THE UNIVERSITY OF MICHIGAN

Department of Pathology

ANNUAL REPORT



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



1 July 1994 - 30 June 1995

THE UNIVERSITY OF MICHIGAN

Department Of Pathology

ANNUAL REPORT



1 July 1994 - 30 June 1995

LIST OF FACULTY

LIST OF FACULTY

Name	Rank	Institutional Affiliation
Abell, Murray R.	Professor Emeritus	The University of Michigan
Abrams, Gerald D.	Professor	The University of Michigan
Annesley, Thomas M.	Associate Professor	The University of Michigan
Appelman, Henry, D.	Professor	The University of Michigan
Baker, James R.	Associate Professor	The University of Michigan
Barr Jr., Mason+	Professor	The University of Michigan
Beals, Theodore F.	Assistant Professor	Veterans Affairs Medical Center
Blaivas, Mila I.	Clinical Associate Professor	The University of Michigan
Bonadio, Jeffrey	Assistant Professor	The University of Michigan
Caplan, Michael J.	Clinical Assistant Professor	The University of Michigan
Capps, Rodney D.	Assistant Professor	The University of Michigan
Chensue, Stephen W.	Assistant Professor	Veterans Affairs Medical Center
Crockett-Torabi, Elahe	Research Investigator	The University of Michigan
D'Amato, Constance J.	Assistant Professor	The University of Michigan
Davenport, Robertson	Assistant Professor	The University of Michigan
de la Iglesia, Felix**	Adjunct Research Scientist	Warner-Lambert/Parke Davis
Dixit, Vishva M.	Associate 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.	Professor	The University of Michigan

Name	Rank	Institutional Affiliation
Flint, Andrew	Associate Professor	The University of Michigan
Frank, Thomas S.	Assistant Professor	The University of Michigan
Friedman, Bruce A.	Professor	The University of Michigan
Giacherio, Donald	Assistant Professor	The University of Michigan
Gikas, Paul W.	Professor	The University of Michigan
Gordon, David	Associate Professor	The University of Michigan
Greenson, Joel	Assistant Professor	The University of Michigan
Hanks, Carl T.*	Associate Professor	The University of Michigan
Headington, John T.	Professor	The University of Michigan
Heidelberger, Kathleen P.	Professor	The University of Michigan
Hendrix, Robert C.	Professor Emeritus	The University of Michigan
Hicks, Samuel P.	Professor Emeritus	The University of Michigan
Hinerman, Dorin L.	Professor Emeritus	The University of Michigan
Johnson, Kent J.	Professor	The University of Michigan
Jones, Michael L.	Assistant Research Scientist	The University of Michigan
Judd, W. John	Professor	The University of Michigan
Killen, Paul D.	Assistant Professor	The University of Michigan
Kunkel, Steven L.	Professor	The University of Michigan
Lowe, John B.	Associate Professor	The University of Michigan
Lukacs, Nicholas	Assistant Research Scientist	The University of Michigan
McClatchey, Kenneth D.	Professor	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
Miller, Richard A.	Professor	The University of Michigan
Mitra, Raj S.	Assistant Research Scientist	The University of Michigan
Naylor, Bernard	Professor	The University of Michigan
Nickoloff, Brian J.	Associate Professor	The University of Michigan
Nunez, Gabriel	Assistant Professor	The University of Michigan
Oberman, Harold A.	Professor	The University of Michigan
Phan, Sem H.	Professor	The University of Michigan
Pierson, Carl L.	Assistant Professor	The University of Michigan
Rachmaninoff, Nikolai	Lecturer	The University of Michigan
Rasche, Rodolfo	Clinical Assistant Professor	The University of Michigan
Remick, Daniel G.	Associate Professor	The University of Michigan
Repola, Kenneth L.	Lecturer	The University of Michigan
Ross, Charles W.	Assistant Professor	The University of Michigan
Rowe, Nathaniel H.*	Professor	The University of Michigan
Schmidt, Robert W.	Professor Emeritus	The University of Michigan
Schnitzer, Bertram	Professor	The University of Michigan
Selvaggi, Suzanne M.	Assistant Professor	The University of Michigan
Shanberge, Jacob N.	Clinical Professor	William Beaumont Hospital
Sheldon, Susan	Assistant Professor	The University of Michigan
Shope, Thomas C.+	Associate Professor	The University of Michigan
Silverman, Eugene M.	Clinical Associate Professor	The University of Michigan
Sima, Anders A.F.	Professor	The University of Michigan

Name	Rank	Institutional Affiliation
Smolen, James E.+	Associate Professor	The University of Michigan
Stoolman, Lloyd M.	Associate Professor	The University of Michigan
Sulavik, Denise	Lecturer	The University of Michigan
Till, Gerd O.	Professor	The University of Michigan
Varani, James	Professor	The University of Michigan
Ward, Peter A.	Professor and Chairman	The University of Michigan
Warren, Jeffrey S.	Associate Professor Director, Clinical Laboratories	The University of Michigan
Weatherbee, Lee	Associate Professor	Veterans Affairs Medical Center
Weiss, Bernard	Professor	The University of Michigan
Weiss, Sharon W.	Professor and Director, Anatomic Pathology	The University of Michigan
Wolter, J. Reimer++	Professor Emeritus	The University of Michigan

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


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1.	University Hospitals Blood Bank (Harold A. Oberman, M.D.)	321-324
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DEPARTMENTAL OVERVIEW

DEPARTMENTAL OVERVIEW
1994/1995

The academic year 1994-95 has been highly successful for the Department of Pathology. During the Summer and Fall of 1994, the Department underwent a review process, which occurs every five-seven years. This is followed by an on-site review by external consultants and is, in essence, a "report card" on the accomplishments of the sitting Chairman. In the data base that has been assembled, the success of the Department in all of its aspects has been evaluated. Of interest is the fact that we have moved into a position of number nine of all academic Department's of Pathology in terms of NIH support. Based on frequency of citation of faculty publications, we are clearly in the top five academic Departments of Pathology in the United States. These accomplishments are due to the very broad base of strengths in the Department in the areas of teaching, service and research and reflect the scholarly accomplishments of the faculty.

As we enter into the new academic year, there are two outstanding issues that will affect the health and vitality of the Department. These bear on space and the Medical Service Plan of the Department. Regarding the former, the Department is currently out of space. We have no space from which to create offices for new faculty, and we have no space for recruitment of new faculty who require research laboratory space. Except for the Departmental purchase of approximately 6,000 sq. ft. of research space in Medical Science Research Building I in the Spring of 1986, since my assumption of Chairmanship of the Department of Pathology in 1980, we have not received from the Medical School any additional space allocation. Currently, the plan is to reassign space in the Pathology Building as clinical activities are moved out the structure. However, the ability to secure this space for new faculty offices and research laboratories will await accomplishment of three other construction projects: the West "bump" addition to University Hospital, construction of laboratory space at the new East Medical Campus, and renovation of the clinical laboratory space in the University Hospitals. In all likelihood, it will be late Fall of 1997 before any moves out of the Pathology Building can be made. Unless the Medical School and Hospitals can provide interim space relief, the Department will be placed in a position of substantial jeopardy.

With reference to our Medical Service Plan (MSP), the institution is putting into place a version of a combined Medical Service Plan which has a profit sharing plan with the University Hospitals, the first of its kind at the Medical Center. These arrangements address the key issue of how to reorganize highly successful Medical Service Plan programs in the face of mounting pressures to respond to care that is either largely managed or contracted. The new program (combining the Clinical Delivery System headed by the Hospital Director and the Medical Service Plan Executive Committee headed by the Dean) will provide for a centralization of clinical activities, contracting and disbursement of revenues. The three key issues in this new system are: (a) retention of effective incentives for individuals and departments; (b) decisions on revenue disbursements (both routine operating revenues as well as profit sharing); and (c) governance in this new system. In the context of the last item, centralization of power in the Medical Service Plan Executive Committee and the Clinical Delivery System Executive Committee puts into the hands of the Committee members a great deal of authority which in the past has rested chiefly in the hands of the sitting Clinical Chairmen. Developing a system of effective and

equitable governance and having in place a program that will not lose focus of the academic missions of both the Medical School and the University Hospitals will be some of the challenges of the immediate future.

Respectfully submitted,

Peter A. Ward, M.D.
Professor and Chairman

INDIVIDUAL FACULTY REPORTS

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Services - 4 1/2 months.
B. Necropsy Service - on call.
C. Pathologist, Cardiac Transplant Team.
D. Consultant for Gastrointestinal Pathology.
E. Consultant for Cardiovascular Pathology.

II. TEACHING ACTIVITIES:

A. Freshman Medical Class:
   1. Pathology 500, Course Director, Lecturer, "Basic Concepts of Disease" - 20 lecture hours.
   2. Multidisciplinary Conferences - six contact hours.
   3. Introductory Histopathology Sequence, Sequence Director, Lecturer, Lab Instructor - 18 contact hours (six lectures, 12 lab hours).

B. Sophomore Medical Class:
   1. Cardiovascular Sequence - five lecture hours.
   2. Cardiovascular Sequence - Pathology Lab Coordinator.
   3. Pathology Lab Instructor - 32 contact hours.
   4 Surgical Pathology, Individual Studies Seminar, 15 contact hours.

C. Senior Medical Class:
   1. Pathology Clerkship Mentor - 20 contact hours.

D. Inteflex (I-3):
   1. Medical Economics - five contact hours.

E. Undergraduate LS&A:
   1. Biology #224 - 2 contact hours.

F. Hospital Conferences:
   1. Cardiovascular Pathology Conference - monthly.
   2. Internal Medicine CPC's - occasional.
   3. Internal Medicine Necropsy Review - occasional.

G. House Officers:
   1. Training in Surgical and Necropsy Pathology.

H. Invited Lectures:
   1. Freshman Orientation, August 1994.
   2. Visiting Dissertation Opponent, Karolinska Institute, Stockholm, Sweden, February 1995.
   3. Northern Michigan Summer Conference, June 1995 (Department of PGM and HPE).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None

PROJECTS UNDER STUDY:

A. Pathologic-Radiologic Correlation in Aortic Disease, with D. Williams.
B. Pathogenesis of venous thrombosis, with T. Wakefield.
C. Tissue reactions to implanted vena caval filters, with L. Greenfield.
D. Mycophenolate in prevention of cardiac allograft rejection, with J. Nicklas.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member, Pathology House Officer Selection Committee.

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

A. Member, Historical Center for the Health Sciences Liaison Committee.
B. Member, Component I Committee.
C. Ombudsperson, Medical Faculty.
D. Member, Executive Committee on Clinical Affairs.
E. Member, Provost's Task Force on Retirement.
F. Chair, Panel of Inquiry into Federally Sponsored Human Radiation Research at U of M (OVPR).

REGIONAL AND NATIONAL:

A. Editorial Board, Modern Pathology.
B. Deputy Medical Examiner, Washtenaw County.
C. Manuscript Reviewer for Cancer, Archives of Pathology and Laboratory Medicine.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kazerooni, E.A., Williams, D.M., Abrams, G.D., Deeb, G.M. and Weg, J.G.: Aortobronchial fistula 13 years following repair of aortic transection. Chest, 106:1590-1594, 1994.
2. Williams, D.M., Andrews, J.C., Chee, S.S., Marx, M.V. and Abrams, G.D.: Canine model of acute aortic rupture: Treatment with percutaneous delivery of a covered Z Stent-Work in progress. J. Vascular and Interventional Radiol., 5:797-803, 1994.
3. Greenfield, L.J., Proctor, M.C., James, E.A., Abrams, G.D. and Moursi, M.M.: Staging of fixation and retrievability of Greenfield filters. J. Vasc. Surg., 20:744-750, 1994.

BOOKS/CHAPTERS IN BOOKS

1. Abrams, G.D., in, Price, S.A. and Wilson, L.M. (eds.), Pathophysiology: Clinical Concepts of Disease Processes, 5th ed. Mosby, In Press, 1995.
   - Chapter 1: General Concepts of Disease. Health vs. Disease.
   - Chapter 3: Cellular Injury and Death.
   - Chapter 4: Response of the Body to Injury. Inflammation and Repair.
   - Chapter 6: Response of the Body to Infectious Agents.
   - Chapter 7: Disturbances of Circulation.
   - Chapter 8: Disturbances of Growth, Cellular Proliferation, and Differentiation.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Director, Drug Analysis and Toxicology Laboratory.
B. Consultant to Veterans Administration Hospital, Ann Arbor, Michigan.
C. Laboratory Director, Chelsea Family Practice, M-Care Facility.
D. Laboratory Director, Briarwood Medical Group, M-Care Facility.
E. Laboratory Director, Briarwood Family Practice Facility.
F. Laboratory Director, Chelsea Internal Medicine Associates.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students:
   1. Course Director, Fundamentals of Laboratory Medicine (PTHCLNL.101) Component IV Medical School Curriculum.
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.
   4. Clinical Pathology Curriculum Committee.
   5. Coordinator, Clinical Pathology Block B.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Multicenter Randomized Dose Ranging Study Comparing the Safety and Efficacy of OG37-325 Oral Solution to Sandimmune in Renal Transplant Patients", $45,000, Sandoz Pharmaceuticals, 1993-1995.

PROJECTS UNDER STUDY:

A. Metabolism, analysis, and therapeutic effect of OG37-325 (CsG) in renal transplant patients.
B. Distribution of cyclosporine and metabolites in blood and tissues.
C. Measurement of therapeutic drugs using alternative fluids beyond serum.
D. Esoteric analysis of drugs by gas chromatography/mass spectrometry.
E. Microbore applications to the analysis of drugs.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Drug Analysis and Toxicology Laboratory.

B. M-Labs Technical Group.

MEDICAL SCHOOL/HOSPITAL:

A. Pharmacokinetics Quality Improvement Team.

REGIONAL AND NATIONAL:

A. Board of Directors, American Board of Clinical Chemistry.
B. Clinical Chemistry Examination Committee, American Board of Clinical Chemistry.
C. Task Force on Sponsorship, American Board of Clinical Chemistry.
D. Board of Directors, National Registry in Clinical Chemistry.
E. Toxicology Examination Committee, National Registry in Clinical Chemistry.
F. Credentials Committee, National Registry in Clinical Chemistry.
G. Faculty, National Toxicology Review Course, American Association for Clinical Chemistry.
H. Member, NCAA Drug Testing Team.
I. Member, Academy of Clinical Laboratory Physicians and Scientists.
J. Member, Clinical Ligand Assay Society.
K. Member, American Association for Advancement of Sciences.
L. Member, Association of Clinical Scientists.
M. Executive Committee, TDM/Clinical Toxicology Division, American Association for Clinical Chemistry.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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

OTHER:

A. Clinical Chemistry, Reviewer.
B. Mayo Clinic Proceedings, Reviewer.
C. Journal of Clinical Immunoassay, Reviewer.
D. Journal of International Federation of Clinical Chemistry, Reviewer.
E. Biomedical Chromatography, Reviewer.
F. Therapeutic Drug Monitoring, Reviewer.
G. Selected Editor, Proceedings of the Third International Congress on Therapeutic Drug Monitoring.

INVITED LECTURES/SEMINARS:

1. "Analytical Aspects of Cyclosporin G Analysis", University of Florida, Gainesville, Florida, August, 1994.
2. "Consensus Recommendations on Cyclosporine Monitoring in Organ Transplantation", 1995 International Consensus Conference on Immunosuppressive Drugs, Lake Louise, Alberta, Canada, May, 1995.
3. "Overview of New Immunosuppressants", University of Windsor, Ontario, Canada, May, 1995.
4. "Quality Control and Quality Assurance in Clinical Toxicology", American Association for Clinical Chemistry, Detroit, Michigan, May, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Annesley, T.M. and Clayton, L.T.: Determination of felbamate in human serum by high performance liquid chromatography. Ther. Drug Monitor. 16:419-424, 1994.
2. Shaw, L.M., Annesley, T., Gilmore, B. and Brayman, K.: Measurement of OG37-325 by high performance liquid chromatography. Transplant. Proc. 26:3010-3012, 1994.
3. Annesley, T.M., Hunter, B.C., Fidler, D. and Giacherio, D.A.: Stability of tacrolimus (FK506) and cyclosporin G in whole blood. Ther. Drug Monitor., In Press, 1995.
4. Shaw, L.M., Annesley, T.M., Kaplan, B. and Brayman, K.L.: Analytical requirements for immunosuppressive drugs in clinical trials. Ther. Drug Monitor., In Press, 1995.
5. Oellerich, M., Armstrong, V.W., Kahan, B., Shaw, L., Holt, D.W., Yatscoff, R., Lindholm, A., Hallocan, P. and Annesley, T.M.: Report of the concensus panel on cyclosporine monitoring in organ transplantation. Ther. Drug Monitor., In Press, 1995.

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

1. Kugler, A.R., Olson, S.C., Webb, C.L., Annesley, T., Nordblom, G.D. and Koup, J.R.: Cross-reactivity of fosphenytoin (cerebyx) in two human plasma phenytoin immunoassays. Pharm. Res. 11:102, 1994.
2. Annesley, T.M.: Gabapentin. Ther. Drug Monitor. Clin. Toxicol. News. 10:5-6, 1995.
3. Annesley, T.M.: Quality assurance and quality control in clinical toxicology. Ther. Drug Monitor. Clin. Toxicol. News. 10:2-3, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. General surgical pathology - four and one-half months.
B. Gastrointestinal and hepatic pathology consultation services - six months.

II.. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students:
   1. Pathology 600 - five full class lectures.
   2. Pathology 630 (dental) - one full class lectures.
   3. Senior medical student, elective rotation in pathology, supervisor one month.
B. House Officers:
   1. Surgical pathology diagnosing room instruction for assigned house officer - 4½ months.
   2. Gastrointestinal and hepatic pathology tutoring - full time.
C. Interdepartmental:
   1. G-I Tumor Conference - Every other Wednesday (three hours/month).
   2. Liver Biopsy Conference - one hour per month.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Hepatic histopathologic changes in methotrexate-treated psoriatics, with Andrew Flint and members of the Gastroenterology Division.
B. Helicobacter-associated gastritis and non-ulcer dyspepsia with Grace Elta.
C. The fate of the transplanted liver in chronic alcoholic patients with Michael Lucey and Kyle Carr.
D. National Study of Thymosin Treatment of Chronic Hepatitis B with Milton Mutchnick.
E. Crohn's disease of the appendix with Jane Huang.
F. Recurrent autoimmune hepatitis in the transplanted liver with Michael Lucey and Kyle Carr.
G. Classification of gastric polyps with Priscilla Chamberlain.
H. Genetic changes in hepatoma with Graeme Macdonald and Joel Greenson.

I. Stromal tumors of small intestine with Joe Tworek and Joel Greenson.
J. Carcinoma of ampulla, distal common bile duct and pancreatic head with Margaret Anderson and Joel Greenson.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Member, Cancer Work Group, University Hospital.
B. Co-Coordinator, Gastrointestinal Sequence for 2nd year medical students.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Lecturer, "The Role of the Pathologist in the Diagnosis and Management of IBD", presented at the Inflammatory Bowel Disease: Memphis Update, Memphis, Tennessee, September 24, 1994.
2. Lecture, "Gastrointestinal Lymphomas: A Gastrointestinal Pathologist's Anti-Intellectual Approach". In Symposium on Gastrointestinal Lymphoproliferative Disorders--the Surgical Pathologist's Approach. XX International Congress of The International Academy of Pathology, Hong Kong, October 12, 1994.
3. Lecture: "It's a Shame to Waste a Liver Biopsy, so Let's Milk It for All It's Worth". Eleventh Annual Eisenstein Memorial Hospital, Mercy Hospital, Port Huron, Michigan, October 21, 1994.

4. Lecturer, "The Adenoma Carcinoma Sequence in the Colon", presented at A Day in Gastrointestinal Pathology and Cytopathology, The University of Western Ontario, London, Ontario, November 4, 1994.
5. Lecturer, Update in Gastrointestinal Pathology and Slide Seminar with Dr. Owen, The First Annual Practical Pathology at Whistler, Whistler, B.C., Canada, February 12-15, 1995.
6. Lecturer, "The Role of the Pathologist in IBD", presented at Inflammatory Bowel Disease (IBD). A Multidisciplinary Discussion, Detroit-Macomb Hospital, February 25, 1995.
7. Short Course, "Inflammatory Conditions of Esophagus, Stomach and Duodenum", with Donald Antonioli, United States and Canadian Academy of Pathology Annual Meeting, Toronto, Ontario, March, 1995.
8. Lecturer, GI Pathology, Second Annual Seminar in Pathology, Pittsburgh, Pennsylvania, May 4-7, 1995. Sponsored by the United Hospital Center, Clarksburg, West Virginia.
9. Lecturer, "Annoying Gut Biopsies", presented at the Suffolk County Society of Pathologists, Great Neck, New York, May 25, 1995.
10. Visiting Professor, Department of Pathology, Stony Brook University Hospital, Stony Brook, New York, May 26, 1995. Lecture on: "Differential Diagnosis of the Acutely Presenting Colitides".
11. Visiting Professor, Department of Pathology, Albany Medical College. Lectures and Seminars in GI Pathology, Albany, New York, June 6-8, 1995.
12. Seminar, "Neoplastic Diseases of Intestine", American Society of Clinical Pathologists, Chicago, Illinois, June, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Appelman, H.D.: Gastritis: Terminology, Etiology, and Clinicopathological Correlations: Another Biased View. Hum. Pathol. 25:1006-1019, 1994.
2. Goldblum, J.R., Appelman, H.D.: Stromal tumors of the duodenum. A histologic and immunohistochemical study of 20 cases. Am. J. Surg. Pathol. 19:71-80, 1995.
3. Henley, K.S., Lucey, M.R., Normolle, D.P., Merion, R.M., McLaren, I.D., Crider, B.A., Mackie, D.S., Shieck, V.L., Nostrant, T.T., Brown, K.A., Campbell, D.A., Ham, J.M., Appelman, H.D., and Turcotte, J.G.: A double-blind, randomized, placebo-controlled trial of prostaglandin E_1 in liver transplantation. Hepatology 21:366-372, 1995.
4. DelBuono, E.A., Appelman, H.D. and Frank, T.S.: Role of polymerase chain reaction in the diagnosis of cytomegalovirus infection in liver transplant patients. Int. J. Surg. Pathol. 2:221-226, 1995.
5. Chey, W.D., Kochman, M.L., Traber, P.G., Appelman, H.D. and Gumucio, J.J.: Possible nizatidine-induced subfulminant hepatic failure. J. Clin. Gastroenterol. 20:164-167, 1995.
6. Silverman, E.M., Sapala, J.A., Appelman, H.D. Regression of Hepatic Steatosis in Morbidly Obese Persons After Gastric Bypass. Am. J. Clin. Pathol., In Press.

A.. Referee for the following journals:

1. Molecular and General Genetics.

2. Biochemistry.
3. Journal of Biological Chemistry
4. Molecular Microbiology.

CHAPTERS IN BOOKS:

1. Lewin, K.J. and Appelman, H.D.: Tumor of the Esophagus and Stomach, Fascicle, In Press.

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

1. Greenson, J.K., Appelman, H.D., Boland, C.R.: Genomic defects in hepatocellular carcinoma: The role of DNA mismatch repair genes. Gastroenterol. 108:A500, 1995.
2. Goff, J.S., Barnett, J.L., Pelke, T., Appelman, H.D. Collagenous Colitis: Natural History and Clinical Remission Rates. Gastroenterol. 108:A824, 1995.
3. Macdonald, G.A., Greenson, J.K., DelBuono, E.A., Grady, W.G, Frank, T.F., Lucey, M.R., Appelman, H.D. "Mini"-microabcess syndrome in liver transplant recipients. Gastroenterol. 108:A1114, 1995.
4. Mutchnick, M.G., Lindsay, K.L., Schiff, E.R., Cummings, G.D., Appelman, H.D. Thymosin α_1 treatment of chronic hepatitis B: A multicenter, randomized, placebo-controlled double blind study. Gastroenterol. 108:A1127, 1995.

JAMES R. BAKER, JR., M.D.

ASSOCIATE PROFESSOR OF PATHOLOGY
DIRECTOR, TISSUE TYPING LABORATORY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Director, Histocompatibility and Immunogenetics Laboratory.

II. TEACHING ACTIVITIES:

A. Director, Basic Immunology Course for Allergy Fellows-In-Training.
B. Instructor, ICS Course for Fellows-In-Training.
C. Instructor, Host Defense Course, First Year Medical School Students.
D. Attending, General Internal Medicine Service.
E. Instructed Pathology Residents, Renal Fellows and Allergy Fellows in HLA Typing.
F. Supervised graduate students undergraduate students in research: David Miller, Brent Wiersma.
G. Supervisor for:
Allergy fellows: Drs. Katherine Liddle, Gregory Gilmet.
Postdoctoral fellows: Drs. Ali Motani, Charles Boyd.
Medical students: Sasha Krupnik.
H. Internal Medicine Grand Rounds.
I. Director, Allergy Training Program.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Immune Response to Thyroid Peroxidase", NIAID - National Institutes of Health, RO1 AI37141-01, budget approximately $653,708/year, January 1, 1995 - December 31, 1997.
B. "Arthritis Core", University of Michigan-MAC, National Institutes of Health, 2 PO AR20557-15, budget approximately $653,708/year, January 1, 1993 - December 31, 1997.
C. "Hybridoma Core", Michigan Diabetes Research and Training Center, National Institutes of Health, 5 P60 DK20572-16, budget approximately $171,413/year, December 1, 1992 - November 30, 1997.
D. Long-Term Effects of Mycophenolate Mofetil in Renal Transplants", Syntex Corporation (Study ICM MYC/1880/USA), $53,904/year, July 1, 1993 - June 30, 1997.
E. "Randomized, Controlled, Dose Ranging Study of Mycophenolate Mofetil", Syntex Corporation (Study ID 2176), $227,296/year, August 12, 1993 - August 11, 1996.
F. "Development of Starburst Dendrimers as a Gene Transfer Agent", Michigan Molecular Institute, budget approximately $244,941/year, January 1, 1994 - June 30, 1995.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Executive Board, Michigan Diabetes Research and Training Center.
B. Dean's Committee on Restructuring Immunology.
C. Hybridoma Core Steering Committee.
D. Chief, Division of Allergy, Department of Medicine.

REGIONAL AND NATIONAL:

A. Histocompatibility Committee, Organ Procurement Agency of Michigan.
B. Chair, Awards Committee, American Thyroid Association.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Genentech, San Francisco, California.
2. Life Technologies, Gaithersburg, Maryland.
3. Pfizer, New York, New York.
4. Promega, Madison, Wisconsin.
5. Michigan Thyroid Association.
6. Grand Rounds, Wayne State University, Detroit, Michigan.
7. Genzyme, Cambridge, Massachusetts.

SCIENTIFIC ACTIVITIES:

A. Reviewer, Journal of Clinical Endocrinology and Metabolism.
B. Reviewer, Annals of Internal Medicine.
C. Reviewer, Journal of Clinical Investigation.
D. Reviewer, Endocrinology.
E. Reviewer, Journal of Leukocyte Biology.
F. Reviewer, Autoimmunity.
G. Reviewer, Thyroid.
H. Reviewer, Journal of Biological Chemistry.
J. Reviewer, The New England Journal of Medicine.
K. Reviewer, Journal of Endocrinological Investigation.
L. Reviewer, The American Journal of Medicine.
M. Regional Accreditation Commissioner, American Society for Histocompatibility and Immunogenetics.
N. Editor, JAMA Primer.

WORKSHOPS/PANEL DISCUSSIONS:

A. American Thyroid Association.
B. Endocrine Society.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

1. Fosso, C.K., Miller, M.J., Solomon, W.R. and Baker, J.R., Jr.: Adverse effects of 3-hydroxy-3-methylglutaryl-coenzyme a reductase inhibitors associated with elevated serum IgE and eosinophilia. J. Allergy Clin. Immunol. 95:1053-1055, 1995.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Kukowska-Latallo, J., Johnson, J., Belinska, A., Spindler, R., Tomalia, D. and Baker, J.R., Jr.: Transfection of eukaryotic cells using Starburst™ Dendrimer DNA conjugates (Submitted).
2. Arscott, P.L., Koenig, R.J., Kaplan, M.M., Glick, G.D. and Baker, J.R., Jr.: Identification of a localized autoantibody epitope in thyroid peroxidase (TPO) that is associated with Hashimoto's disease (Submitted).
3. Lebedovych, L., Johnson, K.J., McMorris, M.S., Gilardy, A.K., Hirschl, R.B., Ward, P.A. and Baker, J.R., Jr.: Characteristics of late allergic response in rats passively sensitized with monoclonal IgE antibodies (Submitted).
4. Belinska, A., Kukowska-Latallo, J., Johnson, J., Spindler, R., Tomalia, D. and Baker, J.R., Jr.: Variables in cellular uptake and localization associated with transfection using different types of Starburst™ Dendrimer/DNA conjugates (In Preparation).
5. Gheraty, P., Chang, F., Belinska, A., Kukowska-Latallo, J. and Baker, J.R., Jr.: *In vivo* transfection of tumors using Dendrimer/DNA complexes (In Preparation).

BOOKS AND CHAPTERS IN BOOKS:

1. Kloos, R.T. and Baker, J.R., Jr.: Thyroiditis, in, Robert, E.R. (ed), Conn's Current Therapy, W.B. Saunders Company, 1996, In Press.
2. Baker, J.R., Jr.: Immunogenetics, the HLA system, and endocrine disease. in, Becker, K.L. (ed), Principles and Practice of Endocrinology and Metabolism Second Edition, J.B. Lippincott Company, 1995.

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

1. Shanley, T.P., Johnson, K.J., Lebedovych, L., O'Connor, C., Jones, M.L., Ward, P.A. and Baker, J.R., Jr.: Upregulation of chemokines, cytokines and adhesion molecules in a rat model of late-phase allergic lung inflammation. Poster presentation, The American Academy of Allergy and Immunology, New York City, New York, February, 1995.
2. Gilmet, G.P., Lebedovych, L., McMorris, M., Johnson, K.J., Ward, P.A., Baker and J.R., Jr.: Histamine release does not relate to the development of the late allergic response (LAR) in rats passively sensitized with IgE. Poster presentation, The American Academy of Allergy and Immunology, New York City, New York, February, 1995.
3. Kukowska-Latallo, J., Johnson, J., Bielinska, A., Tomalia, D., Spindler, R., Baker and J.R., Jr.: Efficient transfer and expression of genetic material in eukaryotic cells using Starburst™ Dendrimer conjugates. Oral presentation, Experimental Biology, Atlanta, Georgia, April, 1995.
4. Bielinska, A., Johnson, J., Kukowska-Latallo, J., Tomalia, D., Spindler, R. and Baker, J.R., Jr.: Unique characteristics of Starburst™ Dendrimers in *in vitro* DNA transfer. Poster presentation, Experimental Biology, Atlanta, Georgia, April, 1995.
5. Bielinska, A., Kukowska-Latallo, J., Johnson, J., Geraghty, P., Chang, A., Tomalia, D., Miller, D., Spindler, R. and Baker, J.R., Jr.: The efficient development of cells persistently expressing

transferred genetic material using Starburst™ Dendrimers. Oral Presentation, Clinical Research, San Diego, California, May, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Pathology House Officer monthly elective: Diagnostic Electron Microscopy.
B. Diagnostic Electron Microscopy Case Conference, bi-weekly.
C. Pathology House Officers, fine needle aspiration technique and interpretation.
D. Instructor, National Laboratory Practicum Program, Department of Veterans Affairs

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Pathologist for: Veterans Administration Cooperative Study #268, "A New Strategy to Preserve the Larynx in the Treatment of Advanced Laryngeal Cancer". (G. Wolf, Principal Investigator).
B. A Prospective, Controlled, Randomized and Double-Blind Multi-Center Clinical Evaluation of Monoclonal Antibody 17.13.C1.10 for its Capability to Detect Head and Neck Squamous Cell Carcinoma in Primary Site Malignancies and Lymph Nodes. (Co-Investigators: Baker, Beals, Carey, Krause, McClatchey, Wolf).
C. Predicting Response to Chemotherapy in Head and Neck Cancer. (Bradford, Principal Investigator).

PROJECTS UNDER STUDY:

A. Clinical relevance of ultrastructural characteristics of small cell carcinoma.
B. Role of plastic embedded cell-blocks and electron microscopy in fine needle aspiration.

C. Growth of cells on microcarriers (with J. Varani).
D. Cell damage caused by oxidants (with D. Hinshaw).
E. DNA content as a predictor of chemotherapeutic response and prognosis in squamous cell carcinoma of the larynx (with C. Gregg and G. Wolf).
F. Differentiation of isolated renal tubular cells in culture (with D. Humes).
G. Incidence of human papilloma virus infection in prostate tissues. Comparison of benign hyperplasia and adenocarcinoma. (with L. Wideroff, NIH).
H. Apoptosis in lung injury (with J. L. Curtis).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Electron Microscopy Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Clinical Executive Committee, elected member, Veterans Affiars Medical Center.
B. Invasive Procedures Review Committee, Veterans Affairs Medical Center.
C. Electron Microscopy Committee, Chair, Veterans Affairs Medical Center.
D. Medical Records Committee, Veterans Affairs Medical Center.
E. Automated Data Processing Committee, Veterans Affairs Medical Center.
F. Medical School Admissions Committee.
G. Cancer Committee, Veterans Affairs Medical Center.

REGIONAL AND NATIONAL:

A. Department of Veterans Affairs, National Electron Microscopy Review Group.
B. Armed Forces Institute of Pathology, Scientific Advisory Board.
C. Association of Pathology Chairs, Veterans Affairs Committee, Consultant.
D. National Veterans Affairs Pathology Field Advisory Board.
E. American Society of Clinical Pathologists, Quality Management Cytology Committee.
F. College of American Pathologists, Cytopathology Committee.
G. National Veterans Affairs Cytopathology Committee, Chair.
H. National Veterans Affairs Surgical Pathology Committee, Chair.
I. Clinical Information Council.
J. Laboratory Medicine Committee, Veterans Health Administration, Department of Defense, National Institutes of Health, Indian Health Service.
K. Interagency Coordinating Committee for Minority Health Care Careers, VHA, DOD, HHS, Commerce, DOE, NASA.
L. Reviewer: Gastroenterology, Biotechnic and Histochemistry, Diagnostic Cytopathology, Acta Cytologica, Analytical and Quantitative Cytology and Histology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

A. Diagnostic Problems in Cytopathology (Department of Internal Medicine, Pulmonary Conference Series).
B. Veterans Affairs Restructuring. National Veterans Affairs Electron Microscopy Meeting, Durham, North Carolina, February 21, 1995.

C. Short Course, "Closed Lung Biopsy Interpretation" with A. Flint, USCAP, Toronto, Ontario, March, 1995.
D. TraVAlab. National Satellite Television Conference, April 27, 1995.
E. National Conference on Occupational Safety. Veterans Affairs Perspective, Norfolk, Virginia, March, 1995.
F. Diagnosis of Bronchial Lesions. Michigan Society of Pathology, Lansing, Michigan, June 10, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Bradford, C.R., Zhu, S., Wolf, G.T., Poore, J., Fisher, S.G., Beals, T., McClatchey, K.D. and Carey, T.E.: Veterans Affairs Laryngeal Cancer Study Group. Overexpression of P53 predicts organ preservation using induction chemotherapy and radiation in patients with advanced laryngeal cancer. 1994.
2. Beals, T.F. and Travers, E.M.: The Cytopathology poficiency program of the Department of Veterans Affairs. Lab. Med. 25:234-236,1994.
3. Wolf, G.T., Fisher, S.G., Truelson, J.T. and Beals, T.F.: DNA content and regional metastases in patients with advanced laryngeal squamous carcinoma. Laryngoscope 104:479-483,1994.
4. Goldblum, J.R., Beals, T.F. and Weiss, S.W.: Neuroblastoma-like neurilemoma. Am. J. Surg. Pathol. 18:266-273, 1994.
5. Shanley, C.J., Braun, D.K., Brown, K., Turcotte, J.G., Greenson, J.K., Beals, T.F., Tiballi, R.N. and Campbell, D.A., Jr.: Fulminant hepatic failure secondary to herpes simplex virus hepatitis. Transplantation 59:145-149, 1995.
6. Wideroff, L., Schottenfeld, D., Carey, T.E., Beals, T., Fu, G., Sakr, W., Sarkar, F., Schork, A., Grossman, H.B. and Shaw, M.W.: Human Papillomavirus DNA in malignant and hyperplastic prostate tissue of black and white males. The Prostate (1995).

BOOKS AND CHAPTERS IN BOOKS:

None.

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

1. Beals, T.F.: Letter on Intracytoplasmic lumen in anaplastic lymphomas. Mod. Pathol. 8:344,1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Eight and one-half months of Neuropathology Service.
B. Four weeks of Autopsy Service and five weekends autopsy calls.
C. Muscle and nerve biopsies referred by other hospitals in- and out-of-state throughout the year.
D. Consultations on brain biopsies, autopsied brains and rheumatology cases.

II. TEACHING ACTIVITIES:

A. Taught residents, fellows and staff in Neurology, Rheumatology and Pediatrics and medical students on muscle and nerve biopsies.
B. Taught Pathology Residents how to perform and read-out autopsies.
C. Lectured on muscle, nerve and brain pathology to residents in Pathology, Neurology, and Neurosurgery.
D. Conferences on muscle cases with Neurology Department.
E. Neuropathology cases review with Pathology Residents.
F. Conferences with Neuromuscular staff.
G. Conferences and lectures for Neurosurgery Residents and staff.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Histochemistry and morphometry of skeletal muscle in patients with hypertension and diabetes. With Hypertension Clinic and Sweden.
B. Histology and histochemistry of orbicularis muscle, normal and aging.
C. Histochemistry, morphometry and EM of levator palatini muscle in children with cleft palate.
D. Histology of animal models of rheumatoid arthritis with Arthritis and Rheumatology Section.
E. Correlation of morphology and imaging studies in cases of craniopharyngioma with Neuroradiology.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL:

A. Member of the Admissions Committee.

REGIONAL AND NATIONAL:

A. Lectures on muscle and nerve pathology to EMG/PM&R/ neurology, residents and fellows in Medical College of Ohio, Toledo, Ohio.
B. Workshop on handling muscle and nerve biopsies with the overview of muscle and nerve pathology at the Ohio Histotechnologists meeting in Perisburg, Ohio, June 3, 1995.
C. Workshop "Neuropathology for general pathologists." For M-Labs clients, University of Michigan, May 6, 1995.
D. Member, American Association of Neuropathologists, IAP, and AAN.
E. Attended IAP, American Association of Neuropathologists and International Society of Neuropathologists meetings.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

1. Pu, A.T., Sandler, H.M., Radany, E.H., Blaivas, M., Page, M.A., Greenberg, H.S., Junck, L. and Ross, D.A.: Low grade gliomas: Preliminary analysis of failure patterns among patients treated using 3-D conformal external beam irradiation. Int. J. Radiation Oncol. Biol. Phys. 31:3; 461-466,1995.
2. Colon, G.P., Quint, D.J., Blaivas, M. and McGuillicuddy, J.E.: Cardiac sarcoma metastatic to the brain. Accepted to J. Neurosurg. A. J. Rad.
3. Gebarski, S.S. and Blaivas, M.: Imaging of normal leptomeningeal melanin. Accepted to A. J. Rad.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Tworek, J., Mikhail, A. and Blaivas, M.: Meningioma: Local recurrence and metastasis. Diagnosed by Fine Needle Aspiration. Submitted to Acta Cytol.

