Ophthalmol, Germany 86:132-137, 1989.
15. Wolter, JR: Fluid state of malignant melanoma growth presenting as exudative retinal detachment. Ophthalmologica, Switzerland 199:34-40, 1989.
16. Wolter, JR, Till, GO: Multinucleated giant cells on Bruch's membrane late in recurrent retinal and subretinal hemorrhaging. Ophthalmologica, Switzerland, in press.
17. Wolter, JR: Precipitates on cornea and lens implant in pseudophakia. Implants in Ophthlmol, Singapore, in press.
18. Wolter, JR: Pathology and general significance of fibrin deposition on lens implants. J Cataract nd Refract Surg, in press.
19. Wolter, JR, Soong, HK: Flat sections for detailed endothelial pathology of corneal buttons. Refract and Corneal Surg, in press.

SECTION REPORTS

DIVISION OF ANATOMIC PATHOLOGY

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1988 - 30 JUNE 1989

The 1988-1989 fiscal year marks the completion of three years of operation of the new University Hospital. During this period, with unprecedented levels of hospital occupancy and clinic utilization, the overall volume of clinical activities in many departments has risen steadily, leading to a parallel increase in the routine activities of many laboratory services, including those of the Division of Anatomic Pathology. At the same time the volume of activity has been increasing, there has been a growing dependency on histopathologic and cytologic techniques for patient monitoring in critical care situations, producing a steady increase in the frequency and intensity of our consultative interaction with clinical colleagues. This, in turn, is leading to significant adjustments in professional and technologic staffing.

The activities of the several services of the Division are outlined below.

Gerald D. Abrams, M.D.
Director, Anatomic Pathology

AUTOPSY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

The Autopsy Service of The University of Michigan continues to perform autopsies on University of Michigan patients. Additionally, autopsies are performed on Washtenaw Country Medical Examiners' cases, as well as Alzheimer's and Disease Related Disorder patients from throughout the region. Modifications in the Autopsy Service have made been and are outlined below.

TIMELY COMPLETION OF AUTOPSIES

Several changes have been made in an attempt to decrease the turn-around time for the completion of autopsies. These changes include:

A. Reduction of Late List from 60 to 45 days. Residents now have 45 days (a reduction from the previous 60 day limit) to complete their autopsies and turn them in for final typing. The intent is to have all autopsies completed within the CAP 60 day guidelines.

B. Routine histology sections returned in two weeks. Routine histologic sections are to be completed within two weeks from the time when gross tissue is handed in. If sections cannot be completed within this time frame, overtime will be authorized.

C. Typing returned in two weeks. The typing of autopsy protocols will be completed within two weeks from the time the gross dictation is handed in. If the completion of typing cannot be done within this time frame, overtime will be authorized.

D. Neuropathology slides returned in three weeks. Neuropathologic slides will be returned within three weeks of the date of the autopsy. If the completion of the slides cannot be done within this time frame, overtime will be authorized.

It is anticipated that a combination of the above measures will decrease the turn-around time for the completion of autopsies.

QUALITY ASSURANCE

A quality assurance program has been initiated. Presently, this is a two-part program.

A. Quarterly Quality Assurance Report. On a quarterly basis, the length of time to complete autopsies is calculated and the data filed with the Quality Assurance Committee. This data is used to identify problem areas.

B. Review of cases. All autopsy protocols which are sent to outside individuals (i.e. family, referring physicians) are reviewed for completeness and accuracy by the Director of the Autopsy Service. One hundred such protocols were

reviewed during the past year. resulting in the revision oven protocols prior to release from the Department of Pathology.

MEDICAL EXAMINER CASES

The Attorney General of Michigan has ruled that counties cannot force other counties to accept medical examiner cases and, furthermore, cannot force them to pay the cost of autopsies. As a result of this ruling, our ability to return forensic cases to the county of injury has been restricted and the number of medical examiner cases which we have performed have increased from 35 (1987/88) to 49 (1988/89). Legislation is pending which would require the county of injury to accept cases. However, at the time of the submission of this report, this legislation has not been formally passed.

FROZEN SECTION/AUTOPSY CALL SCHEDULES

The weekend autopsy call schedule has been formally separated from the week-long frozen section call schedule. As a result of this separation, there will be an increase in the number of Departmental faculty participating on the Autopsy Service. A yearly schedule for weekend autopsy call will be created.

AUTOPSY STATISTICS

	1988/89
Total U of M Autopsies	383
M-Labs Cases	11
Outside Cases	7
Medical Examiner Cases	49
In-Hospital Deaths	26
Outside Cases	23
Percent of U of M Deaths Autopsied (includes Tetralogy Cases)	40%

	85/86	86/87	87/88	88/89
Total Autopsies	394	381	385	383
Autopsy Rate, U of M	38%	36%	35%	40%
Medical Examiner Cases	70	62	35	49
Number of Attending Staff	16	15	15	16

Daniel G. Remick, M.D.
Director,
Autopsy Service

CYTOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1987- 30 JUNE 1988

Workload has increased dramatically in recent months due to the influx of gynecologic cytology specimens from outside the Medical Center. This has resulted in a projected increase of 100 percent in gynecologic cytology for the coming year. Non-gynecologic cytology shows a continued, but much more modest, upward trend of about 4 percent. While we are currently coping with the increased workload, we live in apprehension of ever losing a cytotechnologist since replacing these skilled persons has become extremely difficult.

During the past year we again experienced having a 5th year resident attached full time to cytopathology. As previously, we believe it was an outstanding success both as a learning experience for the resident and as a contribution to the running of the laboratory, including relieving the senior staff of certain activities, e.g. attendance at all fine needle aspirates, about 400 per year.

During the year the laboratory gave hospitality to visiting pathologists from Brazil, Greece and Sweden.

Bernard Naylor, M.D.
Director
Cytopathology Laboratory

DERMATOPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

The Dermatopathology Service receives case material from four different sources: (1) UMMC (ID) cases; (2) outside contractual (MD) cases; (3) personal consultations (HE) cases and; (4) cases from outside sources reviewed for patients referred to UMMC for additional care and management, (TD) cases. There was an increase in each category in 1988-1989 over 1987-1988.

Dr. J.T. Headington has been given the responsibility for directing the activities of the Pigmented Lesion Clinic and the Melanoma Conference and Drs. J.T. Headington and B.J. Nickoloff will be participants in the newly scheduled Cutaneous Lymphoma Conference. These activities reflect increased numbers of patients requiring care for melanomas and lymphomas.

Teaching has continued to involve both Pathology and Dermatology house officers on a daily basis during scheduled rotations, and has also included visiting scholars from other institutions, both national and international.

The Dermatopathology Service significantly interfaces with the research activities of Immunopathology and the Clinical Flow Cytometry Laboratory. During 1988-1989 we anticipate the beginnings of the use of in-situ hybridization techniques for selected problems as well as expanded use of T-cell receptor gene rearrangement studies.

John T. Headington, M.D.

Brian J. Nickoloff, M.D., Ph.D.

ELECTRON MICROSCOPY SERVICE
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

The Electron Microscopy Service continues to process a large number of cases on both clinical as well as research material. During this past year a total of 860 cases were processed. Of this total, 432 represented clinical biopsies. The breakdown of the clinical biopsies revealed that 132 of the biopsies were kidney biopsies with the majority of the remainder being nerve and muscle biopsies and miscellaneous tumors. In the diagnoses of many tumors electron microscopy continues to be a valuable tool particularily when used in conjunction with immunoperoxidase and is indispensable in the diagnosis of peripheral neuropathies and glomerulonephritis.

The research use of electron microscopy continues to expand with 428 samples processed for electron microscopy. Samples of virtually every organ of the body were processed with most tissues being lung and kidney. In addition electron microscopy is used extensively in the analysis of isolated cell populations and in tissue culture.

Studies are also under way using the techniques of immunoelectronmicroscopy to localize specific antigens in tissues using immune gold and peroxidase techniques. Studies are also under way to localize oxygen radical products in tissues in acute inflammation.

In summary, the electron microscopy service continues with its heavy service load in addition to its expanding research obligations with 22 different research investigators utilizing this critical core facility during this past year.

Kent J. Johnson, M.D.
Director
Electron Microscopy Service

NEUROPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

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. Constance J. D'Amato, B.S., Assistant Professor and Mila Blaivas, M.D., Ph.D., Clinical Assistant Professor, spent 60% of their time on the Neuropathology Service. Full time faculty was Paul E. McKeever, M.D., Ph.D., Associate Professor.

CLINICAL ACTIVITIES:

The following examinations were completed with the cooperation of our excellent neurohistology, electron microscopic, general histology, immunohistology, and secretarial staff.