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

1. Weber, J., Erdody, D., Barrow, L., Blaivas, M., Jones, J.M. and Weisler, M.H.: Neuromuscular mutant mnd 2 on mouse chromosome 6: genetic and physical maps. Presented at the meeting Cold Spring Harbor Lab, August 31-September 4, 1994.
2. Gebarski, S.S. and Blaivas, M: Imaging of normal leptomeningeal melanin. Presented at the annual Radiology Society of North America meeting in November 1994, Chicago.
3. Tran, D.D., Levy, R. and Blaivas, M.: Gliofibroma: A rare CNS tumor with propensity in pediatric group and favorable prognosis. Case report and review of literature. Presented at the annual meeting of the American Society of Neuroradiologists in Chicago, April-May, 1995.
4. Eldevik, O.P., Blaivas, M., Gabrielsen, T.O. and Chandler, W.F.: Craniopharyngiomas: correlation between radiological findings, histology and outcome. Presented at the American Society of Neuroradiology meeting in Chicago, April-May, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Attending Staff, University of Michigan Autopsy Service.

II. TEACHING ACTIVITIES:

A. Graduate Students, John Germiller (MSTP), Jeffrey Rouleau (Bioengineering), Robert Guldberg (Bioengineering) and Kuo-Fung Tseng (Bioengineering).
B. Postdoctoral Fellows, Wushan Yin, M.D., Jianming Fang, M.D.
C. Undergraduate Students: None
D. Courses:
   1. Pathology 600: Laboratory Instructor.
   2. Molecular Cell Biology: Section Head, extracellular matrix.
   3. Pathology 581: Course Director.
E. Continuing Medical Education:
   1. "Collagen Disorders", Short Course on Molecular Diagnostics, Genetic Counseling and the Human Genome Project, University of Michigan, August 10, 1994.
   2. "Gene therapy for wound healing: using DNA as a pharmaceutical." Gene Therapy Seminar Series, March 30, 1995.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Direct Gene Transfer into Osteogenic Cells *In Vivo*," U-M Office of the Vice-President for Research.
B. Principal Investigator, "Direct Osteoinductive Gene Transfer," Sponsored Research Agreement, Matrigen, Inc.
C. Principal Investigator, "LTBP Genes and Proteins: Regulators of TGF-β Activity," National Institutes of Health, AR44043.

PROJECTS UNDER STUDY:

A. Molecular cloning of microfibril constituents.
B. Direct gene transfer *in vivo*.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Member, Pre-Clinical Advisory Program, 1988 - present.
B. Biomechanics Core Steering Committee, Multipurpose Arthritis and Musculoskeletal Diseases Center, 1991 - present.
C. Member:
   1. University of Michigan Multipurpose Arthritis Center.
   2. Michigan Cancer Center.
   3. University of Michigan Program Bioengineering Program.
D. Patents:
   1. "Methods and composition for Stimulating Bone Cells." (08/316,650).
   2. "Methods and Composition for Stimulating Bone Cells." (PCT/US95/02251).
   3. "Latent TGF-Beta Binding Protein Genes, Composition and methods." (US Patent Office serial number is pending.).

DEPARTMENTAL:

A. Oversight Committee, Graduate Program, 1989-present.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Ad-hoc Reviewer:
   1. Journal of Bone and Mineral Research.
   2. American Journal of Human Genetics.
   3. Genomics.
   4. Developmental Dynamics.
   5. American Journal of Medical Genetics.
   6. Journal of Biological Chemistry.
B. Consultant Editor:
   1. European Journal of Experimental Musculoskeletal Research, 1991-present.
C. Study Section:
   1. NIH, NIDR, Special Emphasis Panel, Small Grant Program, April 18, 1995.
   2. NIH, NIAMSD, Ad Hoc Program Project Review Meeting, July 10, 1995.

INVITED LECTURES/SEMINARS:

1.. "Direct gene transfer into osteogenic cells *in vivo*." Cold Spring Harbor Meeting on Gene Therapy, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, September 23, 1994.
2. "Direct gene transfer into skeletal tissues *in vivo*." Invited lecture, Genetics Institute, Boston, Massachusetts, November 16, 1994.

3. "Bone growth via gene transfer." Invited presentation, Great Lakes Biotechnology Conference, Dearborn, Michigan, April 4-5, 1995.
4. "LTBP genes and proteins: regulators of TGF-β activity." Invited lecture, Elastin and Elastic Fibers Gordon Conference, Meriden, New Hampshire, July 24, 1995.
5. "Bone structure and function: lessons from transgenic mice." Plenary lecture, Fifth International Conference on the Chemistry and Biology of Mineralized Tissues, Kohler, Wisconsin, October 23, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Yin, W., Smiley, E., Germiller, J., Sanguineti, C., Lawton, T., Pereira, L., Ramirez, F. and Bonadio, J.: Primary structure and developmental expression of *Fbn-1*, the mouse fibrillin gene. J. Biol. Chem. 270:1798-1806,1995.
2. Yin, W., Smiley, E., Germiller, J. and Bonadio, J.: Isolation of a novel latent TGF-β binding protein gene (LTBP-3). J. Biol. Chem. 270:10147-10160,1995.
3. Li, X., Yin, W., Perez-Jurado, L., Bonadio, J. and Francke, U.: Mapping of human and murine genes for latent TGF-β binding protein-2 (*LTBP-2*). Mammalian Genome 6:42-45,1995.
4. Jepsen, K.J., Goldstein, S.A., Kuhn, J.L., Schaffler, M.B. and Bonadio, J.: Type I collagen mutation compromises hierarchical toughening of long bone: implications for the pathogenesis of skeletal fragility. J. Orthop. Res., In Press.
5. Tseng, K-F., Bonadio, J., Stewart, T.A. and Goldstein, S.A.: The effects of local overexpression of human growth hormone by osteoblasts on murine cortical bone. J. Orthop. Res., In Press.
6. Fang, J-M., Li, X., Smiley, E., Yin, W., Francke, U., Mecham, R.P. and Bonadio J.: Isolation and characterization of the mouse laent TGF-β binding protein-2 gene (*Ltbp-2*). J. Biol. Chem., In Press.
7. Yin, W., Smiley, E., Fang, J-M. and Bonadio, J.: The large latent TGF-β1 complex is assembled via an intermolecular disulfide bond between the TGF-β1 small latent complex and TGF-bp structural motifs in the latent TGF-b binding protein. J. Biol. Chem., In Press.

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

1. Bonadio, J. and Goldstein, S.A.: Direct gene transfer into skeletal tissues *in vivo*. Cold Spring Harbor Gene Therapy Meeting, Cold Spring Harbor, New York, September 21-25, 1994.
2. Rouleau, J.P., Goldstein, S.A., Fang, J. and Bonadio, J.: Direct gene transfer into fracture repair cells *in vivo*. 41st Annual Meeting, Orthopaedic Research Society, Orlando, Florida, February 13-16, 1995.
3. Tseng, K-F., Goldstein, S.A., Bonadio, J. and Schaffler, M.B.: The effect of growth hormone overexpression on the mechanical and morphological properties of murine cortical bone. 41st Annual Meeting, Orthopaedic Research Society, Orlando, Florida, February 13-16, 1995.

PETER BRAWN, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. AP/CP Pathology, Veterans Administration Hospital.

II. TEACHING ACTIVITIES:

A. Pathology House Officers, Surgical Pathology/Autopsy, Department of Veterans Affairs Medical Center.

III. RESEARCH ACTIVITIES:

None.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Member, Research and Development Committee, Department of Veterans Affairs Medical Center.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Oncology Reports.

PROFESSIONAL ORGANIZATIONS:

A. Member, International Society of Urological Pathology.
B. Editorial Board, Oncology Reports.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Brawn, P.N., Foster, D.M., Jay, D.W., Kuhl, D., Speights, V.O., Johnson, E.H., Coffield, K.S., Lind, M.L., Karl, R. and Weaver, B.: Characteristics of prostatic infarcts and their effect on serum prostate-specific antigen and prostatic acid phosphatase. Urology 44:71-75,1994.
2. Brawn, P.N., Johnson, E.H., Speights, V.O., Riggs, M., Kuhl, D., Abel, P.D., Lind, M. and Bell, N.: Incidence, racial differences and prognostic significance of prostate carcinomas diagnosed with obstructive symptoms. Cancer 74:1607-1611, 1994.
3. Brawn, P.N., Kuhl, D., Speights, V.O., Johnson, C.F. and Lind, M.: The incidence of unsuspected metastases from clinically benign prostate with unsuspected carcinoma. Archives of Path. and Lab. Med., In Press.

4. Speights, V.O., Brawn, P.N., Foster, D.M., Spikerman, A.M., Kuhl, D. and Riggs, M.W.: Evaluation of age-specific normal ranges for prostate-specific antigen. Urology 45:454-458, 1995.
5. Sharpe, J.C., Gilbertson, J.S., Brawn, P.N., Abel, P.D. and Foster, C.S.: Modulated expression of HLA Class I and Class II determinants in hyperplastic and malignant prostatic disease. British J. Urology 74:609-617, 1994.
6. Studies done jointly with the Pathology Departments of Case Western University School of Medicine, Mayo Clinic, Texas A & M University School of Medicine, University of Liverpool and the University of Colorado and studies done jointly with the Urology Departments of Texas A & M University School of Medicine, Hammersmith Hospital and the University of Colorado (submitted or in press - exact status unknown).
7. Brawn, P.N., Jay, D.W., Foster, D.M., Kuhl D., Speights, V.O., Johnson, E.H., Riggs, M., Lind, M.L., Coffield, K.S. and Weaver B.: Prostatic acid phosphatase levels (Enzymatic Method) from completely sectioned, clinically benign, whole prostates. Prostate, In Press.

CHAPTERS IN BOOKS:

1. Brawn, P.N.: Histologic features of metastatic prostate carcinoma, in, Foster, C. and Bostwick, D. (eds), "Pathology of the Prostate" Major Problems in Pathology Series, W. B. Saunders, In Press.
2. Brawn, P.N.: Adenocarcinoma of prostate - grading of prostate carcinoma, in, Ro, J., Ayela, A., Amen, M. and Grignon, D. (eds), Surgical Pathology of the Prostate Gland, W. B. Saunders (projected publication - April, 1996).

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

1. Abstracts of several published articles reprinted in Yearbook of Pathology and Clinical Pathology, The International Monitor in Oncology.

MICHAEL J. CAPLAN, M.D.
CLINICAL ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 AUGUST 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Director, Forensic Pathology and Medicolegal Autopsies.
B. Supervision of Medicolegal Autopsies (ten months, six days per week).
C. Supervision of Hospital autopsies (six weeks, plus six weekends).
D. Coordinator, Deputy Medical Examiner activities for University Hospitals, Coordinator of Deputy Medical Examiner call schedule and consultant to Deputy Medical Examiners for University Hospitals.
E. Deputy Medical Examiner for University Hospitals (six weeks).
F. Courtroom testimony, Washtenaw County District and Circuit courts in Ann Arbor, Pittsfield Township and Ypsilanti.

II. TEACHING ACTIVITIES:

A. Presentation to Pathology House Officers: Monthly Forensic Pathology Conference (one hour; September 1994 - May 1995).
B. Anatomic Pathology Conference Presentation: "Putting the Autopsy in its Place - The Evaluation of Bodies Found in Water".
C. Presentation to University of Michigan Nursing Students, "Introduction/Orientation to the Autopsy Room".
D. Presentation to Fourth-Year Medical Students, Laboratory Medicine Elective, "Introduction to Forensic Pathology/Medicolegal Autopsy".
E. Presentations to Fourth Year Medical Students, Pathology Elective, "Basic Principles of Forensic Pathology and Death Certification".
F. Presentation to Ann Arbor Community High School Students, "Introduction to Forensic Pathology".
G. Presentation to Pathology House Officers, Fellows, and Junior Faculty: "Forensic Pathology Review for ASCP Pathology Resident In-Service Examination, American Board of Pathology Certifying Examinations".
H. Presentations to Michigan State Police Officers in Training (Cadets), "The Rule of The Forensic Pathologist/Medicolegal Autopsy in Death Investigation".
I. Coordinator and Instructor of Training Program for Deputy Medical Examiner Investigators (nonphysicians), St. Joseph Mercy Hospital.
J. Presentation to Pathology House Officers: "The Evaluation of Gunshot Wounds".

III. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Medicolegal Autopsies (Forensic Pathology).
B. Coordinator, Deputy Medical Examiner System, University Hospitals.

INTERDEPARTMENTAL/INTERDISCIPLINARY:

A. Consultant, Office of Clinical Affairs/Risk Management.
B. Participant, Sentinel Events, University Hospitals.

IV. INVITED LECTURES AND SEMINARS:

1. Presentation, Huron Valley Ambulance Annual Conference: "Atypical Asthma: A Retrospective Look".
2. Panel Discussion, Medical Association of Medical Examiners Annual Meeting, "Medical Examiner Issues in Organ and Tissue Procurement".
3. Presentation, Michigan Association of Medical Examiners Annual Meeting, "Putting the Autopsy in its Place: The Evaluation of Bodies Found in Water".
4. Presentation, Oakland County Medical Examiner Annual Conference, "Goals and Objectives of the Medicolegal Autopsy and the Evaluation of Postmortem Changes".
5. Presentation, University of Michigan Department of Public Safety. Big Ten-Wide Conference, "The Investigation of Deaths on Campus".

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Director, Clinical Laboratories, Veterans Affairs Medical Center, responsibilities include, equipment and methodology evaluation, review and consultation regarding quality management programs, personnel counseling and grievance procedures.
B. Hematology, daily evaluation of pathologist referred blood smears, bone marrow smears, Veterans Affairs Medical Center.
C. Surgical/Frozen Section Diagnosis, (four months/year, approximately 2,200 cases/year).
D. Autopsy Service, rotational basis, on call 13 weeks/year.
E. Special Chemistry/Immunology, daily interpretation of protein electrophoreses, isoenzyme studies, and problem ligand studies, Veterans Affairs Medical Center (six months/year).
F. Blood Bank, consults and investigations, full time as needed, Veterans Affairs Medical Center.

II. TEACHING ACTIVITIES:

A. Medical School, Pathology 600 laboratory course, (two semesters, 30 contact hours).
B. Graduate course, Epidemiology 520, four lecture hours.
C. Pathology house officers, Surgical Pathology/Autopsy supervision and instruction, (four months/year).
D. Technologists and technicians, ongoing instruction on clinical laboratory topics.
E. Graduate students, research training toward doctoral degrees.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Cytokine Cascades in Granuloma Formation", VAMC Merit Review Grant, $85,000 annually - 1993-1997.

PROJECTS UNDER STUDY:

A. Cytokine manipulation of mycobacterial (TH1) and schistosomal (TH2) Ag mediated forms of hypersensitivity granuloma formation.
B. Production and regulation of interleukin-1 receptor antagonist during immune/inflammatory responses.
C. Role of chemotactic cytokines, MCP, MIP and RANTES, in granulomatous inflammation.
D. Regulation of chemotactic cytokine production by leukocytes and stromal cells.
E. Analysis of eosinophil recruitment factors in *Schistosoma mansoni* egg-induced granulomatous inflammation.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member of graduate student thesis committees.
B. Interviewing of resident and faculty applicants.

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. Editorial Review:
   1. American Journal of Pathology.
   2. Journal of Immunology, Associate Editor.
   3. Agents and Actions, Section Editor.
   4. American Journal of Respiratory Cell and Molecular Biology.
   5. Laboratory Investigation.
   6. Paristiology.
B. Medical Advisory Committee, American Red Cross, SMBSR.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited lecturer and chairperson, Minisymposium on Immunopathology of Cytokines, FASEB, Atlanta Georgia, April 9-13, 1995.
2. Case presentations at Tumor Board and Morbidity and Mortality Conferences.
3. Tissue evaluation for clinical researchers.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Chensue, S.W., Warmington, K.S., Ruth, J., Lincoln, P., Kuo, M-C. and Kunkel, S.L.: Cytokine responses during mycobacterial and schistosomal antigen-induced pulmonary granuloma formation. Production of Th1 and Th2 cytokines and relative contribution of tumor necrosis factor. Am. J. Path . 145:1105-1113, 1994.
2. Chensue, S.W., Warmington, K.S., Ruth, J., Lincoln, P.M. and Kunkel, S.L.: Crossregulatory Role of γ-IFN, IL-4 and IL-10 in schistosome egg granuloma formation: In vivo regulation of Th activity and inflammation. Clin. Exp. Immunol. 98:395-400, 1994.
3. Kunkel, S.L., Strieter, R.M., Lukacs, N.W. and Chensue, S.W.: Molecular aspects of granulomatous inflammation. J. Immunol. Immunopharmacol. 14:71-77, 1994.
4. Chensue, S.W., Warmington, K.S., Lukacs, N.W., Lincoln, P.M., Burdick, M.D., Strieter, R.M. and Kunkel, S.L.: Monocyte chemotactic protein (MCP-1) expression during schistosome egg granuloma formation: Sequence of production, localization, contribution and regulation. Am. J. Pathol. 146:130-138, 1995.

5. Lukacs, N.W., Strieter, R.M., Shaklee, C.L., Chensue, S.W. and Kunkel, S.L.: Macrophage inflammatory protein-1α influences eosinophil recruitment in antigen-specific airway inflammation. Eur. J. Immunol. 25:245-251, 1995.
6. Lukacs, N.W., Strieter, R.M., Chensue, S.W., Widmer, M. and Kunkel, S.L.: TNF-a mediates recruitment of neutrophils and eosinophils during airway inflammation. J. Immunol. 154:5411-5417, 1995.
7. Chensue, S.W., Warmington, K., Ruth, J., Lincoln, P., Kuo, M-C and Kunkel, S.L.: Cytokine function during mycobacterial and schistosomal antigen-induced pulmonary granuloma formation. Local and regional participation of γ-IFN, IL-10 and TNF. J. Immunol. 154:5969-5976, 1995.

BOOKS/CHAPTERS IN BOOKS:

1. Luckacs, N.W. and Chensue, S.W.: The role of chemokines in granulomatous diseases. Chemokines in Disease. Strieter, R.M., Koch, A. (eds) In Press.
2. Kunkel, S.L., Lukacs, N.W., Chensue, S.W. and Strieter, R.M. 1995 Chemokines and the inflammatory response. In, Cytokines in Health and Disease, Marcel Dekker, Inc. New York, New York. Edited by D. Remick and Frieland.

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

1. Ruth, J., Bienkowski, M., Warmington, K., Lincoln, P.M., Kunkel, S.L. and Chensue, S.W. Differential IL-1 receptor antagonist (IL-1ra) expression during Th1 and Th2-mediated granuloma formation. FASEB J. 9:A961, 1995.
2. Chensue, S.W., Ruth, J.H., Warmington, K.S., Lincoln, P.M. and Kunkel, S.L. Cytokine-mediated regulation of macrophage IL-12 production in vitro and in vivo. 9th International Congress of Immunology, San Francisco, CA July 23-29. A435, 1995.

ELAHE CROCKETT-TORABI, Ph.D.
ASSISTANT RESEARCH SCIENTIST
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Training and supervision of premedical/medical students in research.

III. RESEARCH ACTIVITIES:

A. Signal transduction pathways of neutrophil activation through Mac-1 molecule.
B. Mechanisms of L-selectin-induced neutrophil activation.
C. Signal transduction pathways of neutrophil activation through FcγR.
D. Mechanisms of immune complex-induced human neutrophil activation.

SPONSORED SUPPORT:

A. Principal Investigator, "Mechanisms of Fc Dependent Neutrophil Activation", NIH-1R29 AI/GM 31436 (85%), $556,500/total costs, July 1, 1991 - July 1, 1996.
B. Principal Investigator, "Mechanisms of L-Selectin Dependent Human Neutrophil Activation", American Heart Association of Michigan Grant-in-Aid, 63GB956 (15%), $28,000 total direct costs/year, July 1, 1995 - June 30, 1996.

IV. ADMINISTRATIVE ACTIVITIES:

None.

V. OTHER RELEVANT ACTIVITIES:

A. Designed the T-shirt logo for The 9th International Congress of Immunology, 1995.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Crockett-Torabi, E., Smith, C.W., Sullenbarger, B. and Fantone, J.C.: Activation of human neutrophils through L-selectin and Mac-1 molecules. J. Immunol. 154:2291-2302,1995.
2. Crockett-Torabi, E., Sullenbarger, B. and Fantone, J.C.: Tyrosine phosphorylation is coupled to L-selectin-mediated signal transduction and superoxide release by human neutrophils. Submitted to J. Immunol.

BOOKS/CHAPTERS IN BOOKS:

1. Crockett-Torabi, E. and Fantone, J.C.: Signal transduction and adhesion molecules, in, Ward, P.A. and Fantone, J.C. (eds), Adhesion Molecules and the Lung, Marcel Dekker, Inc., New York, New York.

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

1. Crockett-Torabi, E.. Sullenbarger, B. and Fantone, J.C.: Tyrosine phosphorylation is coupled to L-selectin-mediated signal transduction and superoxide release in human neutrophils. FASEB J. 9:1315A, 1995. Experimental Biology 95. Invited Speaker, "Leukocyte activation and adhesion molecules", mini-symposium. ASIP.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Neuroscience Sequence, Neuropathology for Second Year Medical Students, one hour lecture, eight hours laboratory, and sequence coordinator for the 8 week sequence.
B. Neuropathology for Pathology house officers. This exercise is integrated with Clinical Activities A, B, and D.
C. Neuropathology 858. Intensive laboratory-lecture course for house officers and fellows, in Pathology and in the several clinical services concerned with the nervous system, and medical students, graduate students, and faculty; implement general plan of course and lecturing. Annual, 18 hours. One credit hour elective.
D. Neuropathology teaching for house officers and fellows from the several clinical services concerned with the nervous system, and medical students who take an elective rotation in Neuropathology.
E. Teach laboratory techniques and basic neuroanatomy and neuropathology to our laboratory technologists.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Co-Investigator with Dr. Anders Sima on MADRC Project, The Pathology of Diffuse Lewy Body Disease. June, 1994 -.
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 Dr. Roger Albin, in the Michigan Alzheimer Disease Research Center.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Anatomic Pathology Committee.
B. Coordinator, Neuropathology 858 Course.

MEDICAL SCHOOL/HOSPITAL:

A. Co-coordinator for the Neuroscience Sequence (new curriculum).
B. Neuroscience Curriculum Committee, Chairman.
C. Coordinator for Neuropathology, Neuroscience Sequence.
D. Neuroscience Examination Committee, Chairman.
E. Admissions Committee, the University of Michigan Medical School.
F. Executive Committee of the Admissions Committee.

REGIONAL AND NATIONAL:

A. American Association of Neuropathologists.
B. American Academy of Neurology.
C. Society for Neuroscience.
D. Michigan Chapter: Society for Neuroscience.
E. Teratology Society.
F. Neurobehavioral Teratology Society.

V. OTHER RELEVANT ACTIVITIES:

A. Member, Dementia Subcommittee of the Chronic Disease Advisory Committee (State of Michigan).
B. Member, Executive Committee of the Postmortem Examination Work group of the Dementia Subcommittee (State of Michigan).
C. Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Committee.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

None.

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

1. Sima, A.A.F., D'Amato, D.J., Defendini, R.F., Jones, M.Z., Foster, N.F., Lynch, T. and Wilhelmsen, K.C.: Primary limbic lobe gliosis; familial and sporadic cases. Brain Pathology 4: 33-14, 1994.
2. Sima, A.A.F., D'Amato, C.J., Foster, N.L., Lynch, T., Defendini, R.F. and Wilhelmsen, K.C.: Neuronal and glial inclusions in familiar progressive limbic lobe sclerosis. J. Neuropathol. & Exper. Neurol. 54:459, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Introductory course in Blood Banking/Transfusion Medicine for Pathology House Officers.
B. Daily teaching rounds for Pathology House Officers assigned to the Blood Bank.
C. Clinical Pathology Grand Round: "DiGeorge's Syndrome", March 3, 1995.
D. Clinical Pathology Grand Round: "Transfusion Reactions", May 19,1995.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Cytokine Roles in Hemolytic Transfusion Reactions", National Institutes of Health, K08-HL02757.

PROJECTS UNDER STUDY:

A. Cytokine production in hemolytic transfusion reactions.
B. Endothelial cell responses in transfusion reactions.
C. Safety and efficacy of solvent/detergent treated plasma.
D. Polymorphisms and function of CR1 on erythrocyte membranes.
E. Reactivation of cytomegalovirus in lymphocytes of blood donors.
F. Mechanisms of immune suppression by blood transfusion.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Transfusion Committee.
B. Quality Improvement Team in Outpatient Care.
C. Department of Pathology Internal Review Committee.

V. OTHER RELEVANT ACTIVITIES:

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

D. Executive Committee, Michigan Association of Blood Banks.
E. Program Committee, Michigan Association of Blood Banks.

INVITED LECTURES AND SEMINARS:

1. Invited speaker: "The Role of Cytokines in Transfusion Reactions", Hematology Grand Rounds, McMaster University, Hamilton, Ontario, October 7, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Davenport, R. D.: The role of cytokines in hemolytic transfusion reactions. Immunol. Invest. 24:319-331, 1995.
2. Davenport, R. D., Polak, T.J. and Kunkel, S.L.: Leukocyte associated procoagulant activity induced by ABO incompatibility. Transfusion. 34:943-949, 1994.
3. Davenport, R. D.: Cytokines and red cell incompatibility. Cur. Opin. Hematol. 1:452-456, 1994.
4. Davenport, R. D.: Cytokines as intercellular Signals in hemolytic transfusion reactions. J. Biol. Signals. In press.

VII. ABSTRACTS, AND PRESENTED PAPERS:

1. Davenport, R. D., Polak, T. J. and Kunkel, S. L.: Differential regulation of monocyte derived cytokines in response to C5a and IgG coated red cells. Transfusion 34:79S, 1994.
2. Davenport, R. D. and Kunkel, S. L.: IgG receptor roles in red cell binding to monocytes and macrophages. Transfusion 34:79S, 1994.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for the following activities:
      a. Student Training and Doctoral Committees.
      b. Joint Student Training in Pharmacology and Toxicology with Florida A&M School of Pharmacy, Toxicology Program.
      c. Direct Postdoctoral Research Fellowship Program in Experimental Pathology.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. All research activities are conducted with intramural support from Parke-Davis.
B. Collaborates with K. Johnson in the development of morphometric models for the evaluation of pathologic changes.
C. Consultant in quantitative microscopy, Morphology Core Lab.
D. Development of image analysis network system.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Co-chair with Dr. P.A. Ward, Joint University of Michigan/Parke-Davis Research-Pathology Program.

MEDICAL SCHOOL/HOSPITAL:

A. None.

REGIONAL AND NATIONAL:

A. Member, Scientific Advisory Committee, NSF Center for Light Microscopy, Carnegie Mellon University, Pittsburgh, Pennsylvania.
B. Member, Organizing Committee, International Symposium on "Peroxisomes: Biology and Role in Toxicology and Disease".

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Editorial Board Member, Drug Metabolism Reviews.
B. Editorial Board Member, Toxicologic Pathology.

VI. INVITED LECTURES/SEMINARS:

1. "Subcellular Organelle Effects of Tetrahydrocminoacridine on Human and Rodent Liver Cells", Drug information Association, Euromeeting, Paris, France, April, 1995.
2. "Structural Diversity of Peroxisome Proliferators and Effects on Mammalian Liver Cells", International Symposium on Peroxisomes: Biology and Role in Toxicology and Disease, Aspen, Colorado, June, 1994.
3. "Comparative Histopathology of Rats and Monkeys Continuously Infused with Recombinant Human EGF 1-48 for Four Weeks", American College of Veternary Pathologists, Montreal, Canada, November, 1994.
4. "Anti-peptide Antibody Production after Four Weeks of Continuous Infusion of Recombinant Epidermal Growth Factor EGF 1-48", Symposium on the Immunobiology of Proteins and Peptides, Rio Rico, Arizona, November, 1994.
5. "Immunogenicity of Recombinant Epidermal Growth Factor Fragmant EGF 1-48 in Monkeys after a Four Week Intravenous Infusion", Symposium on the Immunobiology of Proteins and Peptides, Rio Rico, Arizona, November, 1994.
6. "Morphologic Changes in Rats Treated Postnatally with Recombinant Human Epidermal Growth Factor 1-48", Society of Toxicology, Baltimore, Maryland, February, 1995.
7. "Cell Proliferation and Apoptosis in Rat Gastrointestinal Tract upon Continuous Infusion of Recombinant Human EGF 1-48", American Society of Investigative Pathology, Atlanta, Georgia, April, 1995.
8. "Cell Proliferation in the Gastrointestinal Tract of Cynomolgus Monkeys upon Continuous Intravenous Infusion of Recombinant Human EGF 1-48", American Society of Investigative Pathology, Atlanta, Georgia, April, 1995.
9. "Identification of Putative Protein Tyrosine Phosphatase Genes in Rat Regenerating Pancreas Using Polymerase Chain Reation", American Association for Cancer Research, Toronto, Canada, April, 1995.
10. "Hypolipidemic-Induced Quantitative Microscopic Changes in Rat Liver Mitochondria. VII International Congress of Toxicology, Seattle, Washington, July, 1995.
11. "Subcellular Organelle Effects of Tacrine (Cognex) in Human and Rat Hepatocytes", VII International Congress of Toxicology, Seattle, Washington, July, 1995.
12. "Regression of Multi-Organ Cellular Hyperplasia Induced by Recombinant Human EGF 1-48 in Cynomolgus Monkeys", American College of Veternary Pathologists, Atlanta, Georgia, November, 1995.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Bleavins, M.R. and de la Iglesia, F.A.: Cynomolgus monkeys (Macaca fascicularis) in preclinical immune function safety testing: Development of a delayed-type hypersensitivity procedure. Toxicology. 95:103-112, 1995.
2. Sigler, R.E., Gough, A.W. and de la Iglesia, F.A.: Pancreatic acinar cell neoplasiain male Wistar rats following two years of Gabapentin exposure. Toxicology. 98:73-82, 1995.

3. Feuer, G., Dhami, M.S.I. and de la Iglesia, F.A.: Changes by progesterone derivatives in fatty acids from phosphatidylethanolamine fractions in rat liver endoplasmic reticulum. Exp. Toxicol. Pathol. 46:169-176, 1995.
4. Fowler, L., Sigler, R.E., de la Iglesia, F.A., Reddy, J.K. and Lalwani, N.D.: Absence of Ki-RAS mutations in exocrine pancreatic tumors from male rats chronically exposed to Gabapentin. Mut. Res. 327:151-160, 1995.
5. Breider, M.A., Bleavins, M.R., Reindel, J.F., Gough, A.W. and de la Iglesia, F.A.: Cellular hyperplasia in rats following continuous intravenous infusion of recombinant human epidermal growth factor. Vet. Path. In Press.
6. Bleavins, M.R., de la Iglesia, F.A., McCay, J.A., White, K.L. and Munson, A.E.: Immunotoxicologic studies with CI-959, A novel benzothiphene cell activation inhibitor. Toxicology. In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. de la Iglesia, F.A., Di Fonzo, C.J., Martin, R.A., McGuire, E.J. and Feuer, G.: Quantitative microscopic changes of the functionally impaired hepatic endoplasmic reticulum in a proposed cholestasis rat model. Submitted for publication.
2. de la Iglesia, F.A., Martin, R.A., Walker, R.M. amd Feuer, G.: Metabolic effects of antiinfective agents on the liver of common marmosets (*Callithrix jacchus*). Submitted for Publication.
3. McGuire, E.J. and de la Iglesia, F.A.: Hypolipidemic effects on rat liver mitochondria studied by quantitative microscopy. Submitted for publication.
4. Lalwani, N.D., Dethloff, L.A., Robertson, D.G., Brott, D.A. and de la Iglesia, F.A.: Transient changes in rat liver cell replication and proliferating cell nuclear antigen induced by the peroxisome proliferator Wy-14, 643. Submitted for publication.
5. Dethloff, L.A., Graziano, M.J., Goldenthal, E., Gough, A.W. and de la Iglesia, F.A.: Perspective on the carcinogenic potential of phenytoin based on rodent tumor bioassays and human epidemiological data. Submitted for publication.
6. Monteith, D.K., Theiss, J. and de la Iglesia, F.A.: Subcellular organelle effects of tetrahydroaminoacridine (Tacrine) on human and rodent liver cells. Submitted for publication.
7. Reindel, J.F., Pilcher, G.D., Gough, A.M. and de la Iglesia, F.A.: Recombinant human EGF 1-48 induced changes in the digestive system of Cynomolgus monkeys. Submitted for publication.

BOOKS/CHAPTERS IN BOOKS:

1. Cameron, R., Feuer, G. and de la Iglesia, F.A.(eds): Drug Induced Hepatotoxicity, Handbook of Experimental Pharmacology, Springer Verlag Publishers, Heidelberg, 1995. In Press.
2. Feuer, G. and de la Iglesia, F.A.: Biochemical and morphological correlates in experimental models of hepatotoxicity, in, Cameron, R.G., Feuer, G. and de la Iglesia, F.A. (eds), Drug Induced Hepatotoxicity, Springer Verlag Publishers, Heidelberg, 1995. In Press.
3. Cameron, R.G., de la Iglesia, F.A. and Feuer, G.: Hepatotoxicity of cardiovascular drugs, in, Cameron, R.G., Feuer, G. and de la Iglesia, F.A. (eds), Drug Induced Hepatotoxicity, Springer Verlag Publishers, Heidelberg, 1995. In Press.

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

1. Reindel, J., Pilcher, G., Walsh, K., Gough, A. and de la Iglesia, F.A.: Gross and histologic findings following intravenous administration of recombinant human epidermal growth factor 1-48 for two weeks in Cynomolgus monkeys. Toxicol. Pathol. In Press.
2. Breider, M., Bleavins, M., Reindel, J., Gough, A. and de la Iglesia, F.A.: Multistemic cellulay hyperplasia in Wistar rats Induced by continuous intravenous infusion of human recombinant epidermal growth factor 1-48. Toxicol. Pathol. In Press.

3. Reindel, J., Breider, M., Pilcher, G., Bleavins, M., Altrogge, D., Gough, A. and de la Iglesia, F.A.: Comparative histopathology of rats and monkeys continuously infused with recombinant human EGF 1-48 for four weeks. Vet. Path. 31:622, 1994.
4. Bleavins, M.R., Alvey, J.D. and de la Iglesia, F.A.: Anti-peptide antibody production after four weeks of continuous infusion of recombinant epidermal growth factor EGF 1-48. Proceedings Symposium on Immunobiology of Proteins and Peptides, 1994.
5. Bleavins, M.R., Alvey, J.D., Pilcher, G.D. and de la Iglesia, F.A.: Immunogenicity of recombinant epidermal growth factor fragment EGF 1-48 in monkeys after a four week continuous intravenousiInfusion. Proceedings Symposium on Immunobiology of Protein and Peptides, 1994.
6. Reindel, J., Altrogge, D., Breider, M., Gough, A. and de la Iglesia, F.A.: Regression of multi-organ cellular hyperplasia induced by recombinant human EGF 1-48 in cynomolgus monkeys. Vet. Pathol. In Press.
7. Lalwani, N.D., Haskins, J., Bleavins, M.R., Pilcher, G.D. and de la Iglesia, F.A.: Cell proliferation and apoptosis in rat gastrointestinal tract upon continuous infusion of recombinant human EGF 1-48. FASEB J. A704, 1995.
8. Lalwani, N.D., Bleavins, M.R., Haskins, J., Pilcher, G.D. and de la Iglesia, F.A.: Cell Proliferation in the gastrointestinal tract of Cynomolgus monkeys upon continuous intravenous infusion or recombinant human EGF 1-48. FASEB J. A704, 1995.
9. Haskins, J.R., Lalwani, N.D., Bleavins, M.R. and de la Iglesia, F.A.: Quantitative microscopic characterization of continuous intravenous EGF 1-48 effects on cecal and colonic mucosa of nonhuman primates. Submitted to The Toxicologist 16.
10. Haskins, J.R., Lalwani, N.D., Bleavins, M.R. and de la Iglesia, F.A.: Morphometric evaluation of epidermal growth factor EGF 1-48 effects on the small intestine of Cynomolgus monkeys. Submitted to The Toxicologist 16.
11. Reindel, J., Henck, J., Parker, R. Gough, A., Anderson, J. and de la Iglesia, F.A.: Morphologic changes in neonatal rats treated postnatally with recombinant human EGF 1-48. The Toxicologist 15:179, 1995.
12. McGuire, E.J., Haskins, J.R., Lucas, J.A., and de la Iglesia, F.A.: Hypolipidemic-induced quantitative microscopic changes in rat liver mitochondria. Abstracts, VII International Congress of Toxicology, 7:47-P-7, 1995.
13. Fowler, M.L., Tefera, W., de la Iglesia, F.A. and Lalwani, N.D.: Identification of putative tyrosine phosphatase genes in rat regenerating pancreas using polymerase chain reaction. Proceedings, Amer. Assoc. Cancer Res. 36:519, 1995.
14. Bleavins, M.R., Johnson, K. and de la Iglesia, F.A.: Comparative effects of two forms of recombinant human epidermal growth factor in mercuric chloride-induced kidney injury. Submitted to The Toxicologist 16.
15. Monteith, D.K., Theiss, J. and de la Iglesia, F.A.: Subcellular effects of tacrine in human and rat hepatocytes. Abstracts, VII International Congress of Toxicology, 7:60-P-14, 1995.
16. de la Ig;esia, F.A., McGuire, E.J.m Haskins, J.R. and Lalwani, N.D.: Structural diversity of peroxisome proliferators and effects on mammalian cells. Abstracts, Int. Symposium on Peroxisomes: Biology and Role in Toxicology and Disease, 1995.

KENNETH O. DEVANEY, M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Service - 12 weeks.
B. Cytopathology Service - two weeks.
C. Primary Consultant for Bone and Joint Pathology.
D. Secondary Consultant for Soft Tissue Pathology.
E. Secondary Consultant for Head and Neck Pathology.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Sophomore Medical Class:
   1. Pathology 600 - lecture - three contact hours.
B. House Officers:
   1. Training in Surgical Pathology.
   2. Lectures - two hours.
   3. Surgical Pathology Consultation Conference - four hours.
   4. Pathology Resident Elective in Musculoskeletal Pathology (M. Putzi, M.D.- Feb. 1995) - four weeks.
   5. Pathology Resident Elective in Musculoskeletal Pathology (J. Homeister, Ph.D., M.D. - April, 1995) - four weeks.
C. Interdepartmental:
   1. Sarcoma conference - monthly: 24 hours.
   2. Department of Orthopedic Surgery, Orthopedic Pathology Lecture Series: two hours lecture.
   3. Department of Orthopedic Surgery, Quarterly Interdisciplinary Musculoskeletal Tumor conference: four hours.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT (PENDING APPROVAL):

A. Wolf, G.T., Bradford, C., Carey, T., Esclamado, R., Terrell, J., Urba, S, Wicha, M., Eisbruch, A., Lawrence, T., Beals, T., Devaney, K., McClatchey, K., Nunez, G., Wahl,

R., Mason, H. and Strawderman, M.: Concomitant chemotherapy and radiation for organ preservationin patients with advanced (stage III, IV) laryngeal cancer.

PROJECTS UNDER STUDY:

A. Low grade fibrosarcomas of the soft tissues.
B. Angiosarcomas developing in the first two decades of life.
C. The utility of MIC2 antibody staining in the evaluation of neuroendocrine tumors.
D. Clonality in fibromatosis.
E. Androgen receptor gene expression in fibromatosis.
F. MDM2 and p53 expression in fibromatosis.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Quality Assurance/ Quality Control Representative for Section of Surgical Pathology, Department of Pathology, University of Michigan Hospitals-1995-present.

UNIVERSITY:

A. Member, Musculoskeletal Core, Year II Curriculum.

REGIONAL AND NATIONAL:

A. Member, Arthur Purdy Stout Society of Surgical Pathologists.
B. Ad hoc Reviewer, *Cancer* .

V. OTHER RELEVANT ACTIVITIES:

WORKSHOPS:

1. "Radiologic-Pathologic Correlation in the Diagnosis of Solitary Skeletal Lesions", (Donald E. Sweet, M.D. and Kenneth Devaney, M.D., Course Directors), presented at the 1995 Annual Meeting of the United States and Canadian Academy of Pathology (Toronto, Canada).

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Devaney, K.: Intra-abdominal desmoplastic small round cell tumor of the peritoneum in a young man. Ultrastructural Pathology 18:389-398, 1994.
2. Devaney, K., Vinh, T.N. and Sweet, D.E.: Surface-based hemangioma of bone- a review of cases. Clinical Orthopedics and Related Research. 300:233-240, 1994.

3. Devaney, K., Vinh, T.N. and Sweet, D.E.: Skeletal-extraskeletal angiomatosis - a clinicopathologic study of 14 cases; nosologic considerations. J. Bone Joint Surg. 76A:878-891, 1994.
4. Devaney, K., Goodman, Z.D. and Ishak, K.G.: Hepatobiliary cystadenoma and cystadenocarcinoma-a clinicopathologic review of 68 cases. Am. J. Surg. Path. 18:1078-1091, 1994.
5. Meyers, S.P., Yaw, K. and Devaney, K.: Giant cell tumor of the thoracic spine: MR appearance. Am. J. Neurorad. 15:962-964, 1994.
6. Devaney, K., Abbondanzo, S.L., Shekitka, K.M., Wolov, R.B. and Sweet, D.E.: MIC2 detection by antibody to HBA71 in tumors of bone and adjacent soft tissues. Clinical orthopedic and related research 310:176-187, 1995.
7. Wenig, B.M., Devaney, K. and Wenig, B.L.: Nonneoplastic lesions of the oropharynx and larynx which may simulate malignancy. Pathol. Annual 30:143-187, 1995.
8. Devaney, K., Abbondanzo, S.L., Shekitka, K.M., Wolov, R.B. and Sweet, D.E.: p53 protein and proliferating cell nuclear antigen (PCNA) in small round cell tumors of bone and adjacentsoft tissue - a study of 60 cases. Int. J. of Surg. Path. 2:259-268, 1995.
9. Devaney, K., Ferlito, A. and Silver, C.: Cartilaginous tumors of the larynx. Annals of Otolaryngology, Rhinology, and Laryngology 104:251-255, 1995.
10. Ferlito, A. and Devaney, K.: Developmental lesions of the head and neck: terminology and biological behavior. Annals of Otolaryngology Rhinology, and Laryngology, In Press.
11. Skodras, G., Snodgrass, J. and Devaney, K.: Bladder carcinoma with extensive choriocarcinomatous differentiation - whence the "primary choriocarcinoma of the bladder?". J. Urologic Path., In Press.
12. Ferlito, A., Rinaldo, A. and Devaney, K.O.: Malignant laryngeal tumors: phenotypic evaluation and clinical implications. Annals of Otolaryngology, Rhinology, and Laryngology, In press.
13. Ferlito, A., Devaney, K., Rinaldo, A., Milroy, C.M. and Carbone, A.: Adenoid squamous cell carcinoma of the head and neck. Annals of Otolaryngology, Rhinology, and Laryngology, In Press.
14. Buetow, P.C., Buck, J.L., Pantangra-Brown, L., Res, P.R., Devaney, K., Goodman, Z.D. and Cruess, D.F.: Biliary cystadenoma and cystadenocarcinoma: imaging and radiologic findings in 34 cases with clinical and pathologic correlation emphasizing the significance of ovarian stroma. Radiology, In Press.
15. Devaney, K. and Ferlito, A.: Yolk sac tumors (endodermal sinus tumors) of the head and neck. Annals of Otolaryngology, Rhinology, and Laryngology, In Press.
16. Wenig, B.M., Devaney, K. and Bisceglia, M.: Inflammatory myofibroblastic tumor of the larynx: a clinicopathologic study of eight cases. Cancer, In press.
17. Ferlito, A., Carbone, A, DeSanto, L.W., Barnes, L., Rinaldo, A. and Devaney, K.O.: "Early" cancer of the larynx: the concept as defined by clinicians, pathologists, and biologists. Annals of Otolaryngology, Rhinology, and Laryngology, In Press.
18. Ferlito, A. and Devaney, K.: The squamous neoplastic component in unconventional squamous carcinoma of the larynx: diagnostic, therapeutic and prognostic implications. Annals of Otolaryngology, Rhinology, and Laryngology, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Abbondanzo, S.L. and Devaney, K.: Hodgkin's disease involving bone and adjacent soft tissue in adults: a clinicopathologic and immunophenotypic study of 7 cases.
2. Devaney, K., Abbondanzo, S.L. and Wenig, B.M.: Olfactory neuroblastoma and related sinonasal round cell lesions- MIC2, bcl-2, and p53 immunohistochemistry.
3. Devaney, K. and Popek, E.: Langerhans cell histiocytosis presenting with skeletal involvement in the first two years of life- a report of 22 cases.

CHAPTERS IN BOOKS:

1. Devaney, K.: Sclerosing lesions of bone, in, Rosenberg, A.E. and Schiller, A.L. (eds), Orthopaedic Pathology, W. B. Saunders, Philadelphia, Pennsylvania 1995, In Press.
2. Devaney, K. and Ferlito, A.: Cartilaginous and osteogenic neoplasms, in, Ferlito, A. (ed), Surgical Pathology of Laryngeal Neoplasms, Chapman and Hall, London, England 1995, pp 393-424.
3. Devaney, K.: Vascular neoplasms, in, Ferlito, A.: (ed), Surgical Pathology of Laryngeal Neoplasms, Chapman and Hall, London, England 1995, pp 341-374.
4. Devaney, K.: Fibrous and histiocytic neoplasms, in, Ferlito, A.: (ed), Surgical Pathology of Laryngeal Neoplasms. Chapman and Hall, London, England 1995, pp 295-320.

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

1. Devaney, K., Goodman, Z.D., Epstein, M.S., Zimmerman, H.J. and Ishak, K.G.: The histologic spectrum of hepatic sarcoidosis- a study of 100 cases. 1994 Year Book of Digestive Diseases.
2. Devaney, K., Abbondanzo, S.L. and Wenig, B.M.: Olfactory neuroblastoma and related sinonasalround cell lesions- MIC2, BCL-2, and p53 Immunohistochemistry. Modern Pathology 8:100A, 1995.
3. Devaney, K. and Popek, E.: Langerhans cell histiocytosis presenting with skeletal involvement in thefirst two years of life- a report of 22 cases. Modern Pathology 8:143A, 1995.
4. Wenig, B.M. and Devaney, K.: Myofibroblastic pseudotumors of the larynx (MPL). Modern Pathology 8:104A, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Supervised the following graduate students: Muneesh Tewari, Akhilesh Pandey, Haining Shao.
B. Supervised the following post doctoral fellows: Vidya Sarma, David Beidler, Jim Bretz, Claudius Vincenz.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Mechanisms of Glomerular and Tubular Injury", NIH-DK39255-03, 10% effort, Budget - $58,524 current year, $292,620 Total, 78/31/92-08/01/97.
B. Principal Investigator, "Heparin and Aortic Smooth Muscle Cell Proliferation", NIH-1RO1 HL4785701A1, 20% effort, Budget $86,621 current year, $421,592 Total, 08/01/92 - 07/31/95.
C. Principal Investigator, "Novel Zinc Finger Protein that Inhibits TNF Cytotoxicity", NIH-9RO1-CA61348, 20% effort, Budget $163,278 current year, $1,201,474 Total, Period 07/01/93 - 06/31/98.
D. Principal Investigator, "Thrombospondin 2; Structure, Expression and Function", NIH-RO1 - CA58182-06, 20% effort, Budget $143,657 current year, $1,236,526 Total, 8/04/92 to 05/31/97.
E. Principal Investigator, "Erb-B2 Expression and Resistance to TNF Killing", NIH-LA-64803. 10% effort, Budget $148,779 current year, $858,304 Total, 07/01/94 - 06/31/98.

PROJECTS UNDER STUDY:

A. Characterization of the components of the cell death pathway.
B. Mechanisms of action of tumor necrosis factor.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interview prospective graduate students for:
   1. Molecular and Cell Biology Program, and
   2. Medical Scientist Training Program.

B. 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:
   1. Journal of Biological Chemistry.
   2. Journal of Clinical Investigation.
   3. Journal of Cell Biology.

B. Pathology A Study Section (Ad-hoc).

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Invited Speaker, AHA, Lathrop Village, Michigan, 1994.
2. Invited Speaker, Keystone Symposia, Silverthorne, Colorado, 1994.
3. Invited Speaker, Thomas Jefferson University, Philadelphia, Pennsylvania, 1994.
4. Invited Speaker, New York University, New York, New York, 1994.
5. Invited Speaker, XIV Washington International Symposium, Washington, DC, 1994.
6. Invited Speaker, Gordon Research Conference, Meriden, New Hampshire, 1994.
7. Invited Speaker, Mayo Clinic, Scottsdale, Arizona, 1994.
8. Invited Speaker, AMGEN, Thousand Oaks, California, 1994.
9. Invited Speaker, Scios Nova, Inc., Mountain View, California, 1994.
10. Invited Speaker, American Society for Biochemistry and Molecular Biology Fall Symposium, Lake Tahoe, California, 1994.
11. Invited Speaker, Parke-Davis Pharmaceuticals, Ann Arbor, Michigan, 1994.
12. Invited Speaker, University of Minnesota, Institute of Human Genetics, Minneapolis, 1994.
13. Invited Speaker, IDUN Pharmaceuticals, San Diego, California, 1995.
14. Invited Speaker, Mayo Clinic, Scottsdale, Arizona, 1995.
15. Invited Speaker, March Atherosclerosis Forum, Courchevel, Switzerland, 1995.
16. Invited Speaker, American Society of Investigative Pathology, Toronto, Canada, 1995.
17. Invited Speaker, Tularik, Inc., San Francisco, California, 1995.

18. Invited Speaker, Gordon Conference, New London, New Hampshire, 1995.
19. Invited Speaker, Association of Pathology Chairs, Apoptosis Seminar, Vail, Colorado, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Qabar, A.N., Lin, A., Wolf, F.W., O'Shea, K.S., Lawler, J. and Dixit, V.M.: Thrombospondin 3 is a developmentally regulated heparin binding protein. J. Biol. Chem. 269:1262-1269, 1994.
2. Suchard, S.J., Mansfield, P.J. and Dixit, V.M.: Modulation of Thrombospondin Receptor Expression During HL-60 Cell Differentiation. J. Immunol. 152:877-888, 1994.
3. Shao, H., Lou, L., Pandey, A., Pasquale, E.B. and Dixit, V.M.: cDNA cloning and characterization of a ligand for the Cek5 receptor protein-tyrosine kinase. J. Biol. Chem. 269:26606-26609, 1994.
4. Pandey, A., Lazar, D.F., Saltiel, A.R. and Dixit, V.M.: Activation of the Eck receptor protein tyrosine kinase stimulates phosphatidylinositol 3-kinase activity. J. Biol. Chem. 269:30154-30157, 1994.
5. Hu, H.M., O'Rourke, K., Boguski, M.S. and Dixit, V.M.: A novel RING finger protein interacts with the cytoplasmic domain of CD40. J. Biol. Chem. 269:30069-30072, 1994.
6. Shao, H., Lou, L., Pandey, A., Verderame, M.F., Siever, D.A. and Dixit, V.M.: cDNA cloning and characterization of a Cek7 receptor protein-tyrosine kinase. ligand that is identical to the ligand (ELF-1) for the Mek-4 and Sek Receptor protein-tyrosine kinases. J. Biol. Chem. 270:3467-3470, 1995.
7. Tewari, M. and Dixit, V.M.: Fas- and TNF-induced apoptosis is inhibited by the poxvirus crmA gene product. J. Biol. Chem. 270:3255-3260, 1995.
8. Shao,H., Pandey, A., O'Shea, K.S., Seldin, M. and Dixit, V.M.: Characterization of B61, the ligand for the eck receptor protein-tyrosine kinase. J. Biol. Chem. 270:5636-5641, 1995.
9. Pandey, A., Shao, H., Marks, R.M., Polverini, P.J. and Dixit, V.M.: Role of B61, the ligand for the eck receptor tyrosine kinase in TNF-a induced angiogenesis. Science 268:567-569, 1995.
10. Sarma, V., Lin, Z., Clark, L., Rust, B.M., Tewari, M., Noelle, R.J. and Dixit, V.M.: Activation of the B-cell surface receptor CD40 induces A20, a novel zinc finger protein that inhibits apoptosis. J. Biol. Chem. 270:12343-12346, 1995.
11. Qabar, A. Derick, L., Lawler, J. and Dixit, V.M.: Thrombospondin 3 is a pentameric molecule held together by interchain disulfide linkage involving two cysteine residues. J. Biol. Chem. 270:12725-12729, 1995.
12. Chinnaiyan, A.M., O'Rourke, K., Tewari, M. and Dixit, V.M.: FADD, a novel death domain-containing protein, interacts with the death domain of Fas and initiates apoptosis. Cell 81:505-512, 1995.
13. Tewari, M., Quan, L.T., O'Rourke, K., Desnoyers, S., Zeng, Z., Beidler, D.R., Poirier, G.G., Salvesen, G. and Dixit, V.M.: Yama/Cpp32ß, a mammalian homolog of CED-3, is a CrmA-inhibitable protease that cleaves the death substrate poly(ADP-ribose) polymerase. Cell 81:801-809, 1995.

14. Beidler, D.R., Tewari, M., Friesen, P.D., Poirier G. and Dixit, V.M.: The baculovirus p35 protein inhibits Fas and tumor necrosis factor-induced apoptosis. J. Biol. Chem. 270:16526-16528, 1995.
15. Pandey, A., Duan, H. and Dixit, V.M.: Characterization of a novel src-like adapter protein that associates with the eck receptor tyrosine kinase. J. Biol. Chem. 270:19201-19204, 1995.
16. Tewari, M., Beidler, D.R. and Dixit, V.M.: CrmA-inhibitable cleavage of the 70-kDa protein component of the U1 small nuclear ribonucleoprotein during Fas- and TNF-induced apoptosis. J. Biol. Chem. 270:18738-18741, 1995.
17. Tewari, M., Telford, W.G., Miller, R.A. and Dixit, V.M.: CrmA, a poxvirus-encoded serpin, inhibits cytotoxic T-lymphocyte-mediated apoptosis. J. Biol. Chem., In Press.
18. Rothe, M., Sarma, V., Dixit, V.M. and Goeddel, D.V.: TRAF2 mediates activation of NF-kB by TNF receptor 2 and CD40. Science, In Press.
19. Jäättelä, M., Benedict.M., Tewari, M., Shayman, J.A. and Dixit, V.M.: Bcl-x and Bcl-2 inhibit TNF and Fas-induced apoptosis and activation of phospholipase A_2 in breast carcinoma cells. Oncogene, In Press.
20. Pandey, A., Duan, H., Di Fiore, P.O. and Dixit. V.M.: The ret receptor protein tyrosine kinase associates with the SH2 containing adapter protein Grb10. J. Biol. Chem., In Press.

GREGORY R. DRESSLER, M.D., Ph.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 AUGUST 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Mentored Ph.D. candidate, Dawn Phelps, who received degree in April, 1995 from George Washington University, Washington, D.C.

MEDICAL SCHOOL/HOSPITALS:

None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, Howard Hughes Medical Institute - 001819, "Analysis of Mammalian Developmental Control Genes", (50%), October 1, 1994-September 30, 1997. Approximately $221,500 current year (includes staff salaries, supplies and equipment) excluding PI's salary and benefits. The actual budget is negotiated yearly.

PENDING:

A. Principal Investigator, "PAX-2 in Normal and Cystic Epithelium Develpment", NIH/NIDDK, (25%), September 30, 1995-September 29, 2000. Direct costs approximately $100,000 requested annually.
B. Co-Principal Investigator (Dr. Kate Barald, Principal Investigator), "Role of Hindbrain in Molecular Development and Innervation of the Inner Ear, NSF, (10%), April 1, 1996-March 31, 1999. Total costs: $534,681.
C. Sponsor, WELLCOME TRUST, "Regulation of PAX-2 in Normal and Cystic Epithelium", Fellowship Recipient: Julie Martin, Awardee, Gregory Dressler, Sponsor, (5%), January 2, 1996-December 31, 1998. Direct costs/year (supplies only)- $5,400.

PROJECTS UNDER STUDY:

A. The identification of co-factors required for Pax protein mediated transcription activation.
B. The effect of tumor suppressor genes on Pax gene regulation in renal cell carcinoma.
C. The development of novel methods for identifying genes regulated by Pax proteins.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None.

REGIONAL AND NATIONAL:

None.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited lecturer - Nephrology Conference, Renal Division, College of Physicians and Surgeons of Columbia University, New York, New York, April 10, 1995.
2. Invited speaker for 2nd International Conference on Molecular and Clinical Genetics and Childhood Renal Tumors, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, May 25-27, 1995.
3. Invited speaker for the Seventh International Symposium on Basement Membranes, National Institutes of Health, Bethesda, Maryland, June 29-30, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ryan, G., Steele-Perkins, V., Morris, J., Rauscher, F.J. III and Dressler, G.R.: Repression of PAX-2 by WTI during normal kidney development. Development 121:867-875, 1995.
2. Gnarra, J.R. and Dressler, G.R.: Expression of Pax-2 in renal cell carcinoma and growth inhibition by antisense oligonucleotides. Cancer Research, In Press.

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

None.

BOOK CHAPTERS IN BOOKS:

1. Dressler, G.R.: Developmental control genes, in, Schloendorff, D. and Bonventre, J. (eds), The Molecular Biology of the Kidney in Health and Disease, Marcel Dekker, New York, 1995, In Press.

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

1. Dressler, G.R.: The pros and cons of c-ret. Current Biol. 4:354-356, 1994.
2. Patterson, L.T. and Dressler, G.R.: Regulation of kidney development: new insights from an old model. Curr. Opin. Genet. Develop. 4:696-702, 1994.
3. Dressler, G.R.: Transcription factors in renal development: The WTI and Pax-2 story. Seminars in Nephrology 15:263-271, 1995.
4. Dressler, G.R.: The genetic control of renal development. Curr. Opin. Hyper. Nephrol. 4:253-257, 1995.
5. Dressler, G.R.: The molecular basis of early kidney development: studies with the Pax-2 gene. Medical and Pediatric Oncology, 1995, In Press.
6. Dressler, G.R.: Pax-2 function in early nephrogenesis. Contributions to Nephrology, 1995, In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

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. Participant, Clinical Pathology Grand Rounds.
D. Instructor for Medical Student (M-4) rotation through Chemistry Laboratories.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. USPHS (NIDDKD) 2P60AM20572-10: Michigan Diabetes Research and Training Center, Director Ligand Assay Core Facility, $130,000/year, 1993-1998.
B. USPHS (NICHD) 5T32HD07048-18: Training Program in Reproductive Endocrinology, Co-Investigator, $149,898/year, 1990-1995.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Director, Central Ligand Assay Laboratory.

MEDICAL SCHOOL/HOSPITAL:

A. Director, Chemistry Core Facility, Michigan 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:

1. President, Midwest Clinical Ligand Assay Society, 1994-95.
2. Executive Committee Member of the Clinical Ligand Assay Society, 1994-1995.

3. Chairman of Scientific Program (Roundtables) of the 1996 Annual Meeting of the Clinical Ligand Assay Society to be held in Los Angeles, California.
4. Roundtable Presentor: Annual Meeting 1995 Toronto, Ontario, Clinical Ligand Assay Society. Estradiol Calibration. What's Right?

VI. INVITED LECTURES AND SEMINARS:

None.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1 Benghuzzi, H.A., Possley, R and England, B.G.: The use of tricalcium-phosphate-lysine implants to deliver estrogen in a sustained level for one year in adult castrated rams. Proceedings of the 13th Southern Biomedical Conference, pp. 79-82, 1994.
2. Benghuzzi, H.A. and England, B.G.: The effect of highly compressed TCPL mixed particle sizes on the delivery rate of steroid hormones. Proceedings of the 13th Southern Biomedical Conference, pp. 486-489, 1994.
3. Benghuzzi, H.A., Bajpai, P.K. and England, B.G.: Physical properties and potential behavior of TCPA devices *in vitro*. Proceedings of the 13th Southern Biomedical Conference, pp 474-477, 1994.
4. Flinn, M.V. and England B.G.: Socioeconomic conditions affecting childhod glucocorticoid stress response (abstract). American Journal of Physical Anthropology Supplement 18:87-88, 1994.
5. Decker, S.A., Flinn, M.V. and England, B.G.: Interactions of social status with daily cortisol and testosterone in male caribbean villagers. American Journal of Physical Anthropology Supplement 18:77-78, 1994.

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

1. Benghuzzi, H.A., Bajpai, P.K. and England, B.G.: Physiological responses of long-term sustained delivery of DHT and estradiol by ceramic delivery systems. The 21st Annual Meeting of the Society for Biomaterials. San Francisco, California, March 18-22, 1995.
2. Benghuzzi, H.A., Lemos, L., Carson, A. and England, B.G.: Cytopathoilogical evaluation of tissue compromising the TCPL delivery devices. Scanning electron microscopy international: Cells and Materials, Houston, Texas, May 7-12, 1995. (Invited Presentation).
3. Benghuzzi, H.A. and England, B.G.: Long-term sustained delivery of androgens by means of TCPL devices and the effect on high-density lipoprotein in castrated rams. 32nd Annual Meeting of the Rocky Mountain Bioengineering Symposium, Cooper Mountain, Colorado, April 7-9, 1995.
4. Benghuzzi, H.A. and England, B.G.: The role of sustained delivery of steroid hormones on the gonadotropin secretions using adult rams as a model. Scanning

Electron Microscopy International: Cells and Materials, Houston, Texas, May 7-12, 1995. (Invited Presentation).

5. Benghuzzi, H.A. and England, B.G.: The effect of sustained delivery of danazol and antioxidants on lipoprotein profiles of adult female mice. 32nd Annual Meeting of the Rocky Mountain Bioengineering Symposium, Cooper Mountain, Colorado, April 7-9, 1995.
6. Bush, D., England, B.G., Tucci, M., Cason, A., Lemos, L. and Benghuzzi, H.A.: The effect of TCPL devices on tissue-implant interface using adult sheep as a model. 32nd Annual Meeting of the Rocky Mountain Bioengineering Symposium, Cooper Mountain, Colorado, April 7-9, 1995.
7. England, B.G. and Benghuzzi, H.A. TCPL Delivery System: The effect of various steroid concentrations in adult rams. Scanning Electron Microscopy International: Cells and Materials, Houston, Texas, May 7-12, 1995. (Invited Presentation).
8. Benghuzzi, H.A. and England, B.G.: Biphasic continuous delivery of steroid hormones and the regulation of reproductive function in adult ewes. 59th Annual Meeting of the Mississippi Academy of Sciences, February 9-10, 1995, Vol. 40, Issue 1 p. 64.
9. Flinn, M.V., Quinlan, M., Quinlan, R., Turner, M. and England, B.G.: Glucocorticoid stress response, immune function, and illness among children in a rural Caribbean village (abstract). American Society of Physical Anthropology Annual Meeting, San Francisco, California, 1995.
10. Turner, M.T., Flinn, M.V. and England, B.G.: Mother-infant glucocorticoid stress response in a rural Caribbean village (abstract). American Society of Physical Anthropology Annual Meeting, San Francisco, California, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Autopsy Service.

II. TEACHING ACTIVITIES:

A. Director, Resident Training Program.
B. Graduate Program Committee (Chairman).
C. Course Director - Pathology Teaching Laboratories.
D. Director - Component I and II: Medical Student Curriculum.
E. Laboratory Instructor, M1 Histopathology Sequence.
F. Lecturer, M1 Host Defense Sequence.
G. Coordinator, Department of Pathology Summer Clinical Program for Minority Medical Students.
H. Pulmonary Pathology Conference (six per year to Pulmonary Division, Department of Internal Medicine).
I. Graduate Student Ph.D. Thesis Committee (three).
J. Medical Student Advisor (3rd and 4th year).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Mechanisms of Myocardial Ischemia/Reperfusion Injury", NIH-R01-HL44085.
B. Co-Investigator, "Regulation of IL-Gene Expression", (D.G. Remick, Principal Investigator) NIH GM50401.

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chairman's Advisory Committee.
B. Coordinator - Educational Programs.
C. Department ACAPT Committee.
D. Human Resource Committee.
E. Research Space Advisory Committee.
F. Faculty Sexual Harassment Contact Person.

MEDICAL SCHOOL/HOSPITAL:

A. Medical School - Executive Committee.
B. CD/ACD Education Committee.
C. Component I Committee.
D. Component II Committee.
E. Medical Student Basic Science Academic Review Board.
F. Medical Student Clinical Academic Review Board.

REGIONAL AND NATIONAL:

A. NIH Site Visit, SCOR: Myocardial Injury, Washington, D.C., 1995.
B. AHA of Michigan, Grant Review Committee, 1995.
C. USMLE, Pathology Test Group.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Editorial Board, Laboratory Investigation.
B. Editorial Board, Biological Signals.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Brieland, J.K., Freeman, P., Kunkel, R., Chrisp, C., Hurley, M., Fantone, J.C. and Engleberg, C.: Replicative *Legionlla pneumophila* lung infection in intratracheally inoculated A/J mice: A murine model of human Legionnaires' disease. Amer. J. Path. 145: 1537-1546, 1994.
2. Crockett-Torabi, E., Smith, C.W. and Fantone, J.C.: Activation of human neutrophils through L-selectin and Mac-1 molecules. J. Immunol. 154:2291-2302, 1995.

3. Robins, L.S., Fantone, J.C., Oh, M.S., Alexander, G.L., Shlafer, M. and Davis, W.K.: The effect of pass/fail grading and weekly quizzes on first year medical students' performances and satisfaction. Acad. Med. 70: 327-329, 1995.
4. Brieland, J.K., Remick, D.G., Freeman, P.T., Hurley, M.C., Fantone, J.C. and Englebery, M.C.: *In vivo* regulation of replicative legionella pneumophila lung infection by endogenous tumor necrosis factor and nitric oxide. Infection and Immunity. 63:3253-3258, 1995.
5. Brieland, J.K., Flory, C.M., Jones, M.L., Miller, G.R., Remick, D.G., Warren, J.S. and Fantone, J.C.: Regulation of monocyte chemoattractant protein-1 gene expression and secretion in rat pulmonary alveolar macrophages by lipopolysaccharide tumor necrosis factor-α, and interleukin-1 β. Am. J. Resp. Cell Mol. Biol. 12: 104-109, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Rotations, July (1/4), August (2/4), September (1/4), October (2/4), December (4/4), February (2/4), March (1/4), April (2/4), May (2/4), June (2/4).
B. Estrogen and progesterone receptor analysis of paraffin embedded breast carcinomas by image analysis - 91 samples.

II. TEACHING ACTIVITIES:

A. Pathology 600 Lectures:
   1. Obstructive Lung Disease - November 15, 1994.
   2. Neoplasms - November 18, 1994.
   3. Pathology of ARDS - November 22, 1994.
   4. Tissue Reactions to Infectious Agents - November 17, 1994.
   5. Laboratory Instructor, September, 1994 - May, 1995.
   6. Student question and answer sessions, afternoons and evenings, October, 1994 - May, 1995.
B. Pathology 630:
   1. Respiratory Disease I - October 24, 1994.
   2. Respiratory Disease II - October 26, 1994.
C. Residency Training:
   1. Diseases of the Chest I - January 10, 1995.
   2. Diseases of the Chest II - January 17, 1995.
   3. Diseases of the Chest III - January 24, 1995.
   4. Surgical Pathology Consultant's Conference, December, 1994; May, 1995.
D. Other educational activities:
   1. M4 student elective mentor, August, 1994.
   2. Center for Research on Learning and Teaching Workshop: Motivating Students, October 17, 1994; Using Student Feedback, February 6, 1995; Adapting Lectures, February 8, 1995.
   3. Member, M-2 Respiratory Sequence Committee, 1994-1995.
   4. Course Director, M-4 Student Pathology Clerkships.
   5. Workshop on Lung Transplantation, University of Pittsburgh, Pittsburgh, Pennsylvania, November, 1994.
   6. Participant, Thoracic Surgery Residents Core Curriculum.
   7. Facilitator, Pathology for High School Students, Community High School, March, 1995.
   8. Recipient, Kaiser Permanent Award for Excellence in Clinical Teaching, 1995.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Pathology Consultant, Morphologic Studies of Diffuse Interstitial Lung Diseases, A Multi-Institution Project, Reuben M. Cherniak, M.D., National Jewish Hospital, Program Director.
B. Prognostic Markers of Urinary Bladder Cancer (RFACA 91-09), H. Barton Grossman, M.D. (Principal Investigator),Andrew Flint, M.D. (Co-Investigator).
C. Role of Urothelial Cell Activation in Interstitial Cystitis (DK-91-04), Monica Liebert, Ph.D. (Principal Investigator), Andrew Flint, M.D. (Co-Investigator).
D. Interstitial Lung Diseases - Specialized Center of Research (1 P50 HL- 46487-01), Galen Toews, M.D. (Principal Investigator), Andrew Flint, M.D. (Co-Investigator).
E. Monoclonal Antibodies to Bladder Tumor Antigens, H. Barton Grossman, M.D. (Principal Investigator), Andrew Flint, M.D. (Co-Investigator).

PROJECTS UNDER STUDY:

A. Analysis of TGF-ß and its binding protein, decorin, in lung tissue of ARDS patients.
B. Histologic predictors of obliterative bronchiolitis in lung transplant patients.
C. Histologic prognostic indicators of survival in ARDS patients treated with ECMO.
D. Correlation of TGF-ß levels in BAL specimens with histochemical demonstration of TGF-ß in lung tissue sections.
E. Ploidy analysis and P53 expression in Barrett's esophagus.
F. Pathologic effects of perfluorocarbon liquid ventilation of ARDS patients.
G. The clinical usefulness of the abnormal nondiagnostic lung biopsy sample.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interviewed House Officer Candidates (October, 1994-January, 1995).
B. Director, Surgical Pathology Fellowship Program (July, 1994 - March, 1995).
C. Member Credentials Committee, University Hospital D. Member Bylaws Committee of the Arthur Purdy Stout Society, 1992- 1994.
E. Member, Admissions Committee of the University of Michigan Medical School, 1995 - present.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A.. Reviewer, American Review of Respiratory and Critical Care Medicine (formerly the American Review of Respiratory Disease).
B. Reviewer, Human Pathology.
C.. Reviewer, Annals of Thoracic Surgery.

INVITED LECTURES/SEMINARS:

1. Co-Director, Short Course on Closed Lung Biopsy Interpretation, USCAP meeting, Toronto, Canada, March, 1995.
2. "Lung Biopsy Interpretation", Michigan Pathology Society, June, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Flint, A., Martinez, F.J., Young, M.L., Whyte, R.I., Toews, G.B. and Lynch J.P.: The influence of sample number and biopsy site on the histologic diagnosis of diffuse pulmonary disease. Ann. Thoracic Surg., Accepted for publication.
2. Cherniack, R.M., Colby, T.V., Flint, A., Thurlbeck, W.M., Waldronm J.A., Jr., Ackerson. L., Schwarz, M.I. and King, T.E., Jr.: Correlation of structure and function in idiopathic pulmonary fibrosis. Am. J. Respir. Crit. Care. Med. 151:1180-1188, 1995.
3. Orens, J.B., Kazerooni, E.A., Martinez, F.J., Curtis, J.L., Gross, B.H., Flint, A. and Lynch, J.P. III: The sensitivity of high-resolution CT in detecting idiopathic pulmonary fibrosis proved by open lung biopsy. Chest 108:109-115, 1995.

SUBMITTED PUBLICATIONS:

1. Pickhardt, P.J., Kazerooni, E.A. and Flint, A: Diagnosis of lymphangioleiomyomatosis by CT-guided retroperitoneal lymph node biopsy. J. Thoracic Imaging.
2. Lee, C., Liebert, M., Washington, R., Wedemeyer, G., Flint, A. and Grossman, H.B.: Expression of MUC1 antigens in human prostate cancer. J. Urol.

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

1. Iannettoni, M.D., Fazzalari, F., Whyte, R.I., Flint, A. and Bartlett, R.H.: The role of TGF-beta in acute pulmonary fibrosis and bronchiolitis obliterans. Western Thoracic Surgical Association, 1995.
2. Fazzalari, F.L., Iannettoni, M.D., Lesser, E., Schriener, R.J., Flint, A. and Bartlett, R.H.: Pulmonary fibrosis in ARDS supported with ECMO: The role of transforming growth factor beta (TGF-ß). The American Association for Thoracic Surgery, 1995.
3. Flint, A: Biopsy Interpretation of the Lung, book review for American Journal of Surgical Pathology, 1995.
4. Kazerooni, E.A., Martinez, F.J., Flint, A., Cascade, P.N., Gross, B.H. and Lynch, J.P. III: HRCT at 10 mm increments versus 3-level HRCT in idiopathic pulmonary fibrosis: correlation with pathologic scoring. Radiological Society of North America, 1995.
5. Kazerooni, E.A., Martinez, F.J., Flint, A., Gross, B.H., Cascade, P.N. and Towes, G.B.: Correlations of HRCT and pathologic scoring systems for idiopathic pulmonary fibrosis. Radiological Society of North America, 1995.
6. Stern, R.A., Greenson, J.K. and Flint, A.: Evaluation of cell kinetics in hyperplastic polyps using mib-1 and image analysis and bcl-2. Mod. Pathol. 8:69A, 1995.

THOMAS S. FRANK, M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL RESPONSIBILITIES:

A. General surgical pathology.
B. Gynecologic pathology (consultation cases).
C. Immunohistology and Molecular Analysis (intramural and consultation).
D. Weekly Interdisciplinary Gynecologic Oncology Tumor Board.

II. TEACHING ACTIVITIES:

MEDICAL STUDENT

A. Sequence Coordinator, M2 Course: Oncology.
B. M2 medical student lectures:
   1. Neoplasia (five hours), September 1994.
   2. Gynecology (three hours), March 1995.
C. M2 Pathology Laboratory Supervision 1994-1995.
D. Pathology 630 lecture (one hour), October 1994.
E. Preceptor, M4 Student Elective (Molecular Alterations in Adenocarcinoma of the Cervix), March 1995.

HOUSE OFFICER

A. Lecturer, Pathology House Officer Didactic Conferences in Gynecologic Pathology and Molecular Diagnostics (five hours).
B Gynecologic Pathology Consultation Conferences for Pathology House Officers.
C. Monthly Pathology-Gynecology teaching conference for house officers in OB-GYN.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Development of a Human Breast Cancer Cell-Tissue Bank And Database, DOD Grant, 9/1/94-8/30/98 (Co-investigator,15% effort).
B. Genetic Markers In Gynecologic Malignancy, Harris Foundation.

C. Value of ultrasound, CT, and MR in ovarian cancer staging, Radiology Oncology Diagnostic Imaging Group, NIH Grant 1 UO1 CA59400-01, 12/1/92-11/30/95 (co-investigator, 3% effort).
D. Director, UMCCC Tissue Procurement Core (5% effort).

PROJECTS UNDER STUDY:

A. Genetic alterations in epithelial malignancies of endometrium, cervix, and ovary.
B. Development of a human breast cancer cell-tissue bank and database for the study of genetic and immunophenotypic alterations in breast carcinoma (with Steve Ethier, Ph.D., and Sofia Merajver, M.D.).
C. Identification of microorganisms (including bacteria and DNA and RNA viruses) in paraffin-embedded tissues using molecular analysis.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Immunohistology Laboratory.
B. Director, Preserved Tissue Analysis (Molecular Diagnostics for Anatomic Pathology Specimens).

UNIVERSITY:

A. Member, University of Michigan Comprehensive Cancer Center.
B. Member, Kughn Clinical Research Center.

REGIONAL AND NATIONAL:

A. Molecular Pathology Test Committee, American Board of Pathology.
B. Abstract Review Board, United States & Canadian Academy of Pathology (US-CAP).
C. Organizing Committee, Association for Molecular Pathology.
C. Organizer, Annual Symposium: Molecular Diagnostics in Pathology.
D. Editorial Board, Diagnostic Molecular Pathology.
E. Member, American Association for the Advancement of Science.
F. Member, American Society of Clinical Pathologists.
G. Member, A. James French Society.

V. INVITED LECTURES/SEMINARS:

1. Invited lecture, "Introduction to Molecular Oncology", Workshop on Molecular Diagnostics in Pathology (Sponsored by Universities Associated for Research and Education in Pathology), Bethesda, Maryland, November, 1994.
2. Short course, "Diagnostic Molecular Pathology," with Carolyn Mies M.D., US-CAP Toronto, March, 1995.

3. Invited lecture, "Analysis of Nucleic Acids in Paraffin Sections," Binford-Dammin Society, Toronto Ontario, March, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Pearlman M.D., McNeeley S.G., Frank T.S. and Hoeft-Loyer C.: Anti-endotoxin antibody is protective against tubal damage in an *Eschericia Coli* rabbit salpingitis model. Amer. J. Obst. Gynecol. 171:1588-93, 1994.
2. Caduff R.F., Johnston C.M. and Frank T.S.: Mutations of the Ki-*ras* oncogene in carcinoma of the endometrium. Amer. J. Pathol. 146:182-188, 1995.
3. DelBuono E.A., Appelman H.D. and Frank T.S.: The role of the polymerase chain reaction in the diagnosis of cytomegalovirus infection in liver transplant patients. Inter. J. Surg. Pathol. 2:221-226, 1995.
4. Merajver S.D., Pham T.M., Caduff R.F., Chen M., Poy E.L., Johnston C. and Frank T.S.: Somatic mutations in the *BRCA1* gene in sporadic ovarian tumors. Nature Genetic 9:439-443, 1995.
5. Merajver S.D., Frank T.S., Xu J., Calzone K.A., Bennett-Baker P., Chamberlain J., Garber J.E., Collins F.S. and Weber B.L.: Germline BRCA1 mutations and loss of the wild-type allele in tumors from families with early-onset breast/ovarian cancer. Clinical Cancer Research 1:539-544, 1995.
6. Walling D.M., Clark N., Markovitz D., Frank T.S, Braun D.K., Eisenberg E., Krutchkoff D.J., Felix D.H. and Raab-Traub N.: Epstein-Barr virus coinfection and recombination in non-HIV-associated oral hairy leukoplakia. Journal of Infectious Diseases 171:1122-30, 1995.
7. Goldblum J.R., Frank T.S., Poy E.L. and Weiss S.W.: p53 mutations and tumor progression in well-differentiated liposarcoma and dermatofibrosarcoma protuberans. International Journal of Surgical Pathology 3:35-42, 1995.
8. Frank T.S. and Cook S.M.: Analysis of paraffin sections of Crohn's disease for Mycobacteria paratuberculosis using polymerase chain reaction. (Modern Pathology, in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Caduff R.F., Johnston C.M., Svoboda S.M., Poy E.L. and Frank T.S.: Clinical and pathologic significance of microsatellite instability in sporadic endometrial carcinoma.
2. Frank T.S., Svoboda S.M. and Hsi E.D.: Comparison of methods for extracting DNA from paraffin sections for non-isotopic PCR.
3. Greenson J.K., Svoboda S.M., Merion R.M. and Frank T.S.: The histologic progression of recurrent hepatitis C in liver transplant allografts.
4. Stern R.A., Svoboda S.M. and Frank T.S.: Analysis of chronic endometritis for *Chlamydia trachomatis* by PCR.