1. There were 543 neurosurgical cases examined this year from Main, Mott and outside hospitals in consultation. 54 cases (a 20% increase over the previous year) were referrals from other institutions, a portion of which were part of the NIH funded study of BUDR radio-sensitization of gliomas CA33768. Ninety surgical specimens required special neurohistologic procedures.
2. There were 298 brains examined out of 372 autopsies which is 80% of all autopsies at this Medical Center. 32 were from other institutions and hospitals. Drs. Blaivas and McKeever, in collaboration with Ms. D'Amato interpreted macroscopic neuropathology at the University Hospital. While all neuropathology faculty have participated, Dr. Hicks and Ms. D'Amato collaborated to prepare macroscopic and microscopic descriptions of most UM autopsy brains, and other brains referred for consultation. These are given to the house officer prosectors to compare with their findings, and to facilitate completion of the autopsy reports; in consultation they become the report.
3. There were 145 muscle biopsies (a 9% increase), nearly all with histochemistry, some with electron microscopy. There were 60 peripheral nerve biopsies. Teased fiber preparations and electron microscopy were performed on appropriate nerve biopsies. 79 cases were referrals from other institutions. Dr. Mila Blaivas provides quality diagnoses and consultations. The combination of nerve teasing, muscle histochemistry, electron microscopy and morphometry make the service regionally competitive for diagnostic consultation.
4. Drs. Blaivas and McKeever examined, interpreted and reported 134 cases in semithin section and electron micrographs of 85 cases. The majority were nerve, ceroid and neurosurgical biopsy cases.
5. The ceroid service, buffy coat division, reported 9 cases.
6. The Brain Tumor Board of the University of Michigan Cancer Center and Hospitals reviewed neuropathology and clinical aspects of more than 100 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. She also again received "The Excellence in Teaching Award" from the 2nd year medical student class.
2. House Officers, Graduate students, Postgraduate and other students and faculty: These include a conference every other month where neuropathology is reviewed; 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: Dr. Lynne Abruzzo and two Neurology House Officers chose elective rotations on the Neuropathology Service.
4. Dr. James S. Nelson, Head of Neuropathology at Henry Ford Hospital, was appointed Clinical Professor I in the Department of Pathology. Dr. Nelson contributed to neuropathology teaching including Neuropathology 858.

RESEARCH ACTIVITIES:

1. Dr. Hicks' and Ms. D'Amato's research has centered principally on the development of the nervous system in mammals, mechanisms of malformation and recovery from injury caused by radiation, mutant genes or other agents. They also provide neuropathologic support for a biochemical study of Alzheimer's and other dementias conducted by Anne B. Young and John B. Penney, Department of Neurology.
2. Dr. Blaivas and associates continue to investigate ocular muscle (normal and pathology), peripheral nerve grafting and mitochondrial disorders.
3. 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.
4. The Tumor Immunology, Extracellular Matrix and Neurooncology 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.

5. Collaboration with Neurology, and Epidemiology Departments, Eastern Michigan University, the State of Michigan Department of Public Health, the Alzheimer's Disease and Related Disorders Association and Henry Ford 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 1988 - 30 JUNE 1989

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 (22 weeks gestation or any liveborn, to 18 years)	= 206
Necropsies on above	= 127
Necropsy Percentage	= 62%

Of the 127 posts, 55 patients' bodies were released to Anatomy for study and disposal. These posts were performed by Mason Barr, Jr., M.D. Seventy-two patients were posted by the residents and senior staff in Pathology, primarily Dr. Heidelberger. Additional necropsies categorized in the general hospital statistics as "Medical Legal" posts included 9 additional posts on pediatric patients including SIDS cases and both inpatient and emergency room trauma cases.

A total of 382 necropsies for UMMC Hospitals patients was performed (including the 9 pediatric "medical legals"); 55 by Dr. Barr in the Teratology Unit and 327 by the Pathology Department Staff. Thus, 33.2% of the total posts at the UMMC were pediatric posts.

The total number of pediatric surgical specimens (including placentas) examined is almost 2100. This represents an increase of 4-5% from the previous academic year.

Kathleen P. Heidelberger, M.D.
Director
Pediatric Pathology Service

SURGICAL PATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1988 - 30 JUNE 1989

During the 1988 - 1989 fiscal year, the activities of the Surgical Pathology Service have grown in volume and intensity, continuing the trends of the past several years. The total number of surgical specimens accessioned in University Hospital, the number of specimens accessioned through the activities of M-Labs, and the number of cases referred in consultation by pathologists in other institutions have all increased as compared to the prior year's total. The fact that the demands of this steadily increasing workload have been met until now with no increase in professional personnel is a tribute to the stamina and dedication of the Surgical Pathology staff, all of whom have put forth extraordinary effort on an ongoing basis. During the coming year two additional surgical pathologists are joining the group, and this should enhance the opportunity for the entire staff to continue in the departmental tradition of academic leadership.

The increased volume of work in surgical pathology, coupled with an increasing number of requests for same-day processing of tissue, and an increasing need for special studies (e.g. immunohistochemical) has led to a significant change in staffing of the histopathology laboratory. During the 1988-l989 fiscal year, an afternoon shift (two technologists) has been instituted. This has enabled us to meet requests for rapid tissue processing, has facilitated the timely processing of slides for supplemental studies ordered during the working day, and has provided support for the on-call team of pathologists in intraoperative consultations with frozen section during the evening hours. Weekend technologist staffing patterns have also now been arranged to allow for the increasing number of requests for same-day biopsy results on Saturdays and Sundays, especially from the various transplant services.

During the past year another important change in the staffing of the histopathology laboratory has been the addition of a person specially trained to assist in the accessioning, gross description, and handling of routine biopsy specimens. This, in turn, has allowed our House Officers to devote more of their time to the microscopic study and reporting of the day's biopsies.

Finally, the long awaited enlargement of the frozen section laboratory was undertaken at the year's end. At the time of this writing, a "clean" room, dedicated entirely to microscopic study, has been added to the facility, thus separating the handling and dissection of potentially hazardous specimens from the sign-out activity. The space formerly used for sign-out activity is being remodeled to provide for additional specimen handling and for enhanced gross photography of operative specimens.

Gerald D. Abrams, M.D.
Director
Surgical Pathology Service

CLINICAL PATHOLOGY LABORATORIES

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENT REPORT
JULY 1, 1988 - JUNE 30, 1989

Clinical laboratory personnel were extremely busy in the past year with increased volume in addition to the consolidation of laboratories and new initiatives in the areas of quality assurance and cost effective manage ment. Additionally, the M-Labs program continued to mature and 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 Cytogenetics Laboratory, the HLA Typing Laboratory, and in addition, planned for the consolidation of the Gyn/Endocrine Laboratory. Laboratory personnel have demonstrated a profound commitment to high quality laboratory medicine in their approach to the consolidation and the numerous issues that had to be addressed.

In the process of the consolidation, a College of American Pathologists (CAP) Inspection was carried out. The inspection was passed with only a few minor deficiencies and a congratulation by the inspecting team for our initiative in the areas of quality assurance and laboratory-based information systems.

The Quality Assurance Committee, made up of members of the laboratory staff and chaired for Dr. McClatchey by Suzanne Butch, Chief Technologist for the Blood Bank, has demonstrated a visionary approach to quality assurance in the clinical laboratories. The quality assurance program that the laboratory professionals now have in place is exemplary, and compliments national programs now beginning to develop.

The M-Labs program in the clinical laboratories is continuing to grow and mature, becoming part of the daily routine, and for that matter, evening and night shift routine. It is important to note that the M-Labs program is constantly monitored by the M-Labs Technical Group, which is made up of laboratory personnel, insuring 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 efficient, cost effective laboratory system. The continual monitoring of our M-Labs program and ultimately our laboratory program in general has led to changes in our system that have produced a high quality product, not only for M-Labs clients but University Hospitals in general.

Kenneth D. McClatchey, M.D., D.D.S.
Director,
Clinical Pathology

UNIVERSITY HOSPITALS BLOOD BANK AND TRANSFUSION SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1988 - 30 JUNE 1989

PATIENT CARE:

Although concern regarding posttransfusion disease has caused blood transfusions nationwide to plateau, utilization in University Hospitals increased overall approximately 10 per cent during l989-89. This related primarily to increased blood utilization in cardiovascular procedures, expansion of the liver homotransplantation program and implementation of the bone marrow homotransplantation program. It is anticipated that 80-100 liver transplants will be performed annually in this hospital; moreover, it must be noted that many of these patients require re-operation with resultant increased requirements for blood resources. Cardiac surgery patients consistently have required large volumes of Red Blood Cells and platelet concentrates. Efforts currently are under way in cooperation with the Section of Thoracic Surgery and the Department of Anesthesiology to reduce this rate of utilization.