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

1. Caduff R.F. and Frank T.S.: Microsatellite instability in endometrial carcinoma [poster presentation, United States-Canadian Academy of Pathology, 1995]. Modern Pathology, 8:87A, 1995.
2. Stern R.A., Svododa S. and Frank T.S.: Analysis of chronic endometritis for Chlamydia trachomatis using polymerase chain reaction [poster presentation, United States-Canadian Academy of Pathology, 1995]. Modern Pathology, 8:97A, 1995.
3. Greenson J.K., Sbododa S.M., Frank T.S. and Merion R.M.: Histologic progression of recurrent hepatitis C (HCV) in liver transplant (tx) patients: collrelation with PCR detection of HCV RNA and HLA-DQb status [platform presentation, United States-Canadian Academy of Pathology, 1995]. Modern Pathology, 8:130A, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

DEPARTMENTAL:

A. Co-Director of a laboratory section, Pathology 600.
B. Teaching and supervision of five Pathology house officers participating in two-week Pathology Data Systems (PDS) rotations throughout the year.

MEDICAL SCHOOL/HOSPITALS:

A. Program Director of the Thirteenth Annual Symposium on Automated Information Management in the Clinical Laboratory at the Towsley and Power Centers, June 7-9, 1995. Symposium attracted 310 registrants, a 50% increase over the previous year, and 41 vendors.
B. Two hours of programming from the June symposium were packaged as a teleconference for 53 training programs in pathology in the U.S. and Canada. Approximately teniduals per remote site participated for a total teleconference audience of about 530.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Development of a project called the "virtual department of pathology informatics" with educational offerings in pathology informatics for all house officers in the pathology training programs in the U.S. and Canada. Information technologies such as video and audio transmission across the Internet and web publishing will be integrated into the activities of the virtual department as they mature. As part of this activity, a teleconference was offered as a real-time simulcast from the June symposium. Another teleconference directed to pathology house officers around the country is now being planning for October 23, 1995, in cooperation with MLabs. MLabs will be the local

sponsor of the conference as part of their own educational activities. Activities of the virtual department are being coordinated with Medical Center Information Technology (MCIT) and with the University of Michigan Academic Outreach Program (AOP).

B. Grant of $5,000 from the Ameritech Foundation through the Consortium for Research on Telecommunications Policy to study Community Health Information Networks (CHINs) with Professor Will Mitchell, Department of Corporate Strategy, University of Michigan Business School.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chairman, Internal Review Committee for the Department of Pathology. Final report delivered to the Dean of the Medical School on November 17, 1994.
B. Clinical Laboratory Directors Committee.

HOSPITAL:

A. Chief Information Officer Management Team (CIOMT), University of Michigan Medical Center.
B. Co-Director, Medical Center Data Warehouse Project.

UNIVERSITY:

A. Executive Committee, Center for Statistical Consultation and Research (CSCAR), The University of Michigan, 1991-1996.

REGIONAL AND NATIONAL:

A. Council on Medical Informatics of the American Society of Clinical Pathologists (ASCP).
B. College of American Pathologists (CAP) Committee on Informatics.
C. American Board of Pathology, Informatics Test Committee.
D. Guest Editor of a Pathology Patterns (AJCP) supplement on informatics to be published in April, 1996.
E. Editorial Advisory Board, Clinical Laboratory Management Review.
F. Scientific Advisory Panel, LAB-InterLink Inc., 1994.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Information System Support of Managed Care. A lecture presented at the annual meeting of the Clinical Laboratory Management Association (CLMA), Orlando, Florida, August 31, 1994.

2. Integrating Medical Information in the 1990s. A workshop presented at the Fall Meeting of the American Society of Clinical Pathologists, Washington, D.C., October 23, 1994.
3. Rules Deployment in the Clinical Laboratory: An Organizational, Financial, and Technical Viewpoint. A lecture delivered at the Applied Clinical Informatics Symposium, University of Michigan Medical School, Ann Arbor, Michigan, March 10, 1995.
4. Exchanging Healthcare Information on a Regional Basis with a CHIN. A lecture delivered at a symposium entitled "Telecommunications Infrastructure and the Information Economy" sponsored by the Consortium for Research Concerning Telecommunications Policy and Strategy, University of Michigan, Ann Arbor, Michigan, March 11, 1995.
5. (1) Integration of Laboratory Information, a component of a workshop entitled Laboratories and the Electronic Medical Record. (2) The Politics of Running an LIS. Two lectures delivered at the Spring Meeting of the College of American Pathologists (CAP), Orlando, Florida, April 22 and 25, 1995.
6. (1) Upstream and Downstream Integration: The Laboratory Perspective. (2) Regionalizing Laboratory Information: Taking It On the "CHIN." Two lectures delivered at the Thirteenth Annual Symposium on Automated Information Management in the Clinical Laboratories, Ann Arbor, Michigan, June 7-8, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Friedman, B.A.: The laboratory information float. Clin. Lab. Man. Rev. 2:8-10, 1995.

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

1. Friedman, B.A. and Mitchell, W.: Community health information networks (CHINs) and their relationship to telemedicine. A chapter in a book on telemedicine edited by Rashid Bashshur, Ph.D.
2. Friedman, B.A.: Creating a regional laboratory network using a community health information network (CHIN) infrastructure. A chapter in a book commissioned by the Washington G2 Reports and the Clinical Laboratory Management Association on the current statues of laboratory consolidation and integration in a regional context.
3. Friedman, B.A.: Challenges of laboratory information management in a managed care environment. Pathology Patterns informatics supplement of AJCP, April, 1996.
4. Gendler, S. and Friedman, B.A.: Using hub technology to create enterprise-wide information integration. Pathology Patterns informatics supplement of AJCP, April, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

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 and coagulation testing meters in the Emergency Room and operating rooms of Main and Mott Hospitals.
D. Direct work group overseeing the quality assurance program for bedside blood glucose testing.
E. Planning group for establishment of alternate site testing and near the patient testing programs.
F. Technical Director for laboratories at U-M Medical Group off-site clinics.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Medical School:
   1. Developed Chemistry Lab presentations for the M4 Laboratory Medicine Elective.
B. Pathology House Officers:
   1. Lecturer, Clinical Pathology Rounds (two lectures).
   2. Coordinator, Pathology House Officer rotation through General Chemistry Lab and Section of Chemistry.
   3. Review daily sign-out and interpretation of electrophoresis results.
   4. Review of selected topics in Clinical Chemistry.
C. Medical Technologists:
   1. Program Director, Continuing Education Series for Medical Technologists.
D. Postgraduate
   1. Doctoral Thesis Committee for Michael Ducey, Chemistry Department, University of Michigan.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Evaluation of assays for Troponin T and Troponin I as early markers for myocardial injury.
B. Development of an HPLC assay for iohexol and validation of plasma iohexol clearance as an indicator of glomerular filtration rate.
C. Evaluation of portable instruments for the measurement of prothrombin time in alternate laboratory testing sites.
D. Evaluation of the accuracy and precision of the Ektachem 950IRC chemistry analyzer.
E. Evaluation of immuno-rate methods for the determination of digoxin and phenytoin on an automated chemistry system.
F. Evaluation of methods for the direct measurement of LDL-cholesterol.

G. Evaluation of interference in serum chemistry analyses following administration of the experimental hemoglobin based oxygen carrier HBOC-201.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Quality Assurance Committee.
B. Director, Chemistry Laboratory.
C. Director, Point of Care Testing Services.
D. Coordinator, Chemistry Section Continuing Education Program.

MEDICAL SCHOOL/HOSPITAL:

A. Glucose Monitoring/Bedside Testing Work Group.
B. East Medical Campus Laboratory Services Program Planning Group.

REGIONAL AND NATIONAL:

A. Executive Committee, Michigan Section, AACC.
B. Lipids and Lipoprotein Division Member, AACC.
C. Pediatric Clinical Chemistry Division Member, AACC .
D. Consultant, Parke-Davis.
E. Consultant, Selective Technologies Inc., Ann Arbor, MI.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Evaluation of Precision and Accuracy of the "Ektachem 950IRC Automated Chemistry Analyzer." Johnson and Johnson Clinical Diagnostics, Rochester, New York, April, 1995.
2. "Point of Care Testing: Beyond Glucose." Michigan Section AACC Spring Meeting. Ypsilanti, Michigan, May, 1995.
3. "Point of Care Testing." Workshop presented at Clinical Ligand Assay Society National Meeting, Toronto, May, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. O'Connell, T.D., Giacherio, D.A., Jarvis, A.K. and Simpson, R.U.: Inhibition of cardiac myocyte maturation by 1,25 dihydroxyvitamin D_3. Endocrinology. 136:482-488, 1995.
2. Annesely, T.A., Hunter, B.C. and Giacherio, D.A.: Stability of Tacrolimus (FK506) and Cyclosporin G in whole blood. Therapeutic Drug Monitoring, Accepted for publication.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Bleske, B.E., Rice, T.L., Warren, E.W., Giacherio, D.A., Gilligan, L.J., Massey, K.D. and Tait, A.R.: Effect of vehicle on the nasal absorption of epinephrine during cardiopulmonary resuscitation. American Journal of Emergency Medicine.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Occasional coverage of nephropathology service for Drs. K. Johnson and P. Killen.
B. Autopsy service, attending pathologist, 4/3-4/6/95.

II. TEACHING ACTIVITIES:

A. Renal and Urinary Tract Sequence for M-2 students, 18 hours, Fall Term 1994.
B. Pathology Lab Section for M-1 students, ten contact hours, Winter term 1995.

III. RESEARCH ACTIVITIES:

None.

PROJECTS UNDER STUDY:

None.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Assistant Dean for Medical School Admissions.

REGIONAL AND NATIONAL:

A. National Collegiate Athletic Association (NCAA) Drug Testing Appeals Committee.
B. NCAA Drug Testing Crew Chief.
C. NCAA Committee on Competitive Safeguards and Medical Aspects of Sports.
D. Chairman, Board of Directors, Public Citizen, Inc. (Ralph Nader, Initial Chairman and Founder).

V. OTHER RELEVANT ACTIVITIES:

Retirement Furlough. 1/1/94-12/31/94.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

None.

THOMAS J. GIORDANO, M.D., Ph.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 AUGUST 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. General Surgical Pathology - four months.
B. Endocrine Surgical Pathology, Departmental and Outside Consultation Services - 12 months.
C. Genitourinary Surgical Pathology - backup during Dr. Wojno absence.
D. M-Labs Surgical Pathology Consultation - 12 months.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students:
   1. Component II Endocrine Sequence - two lectures on Endocrine Pathology.
   2. Endocrine Pathology Laboratories - preparation of course materials.
B. House Officers:
   1. General Surgical Pathology - four months.
   2. Endocrine Surgical Pathology - 12 months as needed.
   3. Consultation Conferences - four.
C. Interdepartmental:
   1. Endocrine Conference, Department of Surgery - monthly.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, University of Michigan Comprehensive Cancer Center, John and Suzanne Munn Endowment ($10,000) "Differential Gene Expression in Adrenal Cortical Neoplasms."
B. Principal Investigator, University of Michigan Schembechler Adrenal Cancer Fund ($20,000) "Differential Gene Expression in Adrenal Cortical Neoplasms."

PROJECTS UNDER STUDY:

A. Principal Investigator, "Differential Gene Expression in Adrenal Cortical Neoplasms."
B. Principal Investigator, "p53 Mutational Analysis of Adrenal Cortical Neoplasms."
C. Principal Investigator, "Thyroglobulin Expression in Anaplastic Thyroid Carcinoma."

D. Co-Investigator, "Comparative DNA Analysis of Adrenal Cortical Neoplasms," with Dr. Samir Hanash, Department of Pediatrics.
E. Co-Investigator, "Cytogenetics of Adrenal Cortical Carcinoma," with Dr. Thomas Glover, Department of Human Genetics.
F. Co-Investigator, "Pathology of Multiple Endocrine Neoplasia, Type 1," with Dr. Norman Thompson, Department of Surgery.
G. Co-Investigator, "Histologic-Radiologic Correlation of Adrenal Cortical Adenomas," with Dr. Melvin Korobkin, Department of Radiology.
H. Co-Investigator, "Clinicopathologic Correlation of 131-I Therapy of Papillary Thyroid Carcinoma," with Dr. James Sisson, Department of Internal Medicine.
I. Co-Investigator, "Histologic-Radiologic Correlation of Pulmonary Metastases of Papillary Thyroid Carcinoma," with Dr. James Sisson, Department of Internal Medicine.
J. Co-Investigator, "Pitfalls in the Surgical Treatment of Sporadic Insulinoma," with Dr. Norman Thompson, Department of Surgery.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. House Officer Candidate Interviews.

REGIONAL AND NATIONAL:

A. College of American Pathologists, Molecular Pathology Committee (term expired 12/94).

V. OTHER RELEVANT ACTIVITIES:

A. Consultant, U.S. Surgical Corporation.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

1. Giordano, TJ, Alexander, RB, Rosenberg, SA, and Marino, MJ. Histopathologic findings in patients with renal cell carcinoma treated with interleukin-2 and alpha-interferon immunotherapy. (Submitted to International Journal of Surgical Pathology).

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

1. Korobkin, MT, Giordano, TJ, Brodeur, FJ, Frances, IR, Quint, LE, and Dunick, NR.: The relationship between histologic lip?? and CT-MR findings in surgically resected adrenal adenomas. (Submitted to the 81st Scientific Assembly and Annual Meeting of the Radiologic Society of North America).

2. Few, J, Thompson, NW, Simeone, D, and Giordano, T.: Riedel's thyroiditis; treatment with tamoxifen. (Submitted to the Western Surgical Association).

JOEL K. GREENSON, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. General surgical pathology - four and one-half months.
B. Gastrointestinal and hepatic pathology consultation services - six months.
C. Liver transplant pathology - six months.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students:
   1. Pathology 600 - Laboratory Instructor (25 contact hours).
   2. GI Pathology Sequence, assisted Dr. Appelman (10 contact hours).
   3. Preceptor for M-4 rotation (20 contact hours).

B. Dental Students:
   1. Pathology 630-631 one full class lecture (1 contact hour).

C. House Officers:
   1. Surgical pathology diagnosing room instruction for house officers - four and one-half months.
   2. Two didactic lectures on gastrointestinal pathology - May, 1993.
   3. Gastrointestinal and hepatic pathology tutoring - six months.
   4. Four consultation conferences.

D. Interdepartmental:
   1. Liver biopsy conference - one hour per month.
   2. Multidisciplinary GI tumor board - every other week.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A.. Co-investigator R01CA66560-01 ($5,180,000) "Staging Breast Cancer with Positron Emission Tomography", 5% salary support, Richard L.Wahl, M.D. Principle investigator.

PROJECTS UNDER STUDY:

A. Focal active colitis study with Rob Stern and Jeff Barnett from the Division of Gastroenterology.
B. Pancreatic carcinoma study with Margaret Anderson and Henry Appelman.
C. Study of growth kinetics of hyperplastic polyps with Rob Stern and Andrew Flint.
D. Study of recurrent hepatitis C in liver transplant biopsies with Tom Frank, and Bob Merion from the Division of Transplantation Surgery.
E. Study of mini-microabscess disease in liver transplant patients with Henry Appelman, Tom Frank, and Grahame Macdonald, Division of Gastroenterology
F. Study of molecular genetic alterations in hepatocellular carcinomas with Henry Appelman, Richard Boland, and Grahame Macdonald, Division of Gastroenterology.
G. Study of MALT lymphomas arising in Helicobacter pylori gastritis with Eric Hsi and Charlie Ross.
H. Study of LOH of the DCC gene in Dukes B colon cancers with Richard Boland and John Carruthers, Division of Gastroenterology.
I. Study of colorectal carcinoma metastases with collaborators at Ohio State University.
J. Study of ishemic colitis with Caroline Reilly.
K. Study of small bowel stromal tumors with Joseph Tworek and Henry Appelman.
L. Study of cytokines in experimental colitis model with Dan Remick.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Surgical pathology fellowship program
B. Co-Coordinator, Surgical Pathology Staff Service Rotations.

REGIONAL AND NATIONAL:

A. Reviewer, Cancer.
B. Reviewer, Archives of Pathology and Laboratory Medicine.
C. Reviewer, Gastroenterology.
D. Reviewer, Digestive Diseases and Sciences.
E. Reviewer, American Journal of Pathology.
F. Reviewer, Liver Transplantation and Surgery.
G. Member, Training Programs Committee, Gastrointestinal Pathology Society.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Speaker, Medical Grand Rounds, "An Update on GI Pathology", Marion General Hospital, Marion, Ohio, August, 1994.

2. Visiting Professor, "GI Pathology", University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, October, 1994
3. Invited Speaker, "An Overview of Gastritis, Colitis, and Hepatitis", Oklahoma State Association of Pathologists, Oklahoma City, Oklahoma, October, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Brainard, J.A., Greenson, J.K., Vesy, C.J., Tesi, R.J., Papp, A.C., Snyder, P.J., Western, L. and Prior, T.W.: Detection of cytomegalovirus in liver transplant biopsies: A comparison of light microscopy, immunohistochemistry, duplex PCR, and nested PCR. Transplantation 57:1753-1757, 1994.
2. Marmaduke, D., Greenson, J.K., Cunningham, I., Herderick, E. and Cornhill F: Superficial antral vascular ectasia in bone marrow transplant patients. Am. J. Clin. Pathol 102:194-198, 1994.
3. Shanley, C.J., Braun, D.K., Brown, K., Turcotte, J.G., Greenson, J.K., Beals, T.F., Tiballi, R.N. and Campbell, D.A.: Fulminant hepatic failure secondary to Herpes Simplex virus hepatitis: Successful outcome following orthotopic liver transplantation. Transplantation 59:145-149, 1995.
4. Schneebaum, S., Arnold, M.W., Rohrscheib, S., Houchens, D., Greenson, J.K., Young, D., et al: The importance of intraoperative periportal lymph node metastasis identification. Cancer 75:2809-2817, 1995.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Cote, R.J., Houchens, D.P., Saad, A.D, Nines, R.G., Sampsel, J.W., Greenson, J.K., et al: Intraoperative Detection of Occult Colon Cancer Micrometastases Using ^{125}I-Radiolabeled Monoclonal Antibody CC49. (Submitted to Cancer)
2. Hsi, E.D., Greenson, J.K., Singleton, T.P., Siddiqui, J., Schnitzer, B. and Ross, C.W.: Detection of immunoglobulin heavy chain rearrangement by polymerase chain reaction in chronic active gastritis associated with helicobacter pylori. Submitted to Human Pathology.
3. Greenson, J.K., Svoboda, S.M,, Merion, R.M. and Frank TS.: The histologic progression of recurrent hepatitis C in liver transplant allografts, Submitted to Am J Surg Pathol.

BOOK/CHAPTERS IN BOOKS:

1. Greenson, J.K.: Pathology of the Colon, Rectum and Anus, in, Boland, C.R. (ed), Gastroenterology Image Collection, Ed:, Current Medicine, Philadelphia, Pennsylvania, In Press.

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

1. Hsi, E.D., Greenson, J.K., Singleton, T.P., Siddiqui, J., Schnitzer, B. and Ross, C.W.: Detection of immunoglobulin gene rearrangement by polymerase chain reaction in chronic active gastritis

associated with helicobacter pylori. Stowell-Orbison Award Winner & GI Pathology Award Winner, Poster Presentation at USCAP Meeting, 1995. Mod. Pathol. 8:113A, 1995.

2. Greenson, J.K., Svoboda, S.M., Frank, T.S. and Merion, R.M.: Histologic progression of recurrent hepatitis C in liver transplant patients: Correlation with PCR detection of HCV RNA and HLA-DQB Status. Platform Presentation at USCAP Meeting, 1995. Mod. Pathol. 8:130A, 1995.
3. Stern, R.A., Greenson, J.K. and Flint, A.: Evaluation of cell kinetics in hyperplastic polyps using MIB-1 and image analysis and BCL-2. Poster Presentation at USCAP Meeting, 1995. Mod. Pathol. 8:69A, 1995.
4. Stern, R.A., Carpenter, S.L., Barnett, J.L. and Greenson, J.K.: The clinical significance of focal active colitis. Poster at the AGA Digestive Disease Week, 1995. astroenterol. 108:A922, 1995.
5. MacDonald, G.A., Greenson, J.K., Appelman, H.D. and Boland, C.R.: Genomic defects in hepatocellular carcinoma: The role of DNA mismatch repair genes. Poster at the AGA Digestive Disease Week, 1995. Gastroenterol. 108:A500, 1995.
6. MacDonald, G.A., Greenson, J.K., DelBuono, E.A., Grady, W., Frank, T.F., Lucey, M.R. and Appelman, H.D.: "Mini"-microabscess disease in liver transplant recipients. Poster at the AGA Digestive Disease Week, 1995. Gastroentero. l 108:A1114, 1995.
7. Greenson ,J.K.: (Book review). Pulmonary Pathology. Am. J. Surg. Pathol. 19:735, 1995.
8. Greenson, J.K.: (Book review). Liver Biopsy Interpretation, In Press, Am. J. Surg. Pathol.
9. Macdonald, G.A., Greenson, J.K., Saito, K., Appelman, H.D. and Boland, C.R.: Loss of the DNA mismatch repair genes hMSH2 and/or hMLH1 is an early event in hepatic carcinogenesis. Submitted to AASLD Meeting, November, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Dermatopathology, private consultations.
B. Dermatopathology, M-Labs.
C. Dermatopathology, UMH.
D. Dermatopathology, tutorials.
E. Autopsy call.

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. Pigmented Neurocristic Hamartomas.
B. Hair loss in utero.
C. Atlas: The Histology of Alopecia.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Consultant, Pigmented Lesion Clinic.

MEDICAL SCHOOL/HOSPITAL:

A. Director, Dermatopathology Unit.

REGIONAL AND NATIONAL:

A. Board of Directors, National Alopecia Areata Foundation.

INVITED LECTURES AND SEMINARS:

1. Herbert Z Lund Lecture. The Scarring Alopecias, Duke University. Durham, North Carolina, September, 1994.

2. A Tutorial in the Microscopic Diagnosis of Alopecia. American Society of Dermatopathology, New Orleans, Louisiana, February, 1995.
3. Adnexal Tumors. Houston Society of Clinical Pathologists, Houston, Texas, April, 1995.
4. Dermal Dendrocytes. Visiting Professor. Indianapolis, Indiana, April, 1995.
5. Cutaneous Vasculitis. The University of Texas Medical Branch at Galveston, Texas, April, 1995.

V. PUBLICATIONS:

1. Burnstein, M.A., Headington, J.T., Reifler, D.M., Oestreicher, J.T. and Elner, V.M.: Periocular granuloma annulare, nodular type. occurrence in late middle age. Arch Ophthalmol. 112:1590-3, 1994.
2 Kanzler, M.H., Dhillon, I. and Headington, J.T.: Fibroblastic rheumatism. Arch Dermatol. 131:710-712, 1995.
3 Pearson, J.P., Weiss, S.W. and Headington, J.T.: Cutaneous malignant melanotic neurocristic tumors arising in neurocristic hamartomas. Am. J. Surg. Pathol., In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. M2: Pathology 600, two hours with class as part of Congenital Heart Sequence of new curriculum.
B. M4: Pathology clerkship mentor, five students.
C. House Officers in Pathology, six weeks in surgical reading rooms.
D. House Officers in Pathology, gross and microscopic supervision of most pediatric necropsies, twelve months, and adult cases, ten weeks plus on-call weekends.
E. Lecture on Pediatric Necropsy Pathology in Orientation for new House Officers in Pathology.
F. Gross Necropsy Conference, one hour/week, twelve months.
G. Supervised Pediatric Hematology Fellows (one) for AP elective period.
H. Conferences: Faculty, house staff and students:
    1. Pediatric Cardiology Death Conference, monthly, twelve months.
    2. Pediatric Tumor Conference, twice monthly, twelve months.
    3. Pediatrics CPC/General Death Conference, quarterly.
    4. Pediatric Liver-GI Conference, twice monthly, twelve months.
    5. Pediatric General Surgery Conference monthly, twelve months.

III. RESEARCH ACTIVITIES:

A. Continued study of effects of various congenital heart defects on the pulmonary vasculature.
B. Ongoing study with pediatric cardiologists and thoracic surgeons of effects of various stents and therapeutic manipulations on different stenotic vessels.
C. Histopathological component of lung changes associated with various cardiopulmonary therapeutic support mechanisms.

PROJECTS UNDER STUDY:

A. Review of the predictive value of pre-ECMO lung biopsy in determining survival and recovery of pulmonary function (Group study, pathologists, surgeons, pediatricians).

B. Continuing correlation of histopathologic classification of neuroblastoma cell/tumor maturity with different tissue gene expressions.
C. Study of myocardial ventricular fibrosis in various congenital heart defects, with pediatric cardiologists. (Manuscript submitted).
D. Review of predictive value of heart biopsies for death in pediatric transplant patients.

ONGOING RESEARCH:

A. Co-investigator, with Robert Bartlett, Principal Investigator (NIH); study to further develop and research life support systems (Extra Corporeal Life Support Systems).
B. Co-investigator, with Ramiero Hernandez, Principal Investigator (Radiological Diagnostic Oncology Group), Correlative study of pediatric solid tumors - pathology and radiologic imaging.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Executive Committee for Mott/Women's/Holden/Psychiatric Hospitals.
B. Interviewing Pediatric Cardiology fellowship candidates.
C. University of Michigan, Office of the Provost and Executive Vice President for Academic Affairs: Appointed Senior Faculty Panelist - Career Development Fund for Women Faculty.

REGIONAL AND NATIONAL:

A. Member, CAP Council on Anatomic Pathology's Autopsy Committee. (Completed 12/31/94).
B. Appointed member, Nominating Committee, Society for Pediatric Pathology.
C. Member, Abstract Review Board, US and Canadian Academy of Pathology.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. deMello, D.E., Nogee, L.M.., Heyman, S., Krous, H.F., Hussain, M., Merrit, T.A., Hsueh, W., Haas, J.E., Heidelberger, K.P., Schmacher, R. and Colten, H.R.: Molecular and phenotypic variability in the congenital alveolar proteinosis syndrome associated with inherited surfactant protein B deficiency. J. Pediatr. 125:43-50, 1994.
2. Hutchins, G.M.. and The Autopsy Committee of the College of American Pathologists: (Kathleen P. Heidelberger, Member): Practice guidelines for autopsy pathology: Autopsy performance. Arch. Pathol. Lab. Med. 118:19-25, 1994.
3. Hanzlick, R. and The Autopsy Committee of the College of American Pathologists, (Kathleen P. Heidelberger, Member): Cause of death statements. Guidelines for Pathologists., College of American Pathologists, Northfield, Illinois, 1994.

4 Hanzlick, R. and The Autopsy Committee of the College of American Pathologists, (Kathleen P. Heidelberger, Member): The Medical Cause of Death Manual: Instructions for Writing Cause of Death Statements for Deaths Due to Natural Causes. College of American Pathologists, Northfield, Illinois, Fall, 1994.

5. Hutchins, G.M. and The Autopsy Committee of the College of American Pathologists (Kathleen P. Heidelberger, Member): An Introduction to Autopsy Technique., College of American Pathologists, Northfield, Illinois, Fall, 1994.

6. Elhalaby, E.A., Teitelbaum, D.H., Coran, A.G. and Heidelberger, K.P. Entercolitis associated with Hirschsprung's disease: A clinical histopathological correlative study. J. Ped. Surg., Accepted for publication.

7. Barr, M., Jr, Heidelberger, K.P. and Comstock, C.H.: Craniomicromelic Syndrome: A newly recognized lethal condition with craniosynostosis, distinct facial anomalies, short limbs and intrauterine growth retardation. Am. J. Med Genetics, Accepted for publication.

8. Schwartz, S.M., Gordon, D., Mosca, R.S., Bove, E.L., Heidelberger, K.P. and Kulik, T.J.: Collagen content in normal, pressure, and pressure-volume overloaded developing human hearts. Am. J. Cardiol. Submitted, Amer. J. Cardiol.

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

1. Heidelberger, K.P. and Henricks, W.: Case #AU-A-01-1995, The College of American Pathologists'. Autopsy Pathology Apex Program, Winter, 1995.

2. Heidelberger, K.P. and Barr, M.: Case #AU-B-X-1995, The College of American Pathologists' Autopsy Pathology Apex Program, Fall, 1995 (Accepted).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994- 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. With C. J. D'Amato, examine, describe, prepare gross and microscopic reports of many of the brains sent to the Department for consultation as well as some brains from autopsies in the Department. Many of the brains are from patients with various forms of dementia and nervous system diseases and some are from cases of developmental disorder.

II. TEACHING ACTIVITIES:

A. Occasional review of autopsy cases with residents.

III. RESEARCH ACTIVITIES:

A. Dr. Hicks received the Meritorious Contributions to Neuropathology Award from the American Association of Neuropathologists in 1994, the intent of the award being to express "their admiration and gratitude for his excellent contributions to our discipline, some of which are truly classics in the field."

IV. PUBLICATIONS:

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Immunopathological evaluation of skin and renal biopsies.
B. Director, Morphology Core.
C. Renal pathology.
D. Autopsy coverage.

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Oxidants and Protease Interaction in Acute Lung Injury", National Institutes of Health, $834,625/five years.
B. Principal Investigator, "Oxidants and Glomerular Injury", Project V, Renal Center Grant. National Institutes of Health, $246,585/five years.
C. Principal Investigator, "Mechanisms of Glomerular and Tubular Injury", Core B, Renal Center Grant. National Institutes of Health, $147,795.
D. Principal Investigator, "Inflammatory Cells and Lung Injury", Core C, National Institutes of Health, $291,025.
E. Co-Investigator, "DNA Methylation and SLE", with Bruce Richardson, Rheumatology, National Institutes of Health.

PENDING SUPPORT:

A. Co-Investigator, "Aging, Anesthesia and Influenza Infection", with Paul Knight, Anesthesiology, and Dan Remick, Pathology, National Institutes of Health.
B. Co-Investigator, "Amino Acids and Cell Injury", with Joel Weinberg, Nephrology, and James Varani, Pathology, National Institutes of Health.

PROJECTS UNDER STUDY:

A. Pathogenesis of IgG and IgA immune complex lung injury.
   1. Role of oxygen radicals.
   2. Role of proteases.
   3. Role of terminal components of the complement system.
B. Oxidant and protease interaction in inflammation.
C. Pathogenesis of aspiration pneumonitis.
D. Pathogenesis of viral pneumonitis.
E. Pathogenesis of pancreatitis and pancreatitis induced ARDS.
F. Adhesion molecules and cytokines in inflammation.
G. Cyclosporin-induced nephrotoxicity.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Immunopathology Fellowship Program.
B. Renal Pathology Conference - Biweekly.
C. Space Utilization Committee.
D. Stobbe Funds 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.
D. NIH NHLBI Study Section.

V. INVITED LECTURES AND SEMINARS:

1. Visiting Professor, SUNY Buffalo, NY, Department of Anesthesiology.
2. Invited Speaker - "Mechanisms of Glomerulonephritis", Genentech, South San Francisco, California, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Colletti, L.M., Johnson, K. J., Kunkel, R.G. and Merion, R.M.: Mechanisms of hyperacute rejection in porcine liver transplantation. Transplantation 57:1357-1363, 1994.
2. Gilardy, A., Dysko, R.C., Spilman, S.C., Kunkel, R.G., Brammer, D.W. and Johnson, K.J.: Immune complex vasculitis with secondary ulcerative dermatitis in aged C57BL/6NNia mice. Vet. Pathol. 31:292-300, 1994.

3. Young, E.W., Ellis, C.N., Messana, J., Johnson, K.J., Leichtman, A.B., Mikatsch, M.J., Hamilton, T.A., Groisser, D.S., Fradin, M.S. and Voorhees, J.J.: A prospective study of renal structure and function in psoriasis patients treated with cyclosporin. Kid. Int. 46:1216-1222, 1994.
4. Varani, J., Burmeister, B., Sitrin, R.G., Shallenberger, S.B., Gibbs, D.F. and Johnson, K.J.: Expression of serine and metalloproteinases in organ cultured human skin: altered levels in the presence of retinoic acid loss of epidermal cohesion. Amer. J. Pathol. 145:561-573, 1994.
5. Foreman, K.E., Vaporciyan, A.A., Bonish, B., Jones, M.L., Johnson, K.J., Glovsky, M.M. and Ward, P.A.: C5a receptor-induced expression of P-selectin in endothelial cells. J. Clin. Invest. 94:1147-1155, 1994.
6. Richardson, B.C., Lalwani, N.D., Johnson, K.J. and Mark, R.M.: FAS ligation triggers apoptosis in macrophages but not endothelial cells. E. J. Immuno. 24:2640-2645, 1994.
7. Hirschl, R.B., Overbeck, M.C., Parent, A., Hernandez, R., Schwartz, S., Dosanth, A., Johnson, K.J. and Bartlett, R.H.: Liquid ventilation provides uniform distribution of perfluorocarbon in the setting of respiratory failure. Surgery 116:159-168, 1994.
8. Colton, D.M., Hirschl, R.B., Johnson, K.J., Till, G.O., Deen, S.B. and Bartlett, R.H.: Neutrophil infiltration is reduced during partial perfluorocarbon liquid ventilation in the setting of lung injury. Surg. Forum 1055:668-670, 1994.
9. Varani, J., Burmeister, B., Sitrin, R.S., Schallenberger, S., Gibbs, D.F. and Johnson, K.J.: Serine and metalloproteinases in human skin: relation to loss of epidermal cohesion in retinoic acid-treated organ-cultured skin. J. Cell Biochem. 18B:148, 1994.
10. Foreman, K.E., Vaporciyan, A.A., Bonish, B., Jones, M.L., Johnson, K.J., Glovsky, M.M. and Ward, P.A.: C5a receptor-induced expression of P-selectin in endothelial cells. J. Clin. Invest. 94:1147-115, 1994.
11. Young, E.W., Ellis, C.N., Messana, J., Johnson, K.J., Leichtman, A.B., Mihatsch, M.J., Hamilton, T.A., Groisser, D.S., Fradin, M.S. and Voorhees, J.J.: A prospective study of renal structure and function in psoriasis patients treated with cyclosporin. Kid. Intl. 46:1216-1222, 1994.
12. Hirschl, R.B., Parent, A., Tooley, R., McCrachen, M., Johnson, K.J., Schaffer, T.H., Walfson, M.R. and Bartlett, R.H.: Liquid ventilation improves pulmonary function, gas exchange and lung injury in a model of respiratory failure. Annal. Surg. 221:79-88, 1995.
13. Messana, J.M., Johnson, K.J. and Mihatsch, M.J.: Renal structure and function effects after low dose cyclosporin in psoriasis patients: a preliminary report. Clin. Nephrol. 43:150-153, 1995.
14. Varani, J., Perone, P., Inman, D., Burmeister, W. Schallenberger, S., Fligiel, S.E.G., Sitrin, R.G. and Johnson, K.J.: Elaboration of proteolytic enzymes in the presence of factors which do not promote invasion. Am.J. Pathol. 146:210-217, 1995.
15. Yung, R.L., Quddus, J., Chrisp, C., Johnson, K.J. and Richardson, B.C.: Mechanisms of drug induced lupus ± cloned TH2 cells modified with DNA methylation inhibitors *in vitro* cause autoimmunity *in vivo.* J. Immunol. 154:3025-3035, 1995.
16. Shayevitz, J.R., Rodriguez, J.L., Gilligan, L., Johnson, K.J. and Tait, A.R.: Volatile anesthetic modulation of lung injury and outcome in a murine model of multiple organ dysfunction syndrome. Shock 4:61-67, 1995.
17. Varani, J. Burmeister, W., Perone, P., Bleavins, M. and Johnson, K.J.: Retinoic acid interferes with movements of Ca2+ across the plasma membrane of human dermal fibroblasts. FASEB J. 9:581, 1995.

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. Ginsburg, I., Schuger, L., Gibbs, F., Johnson, K.J., Ryan, U.S., Ward, P.A. and Varani, J.: Endothelial cell killing by polymorphonuclear leukocytes: independent and synergistic roles for oxygen radicals and proteases. Submitted for publication to Am. J. Pathol.
3. Varani, J., Jones, J., Gibbs, D.F., Sulavik, C., Dame, M. and Johnson, K.J.: In vitro and in vivo modulation of the acute inflammatory response by all-trans retinoid acid. Submitted for publication.
4. Johnson, K.J., Dixit, V.M. and Varani, J.: Role of thrombospondin in the acute inflammatory response. Submitted for publication.
5. Messana, J.M., Johnson, K.J., Leichtman, A.B., Ellis, C.N., Mihatsch, M.J., Hamilton, F.A., Groisser, D.S., Gartside, M.S. and Voorhees, J.J.: A prospective study of the effects of low dose cyclosporin in renal structure and function in psoriasis patients. Submitted for publication.
6. Kershaw, D.B., Bunchman, T.E, Johnson, K.J., Sedman, A.B. and Kelsch, R.C.: Crescentic glomerulonephritis with subsequent hemolytic uremic syndrome in a child. Submitted for publication.
7. Lowe, N.J., Weider, J.M., Rosenbach, A., Kunkel, R.G., Johnson, K.J., Simpson, K., Glass, F. and Grabie, M.T.: Chronic cyclosporin for severe psoriasis: effects on renal function and structure. Submitted for publication.
8. Hirschl, R.B., Overbeck, M.C., Parent, A., Hernandez, R., Schwartz, S.S., Dosanjh, A., Johnson, K.J. and Bartlett, R.H.: Perfluorocarbon liquid ventilation provides uniform distribution of ventilation in the setting of respiratory failure. Submitted for publication.
9. Hirschl, R.B., Tooley, R., Parent, A., Johnson, K.J. and Bartlett, R.H.: Evaluation of gas exchange, pulmonary function and lung injury during total and partial liquid ventilation in the setting of severe respiratory failure. Submitted for publication.
10. Mulligan, M.S., Shanley, T.P., Jones, M.L., Johnson, K.J., Bonish, B.K. and Ward, P.A.: Cytokine and adhesion molecule requirements in lung injury induced by anti-glomerular molecule requirements in lung injury induced by anti-glomerular basement membrane antibody. Submitted for publication.
11. Lebedovych, L.M., Johnson, K.J., McMorris, M.S., Gilardy, A.K., Hirschl, R.B., Ward, P.A. and Baker, J.R.: Characteristics of the late allergic responses in rats previously sensitized with monoclonal IgE antibodies. Submitted for publication.
12. Gregory, M.J., Smoyer, W.E., Kershaw, D.B., Valenti, R.P., Johnson, K.J., Sedman, A. and Bunchman, T.E.: Long term cyclosporin therapy for pediatric nephrotic syndrome: a clinical and histologic analysis. Submitted for publication.
13. Shayvitz, J.R., Rodriguez, J.L., Gilligan, L., Johnson, K.J. and Tait, A.R.: Volatile anesthetic modulation of lung injury and outcome in a murine model of multiple organ dysfunction syndrome. Submitted for publication.
14. Varani, J., Hirschl, R., Dame, M. and Johnson, K.J.: Neutrophil infiltration is reduced during liquid ventilation: II. In Vitro analysis. Submitted for publication to Am. J. Respir. & Crit. care Med.

15. Yung, R.L., Johnson, K.J. and Richardson, B.C.: New concepts in the pathogenesis of drug-induced lupus. Submitted for publication to Lab. Invest.
16. Colton, D.M., Hirschl, R.B. Till, G.O., Johnson, K.J, Dean, S.B., Patel, S. and Bartlett, R.H.: Neutrophil infiltration is reduced during liquid ventilation: 1. In vivo analysis. Submitted for publication to Amer. J. Respir. & Crit. Care Med.
17. Hirschl, R.B., Tooley, R., Parent, A., Johnson, K.J. and Bartlett, R.H.: Evaluation of gas exchange, pulmonary compliance, and lung injury during total and partial liquid ventilation in the acute respiratory distress syndrome. Submitted for publication to J. Crit. Care Med.
18. Colton, D.M., Hirschl, R.B., Till, G.O., Johnson, K.J, Ichiba, S. and Bartlett, R.H.: Liquid ventilation decreases pulmonary hemorrhage and vascular permeability. Submitted for publication.
19. Annis, K., Sigler, C. Johnson, K.J., Berman, S., Haber, H, Bonalsky, J., Luscombe, F. and Van de Carr, S.: Predictors of angioedema associated with angiotensin converting enzyme inhibitor. Submitted for publication.

BOOKS AND CHAPTERS IN BOOKS

1. Warren, J.S., Johnson, K.J. and Ward, P.A.: Phagocytes and reactive oxygen substances as mediators of acute lung injury, in, Hyers, T. (ed), Diffuse Alveolar Damage and Respiratory Failure, Futura Press, New York, In Press.
2. Till, G.O., Johnson, K.J. and Ward, P.A.: Oxygen free radicals in inflammation, in, Messmer, K. and Hammersen, F. (eds), Prog. Appl. Microcirc., Volume 9, Karger, Basel, In Press.
3. Ward, P.A., Johnson, K.J. and Till, G.O.: Leukocyte oxygen radicals and acute lung injury, in, Proceedings of a Symposium on "Acute Lung Injury", PSG Publishing Co., Littleton, Massachusetts, In Press.
4. Warren, J.S., Ward, P.A. and Johnson, K.J.: Oxygen radicals as "mediators of inflammation", Volume 6, in, Henson, P.M. (ed), The Handbook of Inflammation, Volume 6, Elsevier Biomedical Division, Amsterdam, The Netherlands, In Press.
5. Warren, J.S., Ward, P.A. and Johnson, K.J.: The respiratory burst and mechanisms of oxygen radical mediated tissue injury, in, Sbarra, A.J. and Strauss, R.P. (eds), The Respiratory Burst and its Physiological Significance in Medicine, Plenum Press, New York, New York, In Press.
6. Warren, J.S., Johnson, K.J. and Ward, P.A.: Consequences of oxidant injury, in, Crystal R.G. and West, T.B. (eds), The Lung: Scientific Foundations, In Press.
7. Ward, P.A., Warren, J.S., Johnson, K.J. and Varani, J.: Cytokines and oxygen radical responses, in, Maier, R. (ed), Proceedings of the International Congress on the Immune Consequences of Trauma, Shock and Sepsis: Mechanisms and Therapeutic Approaches, In Press.
8. Ward, P.A., Warren, J.S., Till, G.O., Varani, J. and Johnson, K.J.: Free radicals in lung disease, in, Rice-Evans, C. (ed), Free Radicals, Diseased States and Anti-Radical Interventions, Proceedings of the Special Colloquium, London, England, In Press.
9. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: PAF, cytokines toxic oxygen products and cell injury, in, Molecular Aspects of Medicine, Proceedings of the VIIth Annual Inflammation Meeting, Birmingham, U.K., Pergammon Press, In Press.
10. Ward, P.A., Warren, J.S. and Johnson, K.J.: Oxygen radicals, inflammation and tissue injury, in, Pryor, W. and Godber, S.L. (eds), Free Radical Biology and Medicine, In Press.

11. Warren, J.S., Ward, P.A., and Johnson, K.J.: Oxygen radicals as "mediators of inflammation", in, Volume 6, Henson, P. (ed), The Handbook of Inflammation, Elsevier Biomedical Division, Amsterdam, The Netherlands, In Press.
12. Ward, P.A., Warren, J.S., Johnson, K.J. and Varani, J.: Inflammation, oxygen radicals and tissue injury, in, Oxidative Damage and Repair: Clinical, Biological and Medical Aspects, In Press.
13. 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, Second Edition, J.B. Lippincott Inc., New York, New York, In Press.
14. Varani, J. and Johnson, K.J.: Modulation of endothelial cell injury by all-trans retinoic acid: Role of the anti-inflammatory effects of RA, in, Jesaitis, A. (ed), Molecular basis of oxidative damage by leukocytes. CRC Press, In Press.
15. Johnson, K.J., Varani, J. and Smolen, J.E.: Neutrophil activation and function in health and disease, in, Coffey, R.G. (ed), Granulocyte Responses to Cytokines: Basic and Clinical Research, Marcel Dekker, Inc., New York, In Press.

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

1. Davidson, B.A., Jones, M.L., Helinski, J.D., Johnson, K.J. and Knight, P.R.: Evidence of PMN Chemokine activity in BAL following gastric aspiration. ASA, 1994.
2. Jones, M.L., Davidson, B.A., Shanley, T.P., Johnson, K.J. and Knight, P.R.: Transcriptional and molecular upregulation of tumor necrosis factor-alpha following gastric aspiration. ASA, 1994.
3. Lalwani, N.D., Richardson, B. and Johnson, K.J.: Induction of FAS does not mediate apoptosis in human endothelial cells. AFCR, 1994.
4. Colton, D.M., Hirschl, R.B., Johnson, K.J., Till, G.O., Dean, S. and Bartlett, R.H.: Neutrophil infiltration is reduced during partial perfluorocarbon liquid ventilation in the setting of lung injury. Amer. Coll. Surg., 1994.
5. Colton, D.M., Hirschl, R.B., Till, G.O., Johnson, K.J., Wilkins, A., Compton, C. and Bartlett, R.H.: Partial liquid ventilation (PLV) decreases neutrophil infiltration prior to and after the induction of respiratory failure. Surg. Forum, 1994.
6. Leggat, J.E. Jr., Leichtman, A.B., Kolars, J.C., Schmiedlin-Ren, P., Watkins, P.B. and Johnson, K.J.: Evidence against a central role for P450 3A in cyclosporin induced nephrotoxicity. Amer. Soc. of Transplant Physicians 13:91, 1994.
7. Richardson, B.C., Lalwani, N.D., Johnson, K.J. and Marks, R.M.: Ligation of FAS is sufficient to trigger apoptosis in macrophages but not in cultured human endothelial cells. AFCR, 1994.
8. Leggat, J.E. Jr., Leichtman, A.B., Kolars, J.C., Schmiedlin-Ren, P., Watkins, P.B. and Johnson, K.J.: Cytochrome P450 3A is expressed by renal tubular cells but not by renal vasculature: evidence against a central role for P450 3A in cyclosporin vasculopathy. Dept. Med. Research day, University of Michigan, 1994.
9. Gibbs, D.F., Burmeister, B., Varani, J. and Johnson, K.J.: Characterization of serine and metalloproteinases activities from stimulated rat neutrophils and rat aveolar macrophages. Keystone Symposium, 1994.
10. Lebedovych, L., McMorris, M.S., Ward, P.A., Johnson, K.J, and Baker, J.R.: Variables altering cutaneous and pulmonary infiltrates in an *in vivo* model of delayed-phase allergic inflammation. FASEB J. 8:3943, 1994.

11. Foreman, K.E., Johnson, K.J. and Ward, P.A.: Identification of a receptor binding site for C5a on human umbilical vein endothelial cells. FASEB J. 8:3958, 1994.
12. Johnson, K.J., Yung, R., Quddus, J., Chrisp, C. and Richardson, B.C.: Spectrum of autoimmunity caused by cloned TH2 cells modifies with DNA methyltransferase inhibitors. FASEB J. 8:1535, 1994.
13. Lowe, N.J., Wieder, J., Rosenbach, A., Johnson, K.J., Simpson, K., Glass, E., Grabie, M. and Bainbridge, C.: Cyclosporin therapy for severe psoriasis: chronic effects on renal structure and function. Sixth International Psoriasis Symposium, Chicago, Illinois, 1994.
14. Leggat, J.E., Johnson, K.J., Kolars, J.C., Schmiedlin-Ren, P. Watkins, P.B. and Leichtman, A.B.: Immunohistochemical localization of cytochrome P450 3A in normal and neoplastic kidney and urinary bladder epithelium. J. ASN 5:786, 1994.
15. Vogt, B.A., Johnson, K.J., Shanley, T.P., Alam, J. and Wath, K.A.: Acute glomerular inflammation induced heme oxygenase (HO) in renal tubules and confers resistance to tubular oxidant injury. J. ASN 5:797, 1994.
16. Colton, D.M., Hirschl, R.B., Till, G.O., Johnson, K.J., Ichiha, S., Planton, C.C. and Bartlett, R.H.: Lung vascular permeability as reduced during partial liquid ventilation (PLV) in the setting of respiratory failure. Soc. of University Surgeons, 1994.
17. Wieder, J., Rosenbach. A., Johnson, K.J., Simpson, K., Glass, E., Grabie, M. and Bainbridge, C.: Cyclosporin therapy for severe psoriasis: chronic effects on renal structure and function. Sixth International Psoriasis Symposium, Chicago, Illinois, 1994.
18. Richardson, B.C., Lalwani, N.D., Johnson, K.J. and Marks, R.M.: Ligation of FAS is sufficient to trigger apoptosis in macrophages but not in cultured human endothelial cells. Clin. Res., In Press.
19. Yung, R.L., Powers, D., Johnson, K.J. and Richardson, B.C.: Inducing LFA-1 overexpression on cloned TH2 T cells causes autoreactivity in vitro and lupus-like immunity in vivo. Clin. Res. 42:315A, 1994.
20. Colton. D., Hirschl, R., Till, G.O., Johnson, K.J., Metzger, R., Dean, S. and Bartlett, R.: The pathophysiology of respiratory failure following systemic complement activation. E. Soc. Crit. Care Med., 1995.
21. Leggat, J.E., Johnson, K.J., Kolars, J.C., Schmiedlin-Ren, P., Watkins, P.B. and Leichtman, A.B.: Immunohistochemical localization of cytochrome P450 3A in normal and neoplastic kidney and urinary bladder epithelium. Exp. Biol., 1995.
22. Richardson, B.C., Johnson, K.J. and Lalwani, N.D.: Macrophage apoptosis in active lupus. Ninth International Congress of Immunology, 1995.
23. Bleavins, M., Johnson, K.J. and de la Iglesia, F.A.: Comparative effects of two recombinant human epidermal growth factors (EGF) in mercuric chloride-induced kidney injury. ICT, Seattle, Washington, 1995.
24. Davidson, B.A., Nader-Djalal, N., Jones, M.L., Johnson, K.J. and Knight, P.R.: The proinflammatory cytokine, TNFα is required for full expression of gastric inspiration lung injury. ASA, 1995.
25. Nader-Djalal, N., Davidson, B.S., Helinski, M.S., Shanley, T.P., Johnson, K.J. and Knight, P.R.: Is interleukin-10 invited to the feast in aspiration pneumonitis? ASA, 1995.
26. Foreman, K.E., Till, G.O., Johnson, K.J, and Ward, P.A.: Complement Activation, endothelial cell P-selectors and the role of C5b-C9. FASEB J. 9:198, 1995.

27. Varani, J., Burmeister, W., Perone, P., Bleavins, M., and Johnson, K.J.: Retinoic acid interferes with movement of Ca across the plasma membrane of human dermal fibroblasts. FASEB J. 9:3366, 1995.
28. Gipson, T.S., Shanley, T.P., Jones, M.L., Ward, P.A. and Johnson, K.J.: Molecular cloning and in vivo transcriptional expression of rat TIMP-2 in lung inflammation. FASEB J. 9:4339, 1995.
29. Leggat, J.E., Jr., Johnson, K.J., Kolars, J.C., Schmiedlin-Ren, P., Watkins, P.B. and Leichtman, A.B.: Immunohistochemical localization of cytochrome P450 3A in normal and neoplastic kidney and urinary bladder epithelium. FASEB J. 9:5604, 1995.
30. Johnson, K.J, Swanson, P.C., Yung, R.L., Blatt, N.B., Eagan, M., Norris, J., Richardson, B.C. and Glick, G.D.: Anti-DNA antibodies structure-function and pathogenicity. Amer. Soc. Nephrol., 1995.
31. Yung, R.L., Johnson, K.J, and Richardson, B.C.: LFA-1 overexpression on T cells causes autoimmunity *in vivo.* Amer. Coll. Rheum., 1995.
32. Colton, D.M., Johnson, K.J. and Hirschl, R.B.: Lung vascular permeability is reduced during partial liquid ventilation (PLV) in the setting of respiratory failure. Amer. Thoracic Soc., 1995.
33. Colton, D.M., Till, G.O., Johnson, K.J., Gator, J., Brent, D.O. and Hirschl, R.B.: Partial liquid ventilation (PLV) decreases intraveolar hemorrhage during acute respiratory failure. Amer. Coll. Surg., 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Clinical Pathology Grand Rounds:
   1. Program Director.
   2. Presented lecture entitled: "Automation in the transfusion service".
B. Anatomical Pathology Conferences:
   1. Program Coordinator.
C. Core-Lecture Series in Blood Banking for 1st-year Pathology House Officers:
   1. Program Coordinator.
   2. Presented lectures on:
      a. Pretransfusion testing.
      b. Prenatal/perinatal testing.
      c. Immune hemolysis.
D. Clinical Pathology Case Study Conference:
   1. Program Coordinator.
   2. Participant.
E. Hematology/Oncology Fellows:
   1. Provided instruction in immunohematology to Dr. Melissa Baird (ten contact hours).
F. Pathology Residents:
   1. Residency Training Review Committee.
   2. Coordinated Blood Bank/Immunology/Coagulation and HLA block rotations for house-officer training in clinical pathology.
   3. Provided instruction in immunohematology to house-officers during their Blood Bank Rotation (100 contact hours).
   4. Presented Pizza Seminar entitled: "The Human Blood Groups".
G. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
   1. Program Director - Planned and coordinated the June, 1995 Current Topics in Blood Banking Symposium and Preconference Workshops.
   2. Presented Workshop entitled: "Problem Solving - Tricks of the Trade".
   3. Presented talk entitled: "The Perfect Crossmatch".
   4. Moderated morning session on Transfusion Management.
H. Clinical Pathology M-4 Elective:
   1. Member, Coordinating Committee.
   2. Organized Elective in Transfusion Medicine.
   3. Presented talks on pretransfusion testing, immune hemolysis and prenatal/perinatal testing.

III. RESEARCH ACTIVITIES:

A. Judd, W.J., Beck M.L., Annesley T., Kirkegaard J. and Steiner E.A.: Observations on monoclonal blood grouping reagents. In preparation.
B. Butch S.H., Judd W.J.: Experiences with the computer crossmatch. Accepted for presentation at the Annual Meeting of the American Association of Blood Banks, New Orleans, November, 1995.
C. Judd W.J., Steiner E.A., Knafl P.: Failure to detect potentially significant antibodies in prewarmed tests. Accepted for presentation at the Annual Meeting of the American Association of Blood Banks, New Orleans, November, 1995.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL/NATIONAL:

A. Michigan Association of Blood Banks:
   1. Chairman, Advanced Lectures in Blood Banking Program - coordinated a series of 60 lectures, two full-day workshops and a two-day review session for technologists seeking Certification as a Specialist in Blood Banking.
   2. Member, Annual Meeting Program Committee.
B. American Association of Blood Banks:
   1. Chairman, AABB Press Oversight Committee.
   2. Member, Awards Committee.
C. Member, Editorial Board, Transfusion.
D. Reviewer of articles submitted for publication in Transfusion and Immunohematology.

V. OTHER RELEVANT ACTIVITIES:

HONORS AND AWARDS:

A. Presented the 1995 Kay Beattie Lecture: "Monoclonal Antibodies - Promises and Pitfalls", Annual Meeting of the Michigan Association of Blood Banks, Troy, Michigan, September, 1994.

INVITED LECTURES:

1. "Lectins", Michigan Association of Blood Banks Advanced Lecture Series. St. Joseph Mercy Hospital, Ann Arbor, September, 1994.
2. "Polyagglutination", Michigan Association of Blood Banks Advanced Lecture Series. St. Joseph Mercy Hospital, Ann Arbor, September, 1994.
3. "The Perfect Crossmatch", Michigan Association of Blood Banks, Fall Seminar, Gaylord, Michigan, October, 1994.
4. "Monoclonal Antibodies - Promises and Pitfalls", Michigan Association of Blood Banks, Fall Seminar, Houghton, Michigan, October, 1994.
5. "The Perfect Crossmatch", Michigan Association of Blood Banks, Fall Seminar, Houghton, Michigan, October, 1994.

6. "Monoclonal Antibodies - Promises and Pitfalls", Sparrow Hospital, Lansing, Michigan, October, 1994.
7. "Approaches to Antibody Identification", South Bend Medical Foundation, South Bend, Indiana, October, 1994.
8. "The Perfect Crossmatch", South Bend Medical Foundation, South Bend, Indiana, October, 1994.
9. "Approaches to Antibody Identification", McPherson Hospital, Howell, Michigan, December, 1994.
10. "Approaches to Antibody Identification", South Florida Blood Services. St. Petersburg, Florida, January, 1995.
11. "Monoclonal Antibodies - Promises and Pitfalls", South Florida Blood Services. St. Petersburg, Florida, January, 1995.
12. "Your Brain on Drugs", American Red Cross National Reference Laboratory, Bethesda, Maryland, March, 1995.
13. "101 Ways with a Wet Noodle", Michigan Association of Blood Banks Spring Workshop, Lansing, Michigan, May, 1995.
14. "Your Brain on Drugs", American Association of Blood Banks Reference Laboratory Annual Meeting, Atlanta, Georgia, May, 1995.
15. "Methods in Immunohematology", American Association of Blood Banks Reference Laboratory Annual Meeting, Atlanta, Georgia, May, 1995.

VI. PUBLICATIONS:

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

1. Judd, W.J., Eisenbrey, L., Weaver, M., Back, M., Cisco, S., Deters, J., Gray, J., Hamilton J., Hartrick, M.B.and Morrison M.: State Association Sponsored Program for SBB Candidates. Immunohematology. 10:95-8, 1994.
2. Judd W.J.: Prewarmed tests: con. Transfusion. 35:271-5, 1995.

BOOKS/CHAPTERS IN BOOKS:

1. Judd, W.J.: Blood groups, in, Encyclopedia of Science and Technology, McGraw-Hill, New-York, NY, 1995.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERSTO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFERRED JOURNALS:

1. Butch, S.H., Stoe, M. and Judd W.J.: Solving the same-day admission identification problem. 47th Annual Meeting of the American Association of Blood Banks, San Diego, CA. Transfusion. 34:93, 1994.

ANTHONY A. KILLEEN, M.D., PH.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Director of Molecular Diagnostics.
B. Director of Clinical Chemistry Section.
C. Interpretation and sign-out of protein electrophoretic analyses (Immunology Laboratory).

II. TEACHING ACTIVITIES:

A. Lectures to Medical Students in M4 Laboratory Medicine Elective.
B. Lectures to House Staff on Block B.
C. Lectures to Pathology House Staff and Faculty at Clinical Pathology Rounds.
D. Research advisor to undergraduate: Ms. Lisa Passmore (Chemistry). Research advisor to Medical Student: Mr. Neil Bavikatty.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Identification of genes activated by mineralocorticoid hormones.
B. Regulation of the mineralocorticoid receptor expression.
C. Development of technologies for the Molecular Diagnostics Laboratory.

SPONSORED SUPPORT:

A. American Heart Association (Michigan Chapter) 7/1/95-6/30/96, $27,600, "Identification of mineralocorticoid response genes". Principal Investigator.
B. Michigan Phoenix Memorial Project. 7/1/95-6/30/96, $4,900 "Identification of mineralocorticoid response genes". Principal Investigator.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Molecular Diagnostics Laboratory.
B. Director, Clinical Chemistry Section.
C. Interviewer, Pathology Resident Applicants.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Committee on Laboratory Planning for East Medical Campus.
B. Member, Patient Care Information Systems (PCIS) Committee.

REGIONAL AND NATIONAL:

A. Member, Program and Finance Committee, Academy of Clinical Laboratory Physicians and Scientists (ACLPS).
    1. Editor of ACLPS Newsletter.
    2. Chair, ACLPS Taskforce on networking.
    3. Founding Member, and Newsletter Editor, Association for Molecular Pathology
B. Member, AACC, ASHG, CAP, ACLPS.
C. Organizer of the November, 1994 symposium on Molecular Pathology for the Michigan Society of Pathologists.
D. Manuscript Reviewer, *Clinical Chemistry*.
E. Organizer of the Internet newsgroup "MxDIAG-L", dedicated to Molecular Pathology.

INVITED LECTURES AND SEMINARS:

1. "Applications of Molecular Diagnostics in Clinical Medicine". Central Michigan Community Hospital, Mt. Pleasant, Michign, September, 1994.
2. "Applications of DNA Diagnostics in the Clinical Laboratory". Ohio Society of Clinical Laboratory Sciences, Toledo, Ohio, October, 1994.
3. "Molecular Diagnostics: Trends and Applications". Michigan Society of Pathologists Meeting, University of Michigan, Ann Arbor, December, 1994.
4. "Applications of PCR and LCR in the Clinical Laboratory". Michigan Society of Clinical Laboratory Sciences, Kalmazoo, Michigan, January, 1995.
5. "Sherlock Holmes meets DNA". (Forensic applications of DNA testing). University of Michigan Medical Center Community Relations Public Talks (with two other speakers), April, 1995.
6. "Diagnostic Molecular Biology: PCR in the Clinical Laboratory". Midwest Clinical Ligand Assay Society, April, 1995.

ARTICLES, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR,MISCELLANEOUS PUBLICATIONS IN UNREFERRED JOURNALS:

1. Chai, C., and Killeen, A.A.: Carbamazepine measurements in samples from the Emergency Room. Therapeutic Drug Monitoring 16:407-412, 1994.
2. Song, C., Killeen, A.A. and Leonard, B.E.: Catalase, superoxide dismutase, and glutathione peroxidase activity in neutrophils of sham-operated and olfactory bulbectomised rats following chronic treatment with desipramine and lithium chloride. Neuropsychobiology 30:24-28, 1994.
3. Killeen, A.A.: A visible spectrophotometric assay for submicrogram quantities of DNA, including PCR-amplified DNA. Microchemical Journal, In press.

4. Hitomi, Y., McDonnell, W.M., Killeen, A.A. and Askari, F.K.: Hepatitis C virus core gene sequence fidelity confirms core protein as an appropriate target for HCV vaccine strategies. J Viral Hepatitis, In Press.

EDITORIAL:

1. Willman C.L. (Co-signed with others): The case for American Board of Pathology Certification in Molecular Pathology. Human Pathology 26:467-468, 1995.

ABSTRACTS:

1. A visible spectrophotometric dye binding method for detection and measurement of submicorgram quantities of DNA. Clinical Chemistry 41:S105, 1995.
2. Bavikatty N.B. and Killeen A.A.: Aldosterone increases citrate synthase activity in human mononuclear leukocytes. (Presented at the ACLPS meeting, June 1995, Syracuse, New York). Am J Clin Path, In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Board Certification, Anatomic Pathology.
B. Autopsy Pathology.
C. Diagnostic Renal Biopsy Service.

II. TEACHING ACTIVITIES:

A. Pathology 600 - Pathology Laboratory for Medical Students. (Approximately 60 contact hours).
B. M2 Pathology Lecture - Renal Sequence (60 hours).
C. Co-Coordinator - Renal Sequence (40 hours).
D. Gross Pathology Conference.
E. Renal Pathology Conference.
F. Clinical Pathology Conference (one hour).
G. Renal Pathology for Nephrology Fellows (nine contact hours).
H. Undergraduate Students (two).
I. Dissertation Committees (two).
J. Post Doctoral Fellows (six).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Collagen IV Gene Transcription in cpk/cpk Mice", NIH-RO1-DK44848, (25% Effort) $143,000/first year, 9/30/91-9/29/95.
B. Principal Investigator, Project VI, "TGF-β Induced Collagen IV Gene Transcription", NIH-P50-DK39225, (10% Effort) $49,822/year, 8/1/92-7/30/97.
C. Co-Investigator, "Renal Fibrosis", NIH-RO1, (10% Effort) $198,213/first year, 4/1/93-3/30/98.
D. Co-Investigator, "Role of EDRF in the Juxtaglomerular Apparatus", NIH-RO1-DK40042, (10% Effort) $164,666/first year, 12/1/93-11/30/98.
E. Co-Sponsor, "Aldose Reductase Expression in Diabetes", NIH-Physician Scientist Award, $60,429/year, 4/1/93-3/30/98.

PROJECTS UNDER STUDY:

A. Structure and function of collagen IV.
B. Regulation of collagen IV gene expression.
C. Localization of nephron segment-specific genes by PCR.
D. Regulation/expression of hypertonicity stress proteins.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Postdoctoral candidate recruitment, Immunopathology Training Grant.
B. Anatomic Pathology Accessioning Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Faculty recruitment - Department of Pathology.
B. Faculty recruitment - Department of Internal Medicine.
C. Curriculum development-M1 Pathology.
D. Curriculum development-M2 Urinary System.

REGIONAL AND NATIONAL:

A. Planning Committee, Genetic Basis of Renal Disease. NIDDK, NIH.
B. Ad hoc reviewer, Division of Extramural Activities, NIDDK, NIH.
C. Ad hoc Reviewer, Juvenile Diabetes Foundation.
D. Reviewer:
    1. Laboratory Investigation.
    2. American Journal of Pathology.
    3. Journal of Clinical Investigation.
    4. Journal of Cell Biology.
    5. Journal of Biological Chemistry.
    6. Journal of American Society of Nephrology.
E. AHA-National Cardio-Renal Study Section, 1992-1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Henry, D.N., Monte, M.D., Green, D.A. and Killen, P.D.: Altered aldose reductase gene regulation in cultured human retinal pigmant epithelial cells. J. Clin. Invest. 92:617-623, 1993.

2. Stevens, M.J., Henry, D.N., Thomas, T.P., Killen, P.D. and Greene, D.A.: Aldose reductase gene xpression and osmotic dysregulation in cultured human retinal pigment epithelial cells. Amer. J. Physiol. 265:E428-438.
3. Grande, J.P., Melder, D. and Killen, P.D.: TGF-β1 induces collagen IV gene transcription in NIH-3T3 cells. Lab. Invest. 69:387-395, 1993.
4. Greene, D.A., Sima, A.A.F., Stevens, M.J., Feldman, E.L., Killen, P.D., Henry, D.N., Thomas, T., Dananberg, J. and Lattimer, S.A.: Aldose reductase inhibitors: An approach to the treatment of diabetic nerve damage. Diabetes/Metabolism Rev. 9:189-217, 1993.
5. Chen, M., Todd-Turla, K., Wang, W-H., Cao, X., Smart, A., Brosius, F.C., Killen, P.D., Briggs, J.P. and Schnermann, J.: Endothelin 1 mRNA in glomerular and epithelial cells of the kidney. Amer. J. Physiol. 265:E542-50, 1993.
6. Chen, M., Schnermann, J., Smart, A.M., Brosius, F.C., Killen, P.D. and Briggs, J.P.: Cyclic AMP selectively increases renin mRNA stability in cultured juxtaglomerular granular cells. J. Biol. Chem. 268:24138-24144, 1993.
7. Kroll, T.G., Peters, B.P., Hustad, C.M., Jones, P.A., Killen, P.D. and Ruddon, R.W.: Expression of laminin chains during myogenic differentiation. J. Biol. Chem. 269:9270-9277, 1994.
8. Mitchell, M., Markovitz, D., Killen, P.D., Braun, D.: Bilateral renal malacoplakia presenting as fever of unknown origin: A case report and review of the literature. Clin. Infect. Dis. 18:704-718, 1994.
9. Bergijk, E.C., Baelde, H.J., de Heer, E., Killen, P.D. and Bruijn, J.A.: A key role for fibronectin in experimental glomerulosclerosis. Kidney Int., In Press.
10. Keller, S.A., Jones, J.M., Boyle, A., Barrow, L.L., Killen, P.D., Green, D.G., Kapousta, N.V., Hitchcock, P.F., Swank, R.T. and Meisler, M.H.: Kidney and retinal defects (*Krd*), a transgene induced mutation with a deletion of mouse chromosome 19 that includes the *Pax-2* locus. Genomics, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Kuncio, G.S., Alvarez, R., Shaoran, L., Haverty, T., Killen, P.D. and Neilson, E.G.: Cytokine modulation of the α1(IV) collagen gene in murine renal tubular cells. Submitted.
2. Todd-Turla, K.M., Schnermann, J.B., Briggs, J.P. and Killen, P.D.: Regulation of renal mineralocorticoid and glucocorticoid receptor mRNA in response to adrenalectomy and corticosteroid hormone replacement. Submitted.
3. Funabiki, K., Togawa, M., Chapo, J.A. and Killen, P.D.: The complete primary structure of the murine α3(IV) Collagen Chain. Submitted.
4. Grande, J.P., Jones, M., Swenson, C.A., Killen, P.D. and Warren, J.S.: Lipopolysaccharide induces monocyte chemoattractant protein production by rat mesangial cells. Submitted.
5. Bergijk, E.C., Baelde, J.J., De Heer, E., Killen, P.D, and Bruijn, J.A.: The extracellular matrix in the development of glomerulosclerosis in experimental chronic serum sickness. Submitted.
6. Bergijk, E.C., Baelde, J.J., De Heer, E., Killen, P.D. and Bruijn, J.A.: Cloning of the murine fibronectin V-region and variation of its splicing in experimental immune complex glomerulonephritis. Submitted.
7. Singh, I.J., Killen, P.D. and Leichtman, A.: Atheroemboli in renal transplantation. Submitted.

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

1. Henry, D.N., Togawa, M., Larkin, D., Greene, D.A. and Killen, P.D.: Aldose reductase gene transcription is not an immediate early response to osmotic stress. Amer. Soc. Nephrol. 4:887, 1993.
2. Togawa, M., Henry, D.N., Greene, D.A. and Killen, P.D..: Identification of an osmotically-induced enhancer of aldose reductase gene transcription. Amer. Soc. Nephrol. 4:898, 1993.

3. Schieren, G., Park, M.H., Funabiki, K. and Killen, P.D.: Expression of the murine α5(IV) collagen gene. Amer. Soc. Nephrol. 4:823, 1993.
4. Park, M.H., Funabiki, K., Togawa, M., Chapo, J.A., and Killen, P.D.: The complete primary structure of the murine α5(IV) collagen chain as deduced from the cDNA. Amer. Soc. Nephrol. 4:820, 1993.
5. Funabiki, K., Togawa, M., Chapo, J.A., Hlaing, T. and Killen, P.D.: The complete primary structure of the murine α3(IV) collagen chain as deduced from the cDNA. Amer. Soc. Nephrol. 4:813, 1993.
6. Bergijk, E.C., Baelde, J.J., deHeer, E., Killen, P.D. and Bruijn, J.A.: The role of the extracellular matrix in the development of glomerulosclerosis in experimental immune complex nephritis. Amer. Soc. Nephrol. 4:646, 1993.
7. Bergijk, E.C., Baelde, J.J., deHeer, E., Killen, P.D. and Bruijn, J.A.: Differential expression of collagen type IV subchains in experimental glomerulosclerosis. Submitted.

STEVEN L. KUNKEL, Ph.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Epidemiology 570.
B. Member, Pathology Graduate Program Committee.
C. Member, Molecular Pathogenesis Training Program (Microbiology).
D. Member, Immunopathology Postdoctoral Training Program (Pathology).
E. Member, Operating Committee, Systems and Integrative Biology Training.
F. Member, Experimental Immunopathology Training Program (Pathology).
G. Member and Co-Director, Pulmonary Cellular and Molecular Biology Training Program.
H. Member, Graduate Teaching Award Review Committee.
I. Supervised the following postdoctoral fellows and graduate students: fellows, Drs. Tsuyoshi Kasama, Dan Smith, Glenn VanOtteren, John Orens, Nick Lukacs; graduate student, Rob Smith.
J. Undergraduate students: Marc Milia, Gannon Dudlar, Kolby Keefer, Laural Goldstein, Rick Dwyer, Janet Sherman, Christi Shaklee.
K. Doctoral Thesis Committee Member/Orals Committee for the following graduate students: Jami Foreback, Jin Liao, Jeffrey Ruth, Ron Allen, Rob Smith, Fran Wolber, Jerry Caldwell.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Macrophage/MonocyteSignals in Lung Granuloma Formation", National Institutes of Health, HL-RO1-35276.
B. Principal Investigator, "Monokine Gene Expression/Regulation in Lung Injury", National Institutes of Health, HL-RO1-31237.
C. Principal Investigator for Section II, "Inflammatory Cells and Lung Injury", National Institutes of Health, Program Project HL-31963.
D. Co-Investigator, "The Role of TNF and ICAM-1 in Lung Allograft Rejection", National Institutes of Health, HL-50057.

E. Co-Investigator, "Cytokine Networks Regulating Inflammation of Pulmonary Fibrosis", National Institutes of Health, HL-46487.

PROJECTS UNDER STUDY:

A. Regulation of macrophage signals that dictate immune responsiveness.
B. Regulation of macrophage gene expression.
C. Macrophage-lymphocyte interactions in the initiation, maintenance, and resolution of chronic inflammation.
D. Role of cytokines in tumorgenesis.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Operating Committee Graduate Program.
B. Space Utilization and Research Committee.
C. Interview candidates for Residency/Graduate Program.
D. Divisional Director of General Pathology.
E. Member Self-Study Committee (Department of Pathology Review Committee).

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

A. Member, Committee on Medical Student Research.
B. Medical School representative to University Senate Assembly.
C. Medical School Admission interview Committee.
D. Medical Scientist Training Program Interview Committee.
E. Chairman, Biomedical Research Council Committee.
F. Member, Biomedical Research Council.
G. Member, Michigan Cancer Center.
H. Institute of Gerontology Faculty Search Committee.
I. Pediatrics Faculty Search Committee.
J. Member, Dean's Immunology Task Force.
K. Interim Associate Vice-President for Research, University of Michigan.

REGIONAL AND NATIONAL

A. Section Editor, Journal of Immunology.
B. Associate Editor, American Journal of Pathology.
C. Associate Editor, American Journal of Respiratory Cell and Molecular Biology.
D. Associate Editor, Pathobiology.
E. Associate Editor, Shock.
F. Editorial Board, Mediators of Inflammation.
G. Co-Organizer, 1994 International Cytokine Conference Banff, Alberta Canada.
H Member Program Committee, American Society of Investigative Pathology.

I. Reviewer for the following journals: American Journal of Pathology, American Review of Respiratory Disease, Circulation, Infection and Immunity, Laboratory Investigation, Science, Journal of Immunology, American Journal of Respiratory Cell and Molecular Biology.
J. Grant Reviewer, The Arthritis Society.
K. Grant Reviewer, Veterans Administration.
L. Grant Reviewer, Canadian Cystic Fibrosis Foundation.
M. National Institute of Health Study Section, Respiratory and Applied Physiology, Ad Hoc.
N National Institutes for Health Study Section, Tropical Medicine/Parasitology, Ad Hoc-Teleconference.
O. National Institute of Health Study Section, Oral Biology & Medicine I, Ad Hoc-Teleconference.
P. Scientific Advisory Council, American Lung Association.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Invited Speaker, International Conference on Endotoxins IV - Symposium on Anti-TNF Treatment of Septic Shock, Amsterdam, The Netherlands, August, 1993.
2. Invited Speaker, "Cytokines and the Lung", British Lung Association, Bath England, September, 1993.
3. Invited Speaker, "Microbial Pathogenesis and Immune Reponses", Orlando, Florida, September, 1993.
4. Invited Speaker, American Heart Association, "Conference on Molecular Cellular Biology of the Vascular Wall", Boston, Massachusetts, October, 1993.
5. Visiting Professor, University of Oklahoma Health Science Center, Oklahoma City, Oklahoma, October, 1993.
6. Invited Speaker, Mini State-of-the-Art Address, Central Society for Clinical Research (AFCR), Chicago, Illinois, November, 1993.
7. Invited Speaker, Functionality of the Endothelium in Health and Diseased States: A Comprehensive Review, Mexican Society of Cardiology, Varacrux, Mexico, November, 1993.
8. Visiting Professor, University of Washington, Department of Pathology, Seattle, Washington, January, 1994.
9. Invited Speaker, Keystone Symposium, "Cytokines and the Acute Phase Response", Tamarron, Colorado, February, 1994.
10. Visiting Professor, University of Vermont, Department of Pathology, Burlington, Vermont, February, 1994.
11. Invited Speaker, 3rd International Congress on the Immune Consequences of Trauma, Shock, and Sepsis, Munich, Germany, March, 1994.
12. Invited Speaker, "Cytokines in Disease", The Ninth UCI Symposium on Cancer Research, Irvine, California, March, 1994.
13 Invited Faculty/Speaker, Opening of The University of Chicago Inflammatory Bowel Disease Center, Chicago, Illinois, April, 1994.

14. Invited Speaker, National American Federation Clinical Research "The Year in Pulmonary Medicine", Baltimore, Maryland, April, 1994.
15. Invited Speaker, Athena Neurosciences, San Francisco, California, May, 1994.
16. Invited Speaker, Gordon Conference, "Chemokines", Plymouth State College NH, June, 1994.

VI. PUBLICATIONS

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kasahara, K., Strieter, R.M., Standiford, T.J. and Kunkel, S.L.: Adherence in combination with LPS, TNF, or IL-1B is synergistic for the induction of monocyte-derived IL-8. Pathobiol. 61:57;-66, 1993.
2. Kasama, T., Strieter, R.M., Standiford, T.J., Burdick, M.D. and Kunkel, S.L.: Expression and regulation of human neutrophil-derived macrophage inflammatory protein-1 alpha (MIP-1a). J. Exp. Med. 178:63-72; 1993.
3. Schmouder, R.L., Strieter, R.M. and Kunkel, S.L.: Interferon-gamma regulation of human renal cortical epithelial cell-derived monocyte chemotactic peptide-1. Kidney International 44:43-49, 1993.
4. Chensue, S.W., Warmington, K.S., Hershey, S.D., Terebuh, P.D., Othman, M. and Kunkel, S.L.: Evolving T cell responses in murine schistosomiasis.: Th2 cells mediate secondary granulomatous hypersensitivity and are regulated by CD 8+ T cells *in vivo*. J. Immunol. 151:1391-1400, 1993.
5. Wertheim, W.A., Kunkel, S.L., Standiford, T.J., Burdick, M.D., Becker, F.S., Wilke, C.A., Gilbert, A.R. and Strieter, R.M.: Regulation of neutrophil-derived interleukin-8: The role of prostaglandin E2, dexamethasone, and interleukin-4. J. Immunol. 151:2166-2175, 1993.
6. Standiford, T.J., Kunkel, S.L., Liebler, J.M., Burdick, M.D., Gilbert, A.R. and Strieter RM.: The gene expression of MIP-1a from human blood monocytes is inhibited by IL-4. Am. J. Respir. Cell Mol. Biol. 9:192-198, 1993.
7. Strieter, R.M., Lukacs, N.W., Standiford, T.J. and Kunkel, S.L.: Cytokines and lung inflammation: Mechanisms of neutrophil recruitment to the lung. Thorax. 48:765-769, 1993.
8. Smith, D.R., Kunkel, S.L., Rolfe, M.W., Standiford ,T.J., Orringer, M.B., Whyte, R.I., Burdick, M.D., Lukacs, N.W., Danforth, J.M., Gilbert, A.R. and Strieter, R.M.: The production of a interleukin-1 receptor antagonist by human bronchogenic carcinoma. Am. J. Pathol. 143:794-803, 1993.
9. Standiford, T.J., Rolfe, M.W., Kunkel, S.L., Lynch, III, J.P., Burdick, M.D., Gilbert, A.R., Orringer, M.B. and Strieter, R.M.: Macrophage inflammatory peptide-1 alpha expression in interstitial lung disease. J. Immunol. 151:2852-2863, 1993.
10. Strieter, R.M., Kunkel, S.L., Bone and R.C.: The role of tumor necrosis factor-alpha in disease states and inflammation. Crit. Care Med. 21:1447-1463, 1993.
11. Standiford, T.J., Kunkel, S.L. and Strieter, R.M.: Interleukin-8: A major mediator of acute pulmonary inflammation. Regional Immunol. 5:134-141, 1993.
12. Chensue, S.W., Bienkowski, M., Eessalu, T.E., Warmington, K.S., Hershey, S.D., Lukacs, N.W. and Kunkel, S.L.: Endogenous IL-1 receptor antagonist protein (IRAP) regulates Schistosome

egg granuloma formation and the regional lymphoid response. J. Immunol. 151:3654-3662, 1993.