The autologous bone marrow transplantation program has impacted the work load of the Blood Bank, inasmuch as the laboratory is responsible for processing harvested marrow as well as peripheral blood stem cells. A program for collection of peripheral blood stem cells by cytapheresis was implemented during the past year. This procedure requires 8-10 apheresis procedures on each prospective recipient of bone marrow.

In addition to the above expanded activities, the concern on the part of our patients for posttransfusion disease has been reflected in increasing demands for preoperative autologous blood donation and directed donation. the Southeastern Michigan Red Cross Blood Program has assisted in providing these services.

Maintenance of the above new programs will require augmentation of staff. Furthermore, the expanded demands upon apheresis and blood transfusion programs likely will require expansion of the current donor facility.

The inclusion of "Transfusion Service" in the name of this activity reflects the level of involvement of the laboratory with direct patient care, as exemplified in the hemapheresis and outpatient transfusion programs, as well as in the consultative activities related to blood component utilization and transfusion practices.

TEACHING ACTIVITIES:

Fellowship training in Blood Banking/Transfusion Medicine will be initiated on July 1, 1989, when Dr. Robertson Davenport will become the first Fellow in training. The program will be inspected in late July by the Licensing Committee on Graduate Medical Education. During the past year considerable effort has been devoted to structure of the fellowship program, and compliance with requirements of the LCGME.

A core lecture series in Blood Banking was presented to Pathology House Officers, and five Grand Rounds lectures were presented in the Clinical Pathology curriculum. House Officers from the Departments of Pediatrics and Anesthesiology rotated through the

Blood Bank to receive training experience. In addition, nursing staff of the laboratory provided in-service lectures for nursing units throughout University Hospitals.

The sixteenth annual Postgraduate Course, "Current Topics in Blood Banking", was held on May 31-June 2, 1989. This was the largest postgraduate course presented in the Towsley Center during the past year, as approximately 270 technologists and physicians from throughout the United States attended. Mr. John Judd and Ms. Diana McCoy-Pardington were program directors, assisted by Ms. Suzanne Butch and Dr. Oberman.

PROFESSIONAL ACTIVITIES:

Suzanne Butch, Chief Technologist of the Blood Bank, again served on the Board of Directors of the American Association of Blood Banks, while Mr. John Judd, Associate Professor, served as Vice-Chairman of the Scientific Section Coordinating Committee of the AABB. Mr. Ronald Salisbury, Supervisory Technologist, continued to play a leadership role in the country in implementation of the Cerner laboratory computer system for blood banks. Dr. Oberman is the Associate Editor of TRANSFUSION, the most prestigious journal in the field.

Other professional activities of faculty and staff in the laboratory are included in the Appendix.

RESEARCH ACTIVITIES:

Faculty and staff of the laboratory presented four papers at the meeting of the International Society of Blood Transfusion in London, England, in July, 1988. In addition, three papers were presented by members of the faculty and staff at the Annual Meeting of the American Association of Blood Banks in Kansas City, MO, in October, 1988. These presentations included such topics as modification of pretransfusion testing, blood utilization for various surgical procedures, percutaneous umbilical blood sampling in obstetrics, blood utilization for extracorporeal membrane oxygenator procedures and utilization review. As is noted in the Appendix, as well as in reports of individual Faculty, members of Faculty and staff were sought for lectures throughout the United States and Europe during the past year, attesting to the leadership position of the laboratory. In addition, members of the Faculty and staff of the laboratory published 13 scientific papers or book chapters during the year.

Harold A. Oberman, M.D.
Director,
Blood Bank

CLINICAL BIOCHEMISTRY SECTION

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

SECTION OVERVIEW:

During the past year, another major increase in volume was experienced by the Clinical Biochemistry Section. This reflects both increase in numbers of routine tests ordered and in the numbers of specialty tests available. As described below, there has been a major shift in the instrumentation available in the general chemistry laboratory. The newer Ektachem 700 instruments will improve both the efficiency of the laboratory and decrease technologist training time. The Drug Analysis and Toxicology Laboratory is now certified by the College of American Pathologists in clinical toxicology. Renovation in the Ligand Assay Laboratory has been completed with the installation of proper temperature control equipment. This new laboratory facility will improve the efficiency of operation. In the Clinical Immunology Laboratory, there have been several new procedures developed which anticipated clinical needs in the areas of immunodeficiency disease, autoimmunity and metabolic disease. Lastly, we welcome the inclusion of the GYN-Encocrine Laboratory and Dr. Menon to our group. We are sure that this addition will have a fruitful, cooperative relationship with the rest of the section.

GENERAL CHEMISTRY LABORATORY - Donald Giacherio, Ph.D., Laboratory Director.

The Chemistry Laboratory continues to experience significant increases in test volume. Actual tests performed ar up 9.3% over the preceding year, to just over 2.6 million tests per year. Significant increases have been seen in the more esoteric, labor intensive testing areas of the lab, much due to the increases in M Labs client volume.

Cholesterol screening continues to be a major focus of the laboratory. An ABBOTT *Vision* analyzer has been leased to give the laboratory the flexibility to perform remote site testing for whole blood cholesterol. The laboratory has supplied this instrument and technologists to perform the analysis for a significant number of cholesterol screening projects, many in conjunction with the MedSport Clinic.

Far and away the major accomplishment of the laboratory this past year has been the selection of new chemistry analyzers. After a long search and evaluation process by a committee within the laboratory, the decision was reached to acquire five Kodak Ektachem 700 analyzers. These will serve to consolidate the currently separate adult and pediatric automated testing areas within the laboratory into one workcenter. This multiple random access instrument approach will allow the Chemistry Laboratory to better meet the institutions growing needs for faster turnaround of lab results, and continue to absorb increases in test volumes without proportional increases in budget or personnel.

DRUG ANALYSIS AND TOXICOLOGY LABORATORY - Thomas Annesley, Ph.D., Laboratory Director

During the last year the Drug Analysis Laboratory has again seen an increase in demand for laboratory services. Overall, test volume was up 14%. The important aspect of this increase is the volume of special hospital and M-Labs programs. Cyclosporine testing has increased 27%, with the laboratory now performing 1200 assays per month for this test alone. General drug screens have increased 22%, and specialty toxicology screens have increased over 29%. Worth mentioning is the fact that laboratory income (gross margin) has increased 26%, during which time the lab has actually remained 2% under budget.

The quality and significance of the numbers outlined above reflect the strong efforts of the technical and management staff of the laboratory. Particularly worth noting is the successful cost saving proposal by John Foster as part of the University Hospital Employee Suggestion Program. John's proposal was highlighted in a hospital publication.

After a lengthy delay in required renovations, the Perkin Elmer 5100 Analyzer was installed. The first test offered using this new technology has been the analysis of serum aluminum. Blood and urine lead will be offered shortly, while the development of heavy metal screens is still under development.

The laboratory successfully underwent two accreditation inspections during the last year. The first was a general inspection for accreditation by the College of American Pathologists for certification in clinical toxicology. The laboratory also went through a rigorous inspection as part of a process for accreditation in forensic toxicology. At the present time, the lab awaits word of actual certification in the forensic toxicology area.

LIGAND ASSAY LABORATORY - Barry England, Ph.D., Laboratory Director.

The Ligand Assay Laboratory experienced an increase in specimens processed of approximately 20% over the previous year, to a total volume of 128,163. The laboratory has occupied its newly renovated quarters in Med Sci I and enjoys the use of an intra-laboratory computer network that permits interactive communication between the several microcomputers in the laboratory and universal access to a recently installed laser printer. The presence of this system has made it possible to maintain many of the aspects of the laboratory quality control system that had been lost because of conversion to alternative technologies and changes in data analysis procedures. It is anticipated that the coming year will provide additional computing capability to replace the losses associated with the aforementioned changes and the still uncorrected problems experienced by this laboratory with the conversion to the Cerner Pathnet system.

The Ligand Assay Laboratory continues to convert radioimmunoassay procedures to the more efficient non-radioisotopic immunoassay methods. A total of 10 radioimmunoassay methods have been converted to fluoresence polarization or chemilluminesence methods. Digitoxin, digoxin, tobramicin and gentamicin have been migrated to the fluoresence polarization analyzer (TDx) from Abbott Labs and thyroxine has been moved to the chemilluminesence analyzer (Magic-lite) from Ciba-Corning. Hepatitis B_s Ag, anti-Hepatitis B_s Ag, Hepatitis B_e Ag, anti-Hepatitis B_e Ag and anti-Hepatitis A have all been converted from radioimmunoassays to enzymeimmunoassays. The non-radioisotopic assay procedures have decreased assay turnaround time and reduced the technical time required to complete the assay procedures. In addition, 2 new assay procedures were initiated during the past year, a test for human T lymphocyte virus I (HTLV I) and a specific test for human prostrate specific antigen.