13. Hewett, J.A., Kunkel, S.L. and Roth, R.A.: Relationship between tumor necrosis factor-α and neutrophils in endotoxin-induced liver injury. Am. J. Physiol. 265:G1011-G1015, 1993.
14. Lukacs, N.W., Kunkel, S.L., Burdick, M.D. and Strieter, R.M.: The production of chemotactic cytokines in an allogeneic response: The role of intercellular adhesion molecule-1 and lymphocyte function-associated antigen-3. Am. J. Pathol. 143:1179-1188, 1993.
15. Burdick, M.D., Kunkel, S.L., Lincoln, P.M, Wilke, C.A. and Strieter R.M.: Specific ELISAs for the detection of human macrophage inflammatory protein-1 alpha and beta. Immunol. Invest. 22:441-449, 1993.
16. Antony, V.B., Hott, J.W., Kunkel, S.L., Godbey, S.W., Hartman, D.L., Burdick, M.D. and Strieter RM.: Recruitment of inflammatory cells to the pleural space: chemotactic cytokines, IL-8 and MCP-1 in human pleural fluids. J. Immunol. 151:7216-7223, 1993.
17. Karmiol, S., Remick, D.G., Kunkel, S.L. and Phan, S.H.: Regulation of rat pulmonary endothelial cell interleukin-6 production by bleomycin: Effects of cellular fatty acid composition. Am. J. Respir. Cell Mole. Biol. 9:628-636, 1993.
18. Rolfe, M.W., Standiford, T.J., Kunkel, S.L., Burdick, M.D., Gilbert, A.R., Moore, S.A., Lynch, III, J.P. and Strieter, R.M.: Interleukin-1 receptor antagonist expression in sarcoidosis. Am. Rev. Respir Dis. 148:1378-1384, 1993.
19. Lukacs, N.W., Kunkel, S.L., Burdick, M.D., Lincoln, P.M. and Strieter, R.M.: Interleukin 1 receptor antagonist blocks chemokine production in the mixed lymphocyte reaction. Blood 82:3668-3674, 1993.
20. Koch, A.E., Kronfeld, L.B., Szekanecz, Z., Cho, M.M., Haines, G.K., Harlow, L.A., Strieter, R.M., Kunkel, S.L., Massa, M.C., Barr, W.G. and Jimenez, S.A.: *In situ* expression of cytokines and cellular adhesion molecules in the skin of patients with progressive systemic sclerosis. Pathobiol. 61:239-246, 1993.
21. Davenport, R.D., Burdick, M., Strieter, R.M. and Kunkel, S.L.: Monocyte chemoattractant protein production in red cell incompatibility. Transfusion. 34:16-19, 1994.
22. Liebler, J.M., Kunkel, S.L., Burdick, M.D., Standiford, T.J., Rolfe, M.W. and Strieter, R.M.: The production of IL-8 and MCP-1 by peripheral blood monocytes: Disparate responses to PHA and LPS. J. Immunol. 152:241-249, 1994.
23. Van Otteren, G.M., Standiford, T.J., Kunkel, S.L., Danforth, J.M., Burdick, M.D., Abruzzo, L.V. and Strieter, R.M.: The expression and regulation of macrophage inflammatory protein-1-alpha by murine alveolar and peritoneal macrophages. Am. J. Respir. Cell Mol. Biol. 10:8-15, 1994.
24. Lukacs, N.W., Strieter, R.M., Evanoff, H.L., Burdick, M.D. and Kunkel, S.L.: VCAM-1 influences lymphocyte proliferation and cytokine production during mixed lymphocyte response. Cell. Immunol. 154:88-98, 1994.
25. Strieter, R.M., Koch, A.E., Antony, V.B., Fick, R.B., Standiford, T.J. and Kunkel, S.L.: The immunopathology of chemotactic cytokines: The role of interleukin-8 and monocyte chemoattractant protein-1. J. Lab. Clin. Med. 123:183-197, 1994.
26. Lukacs, N.W., Chensue, S.W., Smith, R.E., Strieter, R.M., Warmington, K., Wilke, C. and Kunkel, S.L.: Production of monocyte chemoattractant protein-1 and macrophage inflammatory protein-1 alpha by inflammatory granuloma fibroblasts. Am. J. Pathol. 144:711-718, 1994.

27. Liebler, J.M., Kunkel, S.L., Allen, R.M., M.D. Burdick and Strieter, R.M.: Interferon-gamma stimulates monocyte chemotactic factor protein-1 expression by monocytes. Mediators of Inflammation. 3:27-31, 1994.
28. Koch, A.E., Kunkel, S.L., Harlow, L.A., Mazarakis, D.D., Haines, G.K., Burdick, M.D., Pope, R.M. and Strieter R.M.: Macrophage inflammatory protein-1α: A novel chemotactic cytokine for macrophages in rheumatoid arthritis. J. Clin. Invest. 93: 921-928, 1994.
29. Kasama, T., Strieter, R.M., Lukacs, N.W., Burdick, M.D. and Kunkel, S.L.: Regulation of neutrophil-derived chemokine expression by interleukin-10. J. Immunol. 252:3559-3569, 1994.
30. Davenport, R.D., Burdick, M.D., Strieter, R.M. and Kunkel, S.L.: *In vitro* production of interleukin-1 receptor antagonist in IgG-mediated red cell incompatibility. Transfusion. 34:297-303, 1994.
31. Smith, D.S., Polverini, P.J., Kunkel, S.L., Orringer, M.B., Whyte, R.I., Burdick, M.D., Wilke, C.A. and Strieter, R.M.: Inhibition of interleukin-8 attenuates angiogenesis in bronchogenic carcinoma J. Exp. Med. 179:1409-1415, 1994.
32. Lukacs, N.W., Strieter, R.M., Elner, V.M., Evanoff, H.L., Burdick, M. and Kunkel, S.L.: Intercellular adhesion molecule-1 mediates the expression of monocyte-derived MIP-1 alpha during monocyte-endothelial cell interactions. Blood. 83:1174-1178, 1994.
33. Lukacs, N.W., Strieter, R.M., Chensue, S.W. and Kunkel, S.L.: Interleukin-4 dependent pulmonary eosinophil infiltration in a murine model of asthma. Am. Rev. Resp. Cell Mol. Biol. 10:526-532, 1994.
34. Orens, J.B., Lukacs, N.W., Kunkel, S.L., Burdick, M.D., Wilke, C.A., Walz, A. and Strieter, R.M.: Regulation of chemokine production by the oxidative metabolism of L-arginine in a human mixed lymphocyte reaction. Cell. Immunol. 156:95-101, 1994.
35. Liebler, J.M., Kunkel, S.L., Allen, R.M., Burdick, M.D. and Strieter, R.M.: Interferon gamma stimulates monocyte chemotactic protein-1 expression by monocytes. Mediators of Inflammation. 3:27-31, 1994.

BOOKS AND CHAPTERS IN BOOKS

1. Lukacs, N.W., Strieter, R.M. and Kunkel, S.L.: Cytokines in acute inflammation, in, Adamson, J.W. (ed), Current Opinion in Hematology, Current Sciences. 26-31, 1993.
2. Remick, D.G. and Kunkel, S.L.: Pathophysiologic alterations induced by tumor necrosis factor, in, International Review of Experimental Pathology, 34B:7-25, 1993.
3. Kunkel, S.L. and Strieter, R.M.: Cytokine networks in leukocyte and endothelial cell activation, in, Rubio, R. (ed), Functionality of the Endothelium in Helath and Diseased States: A Comprehensive Review.
4. Kunkel, S.L., Driscoll, K.E., Ward, P.A., Nickoloff, B. and Strieter, R.M.: Immunopathology of environmental and occupational disease, in, Craighead, J. (ed), Pathology of Environment and Occupational Disease.
5. Kunkel, S.L., Lukacs, N.W., Chensue, S.W. and Strieter, R.M.: Adhesion molecules and chemokines dictate leukocyte recruitment, in, Faist, E. (ed), Proceedings of the Third Internationl Congress on the Immune Consequences of Trauma, Shock, and Sepsis, Munich Germany.
6. Kunkel, S.L., Lukacs, N.W. and Strieter, R.M.: Cytokines and inflammatory disease, in, Sirica, A. (ed), Cellular and Molecular Pathogenesis, Raven Press.

BOOKS EDITED

1. Westwick, J. and Kunkel, S.L.: The Chemokines: Biology of the Inflammatory Peptide Supergene Family, Lindley, I.J.D. (ed), Plenum Press, New York, 1993.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATION IN UNREFEREED JOURNALS.

1. Strieter, R.M., Colletti, L., Walz, A. and Kunkel, S.L.: Interleukin-8 and ENA-78 in the lung. Cytokines and Lung Function, 1993 FASEB Summer Research Conference, Vermont Academy, Saxtons River, Vermont.
2. Strieter, R.M., Swiderski, D.L., Rolfe, M.W., DeMeester, S.R., Burdick, M.D., Deeb, G.M. and Kunkel, S.L.: Cytokines in lung transplantation: The role of TNF and IL-6. British Association of Lung Research, Bath, United Kingdom, September, 1993.
3. Kunkel, S.L., Lukacs, N.M. and Strieter, R.M.: Cytokine networks in lung inflammation. British Association of Lung Research, Bath, United Kingdom, September, 1993.
4. McCullum, C.B., Smith, R.E., Strieter, R.M., Hume, R.I. and Kunkel, S.L.: Constitutive and regulated expression of macrophage inflammatory protein-1a (MIP-1) in primary cerebellar cultures. To be presented to the 1993 Annual Meeting of the Society for Neuroscience, Washington, D.C., November, 1993.
5. Smith, D.R., Polverini, P.J., Kunkel, S.L., Orringer, M.B., Whyte, R.I., Burdick, M.D., Wilke, C.A. and Strieter, R.M.: Interleukin-8: A primary mediator of angiogenesis in human bronchogenic carcinoma. Clin. Res. 41:688A, 1993.
6. Smith, D.R., Kunkel, S.L., Orringer, M.B., Whyte, R.I., Burdick, M.D., Wilke, C.A. and Strieter, R.M.: Interleukin-10 production by human bronchogenic carcinoma. Clin. Res. 41:644A, 1993.
7. Lukacs, N.W., Kunkel, S.L., Chensue, S.W., Evanoff, H.L. and Strieter, R.M.: The role of ICAM-1 in pulmonary granuloma formation. Clin. Res. 41:674A, 1993.
8. VanOtteren, G.M., Standiford, T.J., Kunkel, S.L., Danforth, J.M., Burdick, M.D. and Strieter, R.M.: Effects of ambient oxygen tension on the expression of tumor necrosis factor and macrophage inflammatory protein-1 alpha from murine alveolar macrophages. Clin. Res. 41:689A, 1993.
9. Koch, A.E., Kunkel, S.L., Harlow, L.A., Mazarakis, D.D., Haines, G.K., Burdick, M.D., Pope, R.M., Walz, A. and Strieter, R.M.: Epithelial neutrophil activating peptide-78: A chemotactic cytokine for neutrophils in arthritis. Arthritis and Rheumatism 36:S175, 1993.
10. Koch, A.E., Kunkel, S.L., Harlow, L.A., Mazarakis, D.D., Haines, G.K., Burdick, M.D., Pope, R.M. and Strieter, R.M.: Macrophage inflammatory protein-1 alpha: A chemoattractant for monocytes in arthritis. Arthritis and Rheumatism. 36:S175, 1993.
11. Colletti, L.M., Kunkel, S.L., Burdick, M.D., Walz, A. and Strieter, R.M.: Tumor necrosis factor triggers release of epithelial neutrophil activating protein which plays a role in lung injury following hepatic ischemia-reperfusion. 27th Annual Association for Academic Surgery, Hershey, Pennsylvania, November, 1993.
12. Kunkel, S.L., Polverini, P. and Strieter, R.M.: The role of chemokines in leukocyte recruitment, wound repair, and healing. Keystone Symposium on Acute Inflammation Response, Keystone, Colorado, February, 1994.

13. Donnelly, S.C., Strieter, R.M., Kunkel, S.L., Walz, A., Steedman, D., Grant, I.S., Pollok, A.J., Carter, D.C. and Haslett, C.: Chemotactic cytokines in the established adult respiratory distress syndrome and at-risk patients. Chest 105:98S-99S, 1994.
14. Smith, D.R., Polverini, P.J., Kunkel, S.L., Orringer, M.B., Whyte, R.I., Burdick, M.D., Wilke, C.A. and Strieter, R.M.: The role of interleukin-8 in human bronogenic carcinoma angiogenesis. Am. Respir. Crit. Care Med. 149:A171, 1994.
15. Lukacs, N.W., Kunkel, S.L., Burdick, M.D. and Strieter, RM.: The role of MIP-1 alpha in esinophil recruitment into airway of asthmatic mice. Am. Respir. Crit. Care Med. 149:A529, 1994.
16. Danforth, J.M., Strieter, R.M., Kunkel, S.L., Arenburg, D.A., VanOtteren, G.M. and Standiford TJ.: Lipoteichoic acid induces the gene expression of chemotactic cytokines from human blood monocytes. Am. Respir. Crit. Care Med. 149:A871, 1994.
17. VanOtteren, G..M., Standiford, T.J., Kunkel, S.L., Danforth, J.M., Burdick, M.D. and Strieter, R.M.: Alterations in ambient oxygen tension modulate the expression of tumor necrosis factor and macrophage inflammatory protein 1 alpha from murine alveolar macrophages. Am. Respir. Crit. Care Med. 149:A1100, 1994.
18. VanOtteren, G.M., Strieter, R.M., Kunkel, S.L., Danforth, J.M., Burdick, M.D. and Standiford, T.J.: Compartmentalized expression of RANTES in a murine model of endotoxemai. Am. Respir. Crit. Care Med. 149:A863, 1994.
19. Wilborn, J.W., Burdick, M.D., Evanoff, H.L., Strieter, R.M., Kunkel, S.L and Peters-Golden, M.: Fibroblasts isolated from patients with idiopathic pulmonary fibrosis have a diminished capacity to synthesize prostoglandin E2. Am. Repsir. Crit. Care Med. 149:A628, 1994.
20. Magliato, K.E., Swiderski, D.L., Kunkel, S.L., Wilke, C.A., Burdick, M.D., Deeb, G.M. and Strieter, R.M.: Increased chemokine expression in response to reimplantation: Rat lung transplantation. FASEB J. 8:A663, 1194.
21. Burdick, M.D., Polverini, P.J., Kunkel, S.L., Orringer, M.B., Whyte, R.I., Wilke, C.A. and Strieter RM.: Human bronchiogenic carcinoma angiogenisis is mediated by tumor-derived interleukin-8. FASEB J. 8:A146, 1994.
22. Colletti, L., Kunkel, S.L., Burdick, M.D., Walz, A. and Strieter, RM.: TNF triggers the release of ENA-78 which mediates liver injury following ischemia-reperfusion (I/R). FASEB J. 8:A663, 1994.
23. Scales, W.E., Campbell, D.A., Strieter, R.M. and Kunkel, S.L.: Hepatic and pulmonary pathophysiology associated with common bile duct ligation in the rat. FASEB J. 8:A126, 1994.
24. Allen, R., Kunkel, S.L., Lukacs, N.W., Evanoff, H., Sherman, J., Shaklee, C. and Strieter, RM.: TH1/TH2 cytokine-induced expression of MIP-1 alpha/beta chemokines from pulmonary vascular smooth muscle cells. FASEB J. 8:A802, 1994.
25. Kunkel, S.L., Strieter, R.M., Chensue, S.W., Evanoff, H.L. and Lukacs, N.W.: The interaction of TNF and ICAM-1 in pulmonary granuloma formation. FASEB J. 8:A802, 1994.
26. Kasama, T., Strieter, R.M., Lukacs, N.W., Burdick, M.D. and Kunkel, S.L.: Regulation of neutrophil-derived chemokine expression by interleukin 10. FASEB J. 8:A135, 1994.
27. Lukacs, N.W., Strieter, R.M. and Kunkel, S.L.: Increased airway resistance in the late phase of airway inflammation correlates with esinophil influx and is mediated by IL-4 production in a murine model of asthma. FASEB J. 8:A764, 1994.

28. Walz, A., Strieter, R.M., Kunkel, S.L. and Schnyder-Candrian, S.: Type I and type II interferons down regulate the production of interleukin-8 and ENA-78 in human monocytes. FASEB J. 8:A267, 1994.
29. Karpus, W.J., Lukacs, N.W., McRae, B.L., Strieter, R.M., Kunkel, S.L. and Miller, S.D.: Treatment of mice with anti-MIP-1alpha prevents PLP peptide induced experimental autoimmune encephalomyleitis. FASEB J. 8:A199, 1994.
30. Nickoloff, B.J., Fivenson, D.P., Kunkel, S.L., Strieter, R.M. and Turka, L.A.: Increased expression of keratinocyte IL-10 in tape stripped skin, poison ivy dermatitis, and Sezary syndrome but not psoriatic plaque skin. Clin. Res. 42:231A, 1994.
31. Lukacs, N.W., Strieter, R.M., Evanoff, H.L., Burdick, M.D. and Kunkel, S.L.: Role of ICAM-1 in the disparate expression of chemokine during monocyte-endothelial cell interactions. Clin. Res. 42:307A, 1994.
32. Colletti, L.M., Kunkel, S.L., Burdick, M.D., Wilke, C.A., Scales, W.E. and Strieter, R.M.: Monocyte chemoattractant protein-1 (MCP-1) is released from cultured hepatocytes and from the liver following hepatic ischemia/repurfusion injury. Clin. Res. 42:306A, 1994.
33. Szekanecz, K., Strieter, R.M., Holloran, M.N., Kunkel, S.L., Burdick, M.D. and Koch, A.E.: Cytokine expression in rat adjuvant induced arthritis. Clin. Res. 42:313A, 1994.
34. Koch, A.E., Kunkel, S.L., Fu, R., Haines, G.K., Burdick, M.D., Harlow, L.A., Pope, R. and Strieter, R.M.: Macrophage inflammatory protein-1beta: A chemokine in arthritis. Clin. Res. 42:314A, 1994.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Supervision of ten postdoctoral fellows (Aron Thall, Ph.D., Peter Smith, Ph.D., Yuko Natsuka, Ph.D., Shunji Natsuka, Ph.D., Petr May, Ph.D., E. Paul Scheidegger, M.D., Kazuhiro Yago, M.D., Daniel Legault, M.D., Steven Domino, M.D., Ph.D., and Hedwig Murphy, M.D., Ph.D.).
B. Lecturer - Postdoctoral Research Training Program.
C. Course Leader, Research Colloquium in Experimental Pathology - Pathology 850 - Genetics and Function of Oligosaccharides.
D. Lecturer - Biochemistry 576 - Membranes and Protein Targeting, 1994. "Mammalian glycosyltransferases and selectin ligand biosynthesis".
E. Member of three Ph.D. thesis committees (Kevin Gersten, Emma Masteller, and Akhilesh Pandey).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Oligosaccharide function during murine embryogenesis". Source of award: Howard Hughes Medical Institute.
B. Principal Investigator, "Molecular biology of human α1,3 fucosyltransferases", NIH GM47455 (25% effort), $72,856/year direct cost, $286,925/four years direct cost, 5/1/92 - 4/30/96.
C. Principal Investigator, "Molecular biology of the human H and Se blood group genes", NIH HL48859 (25% effort), $75,995/year direct cost ($276,544/four years direct cost), 8/1/92 - 6/30/96.
D. Program Project - Project #1 Principal Investigator, "Oligosaccharides as Anti-Inflammatory Agents", NIH AI33189 (15% effort), $125,665/year direct cost ($481,355/four years direct cost), 9/1/92 - 4/30/96.
E. Sponsor, Physician Scientist Award, "Structure-function relationships of fucosyltransferases", Daniel J. Legault, 7/1/94 - 6/30/99.

F. Sponsor, Swiss National Foundation Postdoctoral Fellowship, "Expression cloning of α(2,8)polysialyltransferase in carcinoma cells", Swiss Cancer League, Swiss National Research Foundation, E. Paul Scheidegger, 2/1/93 - 1/31/95.
G. Sponsor, Clinical Investigator Award "Structure and function of recombinant selectin ligands", Hedwig Murphy, 09/01/94 - 08/31/99.
H. Sponsor, Reproductive Scientist Development Program, "Cell surface molecules that mediate blastocyst implantation", Steven Domino, 07/01/94 - 06/30/95.

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.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Resident Selection Committee.
B. Internal Review Committee.

REGIONAL AND NATIONAL:

A. Member, Editorial Board, Journal of Biological Chemistry.
B. Member, Pathobiochemistry Study Section, Division of Research Grants, National Institutes of Health.
C. Board of Directors, Society for Glycobiology.
D. Member, Scientific Advisory Board, The Ara Parseghian Medical Research Foundation (for Niemann-Pick disease type C).
E. Special Study Section for NHLBI - Transfusion Medicine Score, March, 1994.
F. Consulting reviewer for Proc. Natl. Acad. Sci. USA, J. Clin. Invest., Cancer Res., J. Immunol.

V. OTHER RELEVANT ACTIVITIES:

A. Howard Hughes Medical Institute, Associate Investigator.

VI. INVITED LECTURES AND SEMINARS:

1. Mammalian genes that determine cell surface glycosylation phenotype. University of Alabama, Birmingham, Alabama, January, 1995.
2. Mammalian genes that determine cell surface glycosylation phenotype. University of California at San Diego, San Diego, California, April, 1994.
3. Phenotypic consequences of glycosyltransferase gene ablation in the mouse. 1995 Gordon Conference on Glycoproteins and Glycolipids, Oxnard, California, February, 1995.

4. Mammalian fucosyltransferase genes and selectin ligand expression. Genetics Institute, Cambridge, Massachusetts, March, 1995.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Sueyoshi, S., Tsuboi, S., Sawada-Hirai, R., Dang, U-C.N., Lowe, J.B. and Fukuda, M.: Expression of distinct fucosylated oligosaccharides and carbohydrate-mediated adhesion efficiency directed by two different α1,3-fucosyltransferases: Comparison of E- and L-selectin-mediated adhesion. J. Biol. Chem. 269:32342-32350, 1994.
2. Rouquier, S., Lowe, J.B., Fertitta, A.L., Kelly, R.J., Lennon , G.G. and Giorgi, D.: Molecular cloning of a human genomic region containing the H blood group α(1,2)fucosyltransferase gene and two H locus-related DNA restriction fragments. Isolation of a candidate for the human Secretor blood group locus. J. Biol. Chem. 270:4632-4639, 1995.
3. Kelly, R.J., Rouquier, S., Giorgi, D., Lennon, G.G. and Lowe, J.B.: Sequence and expression of a candidate for the human Secretor blood group α(1,2)fucosyltransferase gene (FUT2); homozygosity for an enzyme-inactivating nonsense mutation commonly correlates with the non-secretory phenotype. J. Biol. Chem. 270:4640-4649, 1995.
4. Reguigne-Arnould, I., Couillin, P., Mollicone, R., Faure, S., Fletcher, A., Kelly, R.J., Lowe, J.B. and Oriol R: Relative positions of two clusters of human α-L-fucosyltransferases in 19q (FUT1-FUT2) and 19p (FUT6-FUT3-FUT5) within the microsatellite genetic map of chromosome 19. Cytogenet.Cell Genet. In Press, 1995.
5. Masteller, E., Larsen, R.D., Carlson, L.M., Pickel, J.M., Nickoloff, B., Lowe, J.B., Thompson, C.B. and Lee, K.P.: The selectin ligand sialyl Lewis x is developmentally regulated during chicken B cell development and appears to direct lymphocyte homing to the bursa of Fabricius. Development In Press, 1995.
6. Legault, D.J., Kelly, R.J., Natsuka, Y. and Lowe, J.B.: Human α(1,3/1,4)fucosyltransferases discriminate between different oligosaccharide acceptor substrates through a discrete peptide fragment. J. Biol. Chem. In Press, 1995.
7. Thall, A.D., Maly, P. and Lowe, J.B.: Oocyte Galα1,3Gal epitopes implicated in sperm adhesion to the zona pellucida glycoprotein ZP3 are not required for fertilization in the mouse. J. Biol. Chem. In Press, 1995.
8. Henry, S., Mollicone, R., Lowe, J.B., Samuelsson, B. and Larson, G. A.: Second non-secretor allele of the blood group α(1,2)fucosyltransferase (FUT2). Vox Sang. In Press, 1995.
9. Scheidegger, E.P., Sternberg, L.R., Roth, J. and Lowe, J.B.: A human STX cDNA confers polysialic acid expression in mammalian cells. J. Biol. Chem. In Press, 1995.

ARTICLES SUBMITTED OR IN PREPARATION:

1. Gersten, K.M., Natsuka, S., Trinchera, M., Petryniak, B., Kelly, R.J., Hiraiwa, N., Jenkins, N.A., Gilbert, D.J., Copeland, N.G. and Lowe, J.B.: Molecular cloning, expression chromosomal assignment, and tissue-specific expression of a murine α1,3fucosyltransferase locus corresponding to the human ELAM-1 ligand fucosyl transferase (ELFT/Fuc-TIV). Submitted.

2. Smith, P.L., Gersten, K.M., Petryniak, B., Kelly, R.J., Natsuka, S., Natsuka, Y. and Lowe, J.B.: A murine α(1,3)fucosyltransferase expressed in peripheral lymph node post-capillary venular endothelial cells (high endothelial venules) synthesize candidate oligosaccharide ligands for L-selectin. In preparation.
3. Maly, P., Thall, A., Petryniak, B., Saunders, T., Smith, P.L., Cheng, G., von Andrian, U., Smith, P.L. and Lowe, J.B.: Ablation of the murine Fuc-TVII gene eliminates expression of leukocyte E- and P-selectin ligand activity, and L-selectin ligand in peripheral lymph node high endothelial venules. In preparation.
4. Thall, A., von Andrian, U.H., Cheng, G., Petryniak, B., Camper, S., Saunders, T. and Lowe, J.B.: Robust leukocyte E- and P-selectin ligand expression, but subtle defects in leukocyte rolling, in mice deficient in the ELAM ligand fucosyltransferase (ELFT, Fuc-TIV). In preparation.
5. Hiraiwa, N., Domino, S. and Lowe, J.B.: Structure and tissue-specific expression of a murine α(1,2)fucosyltransferase gene. In preparation.
6. Hiraiwa, N., Domino, S,, Saunders, T, and Lowe, J.B.: Dominant pre-implantation lethality in mice directed by aberrant expression of an α(1,2)fucosyltransferase cDNA. In preparation.

BOOKS AND CHAPTERS IN BOOKS:

1. Lowe, J.B.: Oligosaccharide-dependent mechanisms of leukocyte adhesion, in, Zetter, B.R. (ed), Homing Mechanisms and Cellular Targeting, JAI Press, New York, 1994.
2. Lowe, J.B.: Carbohydrate recognition in cell-cell interaction. Molecular Glycobiology, in, Fukuda, M. (ed), Frontiers in Molecular Biology, Oxford University Press, Oxford, United Kingdom, 1994.
3. Lowe, J.B.: Biochemistry and biosynthesis of ABH and Lewis antigens. Characterization of blood group specific glycosyltransferases, in, Cartron, J-P and Rouger, P. (eds), Molecular Basis of Major Blood Group antigens, in, Cartron, J-P. and Rouger, P. (eds), Blood Cell Biochemistry, Volume 6, Plenum Press, London, 1995.

NICHOLAS W. LUKACS, Ph.D.
RESEARCH INVESTIGATOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. "Immune mechanisms of Disease", Epidemiology 570, Course Instructor, Fall, 1994.
B. Supervised Undergraduate students: Christy Shaklee, Kolby Keifer, Laurel Goldstein, Harold Schok, and Drew Pulan.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Leukocyte recruitment in eosinophilic inflammation", American Lung Association Research Grant, $50,000, 7-1-95 to 6-30-97.
B. Principal Investigator, "Production of chemokines during Monocyte:Endothelial cell interactions", American Heart Association of Michigan Grant-in-Aid, $28,000, 7-1-95 to 6-30-96.
C. Co-Investigator, "The role of chemokines in autoimmune encephalomyelitis", NIH RO1 NS34510-01, with William J. Karpus, Ph.D. Microbiology/Immunology, Northwestern University, Chicago, IL. $582,997, Sept., 1995 to Aug., 1999.

PENDING SUPPORT:

A. Principal Investigator, "Role of C-C chemokines in eosinophil airway inflammation", R-29 FIRST Award, National Institutes of Health.

PROJECTS UNDER STUDY:

A. Regulation of cytokine production during eosinophilic airway inflammation.
B. Role of mast cells in chronic inflammation.
C. Regulation of chemokine production during cell-to-cell interactions.
D. Role of chemokines in autoimmune responses.
E. Adhesion molecules in chronic inflammatory responses.
F. Role of stem cell factor (SCF) in acute and chronic inflammation.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None.

REGIONAL AND NATIONAL:

A. Reviewer for the following Journals:
   1. American Journal of Pathology.
   2. Journal of Immunology.
   3. American Journal of Respiratory Cell and Molecular Biology.
   4. Infection and Immunity.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Cell-mediated immune responses, Concordia College, Department of Biology. September, 1994.
2. The role of cytokines in eosinophilic airway inflammation. New approaches for the treatment of allergic diseases and asthma, Boston, Massachusetts, November 14, 1994.
3. Cytokine activation in allergic airway inflammation, Miles Corp., New Haven, Connecticut, January 10, 1995.
4. The role of chemokines during inflammatory diseases, British Immunology Society, March 29, 1995.
5. The role of chemokines in allergic airway inflammation, International Chemokine Meeting. Bath, England, June 29th, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERREED JOURNALS:

1. Lukacs, N.W., Kunkel, S.L., Strieter, R.M. and Chensue, S.W.: The role of chemokines in S. mansoni granuloma formation. Parasitol. Today 10:322, 1994.
2. Smith, R.E., Strieter, R.M., Phan, S.H., Lukacs, N.W., Huffnagle, G.B., Wilke, C.A., Burdick, M.D., Lincoln, P., Evanoff, H. and Kunkel, S.L.: Production and function of murine macrophage inflammatory protein-1a in bleomycin-induced lung injury. J. Immunol. 153:4704-4712, 1994.
3. Chensue, S.W., Warmington, K.S., Lukacs, N.W., Burdick, M.D., Strieter, R.M. and Kunkel, S.L.: Monocyte chemotactic protein (MCP-1) expression during schistosome egg granuloma formation: Sequence of production, localization, and endogenous regulation. Am. J. Pathol. 146:130-138, 1994.
4. Strout, R.G., Alroy, J., Lukacs, N.W., Ward, H.D. and Pereira, M.E.: Developmentally regulated lectins in Eimeria species and their role in avian coccidiosis. J. Parasit. 80:946-951, 1994.

5. Lukacs, N.W., Strieter, R.M., Shaklee, C.L., Buridick, M.D., Chensue, S.W. and Kunkel, S.L.: Macrophage inflammatory protein 1 a influences eosinophil recruitment in antigen-specific airway inflammation. Eur. J. Immunol. 25:245-251, 1995.
6. Lukacs, N.W., Kunkel, S.L., Allen, R., Evanoff, H., Shaklee, C., Sherman, J., Burdick, M.D. and Strieter, R.M.: Stimulus and cell-specific expression of C-X-C and C-C chemokines by pulmonary stromal cell populations. Am. J. Physiol. 268:856-861, 1995.
7. Lukacs, N.W., Strieter, R.M., Chensue, S.W., Widmer, M. and Kunkel, S.L.: TNFa mediates recruitment of neutrophils and eosinophils during allergic airway inflammation. J. Immunol. 154:5411-5417, 1995.
8. Kasama, T., Strieter, R.M., Lukacs, N.W., Lincoln, P.L., Burdick, M.D. and Kunkel, S.L.: Interferon gamma modulates the expression of neutrophil-derived chemokines. J. Invest. Med. 43:58-67, 1995.
9. Smith, R.E., Strieter, R.M., Zhang, K., Phan, S.H., Standiford, T.J. Lukacs, N.W. and Kunkel, S.L. A role for C-C chemokine in fibrotic lung disease. J. Leuk. Biol. 57:782-787, 1995.
10. Kasama, T., Strieter, R.M., Lukacs, N.W., Lincoln, P.M., Burdick, M.D. and Kunkel, S.L.: Interleukin-10 expression and chemokine regulation during the evolution of murine type II collagen-induced arthritis. J. Clin. Invest. 95:2868-2876, 1995.
11. Lukacs, N.W., Strieter, R.M. and Kunkel, S.L.: Cytokine induced allergic airway inflammation. Am. J. Resp. Cell Mol. Biol. 13:1-6, 1995.
12. Standiford, T.J., Strieter, R.M., Lukacs, N.W. and Kunkel, S.L.: Neutralization of IL-10 Increases lethality in endotoxemia: Cooperative effects of macrophage inflammatory protein-2 and tumor necrosis factor. J. Immunol., In Press.
13. Lukacs, N.W., Strieter, R.M., Elner, V., Evanoff, H., Burdick, M.D. and Kunkel, S.L.: Production of chemokines, IL-8 and MCP-1, during monocyte:endothelial cell interactions is induced via matrix protein interactions. Blood, In Press.

BOOKS/CHAPTERS IN BOOKS

1. Kunkel, S.L., Lukacs, N.W., and Strieter, R.M.: Chemokines and their role in human disease. Agents and Actions, In Press, 1994.
2. Strieter, R.M., Lukacs, N.W. and Kunkel, S.L.: 1995. Role of adhesion molecules and cytokines in experimental lung transplantation, in, Ward, P.A. (ed), Adhesion Molecules and the Lung, Marcel Dekker, Inc., New York, New York, 1995.
3. Lukacs, N.W., Strieter, R.M., Standiford, T.J. and Kunkel, S.L.: Characterization of chemokine function in animal models of diseases. Immunomethods, In Press, 1995.
4. Lukacs, N.W. and Chensue, S.W.: The role of chemokines in granulomatous diseases, in, Strieter, R.M. and Koch, A. (eds) Chemokines in Disease, In Press, 1995.

ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFFEREED JOURNALS.

1. Lukacs, N.W., Kunkel, S.L. and Strieter, R.M.: Administration of soluble TNF receptor blocks neutrophil leukocyte infiltration in allergic airway inflammation. Midwest AFCR annual meeting. September, 1994.

2. Lukacs, N.W., Strieter, R.M., Evanoff, H.E., Burdick, M. and Kunkel, S.L.: Regulation of chemokine production during monocyte-endothelial cell interactions. International Cytokine, October, 1994.
3. Kunkel, S.L., Lukacs, N.W., Kasama, T. and Strieter, R.M.: Cytokine regulation of murine type II collagen-induced arthritis: Role of chemokines and interleukin 10. Exp. Biol. 1995.
4. Lukacs, N.W., Strieter, R.M., Lincoln, P. and Kunkel, S.L.: Role of c-kit ligand in allergic airway eosinophilia. Exp. Biol. 1995.
5. Goldstein, L.A., Lukacs, N.W., Kunkel, S.L., Evanoff, H.L. and Strieter, R.M.: IL-8 and MCP-1 production in eosinophilic leukemic cell line, EOL-1. Exp. Biol. 1995.
6. Kunkel, R.G., Strieter, R.M., Kunkel, S.L., Evanoff, H.L. and Lukacs, N.W.: Pulmonary mast cell-derived chemokines. Exp. Biol. 1995.
7. Karpus, W.J. and Lukacs, N.W.: The role of chemokines in oral tolerance: Abrogation of nonresponsiveness by treatment with anti-monocyte chemotactic protein-1 (MCP-1). New York Academy of Science. 1995.
8. Lukacs, N.W., Strieter, R.M., Lamm, W., Kunkel, S.L. and Albert, R.: Increased airway reactivity correlates with neutrophil, not eosinophil, infiltration into BAL during allergic airway inflammation. Amer. Thoracic. Soc. 1995.

KENNETH D. MCCLATCHEY, M.D., D.D.S.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Surgical Pathology, consultant on all head and neck pathology cases, 1983-present.
B. Autopsy, 1983-present:
   1. Consultant on forensic odontology cases.
   2. Assistant Medical Examiner, Washtenaw County.
C. Director of Clinical Microbiology\Virology Laboratory, 1978-present.
D. Ann Arbor Veterans Administration Medical Center - monthly consultant, 1978-present.
E. Associate Chief of Clinical Affairs, 1990-present.
F. Staff, Oral Pathology Laboratory, School of Dentistry, 1973-present.
G. Professor, Department of Otorhinolaryngology, 1991-present.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Pathology 630/580/631; Course Director, 1983-present.
B. Otorhinolaryngology Pathology 856, Director, 1979-present.

III. RESEARCH ACTIVITIES:

A. Consultant, Impact of Follow-Up on Control of High Blood Pressure and Cholesterol. Principal Investigator: Andrea Foote, Ph.D., Institute of Labor and Industrial Relations, The University of Michigan, 1988-present.
B. Co-Principal Investigator, "Screening of Papa Smears Using Fluorescently Labeled Markers;" Principal Investigator, Daisy S. McCann, Ph. D., McCann Associates, Wayne, MI, 1993-94.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Clinical Microbiology/Virology Laboratory, 1978-present.

MEDICAL SCHOOL/HOSPITAL:

A. Medical Liability Review Committee, 1992-present.
B. Member, Patient Care Advisory Committee, The University of Michigan Hospitals, 1989-present.
C. Member, Technical Advisory Committee, State of Michigan, Department of Health, Bureau of Laboratory and Epidemiological Services, 1987-present.
D. Chairman, Standardization and Product Evaluation Committee (SPEC), The University of Michigan Medical Center, 1991-present.
E. Associate Chief of Clinical Affairs, The University of Michigan Hospitals, 1990-1995.

F. Member, Executive Committee on Clinical Affairs, The University of Michigan Medical Center, 1990-1995.
G. Vice Chairman, Claims Control Committee, The University of Michigan Hospitals, 1990-1995.
H. Clinical Practice Work Group, University of Michigan, 1993-present.
I. Health Services Research Coordinating Committee, University of Michigan, 1993-present.

REGIONAL AND NATIONAL:

A. College of American Pathologists.
   1. Member, Standards Committee, 1986-present.
   2. Council on Scientific Affairs, 1987-present.
   3. Chairman, International Committee, 1993-present.
B. National Committee for Clinical Laboratory Standards.
   1. Council of the National Reference System for the Clinical Laboratory, 1983-present.
   2. International Relations Committee, member, 1988-present.
   3. Committee on Standardization of the PAP Technique, chairman, 1988-present.
   4. Committee on Standardization of FNA Technique, Chairman, 1992-present.
   5. Area Committee on Alternate Site Testing, member, 1993-present.
   6. Subcommittee on Point of Care Testing, member, 1993-present.
   7. Member, Board of Governors.
C. American Society of Clinical Pathologists.
   1. ASCP Advisory Council, 1984-94.
   2. Contributor, Laboratory Management, Resident Examination, 1992-present.
D. Technical Advisory Committee, State of Michigan Department of Health, Bureau of Laboratory and Epidemiological Services, 1987-present.
E. American Society for Testing Materials (ASTM).
   1. Committee F31 on Health Care Services, member, 1988-present.