CLINICAL IMMUNOPATHOLOGY LABORATORY - David F. Keren, M.D., Laboratory Director, Jeffrey Warren, M.D., Associate Director.

During the past year, Dr. Warren has assumed the role of Associate Director of the Clinical Immunology Laboratory. This has been especially helpful in managing the laboratory and developing new, relevant procedures. Dr. John Lowe has continued to assist the laboratory with the daily evaluation of clinical material.

As with the other laboratories, the Clinical Immunology Laboratory has experienced a 20% increase in volume. There have been significant improvements in some of our new laboratory procedures. The neutrophil cytoplasmic autoantibody test is now performed by cytospin. This work was accomplished largely through the efforts of Dr. Gary Hammerberg our Visiting Scientist from Eastern Michigan University. The new assay now allows us to distinguish the cytoplasmic from the perinuclear pattern. The former is more specific for Wegener's granulomatosis. We have also improved the cardiolipin antibody test with and 8 point standard curve which allows us to correlate the cardiolipin antibody level with other institutions nation wide. In addition, we have developed a microalbuminuria assay which will be used to follow the large number of diabetic patients at this institutions. Detection of microalbuminuria has been correlated with early renal disease in these patients. The laboratory is performing a collaborative study with the Ligand Assay Laboratory on ways to detect the P24 antigen. This antigen is important in following patients with Acquired Immunodeficiency Syndrome. Lastly, the laboratory has developed a prealbumin assay which should be helpful in establishing the nutritional status of patients. Other institutions have used this assay for geriatric patients and in malnourished children.

David F. Keren, M.D.
Director
Clinical Biochemistry Section

CLINICAL CYTOGENETICS LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

ORGANIZATION:

The Department of Pathology assumed administration of the clinical cytogenetics laboratory one year ago. During this period, we have seen a number of changes.

The laboratory made two moves during the pat year. First, the entire laboratory moved from Mott Hospital to the second floor of Med Sci II. This space was inadequate from the beginning. This additional space was made available in the Pathology portion of MSI. About one-half of the service was moved to this space last month. While having the lab split is inconvenient and not the most efficient way for me to keep on top of things, the new space is very much welcomed by all of us. Overcrowding is, for the first time perhaps in the history of the lab, not presently an issue. Once the lab is completely staffed with new technologists, this new space will, however, be filled.

STAFFING:

The cytogenetics laboratory has been severely hurt by chronic understaffing. Not only was keeping up with routine specimens difficult but the lab could not properly keep on top of new demands and new technologies. As a result, the lab was not able to keep up with expectations for decreased turn around time (base don national trends) and meet the demands of a large increase in the complexity of tests.

I am now pleased to say that new staff has and will be added to the lab. Dr. Susan Sheldon joined us as Assistant Director. Her experience in the area of cytogenetics of hematological disorders will be a boon to the lab. In addition, we have recently been given the "OK" to hire two new cytogenetic technologists and a full time lab aid. This will bring our total number to techs to 8 with one supervisor (1/2 at scope). This will bring our staffing level to a point where each tech is expected to perform less than 200 analyses per year based on our current load of 1600 specimens per year. This is (finally) where we should be to meet current demands. The national expectation from labs like ours (full service and in an academic setting with training demands, etc.) is 175-200 samples per tech per year.

OTHER:

Our shift to Pathnet computer system has begun. This will make sign-outs and reporting faster and more efficient. I am, so far, very impressed with the system.

Thomas W. Glover, Ph.D.
Acting Director,
Clinical Cytogenetics Laboratory

CLINICAL FLOW CYTOMETRY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

The Clinical Flow Cytometry Laboratory has enjoyed a stable year without the major changes that have characterized the recent past. The Laboratory has continued its active role in Diagnostic Clinical Pathology. A total of 1,500 specimens were handled by the laboratory during the past twelve months, which is an increase of 25% over the previous year. Approximately 600 specimens were processed for cell surface markers or cellular DNA content studies. Approximately 50% of these latter specimens were evaluated for hematologic disorders while the remainder of the specimens were for the evaluation of transplant patients or individuals with primary or acquired immune deficiencies. A sizeable proportion of the latter group is in the area of cellular monitoring of transplant patients receiving OKT3 monoclonal antibody therapy. Approximately 600 specimens were studied for platelet-associated immunoglobulins and neutrophil-specific antibodies. Each specimen requires from 10-30 individual staining, quantitation and analytic procedures. Quality control and calibration procedures further add to the specimen load. Thus, the laboratory staff conducted approximately 28,000 individual marker studies in Fiscal Year 88/89. The laboratory continues to provide 12-24 hour turnaround studies on acute leukemia and selected transplant patients. Overall, patient revenue continues to climb and the significant reduction in commodity expenses seen last year has continued through this year as well. This again has led to a gross margin that is 300% better than the gross margin expected by budget.

The Flow Cytometry Laboratory has undergone a major change in how many of the specimens are processed. All primary and acquired immunodeficiencies along with the immune monitoring of post-transplantation patients are now evaluated by direct, 2-color immunofluorescent analysis. In addition, a flow cytometric accessory from Coulter Corporation (Q-prep) has substantially reduced the processing time required for immunofluorescent analysis. Together, these two steps have enhanced our efficiency as a laboratory and decreased the turnaround time for results. In addition, these method changes have allowed us to evaluate lymphopenic patients who could not be consistently analyzed by previous preparation methods.

The Flow Cytometry Laboratory also underwent a major change in its quality control and quality assurance programs. The entire procedure manual was rewritten and a more exhaustive quality control program instituted. This was done in preparation for the recent CAP inspection, which the laboratory passed with deserved accolades. These changes have enabled the laboratory to become a truly "clinical" pathology laboratory.

The molecular diagnostic aspect of the laboratory has been implemented with the use of technologists currently in the laboratory. We have successfully implemented immunoglobulin and T-cell receptor gene rearrangement studies with over 300 assays evaluated during the previous year. Detection of bcr gene rearrangements in chronic myeloproliferative disorders and acute leukemia is also being analyzed in the laboratory. The use of restriction fragment length polymorphisms (RFLP) studies to evaluate allogenic post-bone marrow transplantation patients for evidence of either engraftment of normal marrow or recurrence of disease will be implemented as soon as the allogenic bone marrow transplant program begins here at the University.

New developments in the flow cytometry area in the upcoming year will include further implementation of direct and two-color staining with monoclonal antibodies. Reticulocyte analysis by flow cytometry will also be evaluated as a means of providing the laboratory with a routine, clinical assay. Future developments in the molecular diagnostic area will depend on the clinical demand for the studies and the technical skills that are required. The polymerase chain reaction (PCR) is being evaluated as a possible technique that may enhance the implementation of DNA studies into the clinical laboratory. Also, a semi-automated DNA instrument is being evaluated that may aid in these assays becoming a more routine procedure. A limited number of biotinylated probes are being used on a trial basis to assess the possibility of moving away from P^{32} radioactive probes. Investigative work will continue in the area of hematologic and genotypic markers in acute and chronic leukemias and malignant lymphoma, as well as studying the role of adhesion molecules and homing receptors in various benign and malignant hematopoietic diseases.

Curtis A.Hanson, M.D.
Lloyd M. Stoolman, M.D.

Directors
Clinical Flow Cytometry Laboratory

CLINICAL HEMATOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

LABORATORY ACTIVITIES:

A. There was an overall increase in the total number of tests from 427,000 in 1987-1988 to 463,00 in 1988-1989.

B. The increase in labor-intensive tests is as follows: a) Differential white blood cell increased by 10 per cent despite the introduction of a new policy of carrying out differential counts below 500/cmm once every other day between 8:00 am and 5:00 pm only; b) reticulocyte counts rose by 8 per cent; c) the number of microscopic fluid examinations requiring review by the hematopathologist rose by 30 per cent despite the fact that the criteria for reviewing fluids were relaxed.

C. New procedures: With the start of the autologous bone marrow transplant program, the following procedures were implemented: a) Buffy coat white blood cell differential counts; b) total nucleated cell counts of bone marrow aspirates; and c) total cell and differential cell counts on peripheral blood stem cell harvests.

D. Additional Innovations: To reduce the work load we no longer carry out platelet estimates on all platelet counts but limit them to those counts under 150,000/cmm, which also reduces the number of slides and reagents used for staining. This results in a saving of approximately 45,000 tests per year without loss of revenue. The number of unnecessary tests has been reduced by requiring approval of special procedures by house officers and staff.