INTERNATIONAL:

A. Secretariat, Commission on World Standards of World Association of Societies of Pathology, 1987-present.
B. Chair, Committee on Management of the Blood System, Committee on Blood Safety. Government of Canada, 1993-1995.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Quality Management in the Practice of Laboratory Medicine XI Congress of the Latin American Society of Clinical Pathology, Rio De Janeiro, Brazil, August 24-27, 1994.
2. Medical Record Documentation for Risk and Quality Management. Seminars in Medicine, Component III-IV, University of Michigan Medical School, September 2, 1994.
3. Immunochemical Markers in Head and Neck Cancer, moderator, Fourth Research Workshop on the Biology, Prevention, and Treatment of Head and Neck Cancer, Washington, D.C., September 8-11, 1994.
4. Accreditation in the Clinical Laboratories in the USA, Seminar on Accreditation in Clinical Laboratories, Argentine Society of Clinical Chemistry, Buenos Aries Argentina, September 14-16, 1994.
5. Global Changes in Quality Assurance, International Congress of Environmental and Academic Pathologists, Hong Kong, October 7-15, 1994.

6. Squamous Cell Carcinoma in Respiratory Papillomas Containing High Risk HPV Types, 13th International Papillomavirus Conference, Amsterdam, October 8-12, 1994.
7. Consensus Standardization in Clinical Laboratory Medicine, American Society of State and Territorial Public Health Laboratory Directors, Dearborn, Michigan, October 28, 1994.
8. Productivity Management, Joanne Loring Barker Memorial Seminar, Management Topics in Blood Banking, Ann Arbor, MI, December 12, 1994.
9. Quality Assurance in Blood Banking, Ontario Society of Blood Banks, Toronto, Ontario March 25, 1995.

VI. PUBLICATIONS

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Esclamado, R.M., Disher, M.J., Ditto, J.L., Rontal, E. and McClatchey, K.D.: Laryngeal liposarcoma. Archives of Otolaryngology - Head & Neck Surgery 120:422-426, 1994.
2. Sassler, A.M., McClatchey, K.D., Wolf, G.T., Fisher, S.G. and the Laryngeal Cooperative Study Group. Eosinophilic infiltration in advanced laryngeal squamous cell carcinoma. Laryngoscope 105:1-4, 1995.

ARTICLES SUBMITTED FOR PUBLICATION

1. Beck, J.E., Carey, T.E. and McClatchey, K.D. Identification of HPV6 in Inverted Papilloma Arising in a Renal Transplant Recipient. Submitted for publication-Head and Neck Surg, July, 1994.
2. Hietanen, S.H., Kurvinen, K., Syrjänen, K., Grénman, S., Carey, T.E., McClatchey, K.D. and Syrjänen, S. Mutation of tumor suppressor gene p53 is frequently found in vulvar carcinoma cells. Submitted for publication, September 1994.
3. Beck, J.C., McClatchey, K.D., Lesperance, M.M., Esclamado, R.M., Carey, T.E. and Bradford, C.R. HPV types important in progression of inverted papilloma. Submitted for publication, Otolaryngology Head and Neck Surgery February, 1995.
4. Garetz, Susan L., Hartshorn, Duane L., McClatchey, K.D., Wiatrak, B.J. and Terrell, J.E. Benign pseudotumor of the larynx. Head & Neck Surgery June, 1995.

BOOKS AND CHAPTERS IN BOOKS

1. Travers, E.M. and McClatchey, K.D.: Laboratory Management in, McClatchey, K.D., Clinical Laboratory Medicine, Williams & Wilkins, Baltimore, Maryland, 1994.
2. Contributor, Dybkaer, R., McQueen, M.J., Rej. R. and Wilde, C.E.: Continuous Quality Improvement in Clinical Laboratories, COLABIOCLI, Mexico City, Mexico, 1194.

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

1. Bradford, C.R., Wolf, G.T., Fisher, S.G. and McClatchey, K.D.: Prognostic importance of surgical margins in advanced laryngeal squamous varcinoma. IV International Head & Neck Conference, Arlington, Virginia, September, 1994.
2. Boyd, C.M., Bradford, C.R., McClatchey, K.D. and Hoffman, H.T.: Histologic and immunohistologic correlations in metastatic basal cell carcinoma of the head and neck. IV International Head & Neck Conference, Arlington, Virginia, September,1994.
3. Beck, J.C., Bradford, C.R., Terrell, J.E., McClatchey, K.D. and Carey, T.E.: Identification of HPV 6 in inverted papilloma arising in a renal transplant recipient. International Human Papilloma Virus Conference, Amsterdam, October, 1994.

4. Beck, J.C., McClatchey, K.D., Lesperance, M.M., Esclamado, R.M. and Carey, T.E. and Bradford, C.R.: Presence of human papillomavirus predicts recurrence of inverted papilloma. 1994 Academy of Otolaryngology-Head and Neck Surgery Foundation Annual Meeting, San Diego, California, September, 1994.
5. Bradford, C.R., Wolf, G.T., Fisher, S.G. and McClatchey, K.D.: Prognostic importance of surgical margins in advanced laryngeal squamous carcinoma. Fourth Research Workshop on the Biology, Prevention, and Treatment of Head and Neck Cancer, Crystal City, Virginia, September, 1994.
6. Bradford, C.R., Poore, J., Wilson, M., Carey, T.E., McClatchey, K.D. and Wolf, G.T.: Biologic markers which predict response to chemotherapy in head and neck cancer, Crystal City, Virginia, September, 1994.
7. Moore, C.E., McClatchey, K.D., Wiatrak, B.J., Koopman, C.F., Bradford, C.R., Thomas, G. and Carey, T.E.: Squamous cell carcinoma in respiratory papillomas containing high risk HPV types. 13th Annual Papilloma Conference, Amsterdam, October, 1994.
8. DeBusscher, J.H., Hankerd, R.E. and McClatchey, K.D.: Instability of low-positive and indeterminant results using *Clostridium difficile* toxin A detection kits. 95th General Meeting, American Society for Microbiology, Washington, D.C., March, 1995.
9. Hertz, H.S., Passey, R.B., Gavan, T.L., Graham, G.A., McClatchey, K.D., Moran, R.F., Rand, R.N., Rictchie, R.F., Schaffer, R., Simson, E. and Vanderlinde, R.E.: Sourcebook of Reference Methods, Materials, and Related Information for the Clinical Laboratory; Proposed Guideline, Vol 14, No. 1 (NCCLS Publication NRSCL12-P). National Committee for Clinical Standards, Villanova, Pennsylvania, 1994.

PAUL E. McKEEVER, M.D., Ph.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Daily surgical neuropathology and electron microscopic neuropathology - four months.
B. Consultations on surgical neuropathology from other hospitals.
C. Weekly Brain Tumor Board, review of neurosurgical, neuroradiologic, neuropathologic and clinical-pathologic correlation - six months.
D. Diagnostic neuropathology consultant, Veterans Administration Hospital - four months.
E. Examination of autopsy neuropathologic material - staff rotation and consults to faculty.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Neuroscience Sequence, Neuropathology for Second Year Medical Students.
B. House Officers:
   1. Individual daily instruction of Pathology House Officers over microscope.
   2. Review of neuropathologic postmortem material - staff rotation and consults to residents.
   3. Review all neurosurgically removed material in this hospital in CME-approved biweekly conference - six months.
   4. Shared consultations in conference.
   5. Invited presentations of neuropathologic observations at joint clinical conferences.
   6. Pathology Resident's monthly Neuropathology Conference - four months.
C. Two Pathology House Officers: Scott Silveira and Walter Henricks, and one Neurosurgery House Officer, Michael Polinsky: One month electives in neuropathology.
D. Teach laboratory techniques to Neurohistologists and Research Staff.

REGIONAL AND NATIONAL:

A. Nelson, J.S. and McKeever, P.E.: Clinical Neuropathology. Laser videodisk medical education reference, (in press).
B. 33rd Faculty Annual AFIP Neuropathology Review, Armed Forces Institutes of Pathology, New Orleans, Louisiana.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-Investigator, "Antimetabolite Selectivity: Regional Treatment and Modulation," National Institutes of Health Program Project, NIH CA-42761-04, 1 August 1993 - 31 July 1996.
B. Co-Investigator, "PET Study of Biochemistry and Metabolism of the CNS," (Program Title). "Glioma Imaging with Benzodiazepine Analogs." (Section Title), National Institute of Health Program Project NS-15655, 1 December 1989-30 November 1994.

C. Co-Investigator, "PET, Growth Kinetics and Neuropathology of Brain Tumors," National Institutes of Health Grant, NIH, CA54104, 1 May 1991-30 April 1995.

PROJECTS UNDER STUDY:

A. Glioma tissue marker potential diagnostic and prognostic value with Drs. Mila Blaivas, Thomas W. Glover, David Gordon, Harry S. Greenberg, Robert Jones, Larry Junck, Anthony A. Killeen, Hernando Mena, James S. Nelson, Donald Ross, Susan Sheldon, Myla Strawderman, Jeffrey M. Trent and Sharon W. Weiss. Submitted to NCI.
B. Growth, spread and antigenicity of ENU-induced gliomas in rats with Constance D'Amato and Dr. Terry Hood, submitted to J. Neuro-oncology.
C. Quantitative analysis of DNA in fresh and cultured cells of brain tumors, with Drs. Karin Muraszko, Donald Ross, William Chandler and James Varani.
D. Extracellular matrix products and plasminogen activators of gliomas with Drs. James Varani, Robert Sitrin, Dario Caccamo and Suzanne Fligiel.
E. Magnetic resonance diffusion and cross relaxation of brain tumors with Drs. James Brunberg, Thomas Chenevert and Brian Ross.
F. Characterization of Rosai-Dorfman disease in brain with Drs. Michael Boland and Karin Muraszko.
G. Combined ultrastructural and karyotypic analysis of the VX-2 tumor with Dr. Thomas E. Carey, submitted to Int. J. Cancer.
H. Viral vectors in glioma therapy with Drs. Julian Hoff, Brian Ross and Donald Ross.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chief, Section of Neuropathology.
B. Member, Photography Committee.
C. Member, Immunoperoxidase Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Organization and scheduling of Pathology, Neurology, Neuroradiology and Neurosurgery House Officer Neuropathology teaching conferences, individual instruction and consultation review.
B. Organization of call logistics, specimen handling, and schedules for coverage of diagnostic 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, Radiation Oncology, Neuro- oncology & Neuroradiology.
E. Quality control of microscopic, ultrastructural and immunodiagnostic neuropathology. This included scheduled twice monthly QA/QC meetings and various ad hoc reviews requested by faculty.

REGIONAL AND NATIONAL:

A. Primary Review Pathologist, Children's Cancer Study Group CCG 9891 nationwide study of childhood low grade gliomas.
B. Reviewer for various pathology, neuroscience and neuro-oncology journals.
C. M-Labs Neuropathology Services.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

A. Faculty of Graduate Program of Department of Pathology.
B. Member of the University of Michigan Cancer Center.
C. Member, International Academy of Pathology, 1972--.
D. Member, Alpha Omega Alpha, Eta Chapter, 1972--.
E. Member, American Association of Neuropathologists, 1978--.
F. Member, Society of Neuroscience, 1983--.
G. Member, American Association of Pathologists, 1984--.
H. Member, Children's Cancer Study Group, 1985--.
Pathology Committee, 1989--.
I. Member, Histochemical Society, 1989--.
Councilor, 1994--.
J. Member, Constitution Committee, American Association of Neuropathologists, 1990- .

INVITED LECTURES/SEMINARS:

1. Chairperson, scientific session on brain tumors, American Association of Neuropathologists, and International Society of Neuropathologists, Toronto, Ontario, 1994.
2. Chairperson, scientific session, Brain tumors, United States and Canadian Academy of Pathology, Toronto, Ontario, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Sweasey, T.A., Brunberg, J.A., McKeever, P.E., Sandler, H.M. and Chandler, W.F.: Cystic cervical intramedullary ependymoma with previous intracyst hemorrhage: MR imaging at 1.5T. J. Neuroimaging 4:11-113, 1994.
2. Caccamo, D., Keohane, M.E. and McKeever, P.E.: Plasminogen activators and inhibitors in gliomas: An immunohistochemical study. Modern Pathology 7:99-104, 1994.
3. Meyer, J.R., Quint, D.J., McKeever, P.E., Boland, M. and Ross, D.A.: Giant Rathke's cleft cyst. Am. J. Neuroradiol.. 15:533-536, 1994.
4. Greenberg H.S., Chandler W.F., Ensminger W.D., Sandler, H., Junck, L., Page, M.A., Crane, D., McKeever, P.E., Tankanow, R. and Bromberg, J.: Radiosensitization with carotid intra-arterial bromodeoxyuridine ± 5-fluorouracil biomodulation for malignant gliomas. Neurology 44:1715-1720, 1994.
5. McKeever, P.E., Varani, J., Papadopoulos, S.M., Wang, M. and McCoy, J.P.: Products of cells from gliomas: IX. Evidence that two fundamentally different mechanisms change extracellular matrix expression by gliomas. J. Neuro-Oncol. 1995, In Press.
6. Roberson, P.L., Ten Haken, R.K., McKeever, P.E. and Ensminger, W.D.: Nonuniform liver dose for yttrium-90-microsphere therapy in a rabbit model. J. Nucl. Med., In Press.
7. Levy, R.A., Allen, R. and McKeever, P.E.: Pleomorphic xanthoastrocytomas presenting with massive intracranial hemorrhage. Am. J. Neuroradiol.., In Press.
8. Brunberg, J.A., Chenevert, T.L., McKeever, P.E., Ross, D.A., Junck, L.R., Muraszko, K.M., Dauser, R., Pipe, J.G. and Betley, A.T.: *In vivo* MR determination of water diffusion coefficients and diffusion anisotrophy: Correlation with structural alterations in gliomas of the cerebral hemispheres. Amer. J. Neuroradiol. 16:361-371, 1994.
9. McKeever, P.E., Dennis, T.R., Burgess, A.C., Meltzer, P.S., Marchuk, D.A. and Trent, J.M.: Chromosomal breakpoint at 17q11.2 and insertion of DNA from three different chromo- somes in a glioblastoma with exceptional GFAP expression. Cancer Genet. Cytogenet, In Press.

BOOKS/CHAPTERS IN BOOKS:

1. McKeever, P.E. and Lloyd, R.V.: Pituitary adenomas and related lesions, in, Garcia, J.H. (ed), Diagnostic Neuropathology, Vol IV, Mosby, In Press.
2. McKeever, P.E. and Blaivas, M. : The brain, spinal cord, and meninges, in, Sternberg. S.S., Antonioli, D.A., Carter, D., Mills, S.E., and Oberman, H.A. (eds), Diagnostic Surgical Pathology, Raven Press, Ltd., New York, New York, pp. 409-492, 1994.
3. McKeever, P.E.: Molecular neuropathology in brain tumor diagnosis, in, Kornblith, P.L., Walker, M., and Korn, S.E. (eds), Advances in Neuro-Oncology, Vol 2, Futura, San Diego, California.
4. McKeever, P.E.: Glial Cell Pathology, in, Smith, B.H. and Adelman, G. (eds), Encyclopedia of Neuroscience, Elsevier, Amsterdam, In Press.

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

1. Junck, L., McKeever, P.E., Ross, D.A., Brunberg, J.A., Greenberg, H.S., Betley, A.T. and Grube, S.: Glucose metabolism and cell kinetics in untreated human gliomas studied *in vivo*. Amer. Acad. of Neurology, 1994.
2. McKeever, P.E., Junck, L., Ross, D.A., Brunberg, J.A., Bromberg, J., Wang, M., Onda, K., Grube, S.V. and Greenberg, H.S.: Comparison of MIB-1, BUDR and PCNA labeling index markers of cellular proliferation in grading astrocytic gliomas. Brain Pathol. 4:412, 1994.
3. McKeever, P.E. and Wang, M.: Numerical variations in chromosome specific satellite DNA distinguish glioblastoma, lower grade gliomas and brain. Brain Pathol. 4:412, 1994.
4. McKeever, P.E., Dennis, T.R., Burgess, A.C., Meltzer, P.S. and Trent, J.M.: Chromoso- mal breakpoint at 17q11.2 and DNA insertion near the NF-1 and c-erB-2 gene loci corresponds with expression of glial fibrils in a glioblastoma. FASEB J. 8:A392, 1994.
5. McKeever, P.E., Lawrence, T.S., Davis, M.A., Genik, S.J. and Ensminger, W.D.: Quantitative immunohistochemistry (QIHC) reveals topographic differences in iodode- oxyuridine (IdUrd) uptake by tumor cells. J. Histochem. Cytochem. 42:978; 1994.
6. McKeever P.E. and Wang M.: Internal standardization of archival tissue sections enables evaluation of chromosomal abnormalities by *in situ* hybridization. United States and Canadian Academy of Pathology Meeting, 1995.
7. Junck L., Strawderman M., Ross D.A., Betley, A.T., Brunberg, J.A., Greenberg, H.S. and McKeever, P.E.: Prognostic value of PET-FDG scans in untreated gliomas. Neurol. 45: A387, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

CLINICAL RESEARCH-RELATED ACTIVITIES:

A. The NIH proposal for studying the effects of clinical depression on human reproduction reported last year with a rating of 128 and 6.8 percentile has still not been funded. The NIMH is having particularly difficult times this year, but we have learned that it is likely that it will now be funded with funds released at year's end.

B. We have submitted a proposal to the NIA on endocrine changes associated with the menopause and aging of women. It was site visited and a decision is expected at the end of this month.

C. The system for generating protocols and bar-coded labels to facilitate analysis of samples for a large clinical study involving infertility has been improved and is being used extensively.

D. Working with a mathematician, Steve Pincus, we have demonstrated that a novel method for assessing regularity in time-series data, estimation of approximate entropy, can reveal important differences in patterns of secretion of gonadotropins in sheep. Based on these observations, we have developed a clinical protocol and obtained approval for using it by the IRB and with CRC facilities.

II. TEACHING ACTIVITIES:

A. Lectures:
   1. Served as a primary instructor for a full semester four hours/week laboratory course for dental and health professional students, Pathology 630/631, Fall 1994.
   2. Taught portion of Cellular Biotechnology Training Program 504, Winter 1995 (six hours lectur: Intercellular Communication).

B. Graduate Students:
   1. Karen Heinze, Bioengineering - Doctoral Student transferred supported on NCIR Grant.
   2. William Lemon, Bioengineering, supported on Cellular Biotechnology Training Grant.

C. Undergranduate Students:
   1. Aiman Abbarah, Pre-Medical Student.
   2. Jasmin Ghuznavi, Pre-Medical Student.
   3. Mona Prasad, Pre-Medical Student.

D. Dissertation Committees:
   1. Jeaneatte Buckwalter, Chemistry, Ph.D., 1994.
   2. Michael Poplawski, Electrical Engineering and Computer Science, Current.
   3. David Mauger, Biostatistics, Current.

E. Worked with Visiting Scientist:
   1. Bent G. Boving, Ph.D., Extramural Associate, Department of Embryology, Carnegie Institute of Washington.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIH, P30 HD 18258, A.R. Midgley, Principal Investigator, Center for the Study of Reproduction, 04/01/94 - 03/31/99, $2,583,244, 15%, 04/01/95 - 03/31/96, $509,675.

B. NIH, U54-HD 29184-04, N.Reame, Principal Investigator, National Center for Infertility Research at Michigan, 09/01/91 - 08/31/96, $5,873,767, 40%, 09/01/94 - 08/31/95, $1,206,578.

C. NIH, 1RO1-MH 50030, E.Young, Principal Investigator, Stress and Reproductive Hormones in Depressed Women, 08/01/94 - 07.31.95, $661,569, 10%, 08/01/94 - 07/31/95, $200,215.

D. NIH, U01-AG 12495, A.R. Midgley, Principal Investigator, Menopause and Aging in Women: Central Laboratory, 10/01/94 - 09/30/99, $1,465,338, 20%, 10/01/94 - 09/30/95, $278,005.

E. NIH NIMH/NIDDK, E.Young, Principal Investigator, Stress and Reproductive Hormones in Depressed Women, 08/01/94 - 07/31/97, $661,569, 5%, 08/01/94 - 07/31/95, $200,215.

F. NIH, T32-HD 07048-20, D.Foster, Principal Investigator, Training Program in Reproductive Endocrinology, 07/01/90 - 06/30/95, $762,838, 5%, (no salary support), 07/01/94 - 06/30/95, $163,846.

PENDING:

A. NIH, T32-HD07048 (Renewal), D. Foster, Principal Investigator, Training Program in Reproductive Endocrinology, 07/01/95 - 06/30/00, $1,733,416, 5%, (no salary suppory), 07/01/95 - 06/30/96, Pending.

B. NIH, V.Padmanabhan, Principal Investigator, Physiologic Relevance of FSH Heterogeneity, 12/01/94 - 11/30/98, $458,782, 5%, 12/01/94 - 11/30/95, Pending.

C. NIH, E. Young, Principal Investigator, Cortisol Feedback in Duirnal Rhythm of HPA Axis, 09/01/95 - 08/31/99, $659,179, 5%, 09/01/95 - 08/31/96, Pending.

D. NIH U01-AG 12495-S1, A.R. Midgley, Principal Investigator, Hormonal Prdictors of Perimenopausal Morbidity-Central Laboratory (LAB), 10/01/94 - 09/30/99, $2,260,106, 20%, 10/01/94 - 09/30/95, $754,468, Pending.

E. Assisted in development of new SBIR grant applications which, if successful, will involve the University as a sub-contracto (Mathematician Entrepreneur Steve Pincus and Judith Erb of Innovation Associates).

SCIENTIFIC COLLABORATIONS:

A. Biological Chemistry and Obstetrics and Gynecology: K.M.J. Menon: Localization and regulation of mRNA for LH receptor in rat granulosa cells.

B. Biostatistics; Morton Brown and Dan Normolle: development and implementation of a means for automating the collection of immunoassay data and organizing it in a distributed database for clinical hormone studies.

C. Electrical Engineering: Rich Brown: (with Mark Meyerhoff) NSF-funded project aimed at developing multisite, antibody-based solid state microelectrodes.

D. Nursing: Nancy Reame: joint involvement in exploring the applicability of our recently developed dimeric inhibin assay with samples from perimemopausal women.

E. Pediatrics: Vasantha Padmanabhan: co-investigator of a project in the NCIR grant and development of a new RO1 grant - concerning the regulation of pituitary gonadotropin secretion.
F. Psychology: Jacquelynne Eccles: Completing a long tern, longitudinal study concerning hormones and behavior in adolescents.
G. Innovation Associates, Ann Arbor, MIichigan, Judith Erb, Immunoassayist: assisted in development of a funded SBIR concerning the development of simplified immunoassays able to evaluate fertility and development of a second funded SBIR.
H. Massachusetts General Hospital: Pat Sluss, Reproductive Biologist: development of assays for inhibin, follistatin and activin.
I. Michigan State University, Animal Science: James Ireland, Reproductive Biologist: development of a solid state, two site chemiluminescence-based immunoassay for inhibin.
J. University of Wisconsin, Madison: Brian Goodman, a biomathematician, is collaborating with our laboratory to apply spectral analysis and convolutional algorithms to model stimulus-response relationships in our perifusion system.
K. Wayne State University, Obstetrics and Gynecology: Kamran Moghissi: Co-Associate Director of the NCIR grant and Key Investigator of one of its projects.
L. Wolpert Polymers, Inc., Southfield, MI 48037: Stephen M. Wolpert, Polymer Chemist formerly with Gelman Sciences and KMS Fusion. Helped him develop an SBIR focused on creating a novel affinity matrix-membrane for immunoassays, blotting experiments, etc.
M. Yale University: Steve Pincus, a mathematician associated with Yale, is collaborating with our laboratory to explore ways in which application of his measure of approximate entropy to reproductive hormones will be useful.

PROJECTS UNDER STUDY:

A. Neuroendocrine causation of infertility; mechanisms controlling pituitary gonadotropin secretion.
B. Dynamics and modes of regulatory communication among cells.
C. Development and utilization of a computer-controlled perifusion system for on-line analysis of cellular responses to pulsatile and other controlled signaling including the development and application of novel immunobiosensors and immunoassays.
D. Application of principles of cellular bioengineering to the growth and function of mammalian cells.
E. Development of novel biosensors and immunoassays.
F. Examination of the relationships between changes in hormones, behavior and peer reactions during pre-adolescent development of children.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Director, Center for the Study of Reproduction.
B. Associate Director, National Center for Infertility Research at Michigan (NCIR).
C. Director, Standards and Reagents Core Facility.
D. Director, Assay Development Core, NCIR.
E. Member, RSP Selection Committee.

UNIVERSITY:

A. Director, Reproductive Sciences Program.
B. Member, Executive Committee, University of Michigan Women's Health Initiative.
C. Member, Scientific Advisory Board, Child/Adolescent Health Behavior Research Center, The University of Michigan, 1991-.
D. Member, Michigan Cancer Center, 1993-.
E. Interviewing candidates for Obstetrics/Gynecology, Internal Medicine, Institute of Gerontology
F. Chair, Facilities Committee and Member, Local Arrangements Committee for 1994 Annual Meeting of the Society for the Study of Reproduction to be hosted by the University of Michigan.
G. Chair, Research Grants Review Committee, Michigan Initiative for Women's Health, 1993-1994.

REGIONAL AND NATIONAL:

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

REPRODUCTIVE SCIENCES PROGRAM:

A. The Reproductive Sciences Program completed its five-year review this past year and the response of the external review team and University administration was highly complimentary.
B. Our NIH P30 Center was reviewed and refunded with the highest priority (1.0%) that we have ever achieved. Six of our seven cores were judged to be Outstanding; the seventh was judged as Excellent.
C. The University's Michigan Initiative for Women's Health, established through the initiative of RSP, is now thriving under the co-chairship of Deborah Oakley and Mary Fran Sowers. Dr. Timothy Johnson, Chair of Obstetrics and Gynecology, is participating actively on its Executive Committee.
D. RSP is hosting two national meetings at the University in July, 1994: the biannual Ovarian Workshop and the annual meeting of the Society for the Study of Reproduction. The former will bring about 200 scientists to the University and the latter will bring about 1000.
E. Between these two meetings RSP is hosting a 25th Anniversary celebration with over 200 anticipated attendees.
F. RSP continued to manage increased regulatory compliance in areas of hazardous wastes and radiochemical safety as mandated by Federal, State and University regulation.
G. RSP hosted its Eighth Annual RSP Poster Day, November 5, 1993 (36 posters presented plus talk by former trainee, Mrinalini Rao).

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Retreat, National Center for Infertility Research at Michigan, Ann Arbor, Michigan, July 12, 1994.
2. Ovarian Workshop, Ann Arbor, Michigan, July 21-23, 1994.
3. 27th Annual Meeting of the Society for the Study of Reproduction, University of Michigan, Ann Arbor, Michigan, July 27-27, 1994.
4. Meeting of Directors of NICHD P30 Centers, Charlottesville,, July 31-August 2, 1994.
5. U01 Perimenopausal Meeting, Bethesda, Maryland, October 9-11, 1994.
6. RSP Poster Day, October 14, 1994.
7. National Cooperative Program for Infertility Research, Ann Arbor, Michigan, October 26-28, 1994.
8. U01 Perimenopausal Meeting, Gaithersburg, Maryland, November 2-4, 1994.
9. Annual Meeting of the Society for Neuroscience, Miami Beach, Florida, November 12-16, 1994.
10. Presented RSP Seminar, "Events and Episodes: Signals or Noise?", November 28, 1994.
11. U01 Perimenopausal Meeting, San Francisco, California, February 20-22, 1995.
12. Collaborated with Pat Sluss, Ann Arbor, Michigan, February 27, 1995.
13. U01 Perimenopausal Meeting, Bethesda, Maryland, April 3-4, 1995.
14. National Cooperative Program for Infertility Research, Ann Arbor, Michigan, April 10-12, 1995.
15. U01 Perimenopausal Meeting, Chicago, Illinois, May 22, 1995.
16. Endocrine Society Meeting, Washington, D.C., June 14-17, 1995.

RELEVANT ACTIVITIES:

A. Developing an immunoassay analysis system that will assist many investigators.
B. Implementing ELISA and chemiluminescence-based, solid state, two-site immunoassays in Standards and Reagents Core as a partial replacement for reaioimmunoassays (and thereby reduction in usage of radioactive isotopies).

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Brand, R.M, Lyons, R.H. and Midgley, A.R.: Understanding the dynamics of cellular responsiveness to modifications of metabolic substrates in perifusion. J. Cell. Physiol. 160:10-16,1994.
2. Brand, R.M., Midgley, A.R. and Williams, W.J.: Convolution: a method for data analysis in perifusion systems. Am. J. Physiol. 267:E759-E768,1994.
3. Peegel, H., Randolph, J.,Jr., Midgley, A.R. and Menon, K.M.J.: In situ hybridization of LH/hCG messenger RNA during hormone-induced down regulation and the subsequent recover in rat corpus luteum. Endocrinol. 135:1044-1051,1994.
4. Khoury, R.H., Wang, Q.F., Crowley, W.F., Jr., Hall, J.E., Schneyer, A.L., Toth, T., Midgley, A.R. and Sluss, P.M.: Serum follistatin levels in women: evidence against an endocrine function of ovarian follistatin. J.Clin. Endo. Metab. 80:1361-1368,1995.
5. Midgley, A.R., Brand, R.M., Favreau, P.A., Boving, B.G., Ghazzi, M.N., Padmanabhan, V., Young, E.Y. and Cantor, H.C.: Monitoring dynamic responses of perifused neuroendocrine tissues to stimuli in real time. Invited review, in, Veldhuis and Johnston (eds), Quantitative Neuroendocrinology, a volume in the series Methods in Neuroscience, In Press, 1995.

6. Dabbs, J.M., Jr., Campbell, B.C., Gladue, B.A., Midgley, A.R., Navarro, M.A., Read, G.F., Susman, E., Swinkles, L.M.J.W. and Worthman, C.M.: Reliability of salivary testosterone measurements: a multicenter evaluation. Clinical Chemistry, In Press, 1995.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Ghazzi, M.N., Wise, K.D., Anderson, D.J. and Midgley, A.R., Jr.: Computer-assisted analysis of single-unit neuronal activity obtained using multichannel microprobes. Submitted for publication.
2. Chazzi, M.N., Wise, K.D., Anderson, D.J. and Midgley, A.R., Jr.: Performance of silicon-based multichannel microprobes for monitoring the activity of neurons in deep brain structures: Characterizing the activity of neurons in the anterior hypothalamus. Submitted for publication.
3. Halberstadt, C.R., Lee, G.M., Palsson, B.O. and Midgley, A.R.: Enhanced antibody productivity in a serum-free, low-protein medium from a long-term hybridoma cell culture using the transtubular reactor. Submitted to Biotech. Progress.
4. Halberstadt, C.R., Palsson, B.O., Midgley, A.R. and Curl, R.L.: Optimization of the transtubular bioreactor for the production of monoclonal antibodies from a hybridoma cell line S3H5/γ2bA2. Submitted.
5. Ulloa-Aguirre, A., Midgley, A.R., Jr., Beitins, I.Z. and Padmanabhan, V.: Follicle stimulating isohormones: Biological characterization, invited review for Endocrine Reviews. Submitted for publication.

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

1. Padmanabhan, V., Van Cleef, J., Favreau, P and Midgley, A.R.: Opposing effects of activin and follistatin on LH and FSH secretion from ovine pituitary cells cultured in vitro. Endocrine Society, Washington, D.C., June 14-16, 1995.
2. McConnell, D.S., Padmanabhan, V., Sluss, P.A., Christman, G.M., Reese, K.A., Wang, Q.F., Smith, P.C., Khoury, R.H. and Midgley, A.R.: A two-site solid phase immunohistochemiluminescent assay for measurement of follistatin in human serum. Endocrine Society, Washington, D.C., June 14-16, 1995.
3. Hu, L., Favreau, P.A., Midgley, A.R. and Padmanabhan, V.: Paracrine control of LH and FSH secretion from ovine pituitary cells by galanin. Endocrine Society
4. Plant, T.M., Padmanabhan, V., McConnell, D.S., Majumdar, S.S., Ishwad, P.C., Winters, S.J. and Midgley, A.R., Jr.: Inhibin in the male rhesus monkey: Discordance between physiological and immunological studies. Endocrine Society, Washington, June 14-16, 1995.
5. Heinze, K., Padmanabhan, V., Favreau, P.A. and Midgley, A.R.: Effects of physiologically relevant variations in GnRH pulse patterns on LH secretion. Society for Study of Reproduction, U.C. Davis, July 10-12, 1995.
6. Sherman, S.S., Neer, R., Greendale, G., Sowers, M.F., Gold, E., Matthews, K., McKinlay, S., Midgley, A.R., Powell, L. and Weiss, G.: A multi-ethnic study of the perimenopausal transition. American Society for Bone and Mineral Research, 1995.
6. Lemon, W.J., Padmanabhan, V., Young, E.A., Favreau, P.A., Pincus, S.M. and Midgley, A.R. Jr.: The shape of LH pulses in the hypophyseal portal blood of ovariectomized Suffolk ewes. 27th Annual Meeting, Society or the Study of Reproduction, July 24-27, 1994.
7. McConnell, D.S., Padmanabhan, V., Pollak, T., Groome, N.P., Ireland, J.J. and Midgley, A.R., Jr.: Development of a two-site solid phase immunochemiluminescent assay for measurement of

dimeric inhibin in biological fluids. 27th Annual Meeting, Society for the Study of Reproduction, July 24-27, 1994.

9. Padmanabhan, V., McConnell, D.S., Reame, N.E., Pollak, T. and Midgley, A.R., Jr.: Release of dimeric inhibin is episodic during luteal phase in women. 50th Annual Meeting, The American Fertility Society, November 5-10, 1994.
10. Midgley, A.R., Jr., Pincus, S.M., Karsch, F.J. and Padmanabhan V.: Approximate entropy statistics reveal non-GnRH-dependent subordinate activity in FSH concentrations in the peripheral and hypophyseal portal circulations of ovariectomized sheep. Annual Meeting, Society for Neuroscience, November 13-18, 1994.
11. Reame, N.E., Padmanabhan, V., McConnell, D.S., Pollak, T., and Midgley, A.R., Jr.: Age-related increases in LH and FSH are not associated with a detectable decline in circulating dimeric inhibin or estradiol in ovulatory women. North American Menopause Society, 1994.

RICHARD A. MILLER, M.D., Ph.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY
RESEARCH SCIENTIST
INSTITUTE OF GERONTOLOGY
RESEARCH SCIENTIST
ANN ARBOR V.A. MEDICAL CENTER

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Graduate Students
   1. Responsible during the current academic year for teaching activities for the following:
      a. Thirteen sessions Pathology 850 (Miller).
   2. Program Director, "Experimental Immunopathology Training Grant."
   3. Ph.D. Dissertation Committees, University of Michigan:
      a. Ann Jackson.
      b. Alex Greenwood.
      c. Lynn Billington.
   4. Ph.D. Dissertation Advisor:
      a. Michael Eisenbraum.
      b. Chris Kirk.
   5. Summer Rotations:
      a. George Kunz, Med I.
      b. Hershell Wallen, MSTP I.

B. Postdoctoral fellows:
   1. Jacek Witkowski, M.D., Ph.D.
   2. Michael Angell, Ph.D.
   3. Nathan Bining, Ph.D.
   4. William Telford, Ph.D.
   5. Gonzalo Garcia, Ph.D.

C. Assistant Research Scientist:
   1. R. Lee Mosley, Ph.D.

D. Visiting Research Scientist
   1. Igor Dozmorov, Ph.D.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Activation Defects in Aging T Cells", NIH AG-09801 (15%), $158,814 direct costs/year, 8/1/90-7/31/95. MERIT award.
B. Principal Investigator, "Immune and Muscle Function Assays as Biomarkers of Aging", NIH AG-11067 (15%), $145,000 direct costs/year, 4/1/93 - 3/31/98.
C. Principal Investigator, "Aging Effects on IL-2 Secreting Helper T Cells", NIH AG-03978 (16%), $149,366 direct costs/year, 8/1/92 - 7/31/95.
D. Principal Investigator, "Genetic Control of Longevity in Mice", NIH AG-11687 (8%), $207,174 direct costs/year, 9/1/93 - 8/31/98.
E. Director, "Core Facility for Aged Rodents", NIH AG-08808 (15%), $64,627 direct costs/year, 9/1/94 - 8/31/99. (Component of Claude Pepper Older Americans Independence Center, J. Halter, Program Director).
F. Director, "Research Development Core", NIH AG-08808 (15%), $155,270 direct costs/year, 9/1/94 - 8/31/99. (Component of Claude Pepper Older Americans Independence Center, J. Halter, Program Director).
G. Project Director, "Prevention of Disease by Immunotonic Agents in Mice", NIH AG-08808 (5%), $50,235 direct costs/year, 9/1/94 - 8/31/99. (Component of Claude Pepper Older Americans Independence Center, J. Halter, Program Director).
H. Program Director, "Research Training in Immunopathology", NIH T32-AI-07413 (5%), $117,126 direct costs/year, 4/1/92 - 3/31/97.
I. Co-Director, "Breast Cancer in Elderly Women", (M. Wicha, PI), NIH/NCI P20-AG13094 (5%), $104,307 direct costs/year, 9/30/94 - 8/31/98.
J. Principal Investigator, "New T Cell Subsets in Aging Mice", Allied Signal Research Award, $50,000 direct costs/year, 1/1/95 - 12/31/96.
K. Course Director, "Summer Training Courses in Experimental Aging Research", NIH/NIA R13-AG12917 (0%), $29,358 direct costs/year, 4/1/95 - 3/31/98.

PENDING:

A. Principal Investigator, "Aging Effects on IL-2 Secreting Helper T Cells", NIH-AG-03978 (16%), $149,366 direct costs/year, 8/1/82 - 7/31/95. [Renewal Pending]
B. Principal Investigator, "Restriction Landmark Genome Scanning for Longevity Assurance Genes", R01-AG1168751 (0%), $23,162 direct costs requested/year, 7/1/95 - 6/30/96.
C. Principal Investigator, "T Cell Subsets Defined by P-glycoprotein in Aging Mice", NIH R01-AG03978 (5%), $177,177 direct costs requested/year, 12/1/95 - 11/30/98.
D. Principal Investigator, "Wild Derived Mouse Stocks: New Models for Aging Research", NIA R01-AG13711 (5%), $187,826 direct costs requested/year, 4/1/96 - 3/31/01.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Committee on Master Planning Analysis.
B. Graduate Education Committee.
C. Qualifying Examination Committee.
D. Research Colloquia, Course Coordinator.
E. Director, Experimental Immunopathology Training Program.

MEDICAL SCHOOL/HOSPITAL:

A. Geriatrics Center: Research Development Core Director.
B. Geriatric Center: Director, Core Facility for Aged Rodents.
C. Member, Geriatrics Center Research Operating Committee.
D. Associate Director for Research, Geriatrics Center.
E. Member, Dean's Immunology Task Force.
F. Member, Cell and Molecular Biology Training Program.
G. Member, Rheumatology Training Program.
H. Co-Director, Breast Cancer in elderly Women Project, University of Michigan Cancer Center.