E. The automated hematology counters were upgraded in the laboratory to maintain efficiency and to decrease turn-around time. Two automated differential counters (Coulter-VCS) are being incorporated into the laboratory. Preliminary studies of these new generation instruments indicate that 30%-40% of current white cell differential counts performed manually may be successfully done by the VCS instrument. This saving of personnel time is essential as the number of tests performed increases.

F. Daily bone marrow signout.

G. Daily signout of in-house and UM clients, abnormal blood smears and body and joint fluids takes place 7 days per week.

H. A quality assurance program has been implemented in the area of bone marrow cytochemical stains for leukemia. The house officer on the Hematology Service reviews all cytochemistry requests to determine the appropriateness of the test. This has led to an approximate 40% decrease in cytochemical stains performed, resulting in improved utilization of resources.

TEACHING ACTIVITIES:

A. Pathology House Officers 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-Lab clients.
6. A formal teaching conference for House Officers has been implemented.
7. Review of SWOG cases.
8. Weekly Interdepartmental Lymphoma Conference.
9. Biweekly Hematopathology Conferences.
10. Pediatric Hematology/Oncology fellows participate in signouts.

FY 88/89 GOALS:

A. Implementation of Fellowship program in Hematopathology as of July 1, 1989.

Bertram Schnitzer, M.D.
Curtis A. Hanson, M.D.
Directors
Clinical Hematology Laboratory

CLINICAL MICROBIOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

CLINICAL ACTIVITIES:

The specimen volume increased 11.4% compared to last year's volume; we currently process over 12,000 specimens/month. M-Labs specimen volume increased 128T and accounted for 8.5% of the total laboratory volume.

New tests implemented by the laboratory were: Clostridium difficile culture and toxin assay, Sputum Quality Gram stain procedure, Leptospira culture, E coli K1 antigen test for neonates and Antimicrobial Synergy testing.

Under the direction of Patricia Shalis, numerous microbiology software changes were made to the Cerner program to enhance specimen handling and reporting. She also participated in 13 site visits by laboratory personnel interested in our system.

Laboratory quality and safety issues continued to receive attention as exemplified by the implementation of new quality assurance programs and the introduction of "Q-Probe" sponsored by the College of American Pathologists (CAP). The laboratory successfully completed a CAP inspection this spring. A "Body Substance Precaution" procedure was instituted in compliance with federal guidelines to enhance employee safety while handling potentially infectious material.

DEVELOPMENTAL ACTIVITIES:

Commercially prepared DNA probe kits were valuated for:

- the direct detection of Mycobacterium spp. in sputum
- the combined detection of the Mycobacterium avium complex organisms from culture
- the direct detection on Chlamydia using a chemoluminescent labelled probe.

New antibiotic and antibiotic combination studies were sponsored by various pharmaceutical companies to test for effectiveness against clinical isolates. The Laboratory continues to be participants in a multicenter Bacteroides fragilis group study and recently began contributing information for a multicenter mycology study.

Several cooperative studies with other departments are on-going.

- Two clinical trails with investigational antibiotics are being performed with Pulmonary Medicine.
- Clinical isolates of C. difficile, Enterococcus and Lactobacillus are being isolated and provided to the Infectious Disease section.
- IV catheter contamination studies were conducted with the Pharmacy Department and a PEN team procedure is currently being conducted in the laboratory.
- A vascular graft infection study with the Vascular Surgery section was completed and the results accepted for publication.
- Granulocyte bactericidal function studies for CGD patients are being done for Pediatric Hematology.
- A vaginosis study is underway with the Ob/Gyn section.

EDUCATIONAL ACTIVITIES:

A. PRESENTATIONS AT NATIONAL MEETINGS:

Shalis, P.: "Microbiology applications of Cerner Command Language", 1989 American Society for Microbiology meeting, New Orleans, Louisiana.

B. PRESENTATIONS AT REGIONAL MEETINGS:

Pierson, C.: "Detecting Tuberculosis with DNA Probes- Is it prudent and practical?", and "Impact of Transplants on the Microbiology Laboratory", 1988 Region IV annual meeting of American Society for Medical Technology, Detroit, Michigan.

C. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERED JOURNALS:

1. Lookwood, W., Friedman, C., Bus, N., Pierson, C.L. and Gaynes, R.: "An outbreak of Mycobacterium terrae in clinical specimens associated with potable water," American Review of Respiratory Diseases, in press.
2. 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. of Vascular Surgery, in press.

D. PATHOLOGY HOUSEOFFICER TRAINING PROGRAM:

All Senior Technologists presented an introductory lecture and conducted a laboratory session for the first year houseofficers.

The laboratory provided 19 months of training for 12 Pathology houseofficers. In addition, 16 Pediatric houseofficers and students were rotated through all areas of the laboratory.

E. OTHER EDUCATION ACTIVITIES:

Four technologist were sent to regional and national meetings or workshops.

Assistance was given to two senior medical residents by providing data and advice for their assigned projects leading to departmental presentations:

- "Pseudomonas sepsis"
- "Anaerobic sepsis"

Kenneth D. McClatchey, M.D., D.D.S.
Director
Clinical Microbiology Laboratory

Carl L. Pierson, Ph.D.
Associate Director
Clinical Microbiology Laboratory

MOLECULAR DIAGNOSIS/FLOW CYTOMETRY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

The Molecular Diagnosis/Clinical Flow Cytometry Laboratory has enjoyed a stable year without the major changes that have characterized the recent past. The Laboratory has continued its active role in Diagnostic Clinical Pathology. A total of 1,500 specimens were handled by the laboratory during the past twelve months, which is an increase of 25% over the previous year. Approximately 600 specimens were processed for cell surface markers or cellular DNA content studies. Approximately 50% of these latter specimens were evaluated for hematologic disorders while the remainder of the specimens were for the evaluation of transplant patients or individuals with primary or acquired immune deficiencies. A sizeable proportion of the latter group is in the area of cellular monitoring of transplant patients receiving OKT3 monoclonal antibody therapy. Approximately 600 specimens were studied for platelet-associated immunoglobulins and neutrophil-specific antibodies. Each specimen requires from 10-30 individual staining, quantitation and analytic procedures. Quality control and calibration procedures further add to the specimen load. Thus, the laboratory staff conducted approximately 28,000 individual marker studies in Fiscal Year 88/89. The laboratory continues to provide 12-24 hour turnaround studies on acute leukemia and selected transplant patients. Overall, patient revenue continues to climb and the significant reduction in commodity expenses seen last year has continued through this year as well. This again has led to a gross margin that is 300% better than the gross margin expected by budget.

The Flow Cytometry Laboratory has undergone a major change in how many of the specimens are processed. All primary and acquired immunodeficiencies along with the immune monitoring of post-transplantation patients are now evaluated by direct, 2-color immunofluorescent analysis. In addition, a flow cytometric accessory from Coulter Corporation (Q-prep) has substantially reduced the processing time required for immunofluorescent analysis. Together, these two steps have enhanced our efficiency as a laboratory and decreased the turnaround time for results. In addition, these method changes have allowed us to evaluate lymphopenic patients who could not be consistently analyzed by previous preparation methods.

The Flow Cytometry Laboratory also underwent a major change in its quality control and quality assurance programs. The entire procedure manual was rewritten and a more exhaustive quality control program instituted. This was done in preparation for the recent CAP inspection, which the laboratory passed with deserved accolades. These changes have enabled the laboratory to become a truly "clinical" pathology laboratory.

The molecular diagnostic aspect of the laboratory has been implemented with the use of technologists currently in the laboratory. We have successfully implemented immunoglobulin and T-cell receptor gene rearrangement studies with over 300 assays evaluated during the previous year. Detection of bcr gene rearrangements in chronic myeloproliferative disorders and acute leukemia is also being analyzed in the laboratory. The use of restriction fragment length polymorphisms (RFLP) studies to evaluate allogenic post-bone marrow transplantation patients for evidence of either engraftment of normal marrow or recurrence of disease will be implemented as soon as the allogenic bone marrow transplant program begins here at the University.

New developments in the flow cytometry area in the upcoming year will include further implementation of direct and two-color staining with monoclonal antibodies. Reticulocyte analysis by flow cytometry will also be evaluated as a means of providing the laboratory with a routine, clinical assay. Future developments in the molecular diagnostic area will depend on the clinical demand for the studies and the technical skills that are required. The polymerase chain reaction (PCR) is being evaluated as a possible technique that may enhance the implementation of DNA studies into the clinical laboratory. Also, a semi-automated DNA instrument is being evaluated that may aid in these assays becoming a more routine procedure. A limited number of biotinylated probes are being used on a trial basis to assess the possibility of moving away from P^{32} radioactive probes. Investigative work will continue in the area of hematologic and genotypic markers in acute and chronic leukemias and malignant lymphoma, as well as studying the role of adhesion molecules and homing receptors in various benign and malignant hematopoietic diseases.

Curtis A.Hanson, M.D.
Lloyd M. Stoolman, M.D.
Directors
Clinical Flow Cytometry Laboratory

PATHOLOGY DATA SYSTEM

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

The activities of Pathology Data Systems for the past year can be divided into seven separate categories: (1) system software upgrades and enhancements; (2) new laboratory installations; (3) interrogation and manipulation of the laboratory data base using CCL programs; (4) quality assurance activities; (5) training, teaching, and user relations; (6) workstation development; and (7) hospital computer activities.

Software changes consisted of the installation of two new versions of the Cerner PathNet software (V. 301 in November and V.302 in May) and a new VAX/VMS operating systems (V. 5.01 in May). The changeover to the Cerner software is particularly significant in that it marks the first time since PDS served as the alpha test site for Cerner 300 software that the laboratory computer is running on a standard software product. The overriding goal here has been to work with more stable software and to enhance in-house software management.

Regarding new laboratory installations, the Cytogenetics Laboratory is now in the final stages of being integrated into the overall laboratory computer operations. Efforts to convert the Tissue Typing laboratory to PathNet are continuing. Plans are now underway to bring up the autopsy module of PathNet in the Fall including SNOMED coding of autopsy diagnoses and electronic on-line editing of gross provisional diagnoses and autopsy protocols.

The laboratory data base can be utilized to pursue quality assurance goals using CCL programs. A new employee has been added to the PDS staff, partly funded by Cerner Corporation, to develop such CCL programs. Both she and other within PDS have been actively developing these programs to create data base audits, throughput reports, and reports monitoring utilization of laboratory services. Other quality assurance activities within PDS include system documentation in response to the FDA mandated requirements in blood banking and quality reports in Anatomic Pathology such as one documenting disagreements between frozen section and final surgical pathology diagnoses.

Regarding training, teaching, and user relations, the PDS Forum was reestablished to enhance communication between chief technologists and PDS personnel. Enhanced documentation for clinicians concerning Patient Result Inquiry (PRI) was created. Relations with M-Labs/M-Care clients were enhanced with the development of two new reports: order-by-client report and the overdue report. M-Labs charting was totally revamped. Twenty-four new M-Labs clients were added, two with remote printers. The seventh annual symposium on clinical laboratory computers was held in June. Personnel in PDS were well-represented on the course faculty. The symposium attracted 160 paid registrants from 30 states and 16 system vendors and consultants.

The workstation project under the direction of PDS personnel is continuing. Prototypes of two workstation hardware platforms have been created during the last four months. The intention is to shift production word processing by secretaries to MS-Word and away from the current dedicated IBM word-processing system. Faculty consultation reports in surgical pathology will ultimately be entered into the PathNet system. The VAX cluster will also serve as a file server and as means for backing up the personal files of individual users.

At the hospital and university level, PDS personnel are currently active in a project to integrate information from the heterogeneous and distributed hospital systems at the workstation level for clinicians. Bob Dieterle participated in University negotiations with the Oracle Corp. for a software site license. Oracle is a relational data base manager which will be used to achieve this integration. PDS personnel also actively cooperated with HIS personnel in the conversion to a uniform password/security system for all system users in the hospital.

Bruce A. Friedman, M.D.
Director,
Pathology Data Systems

TISSUE TYPING LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

HISTORICAL:

The Tissue Typing Laboratory of The University of Michigan Medical Center was founded in 1968 by Dr. Richard F.Haines as an adjunct to The Lane Laboratory of New Growth of the Department of Surgery. The latter laboratory had been established in 1960 by Dr. Haines in support of the pending clinical transplantation programs at The University of Michigan. Thus, the Tissue Typing Laboratory became the first of its kind in the state of Michigan and one of few similar laboratories in the country. Following the initiation of the clinical renal transplantation program at The University of Michigan in March, 1964, recipients and donors were matched by the laboratory of Dr. Paul I. Terasaki at The University of California at Los Angeles for some four years. In August, 1968 Dr. Haines visited Dr. Terasaki's laboratory for the purpose of learning the tissue typing techniques. Immediately thereafter tissue typing was added to the activities of the Lane Laboratory. For the next several months local results were confirmed by the submission of duplicate samples to the UCLA laboratory. By October, 1969 sufficient proficiency had been demonstrated such that the tissue typing procedures were granted a fee-for-service status by University of Michigan Hospitals administration.

For the next twenty years the Tissue Typing Laboratory functioned as a unit within the General Surgery Section of the Department of Surgery. During this time the laboratory's procedures were in increasing demand as clinical transplantation expanded to include heart and lung transplants briefly in 1968-71 followed by cornea transplants in 1977, pancreas transplants and a return to heart transplants in 1984, liver transplants in 1985 and bone marrow transplants in 1988. The laboratory also has been associated with numerous disease-association studies, performed paternity testing for eight years, and shared state-wide responsibility for cadaveric donor evaluation for ten years prior to the establishment of the Transplantation Society of Michigan's own histocompatibility laboratory in 1984.

Dr. Haines began a phased retirement as Laboratory Director in the Fall of 1986, but was asked to resume the directorship on an acting basis effective January 1, 1988. On July 1, 1988, the administrative responsibility for the Tissue Typing Laboratory was transferred from the Department of Surgery to the Department of Pathology.

LABORATORY ACTIVITIES:

A. With the exception of paternity testing, the laboratory offers a full range of histocompatibility, or tissue typing, procedures. These include:
   1. ABO Grouping, forward and reverse
   2. Tissue Typing
      a. HLA Class I Antigens
      b. HLA Class II Antigens
      c. SIngle Antigens, customized
   3. Crossmatches
      a. T-Cell/B-Cell
         1) Concurrent Donors
         2) Subsequent Donors
         3) Immediate Pretransplant
      b. T-Cell Only
      c. B-Cell Only
      d. Reverse Lymphocyte
      e. Autologous Lymphocyte
      f. Monocyte
   4. Cytotoxic Antibody Screens
      a. Class I
         1) Standard Serum Tray
         2) Frozen Cell Tray
      b. Class II
         1) Standard Serum Tray
         2) Frozen Cell Tray
   5. Mixed Lymphocyte Cultures (MLC's)

B. All laboratory procedures have been reviewed for appropriateness and assigned a new set of fee codes, which is more extensive than previously.

C. There has been a substantial increase in the number of billable procedures performed. This has been due, largely, to:
   1. Some increase in the renal and heart transplant programs.
   2. Growth of the liver transplant program.
   3. The initiation of the bone marrow transplant program.

D. The laboratory continues to participate, in conjunction with the Department of Ophthalmology, as one of six centers in the national Collaborative Corneal Transplantation Study. This double blind study is examining the effect of 1) HLA matching and 2) crossmatches on the clinical outcome of coneal transplantation.

TEACHING ACTIVITIES:

The laboratory continues to provide practical histocompatibility instruction for Pathology House Officers, interdepartmental invitees and others interested in the experience.

ACCREDITATION:

A. The laboratory was subjected to an on-site College of American Pathologists (CAP) inspection on May 31, 1989. Although a finalized report of the results

has not been received yet, the laboratory was advised by the inspector verbally that the accreditation was assured.

B. The laboratory is in the final year of its three-year accrediation by the American Society for Histocompatibility and Immunogenetics (ASHI). A mutually agreed on date for the necessary on-site inspection for new three-year accreditation has been set as July 6, 1989.

GOALS FOR 1989-90:

A. The laboratory is prepared to augment its list of available procedures by the addition of the following:
   1. Tissue typing for Crossreacting (antigen) Groups (CREG's)
   2. Vascular-endothelial cell crossmatches.
   3. Cytotoxic antibody screening vs. monocytes.
   4. Cytotoxic antibody screening and crossmatching of DTT- (dithiothreitol) treated serum to rule out innocuous IgM false-positivity.

B. Considerable work remains to be done regarding the reorganization and relocation of the historical collection of transplantation patient sera. Additional freezer space has been identified and will be fully utilized.

C. The only major activity in which the laboratory is not currently engaged is paternity testing. The need for such service state-wide is increasing alarmingly. Thus, it appears more appropriate than ever that the laboratory should give serious thought to reinstating this activity.

Richard F. Haines, Ph.D.
Acting Director
Tissue Typing Laboratory

ADMINISTRATIVE/FINANCIAL AFFAIRS SECTION

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 July 1988 - 30 June 1989

The Administrative and Financial Affairs Section, which is under the auspices of the Office of the Chairman and his designee, includes five subsections which are organized as follows:

A. ADMINISTRATIVE SUPPORT CENTER - PATHOLOGY LABORATORIES:

- Thomas D. Morrow, Assistant Administrator for Finance and Operations
- Deborah Day Jansen, Administrative Coordinator for Pathology Laboratories

Surgical Pathology Clerical Area:

- Edith M. Brayton, Office Manager
- June M. Possley, Office Supervisor
- Beverly J. Smith, Administrative Assistant, Personnel and Payroll functions
- Nancy A. Coray, Financial Analyst and Billing Coordinator

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

E. OFFICE OF THE CHAIRMAN:

- Laura Blythe, Staff Assistant
- Mary Anne Tishma, Staff Assistant

In addition to the management of daily activities, each of the units completed major projects. They are as follows:

ADMINISTRATIVE SUPPORT CENTER:

1. The M-Labs Program has continued to expand and this year we have initiated clinical pathology services to Federated Medical Laboratories, Inc. and Port Huron Hospital. Additionally we have initiated service with several other extramural clients.

2. The Pathology Laboratories Handbook intramural and extramural versions (and mini-book) have been input into a database and new manuals have been distributed. Future updates to this manual will be printed and distributed as required, thereby eliminating costly printing and distribution costs for the annual publication of this information. The handbook will be placed into an online data base in Fiscal Year 1990 to allow Hosital staff access.

3. The design process for the Blood Drawing Station which will be located in the new Maternal Care Health Center has been completed.

4. The implementation of a Quality Assurance Program has been completed at the M-Care Satellite Clinics.

5. Completed the renovation and expansion of the Frozen Section Room in the Operating Rooms of the Hospitals.

6. Development of the M-Labs Clinical Pathology billing system with the Hospitals.

CLINICAL FACULTY OFFICES:

1. The AGH Faculty Offices have been renovated to accommodate the arrival of two new faculty members in the Division of Anatomic Pathology. The new faculty include, Sharon W. Weiss, M.D., Professor and Director of the Division of Anatomic Pathology and Chief of Surgical Pathology, and Thomas S. Frank, M.D., Assistant Professor of Pathology. The addition of these faculty will require the support of a new secretarial staff member.

2. Installation of an interactive telepathology system in the office of the Associate Chairman. This system is an "alpha site" installation for emerging technology.

MEDICAL SERVICE PLAN OFFICE:

1. Implemented reports to track referrals by major clients of the M-Labs program in order to determine patient mix and profitability. Emphasis was placed on direct patient and client contact by Billing Office personnel which assisted with the resolution of billing problems.

2. Participated in the external audit of the Pathology Associates Billing Office. Preliminary reports indicate that current procedures and practices meet all requirements.

3. Completed studies that forecasted the negative financial impact caused by reimbursement changes implemented by Medicare and Blue Shield in November 1988 and January 1989 respectively.

MSP OFFICE - OTHER ACTIVITIES:

1. Completed Phase IV of the renovation and remodeling of the Pathology Building including the Ligand Assay Laboratory, Cytogenetics Blood and Bone Marrow Laboratory, Flow Cytometry Research Facility and the locker room area.

2. Word Processing Center:

   Developed manuals for beginning, intermediate and advanced users for Microscoft Word.

3. Prepared data for the Blue Cross Audit, which included gathering of data to substantiate Schedules B and D for Fiscal Year 1987.

4. Developed impact analyses on decrease in reimbursement levels for Medicare and Blue Cross/Blue Shield.

OFFICE OF RESEARCH AND EDUCATION ADMINISTRATION:

1. Implemented a revised recharge system for the Histology Service. This included revising rates and processing charges.

2. Coordinated the renovation of the Conference Room and one research laboratory in the Medical Science Research Building.

3. Designed and implemented a Lotus 1-2-3 program to monitor sick and vacation accruals for the Medical School/Pathology staff.

4. Coordinated the quarterly publication of the Pathology Telephone Directory including inputting and updating of personnel data and distribution of the final directory.

5. Developed and implemented an Orientation Program for employees new to the Department of Pathology. The focus of this program is to inform new employees of policies and procedures as well as the structure of the Department.

6. Participated in the Medical School Information System Goals Group. This group identified and reviewed problems and future needs of system users.

GENERAL:

1. Participated in the review of the Medical Campus Personnel Office with the final report submitted to University officers in March 1989.

2. Managed the Pathology Associates Billing Office with the assistance of the Research and Education Administrator and the Financial Analyst for approximately 8 weeks during the injury and recovery period of the Manager.

3. As Executive Secretary of the A. James French Society of Pathology, planned the First Annual Scientific Meeting of the Society which will be held in October, 1989.

4. Negotiated contracts for MLabs Services for clinical pathology for Federated Medical Laboratories, Inc. and Port Huron Hospital; coordinated the termination of the agreement with Metric Medical Labs for services provided Chelsea Community Hospital.

5. Initiated and directed the implementation of a budgeting system that recognizes and incentive system for principal investigators and establishment of a separate budgeting system for the administration of the House Officer Training Program and the new Director of Anatomic Pathology.

SUMMARY OF FINANCIAL DATA:

1. Grants and Contracts:

73 active grants, contracts and other accounts

Total Direct Expenditures . . .	$3,200,852
Indirect Research Expenditures	$1,555,251
Total Sponsored Projects	$5,002,276
Other Expenditures	$1,896,072
TOTAL EXPENSES	$6,436,533

2. Medical Service Plan:

Average number of active accounts	
Total number of charge entries	$64,617
Gross Anatomic/Clinical Pathology Billings	$7,237,702
Net Anatomic and Clinical Pathology Collections	$3,439,964
Part A. Payment	$2,639,334

3. Pathology Laboratories:

Number of fee code procedures	2,941,785
Number of laboratory test results	11,500,000
Gross Revenue	$71,842,680
Direct Expenses	$25,357,524

Details regarding the financial data included in this report are available in the Office of the Chairman.

Respectfully Submitted,

Eugene J. Napolitan
Administrator

EDUCATIONAL ACTIVITIES*

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1988 - 30 JUNE 1989

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).

This represent the fifth year in which the Sophomore Pathology Course (Path 600) has been taught under a "revised" teaching format. The structure of the course is predicated on the students' acceptance of a significant responsibility for their own education, under faculty guidance. This is achieved through the use of focused faculty lectures, directed laboratory sessions, and more emphasis placed on student home study requiring text reading, utilization of microscopes, and slide sets, and descriptive syllabi. During the past year the number of laboratory groups was increased from four to six. This required a significant increase in faculty effort in the Course. Formal course evaluation indicated that the revised course format continues to function smoothly and is generally well accepted by the students. In particular, the smaller laboratory group size was viewed as having a positive impact on the students' education by both students and faculty. A formal evaluation mechanism of lecturers and laboratory instructors was also developed and implemented this year in an attempt to provide constructive feedback to faculty regarding the quality of their teaching efforts. 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 is the relative lack of contact time that the faculty have with students within the Medical School curriculum compared to peer institutions.

Following review of the combined Dental/Graduate Student Course two years ago a separate graduate student section was formulated as an alternative to teaching systemic pathology to graduate students. This section was composed of approximately 15 students and focused on the study of the cellular/molecular basis of the inflammatory response and the role of the extracellular matrix in disease. This allowed more indepth discussion of the specific topic areas in a small group seminar format and was generally well received by the students. Further development of a graduate course in general pathology separate from the Dental course has continued and will be offered in the upcoming year.

During the past year, a proposal for the development of a graduate program based in the Department of Pathology has been developed and approved by the Horace G. Rackham School of Graduate Studies beginning in 1989. 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.

*House Officer training and postdoctoral research training are discussed elsewhere.

Formal courses given within the Department include:

I. COURSES IN THE "STANDARD" MEDICAL CURRICULUM

A. ICS 500:
   1. Introductory Lectures on General Pathology (20 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 (18 contact hours).

D. Pathology 600:
   1. 67 hours of whole-class lecture, 37 hours of laboratory (in each of six sections) (104 contact hours).

E. Pathology Clerkships:
   1. Elected by 48 students at University Hospitals.

II. COURSES IN THE DENTAL CURRICULUM

A. Pathology 630:
   1. General Pathology Lectures (45 contact hours).

B. Pathology 631:
   1. Pathology Laboratory (90 contact hours) each of three sections (assisted by Oral Pathology staff).
   2. Graduate Student Section.

C. Pathology 858:
   1. Neuropathology (23 contact hours).

III. GRADUATE COURSES IN PATHOLOGY

A. Pathology 580: General Pathology for Biologic Scientists
B. Pathology 581: Cellular and Molecular Basis of Disease
C. Pathology 650: Laboratory Techniques in Experimental Pathology
D. Pathology 850: Special Topics in Pathology

IV. POSTGRADUATE MEDICINE/CONTINUING MEDICAL EDUCATION:

A. Current Topics in Blood Banking, May 31-June 2, 1989.
B. Clinical Laboratory Computers, June 7-9, 1989.

V. CLINICAL CONFERENCES:

The Department of Pathology provides an important educational service tomany 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

M-LABS

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENT REPORT
JULY 1, 1988 - JUNE 30, 1989

he M-Labs program continues to grow in both areas of 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 laborato ry system within the central pathology laboratories. The credit for such an increased profit margin as well as increased volume is attributed to the many laboratory professionals who have labored to make M-Labs work.

-Labs now has over 70 clients, of which approximately 20 can be consid ered major clients. These clients include hospital accounts, independent laboratories, and large doctor office accounts.

The forecase for the coming year for M-Labs is for continued growth with no foreseeable increase in costs of the program. Additionally, the sales and marketing program will be incorporated into the operations section eliminating a daily "on the road" sales staff, yet augmenting the increasing need for client services.

Kenneth D. McClatchey, M.D., D.D.S.
Director,
M-Labs

RESIDENCY TRAINING PROGRAM

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
JULY 1, 1988 - JUNE 30, 1989

The Residency Training Program has recruited five outstanding candidates in the past year as follows: Kyle A. Carr, M.D, Suzanne M. Cook, M.D., John R. Goldblum, M.D., Eric P. Kaldjian, M.D., and Priscilla R. Lindley, M.D. The recruitment activities continue to involve greater and greater work effort with 399 letters of inquiry processed, 196 completed applications received, and 28 candidates invited to interview in the Department.

With the consolidation of laboratories in the Department, new rotations are being developed in the areas of Cytogenetics, HLA Typing, and Gynecologic Endocrinology.

Following the recent recruitment effort, a Residency Advisory Committee was appointed by Dr. Ward to evaluate the growth of the Residency Train ing Program and its future needs. A formal document was developed by the Committee and discussed at the June Faculty Retreat. Highlights of the document include:

1. Senior residents will perform a limited number of autopsies.
2. AP only residents should consider including selected CP rotations as part of their training program appropriate to their career goals.
3. The CP curriculum shall consist of a 15-month core of rotations. Straight AP programs shall follow revised surgical pathology tracking.
4. The Department shall support residents for only those years needed for Board eligibility.
5. Residents who switch from a combined AP/CP program to a straight AP or CP program will not be eligible for a fifth year of support. Those residents involved in the straight AP or CP program and those AP/CP residents who do not need the fifth year for Board eligibility must obtain their own support for any additional non-credential time in the training program.
6. Not more than one AP academic surgical pathology resident shall be recruited per year.
7. Not more than one AP research resident shall be recruited per year.
8. CP only residents cannot be accomodated in the training program except under special circumstances.

The residents again this year took the American Society of Clinical Pathologists' inservice examination and performed very well.

Kenneth D. McClatchey, M.D., D.D.S.
Director
Residency Training Program

VETERANS ADMINISTRATION MEDICAL CENTER
LABORATORY SERVICE

DEPARTMENT OF PATHOLOGY - UNIVERSITY OF MICHIGAN
ANNUAL DEPARTMENTAL REPORT
1 JULY 1987 - 30 JUNE 1988

INTRODUCTION:

The VA Medical Center Laboratory Service maintains a strong and close affiliation with the University of Michigan Medical Center Department of Pathology. Pathology residents receive part of their training at the VA. The regular rotations are those of surgical and autopsy pathology but one-month electives are available in electron microscopy, research methods and in other areas that may be arranged. There are frequent mutual consultation activities and educational seminars that are attended by both staffs. The four full-time VA pathologists are active in the formal and informal teaching of medical students and residents. Research activities are often cooperative in nature.

ANATOMIC PATHOLOGY:

A. Surgical Pathology: 4,324 cases have been completed and all have been initially examined by the resident assigned to surgical pathology and then further processed and reported with the supervision and guidance of a staff pathologist. The resident acts as the coordinator of the surgical pathology section and is responsible for assuring liaison with the clinical services. The teaching activities are intense and involve all of the staff. Interesting and/or difficult cases are discussed in a weekly conference with all residents and staff in attendance.

B. Autopsy Pathology: 101 autopsies were done during this time, the majority dissected primarily by the resident with staff supervision and then examined microscopically and reported with staff guidance.

C. Cytology: 2,670 cytology cases were reported during this time. No regular resident rotation is available in cytology but the material is easily obtained for correlation with surgical, autopsy and electron microscopy. The material is used for teaching as appropriate.

D. Electron Microscopy: An elective resident rotation is available in electron microscopy taught by Dr. Beals. The instrument and resulting photographs are used frequently for correlation with surgical, autopsy and cytology. In early 1989 the electron microscopy section was designated by VA Central Office a center of Excellence within the va system. The result of this designation will be increased number of cases and the goal will be updating the equipment.

THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF PATHOLOGY
HOUSE OFFICERS
1989-1990

David M. Grossman, M.D.
Chief Resident
House Officer VI
(4th Year)

Lynne V. Abruzzo, Ph.D., M.D.
House Officer IV
(4th Year)

Anne C. McQuillian, M.D.
House Officer V
(5th Year)

David M. Graham, M.D.
House Officer IV
(4th Year)

Elizabeth A. Del Buono, M.D.
Assistant Chief Resident
House Officer III
(3rd Year)

Cynthia A. Hegg, M.D.
House Officer IV
(3rd Year)

Steven H. Marden, M.D.
House Officer III
(3rd Year)

Paul F. Mazzara, M.D.
House Officer III
(3rd Year)

Michael J. Caplan, M.D.
House Officer III
(3rd Year)

Randall J. Shannon, M.D.
House Officer III
(3rd Year)

Denise E. Sabatk, M.D.
House Officer III
(3rd Year)

Sarah F. Campbell, M.D.
House Officer II
(2nd Year)

Barbara A. Markey, M.D.
House Officer II
(2nd Year)

Philip L. Perkins, M.D.
House Officer III
(2nd Year)

Loretta J. Register, M.D.
House Officer II
(2nd Year)

Cheryl A. Uliger, M.D.
House Officer II
(2nd Year)

Kyle A. Carr, M.D.
House Officer I
(1st Year)

Suzanne M. Cook, M.D.
House Officer I
(1st Year)

John B. Goldblum, M.D.
House Officer I
(1st Year)

Eric P. Kaldjian, M.D.
House Officer I
(1st Year)

Priscilla R. Lindley, M.D.
House Officer I
(1st Year)

CLINICAL PATHOLOGY:

This division of the Laboratory Service encompasses chemistry, microbiology, hematology and immunohematology. Approximately 1.7 million unweighted tests were done during this period. Although there has not been a formal resident rotation in the clinical area, the resident are encouraged to become familiar with the procedures and the technical staff, participate in in-service teaching as desired and use clinical data that may relate to their formal rotation schedules.

EDUCATION AND TEACHING:

A significant portion of staff time is devoted to "on-the-job" teaching of residents primarily in surgical and autopsy pathology. The small size of the Laboratory Service and the availability of the staff pathologists permits significant informal contact with the residents. Dr. beals presents bi-weekly seminars in electron microscopy for residents at the University. Dr. Weatherbee and Dr. Beals presented a gross pathology conference tot he residents. All four pathologists participated in medical student teaching in the pathology laboratory. Dr. Weatherbee gave two lectures to the second year students in bone pathology. In addition to medical student teaching, Dr. Burkholder also taught in the dental student laboratories.

RESEARCH:

On July 19, 1989, Dr. Chensue replaced Dr. Beals as member of the VA Research and Development Committee and Dr. Weatherbee completed his term as a member of the Human Studies Committee. Dr. Beals is a co-investigator on a number ob funded grants. Dr. Chensue has a VA Merit Review grant through 1990 and had a VA Research Advisory Group grant through 1988. All members of the staff, particularly Dr. Beals and Dr. Chensue, participate as collaborators or consultants with other investigators with the VA and at the University of Michigan.

SUMMARY:

The pathlogists within Laboratory Service at the VA Medical Center are committed to the practice of high quality medicine at this Medical Center. To that end there is continued effort to maintain and improve the close relationship with the University of Michigan. Every effort is made to assure and strengthen the professional interchange between the two institutions. The firm cooperative atmosphere is based on mutual benefits derived by the relationship and aims toward the goal of improved diagnosis and care of patients, continued educational commitment and strengthened research contribution.

Lee Weatherbee, M.D.
Chief, Laboratory Service
Ann Arbor VA Medical Center