REGIONAL AND NATIONAL:

A. Member, National Advisory Council on Aging.
B. Publications Committee, Gerontological Society of America.
C. Board of Scientific Advisors, Buck Center for Research on Aging.
D. Fellow, Gerontological Society of America.
E. Board of Scientific Advisors, American Federation for Aging Research.
F. Chair, Biological Sciences, Gerontological Society of America.
G. Member, Council, Gerontological Society of America.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Aging: Immunology and Infectious Disease. (Section editor)
B. Journal of Gerontology: Biological Sciences.
C. Journal of the American Geriatrics Society. (Section Editor)

INVITED LECTURES/SEMINARS:

1. Plenary Lecturer, 15th Annual Meeting of the Southeastern Pharmacology Society, Clearwater, Florida, September 29-October 1, 1994.

2. Meeting Chair, Genontology Society of America Annual Meeting, Atlanta, Georgia, November, 1994.
3. "Signal Transduction and Aging: Immune Models", Department of Physiology, University of Texas Health Science Center, San Antonio, Texas, February 15, 1995.
4. Plenary Address, ""Immunobiological Changes in Aging", Advances in Geriatrics VII Conference: Biopsychological Aspects of Aging, Miami Area Geriatric Education Center, Miami, Florida, March 9-11, 1995.
5. "Activation Defects in T Cells from Old Mice", Geriatric Research, Education and Clinical Center, University of Florida, Gainesville, Florida, March 13, 1995.
6. Keynote Speaker, "Immune Models for Aging Research", Conference on Gerontology and Aging, University of Illinois, Champaign-Urbana, Illinois, April 14, 1995.
7. "Gerontology as Oncology", Symposium on "Consequences of Age Changes Explored at the Cellular and Subcellular Levels on Organismic Function", Volterra, Italy, May 7-12, 1995.
8. "Candidate Biomarkers of Aging", Gordon Conference on the Biology of Aging, Barga, Italy, May 7-12, 1995.
9. "Human and Animal Models for Aging Research" and "Immune Models for Aging Research", Third Annual Summer Training Course in Experimental Aging Research, San Antonio, Texas, June 4-8, 1995.
10. "Research Funding: The Steep and Thorny Path", Aging and Mobility Summer Research Retreat, Ann Arbor, Michigan, June 13-14, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ghosh, J. and Miller, R.A.: Rapid tyrosine phosphorylation of Grb2 and SHC in T cells exposed to anti-CD3, anti-CD4, and anti-CD45: differential effects of aging. Mechanisms of Aging and Development 80:171-187, 1995.
2. Dozmorov, I.M., Kalinichenko, V.V., Sidorov, I.A. and Miller, R.A.: Antagonistic interactions among T cell subsets of old mice revealed by limiting dilution analysis. J. Immunol. 154:4283-4293, 1995.
3. Li, S.P., Verma, S. and Miller, R.A.: Age related defects in T cell expression of CD40 ligand and induction of in vitro B cell activation. Aging: Immunol. and Infect. Disease, In Press.
4. Witkowski, J.M., Gorgas, G. and Miller, R.A.: Reciprocal expression of P-glycoprotein and TAP1 accompanied by higher expression of MHC Class I antigens in T cells of old mice. J. Gerentol: Biol. Sciences, In Press.
5. Miller, R.A.: Mini-review: aging and cancer - one side of the same coin. (in Italian and English). Giornale di Gerontologia, In Press.
6. Miller, R.A.: Chemical and Biological changes in the aging mouse immune system. Nutrition Reviews 53:S8-S17, 1995.

ARTICLES SUBMITTED FOR PUBLICATION

1. Tewari, M., Telford, W.G., Miller, R.A. and Dixit, V.M.: CrmA, a poxvirus-encoded serpin, inhibits cytotoxic T-lymphocyte-mediated apoptosis. Submitted for publication.
2. Dozmorov, I.M., Lutsenko, G.V., Sidorov, I.A. and Miller, R.A.: Analysis of cellular interactions in limiting dilution cultures. Submitted for publication.

BOOKS/CHAPTERS IN BOOKS

1. Miller, R.A.: Immune system, Chapter 21, in, Masoro, E. (ed), Handbook of Physiology: Section 11: Aging, Oxford University Press, New York, pp.555-590, 1995.
2. Miller, R.A.: Aging and the immune response, in, Scheider, E.L. and Rowe, J.W. (eds), Handbook of the Biology of Aging, Academic Press, New York, In Press.
3. Miller, R. A.: The biology and genetics of aging and longevity, in, Kelley, W.N. (ed), Textbook of Internal Medicine, 3rd Edition, J.B. Lippincott, New York, In Press.
4. Miller, R.A.: Geroncology: the study of aging as the study of cancer, in, Esser, K. and Martin, G.M. (eds), Molecular Aspects of Aging, John Wiley and Sons, New York, pp. 265-278.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Member, Ph.D. Thesis Committee, College of Pharmacy.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Role of Keratinocytes in Cutaneous Inflammation/Immunity", Johns Hopkins Center for Alternatives to Animal Testing, 2/94-1/95.
B. Co-Investigator, "Immunobiology of Kaposi's Sarcoma Tumor Cells", National Institutes of Health, (B.J. Nickoloff, Principal Investigator), 7/1/94-6/30/99.
C. Co-Investigator, "Role of Scatter Factor in AIDS-Kaposi's Sarcoma", (Peter Polverini, Principal Investigator), 7/1/94-6/30/99.

PROJECTS UNDER STUDY:

A. Studies on normal and psoriatic skin-derived dendritic cells.
B. Safety testing: Skin irritation and contact sensitization.
C. Modulation of apoptosis in cultured keratinocytes.

REVIEWER

A. NATO Advanced Study Institute.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None.

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Nickoloff, B.J., Mitra, R.S., Varani, J., Dixit, V.M. and Polverini, P.J.: Aberrant production of interleukin-8 and thrombospondin-1 by psoriatic keratinocytes mediates angiogenesis. Amer. J. Pathol. 144:820-828, 1994.
2. Mitra, R.S., Judge, T.A., Nestle, F.O., Turka, L.A. and Nickoloff, B.J.: Psoriatic skin-derived dendritic cell function is inhibited by exogenous IL-10. J. Immunol. 154:2668, 1995.
3. Nickoloff, B.J., Turka, L.A., Mitra, R.S. and Nestle, F.O.: Direct and indirect control of T-cell activation by keratinocytes. J. Invest. Dermatol. 105:255-295, 1995.

BOOKS/CHAPTERS IN BOOKS:

1. Mitra, R.S. and Nickoloff, B.J.: Cultivation of human epidermal keratinocytes in serum-free growth medium, in, Leigh, I. (ed), Keratinocyte Handbook, Cambridge University Press, pp. 17-19, 1994.

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

1. Nickoloff, B.J., Mitra, R.S. and Turka, L.A.: Transfection of CD28 ligand B7-1 and anti-IL-10 mAb are important for allogenetic T cell response to IFN-a treated keratinocytes. J. Invest. Dermatol. 102:583, 1994.
2. Nestle, F.O., Mitra, R.S., Turka, L. and Nickoloff, B.J.: Strong autoreactivity between dermal dendritic cells derived from psoriatic plaques and blood T cells produces high levels of IL-1 and IFN-α. J. Invest. Dermatol. 102:527, 1994.
3. Mitra, R.S. and Nickoloff, B.J.: Modulation of emigration and maturation of dendritic cells from human skin by cytokines and Phorbol ester. J. Invest. Dermatol. 104:615, 1995.
4. Singer, N.G., Nickoloff, B.J., Mitra, R.S., Lialios, F. and Fox, D.A.: 9th International Congress of Immunology, July, 1995.

R. LEE MOSLEY, Ph.D.
ASSISTANT RESEARCH SCIENTIST
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 AUGUST 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

None.

III. RESEARCH ACTIVITIES:

A. Research proposal applications submitted:
   1. "Quantitation and Characterization of Post-Thymic T Stem Cells" submitted to Leukemia Society of America.
   2. "Frequency and Expansionary Potential of Post-Thymic T Stem Cells from Aged Mice" submitted to American Federation for Aging Research.
   3. "Frequency and Expansionary Potential of Post-Thymic Stem Cells from Aged Mice" submitted to Sandoz Foundation for Gerontological Research.

SPONSORED SUPPORT:

A. American Federation for Aging Research (AFAR); 1 year at $40,000; pending.

PROJECTS UNDER STUDY:

A. Enumeration and Identification of Post-Thymic T Stem Cells.
B. Frequency and Expansionary Potential of Post-Thymic T Stem Cells from Aged Mice.
C. Age-Related Effects of Mucosal T Lymphocytes.

IV. ADMINISTRATIVE ACTIVITIES:

None.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

A. None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. R. L. Mosley, Wang, J., Hamad, M. and Klein, J.R.: Functional heterogeneity of murine intestinal intraepithelial lymphocytes: Studies using TCR$\alpha\beta^+$ IEL lines and fresh IEL isolates reveal multiple cytotoxic subsets Dev. Comp. Immunol.. 18:155-164, 1994.
2. R. L. Mosley, Hamad, M., Whetsell, M. and Klein, J.R.: A novel marker of murine bone marrow hematopoietic stem cells that is expressed on peripheral T cells and is associated with a functionally important molecule on activated cytotoxic T lymphocytes. Hybridoma 13:353-358, 1994.
3. A. W. Gough, Mosley, R.L. and Stubbs, C.J.: Immunopathologic characterization of typhlitis and colitis in juvenile HLA-B27 transgenic rats. Pathobiology 62:221-231, 1995.
4. A. I. Sperling, Greene, J.M., Mosley, R.L., Smith, P.L., DiPaolo, R.J., Klein, J.R., Bluestone, J.A. and Thompson, C.B.: CD43 is a murine T cell costimulatory receptor that functions independently of CD28. J. Exp. Med. 182:139-146, 1995.

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

1. D. H. Teitelbaum, Neidick, B., Valle, J.D. and Merion, R.M. (Sponsor Mosley, R.L.). Inhibitory activity of intestinal intraepithelial lymphocytes (iIEL). FASEB J. 9:A415, 1995.
2. A. Gough,. Breider, M. and Mosley, R.L.: Early pathological changes in dextran sodium sulphate-induced colitis in mice. Vet. Pathology, In Press.

HEDWIG S. MURPHY, M.D., PH.D.
RESEARCH INVESTIGATOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NHLBI Clinical Investigator Development Award KO8 HL03181-01:Structure and Function of Recombinant Selectin Ligands, 09/01/94-08/31/99, $402,916.

PROJECTS UNDER STUDY:

A. Structure and function of recombinant glycoproteins.
B. Endothelial cell expression of selectin ligands.
C. Function and mechanism of generation of endothelial cell superoxide.
D. Endothelial cell signal transduction.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Pathology residents - supervision and teaching during cytopathology rotation and when covering necropsies.
B. Pathology residents - biweekly cytopathology conferences.
C. Senior medical students during pathology electives.
D. Sophomore medical students: Instructor, Pathology 600 laboratory.

III. RESEARCH ACTIVITIES:

A. Cytopathology, with particular reference to serous fluids.

PROJECTS UNDER STUDY:

A. Curschmann's spirals in bronchial aspirates.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director and Co-Director, Cytopathology Laboratory.
B. Advisory Committee on Appointments and Promotions.

REGIONAL AND NATIONAL:

A. North American Review Board, Acta Cytologica.
B. Associate Editor, Acta Cytologica.
C. Editorial Board, Cytopathology.
D. Editorial Consultant, Diagnostic Cytopathology.
E. Chairman, Publications Committee, International Academy of Cytology.
F. Membership Committee, International Academy of Cytology.
G. Budget and Finance Committee, American Society of Cytology.
H. Chairman, Awards Committee, American Society of Cytology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Naylor, B.: Lectures and case presentations: a) Cervical cytology, b) Aspiration cytology of the breast, c) Cytology of pleural, peritoneal and pericardial fluids. 4th International Marmara Medical Days, Marmara University, Istanbul, Turkey, September, 1994.
2. Naylor, B.: Pleural, peritoneal and pericardial fluids: Technical approaches and diagnostic problems. Bay Area Seminars in Cytopathology, University of California, San Francisco, January, 1995.
3. Naylor, B.: Cytology of serous effusions: Technical approaches and diagnostic problems. Teleconference, American Society of Clinical Pathologists, March, 1995.
4. Naylor, B.: a) Cytology of serous effusions: Technical approaches and diagnostic problems, b) Diagnostic seminar. Greater Detroit Society of Pathologists, Detroit, Michigan, April, 1995.

HONORS AND AWARDS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Naylor, B.: Roth M. Graham, D. Sc. (Hon.), B.S. (1917-1978). Diag. Cytopath. 12:373-374, 1993.

BOOKS/CHAPTERS IN BOOKS:

None.

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

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Dermatopathology, University of Michigan Hospitals.
B. Dermatopathology, M-Labs.
C. Dermatopathology, Private Consultations.
D. Dermatology, Melanoma Clinic.
E. Immunopathology Laboratory.
F. MSTP Clinical Phase Mentorship Panel.
G. Cutaneous Oncology Program Scientific Director.

II. TEACHING ACTIVITIES:

A. Pathology and Dermatology House Officers Lecture Series.
B. Clinical Pathology Orientation Lecture and Laboratory.
C. Five Week Medical Student (Year 2) Research Elective.
D. Year One Medical Student Dermatopathology Lecture Series.
E. Dermatology Grand Rounds - Dermatopathology presentations.
F. Ten Week Undergraduate Student Research Elective.
G. Immunopathology Lecture Series.
H. Department of Pathology Graduate Course and Dissertation Committee.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Immunobiology of Kaposi's Sarcoma Tumor Cells", NIH RO-1 (25% effort), $194,727 Annual Direct Costs, June 1994 - June 1999.
B. "Role of Scatter Factors in AIDS-Related Kaposi's Sarcoma", NIH RO-1 (5% effort), $201,011 Annual Direct Costs, June 1994 - June 1999.
C. "Role of Adhesion Molecules in Psoriasis", NIH RO-1 (40% effort), $145,120 Annual Direct Costs, June 1994 - June 1997.
D. "Regulation of Macrophage Angiogenic Activity", NIH RO-1 (10% effort), $155,000 Annual Direct Costs, June 1995 - June 1999.

Total Annual Direct Costs = $695,858.

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. Role of endothelial cell adhesion molecules (ICAM-1, ELAM-1, VCAM-1) in cutaneous leukocyte trafficking.
D. Role of factor XIII a positive dermal dendrocytes in AIDS-related psoriasis.

E. Dissection of cytokine networks in psoriasis, allergic contact dermatitis to poison ivy, and mycosis fungoides.
F. Role of Scatter Factor/C-met in Kaposi's Sarcoma.
G. Role of CD28/BB-1/B7 in Psoriasis.
H. Role of Bcl-x in Psoriasis.

IV. ADMINISTRATIVE ACTIVITIES:

A. Scientific Director: Cutaneous Oncology Program - Cancer Center.

REGIONAL AND NATIONAL:

A. Member, General Medicine A Study Section, National Institutes of Health.
B. Ad-hoc Reviewer, University of Michigan Multipurpose Arthritis Center.
C. Ad-hoc Reviewer, University of Michigan Department of Surgery.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. American Journal of Dermatopathology.
B. Journal of Cutaneous Pathology.
C. Autoimmunity Forum In Dermatology.
D. Journal of American Academy of Dermatology.
E. Journal of Dermatological Science.
F. American Journal of Pathology.

OTHER:

A. Journal of Investigative Dermatology, Reviewer.
B. Journal of Cutaneous Pathology, Reviewer.
C. American Journal of Pathology, Reviewer.
D. American Journal of Dermatopathology, Reviewer.
E. Archives of Dermatology, Reviewer.
F. Journal of American Academy of Dermatology, Reviewer.
G. American Journal of Plastic Surgery, Reviewer.
H. Journal of Cellular Physiology, Reviewer.
I. British Journal of Dermatology, Reviewer.
J. New England Journal of Medicine, Reviewer.
K. Journal of National Cancer Institute, Reviewer.
L. Journal of Clinical Investigation, Reviewer.
M. Journal of Dermatological Science, Reviewer.
N. Journal of Immunology, Reviewer.
O. Journal of Experimental Medicine, Reviewer.
P. Nature, Reviewer.

INVITED LECTURES/SEMINARS:

1. Invited Speaker, "Role of Dermal Dendritic Cells in Psoriasis", 3rd International Symposium on Dendritic Cells in Fundamental and Clinical Immunology, Annecy, France, June 22, 1994.
2. Invited Speaker, "Dermal Dendritic Cell Subsets: Role of the Dermal Immune System", Joint International Society of Dermatopathology/British Society of Dermatopathology, London, England, June 29, 1994.

3. Invited Speaker, "Professional and Non-Professional Antigen Presenting Cells in the Skin", Department of Pathology, Division of Experimental Immunology, Zurich, Switzerland, July 17, 1994.
4. Invited Speaker, "Keratinocyte: T-Cell Interactions in Skin Diseases", 35th Annual Symposium on the Biology of the Skin, Snowmass, Colorado, August 18, 1994.
5. Invited Speaker, "Inflammation - A Dermatological Perspective", International Meeting of the European Academy of Dermatology and Venereology-Skin Therapy Update, Crete, Greece, October 17, 1994.
6. Invited Speaker, "Targeting Co-Stimulatory Molecules B7-1, B7-2, and B7-3 Expressed by Immunocytes in Psoriasis", Inflammation Research Association: Novel Approaches to Immunoregulatory Therapy, San Diego, California, November 11, 1994.
7. Invited Speaker, "Role of Professional and Non-Professional APC's in Skin Disease with Emphasis on Co-Stimulatory Molecules B7-1, B7-2, and B7-3", Department of Pathology, Harvard Medical School, Boston, Massachusetts, December 14, 1994.
8. Invited Speaker, "Keratinocytes as Initiators of Inflammation and Immunologic Antigen Presenting Cell", Center for Alternatives to Animal Testing Symposium on In-Vitro Approaches to Contact Dermatitis, Baltimore, Maryland, March 4, 1995.
9. Visiting Professor, "Chaos and KS", Department of Dermatology, Stanford University, Palo Alto, California, April 13, 1995.
10. Invited Speaker, "Role of IL-12 in Psoriasis", Annual Meeting of Society for Investigative Dermatology, Chicago, Illinois, May 25, 1995.
11. Invited Speaker, "New Animal Model for Psoriasis", Cytokines in Dermatology Symposium, San Francisco, California, June 1, 1995.
12. Invited Speaker, "Dermal Dendritic Cells and Dermatology", Four hour Workshop Presentation, San Francisco, California, June 2, 1995.
13. Presenter, "Role of APC's in Cutaneous Neoplasms", 36th Annual Symposium on the Biology of the Skin - Skin Cancer, Snowmass, Colorado, July 16, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Nickoloff, B.J., Nestle, F.O., Zheng, X.G. and Turka, L.A.: T lymphocytes in skin lesions of psoriasis and mycosis fungoides express B7: A ligand for CD28. Blood. 83:2580-2586, 1994.
2. Naidu, Y.M., Rosen, E.M., Zitnik, R., Goldberg, I., Park, M., Polverini, P.J. and Nickoloff, B.J.: Role of scatter factor (hepatocyte growth factor) in the pathogenesis of AIDS-related Kaposi's Sarcoma. Proc. Nat'l. Acad. Sci. (USA). 91:5281-5285, 1994.
3. Saed, G., Fivenson, D.P. and Nickoloff, B.J.: Mycosis Fungoides exhibits a TH-1 type cell mediated cytokine profile while Sezary syndrome expresses a TH-2 type profile. J. Invest. Dermatol. 103:29-33, 1994.
4. Nestle, F.O., Turka, L.A. and Nickoloff, B.J.: Characterization of dermal dendritic cells in psoriasis: Autostimulation of T lymphocytes and induction of TH-1 type cytokines. J. Clin. Invest. 94:202-209, 1994.
5. Goodman, R., Naidu, Y., Nestle, F., Green, J., Nickoloff, B.J. and Turka, L.A.: Keratinocyte-derived T cell co-stimulation induces preferential production of IL-2 and IL-4, but not IFN-γ. J. Immunol. 152:5189-5198, 1994.
6. Nickoloff, B.J. and Turka, L.A.: Immunologic function of non-professional antigen presenting cells. Insights from keratinocyte: T cell interactions. Immunol. Today. 15:464-469, 1994.
7. Nestle, F.O., Mitra, R.S., Bennett, C.F., Chan, M. and Nickoloff, B.J.: Cationic lipid is not required for uptake and selective inhibitory activity of ICAM-1 phosphorothioate antisense oligonucleotides in keratinocytes. J. Invest. Dermatol. 103:569-575, 1994.

8. Nickoloff, B.J., Fivenson, D.P., Kunkle, S.L., Strieter, R.M. and Turka, L.A.: Keratinocyte IL-10 expression is upregulated in tape stripped skin, poison ivy dermatitis, and Sezary syndrome, but not in psoriatic plaques. Clin. Immunol. and Immunopath. 73:63-68, 1994.
9 Fivenson, D.P., Hanson, C.A. and Nickoloff, B.J.: Localizatioin of clonal T-cells to the epidermis in cutaneous T-cell lymphoma. J. Am. Acad. Dermatol. 31:717-723, 1994.
10. Mitra, R.S., Turka, L.A., Judge, T.A., Nestle, F.O. and Nickoloff, B.J.: Psoriatic skin-derived dendritic cell function is inhibited by exogenous IL-10: Differential modulation of B7-1 (CD80) and B7-2 (CD86) expression. J. Immunol. 154:2668-2677, 1994.
11. Nickoloff, B.J., Kunkle, S.L., Burdick, M. and Strieter, R.M.: SCID mouse: Human psoriatic skin chimeras - Validation of a new animal model. Am. J. Pathol. 146:580-588, 1994.
12. Ohmen, J.D., Hanifin, J.M., Nickoloff, B.J., Rea, T.H., Wyzikowski, R., Nassif, A.S., Chan, S.C. and Modlin, R.L.: Overexpression of IL-10 mRMA in atopic dermatitis: Contrasting cytokine patterns with delayed-type hypersensitivity reactions. J. Immunol. 154:1956-1963, 1995.
13. Wrone-Smith, T., Nunez, G., Johnson, T., Nelson, B., Boise, L.H., Thompson, C.B. and Nickoloff, B.J.: Discordant expression of Bcl-X and Bcl-2 keratinocytes *in vitro* and psoriatic keratinocytes *in vivo*. Am. J. Pathol. 146:1-10, 1995.
14. Nickoloff, B.J., Turka, L.A., Mitra, R.S. and Nestle, F.O.: Direct and indirect control of T cell activation by keratinocytes. J. Invest. Dermatol. 105(suppl):25-29, 1995.
15. Sakimura, L., Yamamura, M., Sieling, P.A., Uyemura, K., Tahery, D., Oliveros, J., Nickoloff, B.J., Rea, T.H. and Modlin, R.L.: Interleukin-7 in the cell mediated immune response to a human pathogen. J. Immunol. 154:2775-2783, 1995.
16. Fivenson, D.P. and Nickoloff, B.J.: Distinctive dendritic cell subsets expressing factor XIIIa, CD1a, CD1b, and CD1c in mycosis fungoides and psoriasis. J. Cut. Path. 22:223-228, 1995.
17. Mastellar, E.L., Larsen, R.D., Carlson, L.M., Pickel, J.M., Nickoloff, B.J., Lowe, J., Thompson, C.B. and Lee, K.P.: The selectin ligand sialyl Lewis X is developmentally regulated during chicken B cell development and appears to direct lymphocyte homing to the bursa of Fabricus. Development. 121:1-11, 1995.
18. Hsi, E.D. and Nickoloff, B.J.: Dermatofibroma and dermatofibrosarcoma protuberans: An immunohistochemical study reveals distinctive antigenic profiles. J. Dermatol. Sci., In Press.
19. Kim, J., Modlin, R.L., May, R.L., Dubinett, S.M., McHugh, T., Nickoloff, B.J. and Uyemura, K.: IL-10 production in cutaneous basal and squamous cell carcinoma: A mechanism for evading the local T cell immune response. J. Immunol., In Press.
20. Nestle, F.O. and Nickoloff, B.J.: Dermal dendritic cells are important members of the skin immune system. J. Invest. Dermatol., In Press.
21. Turka, L.A., Goodman, R.E., Rutkowski, J.L., Sima, A.F., Merry, A., Mitra, R.S., Wrone-Smith, T., Toews, G., Strieter, R.M. and Nickoloff, B.J.: IL-12 A potential link between nerve cells and the immune system. Mol. Med., In Press.
22. Nickoloff, B.J.: Contributions of cytokines to cutaneous barrier function. J. Contact Derm.., In Press.
23. Tsai, C., Diaz, L. Singer, N., Li, L., Mitra, R.S., Nickoloff, B.J., Castor, W., Croffoerd, L.J. and Fox, D.A.: Human T lymphocytes respond to bacterial superantigens presented by cultured rheumatoid arthritis synoviocytes. J. Immunol., In Press.

BOOKS/CHAPTERS IN BOOKS:

1. Mitra, R.S. and Nickoloff, B.J.: Culture of Epidermal Keratinocytes in Serum-Free Growth Medium, in, Leigh, I. (ed), Keratinocyte Handbook, Cambridge University Press, pp. 17-20, 1994.
2. Nestle, F.O. and Nickoloff, B.J.: The Role of Dendritic Cells in Benign and Malignant Lymphocytic Infiltrates of the Skin, in, Burg, G., Karl, H. and Thiers, B. (eds), Dermatologic Clinics on Cutaneous Lymphomas, W.B. Saunders, Philadelphia, Pennsylvania, 12:271- 283, 1994.
3. Karasek, M..A. and Nickoloff, B.J.: Guest Editor and Contributor: Festschrift for Dr. Eugene Farber, International Journal of Dermatology, Volume 33, 1994.

4. Polverini, P. and Nickoloff, B.J.: Role of Scatter Factor and the c-met Protoncogene in the Pathogenesis of AIDS-Related Kaposi's Sarcoma, in, Klein, G. and Van deWoude G.F. (eds), Advances in Cancer Research, Academic Press, New Tork, New York, 66:235-253, 1995.
5. Nickoloff, B.J.: Role of Cytokines in Psoriasis and Other T-cell Mediated Dermatoses, in, Aggarwal, B.A. and Pari, R. K. (eds), Human Cytokines: Their Role in Health and Disease, Science, Inc., pp. 641-650, 1995.
6. Kunkle, S.L., Driscoll, K., Ward, P.A., Nickoloff, B.J. and Strieter, R.M.: Immunopathology of Environmental and Occupational Diseases, in, Craighead, A.G. (ed), Pathology of Envornmental and Occupational Disease, Mosby Publishers, pp. 77-94, 1995.
7. Fivenson, D.F. and Nickoloff, B.J.: Cell Trafficking Networks in Cutaneous T Lymphoma, in, Lambert, W.C. (Ed), NATO Meeting-Basic Mechanisms of Physiological and Aberrant Lymphoproliferation in the Skin, Plenum Publishing, New York, New York, pp.77-94, 1994.
8. Polverini, P. and Nickoloff, B.J.: Role of Scatter Factor as a Mediator of Initiation and Maintenance of AIDS-Related Kaposi's Sarcoma, in, Goldberg, I.D. and Rosen, E.M. (Eds), Epithelial-Mesenchymal Interations in Cancer, Birkhausen Verlag, Basel, Switzerland, In Press.
9. Burg, G., Dummer, R., Domman, S., Nestle, F.O. and Nickoloff, B.J.: Pathology of Cutaneous T-cell Lymphoma, in, Koh, H. (Ed), Lymphomas, W.B. Saunders, Philadelphia, Pennsylvania, In Press, 1995.
10. Fivenson, D.F. and Nickoloff, B.J.: Cytokine Networks in Skin Disease, in, Remick, D.G. (Ed), Cytokines in Health and Disease, Second Edition, Marcel Dekker, Inc., New York, New York, Submitted.
11. Foreman, K. and Nickoloff, B.J.: The Role of Chemokines in Skin Disease, in, Koch, A.E. and Strieter, R.M. (Eds), Chemokines, In Preparation.
12. Wrone-Smith, T. and Nickoloff, B.J.: The Role of Adhesion Molecules in Traffickinf of T Lymphocytes in Skin, in, Bos, J.D. (Ed), Skin Immune System, Second Edition, CRC Press, Inc., In Preparation.

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

1. Nestle, F.O., Turka, L.A. and Nickoloff, B.J.: Hierarchy of the functional significance of B7 expression by antigen-presenting cells: autologous versus allogenic reactions. Arch. Dermatol. Res. 286:145-231, 1994.
2. Saed, G.M. Fivenson, D.P. and Nickoloff, B.J.: Quantitative PCR analysis of cytokines in HUT 78 cells after PUVA exposure. J. Invest. Dermatol. 102:585, 1994.
3. Nestle, F.O., Mitra, R.S., Turka, L.A. and Nickoloff, B.J.: Dermal dendritic cells express higher levels of B7-2 versus B7-1 and their immunomodulatory capacity is reduced by IL-10. J. Invest. Dermatol. 103:443, 1994.
4. Nestle, F.O., Filgueira, L. Groscurth, P. Burg, G. and Nickoloff, B.J.: Dermal dendritic cells process and present soluble protein antigens. J. Invest. Dermatol. 104:566, 1995.
5. Wrone-Smith, T., Nunez, G., Johnson, T., Nelson, B., Boise, L., Thompson, C.B. and Nickoloff, B.J.: Characterization of proteins that promote or prevent apoptosis in benign and malignant keratinocytes. J. Invest. Dermatol. 104:572, 1995.
6. Singer, N.G., Fox, D.A., Lialios, F., Mitra, R.S. and Nickoloff, B.J.: Evidence that a CD6 ligand is expressed by γ-interferon activated keratinocytes. J. Invest. Dermatol. 104:574, 1995.
7. Goodman, R., Turka, L.A., Rutkowski, J.L., Sima, A.F., Merry, A., Mitra, R.S., Wrone-Smith, T., Toews, G., Strieter, R.M. and Nickoloff, B.J.: IL-12 is contained within sensory and sympathetic neurons in skin as well as central peripheral glial cells. J. Invest. Dermatol. 104:587, 1995.
8. Fivenson, D.R., Farla, D.T., Nickoloff, B.J., Polverini, P.J., Kunkle, S.L., Burdick, M. and Strieter, R.M.: Anti-inflammatory cytokines increase during healing of chronic venous ulcers favoring progression to a macrophage dominated late inflammatory/early proliferative phase of wound repair. J. Invest. Dermatol. 104:591, 1995.

9. Mitra, R.S. and Nickoloff, B.J.: Modulation of emmigration and maturation of dendritic cells from human skin by cytokines and phorbol ester. J. Invest. Dermatol. 104:615, 1995.
10. Fivenson, D., Faria, D. Nickoloff, B.J., Polverini, P.J., Kunkle, S. L., Burdick, M. and Strieter, R.: CXC Chemokine effects during chronic wound healing: critical role of the ELR motif in angiogenesis. J. Invest. Dermatol. 104:625, 1995.
11. Nickoloff, B.J., Burg, G. and Nestle, F.O.: Tumor associated antigen presenting cells are deficient in expression of T-cell co-stimulatory molecules B7-1 (CD80) and B7-2 (CD86). J. Invest. Dermatol. 104:646, 1995.
12. Fivenson, D., Elkheimi, M., Christopherson, P., Saed, G. and Nickoloff, B.J.: Modulation of IL-10 expression in HUT 78 cells: Insights into the pathobiology and treatment of CTLC. J. Invest. Dermatol. 104:648, 1995.
13. Hsi, E.D., Goldblum, J., Nickoloff, B.J. and Frank, T.: Detection of human papilloma virus by polymerase chain reaction in immunocompromised patients with keratoacanthomas. J. Clin. Path.
14. Tsai, C. Diaz, L.A. Jr., Mitra, R.S., Nickoloff, B.J., Singer, N.G., Crofford, L. and Fox, D.A.: Rheumatoid fibroblast-like synoviocytes can support T-cell responses to staphyloccocal superantigens.
15. Singer, N.G., Nickoloff, B.J., Mitra, R.S., Lialios, F., Fox, D.A.: Evidence that IFN-γ activated keratinocytes express a CD6 ligand.
16. Sima, A.F., Goodman, R.E., Rutkowski, J.L., Merry, A.L., Mitra, R.S., Wrone-Smith, T., Toews, G., Strieter, R.M., Turka, L.A. and Nickoloff, B.J.:The localization of IL-12 to human and rodent CNS and PNS.
17. Saed, G.M., Fivenson, D.P. and Nickoloff, B.J.: Malignant cells in cutaneous T-cell lymphoma resemble murine TH-2 type helper T lymphocytes. J. Invest. Dermatol.
18. Nickoloff, B.J.: Diagnosis of Lymphomatoid Papulosis. Am. J. Dermatopath.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Autopsy Service (two weeks and one weekend on-call).

II. TEACHING ACTIVITIES:

A. Supervised Dr. Maribel Gonzalez-Garcia, Dr. Ramon Merino, Dr. Didier Grillot and Dr. Philip Simonian (Postdoctoral Fellows).
B. Supervised Mary Benedict (graduate student).and Eric Humke (graduate student).
C. Supervised Eric Humke (graduate student).
D. Laboratory Instructor, Pathology 630/631. Full semester, two hours/week.
E. Speaker, Undergraduate, UROP program (one lecture).
F. Speaker, Molecular Diagnostic, Department of Pathology (one lecture).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Regulation and Function of the Bcl-2 Gene during Thymus Development", National Institutes of Health, $150,000 (total direct costs), 1/1/93-12/31/95.
B. Principal Investigator, "Regulation and Function of Bcl-2 in Germinal Centers", American Cancer Society, $313,368 (total direct costs), 7/1/93-6/30/96.
C. Principal Investigator, "Function of the Bcl-2 Proto-Oncogene During B Cell Development", The Council for Tobacco Research, $264,709, 1/1/94-12/31/96.
D. Principal Investigator, "Genetic Regulation of Apoptotic Cell Death", National Institutes of Health, $725,000 (total direct costs) 8/1/94-7/31/99.
E. Principal Investigator, Research Career Development Award, "Genetic Regulation of Apoptotic Cell Death", National Institutes of Health, $280,000 (total direct costs) 8/1/94-7/31/99.

PENDING SUPPORT:

A. Principal Investigator, "Bcl-xs Mediated Apoptosis of Kaposi's Sarcoma Cells," National National Institutes of Health, $2,282,648 (total direct costs), 9/01/95 - 8/31/00.

PROJECTS UNDER STUDY:

A. Functional characterization of Bcl-2 and Bcl-x genes during lymphoid development.
B. Molecular interactions between Bcl-2 family members.
C. Regulation and role of Bcl-2 and Bcl-x in neuroblastoma.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interviewer, faculty, postdoctoral, and graduate student candidates for research fellowships.
B. Member, Cultural Diversity Assessment Steering Committee, University of Michigan, Ann Arbor, Michigan.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Molecular and Cellular Biology Program.
B. Member, University of Michigan Cancer Center.
C. Member, Transgenic Core Facility Committee, Multipurpose Arthritis Center.
D. Member, Faculty Search Committee, Rheumatology Division.
E. Reviewer, Departmental Grants.
F. Interviewer, MSTP Candidates.
G. Committee Member, Suil Kim, Graduate student, M.D./Ph.D., Training Program, Ph.D.
H. Committee Member, Charlene Ford, Graduate Student, Immunology Program, Preliminary Oral Examination.
I. Christine Hodges, Molecular and Cellular Biology Program, Preliminary Oral Examination.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Reviewer for the following journals: American Journal of Pathology, Blood, Journal of Immunology, Oncogene, Journal of Cell Biology, Laboratory Investigation, Cancer Research.
B. Ad Hoc Reviewer: Research grants, National Institute of Health .

INVITED LECTURES AND SEMINARS

UNIVERSITY OF MICHIGAN

1. Invited Speaker, Nephrology Research Conference, 1994.
2. Invited Speaker, U-M Cancer Center Retreat, 1994.
3. Lecturer, Molecular Diagnostics Course, M-Labs, 1994.
4. Invited Speaker, University of Michigan Cancer Center, 1994.
5. Invited Speaker, Symposium on Apoptosis, 1995.
6. Invited Speaker, Seminar Pulmonary and Critical Care Medicine, 1995.

NATIONAL AND INTERNATIONAL

1. Invited Speaker, Cell Death in Development and Cancer, M.D. Anderson Cancer Center, Houston, Texas, 1994.
2. Invited Speaker, American Society for Histocompatibility and Immunogenetics, Pittsburgh, Pennsylvania, 1994.
3. Invited Speaker, Exploiting Cell Death for Therapeutic Applications, IBC's International Conference, Cambridge, Massachusetts, 1994.

4. Invited Speaker, Conference on Regulation of the Cell Cycle and Apoptosis, University of London, England, 1994.
5. Invited Speaker, XXIII National Congress of Rheumatology, Aquacaliente, Mexico. 1995.
6. Invited Speaker and Session Chair, Apoptosis (programmed cell death), Keystone Symposium, Tamarron, Colorado, 1995.
7. Developmental Biology Study Section, NIH, February 16, 1995.
8. Invited Speaker, Symposium on Apoptosis, Keystone, Colorado, April 17, 1995.
9. Invited Speaker, Wound Healing Society, Annual Meeting, Minneapolis, MN, May 1, 1995.
10. Invited Speaker, Danish Cancer Society, Copenhagen, Denmark, March 7, 1995.
11. Invited Speaker, Second European Workshop on Basic Biology of Head and Neck Cancer, Lung, Sweden, June 8-11, 1995

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Gottschalk, A.R., McShan, C.L., Merino, R., Nuñez, G. and Quintans, J.: Physiological cell death in B lymphocytes. I. Differential susceptibility of WEHI-231 sublines to anti-lg induced physiological cell death and lack of correlation with bcl-2 expression. Int. Immunol. 6:121-130, 1994.
2. Ryan J, Gottlieb C, Ding L, Nunez G, Clarke M: Alteration of the cell cycle regulatory function of p53 by bcl-2. PNAS (USA) 91:5878-5882, 1994.
3. Dole, M.G., Nuñez, G., Merchant, A., Maybaum, J., Rode, C., Bloch, C.A. and Castle, V.P.: bcl-2 inhibits chemotherapy induced apoptosis in neuroblastoma. Cancer Res. 54:3253-3259, 1994.
4. González-García, M., Perez Ballestero, R., Ding, L., Duan, L., Boise, L., Thompson, C. and Nuñez, G.: Bcl-xl is the dominant mRNA from expressed during development and its product localizes to outer mitochondria. Development 120:3033-3042, 1994.
5 Lam, L., Dubyak, G., Chen, L., Nuñez, G., Miesfeld, R.L. and Distelhorst, C.W.: Evidence that bcl-2 blocks glucocorticoid- and thapsigargin- induced apoptosis of mouse lymphoma cells by interfering with calcium mobilization from the endoplastic reticulum. Proc. Natl. Acad. Sci. USA, PNAS (USA) 91:6569-6573, 1994.
6. Cleveland, J., Troppmair, J., Packham, G., Askew, D., Lloyd, P., Gonzalez-Garcia, M., Nuñez, G. and Ihle, J.: *v-raf* suppresses apoptosis and promotes growth of interleukin 3-dependent myeloid cells. Oncogene 4:399-403, 1994.
7. Nuñez, G., Merino, R., Grillot, D. and Gonzalez-Garcia, M.: Bcl-2 and Bxl-x: Regulatory switches for cell death and survival. Immunology Today, In Press.
8. Nunez, Merino R, Brillot D., and Gonzalez-Garcia M.: Bcl-2 and Bcl-x: Regulatory switches for cell death and survival. Immunology Today 15:582-588, 1994.
9. Nunez, G. and Clarke, M.: The Bcl-2 family of ; regulators of cell death and survival. Trends in Cell Biology 4:399-403, 1994.
10. Gratiot-Deans, J., Merino, R., Nunez, G. and Turka, L.A.: Bcl-2 expression during T cell development: Early loss and late return occurs at specific stages of commitment to differentiation and survival. Proc. Natl. Acad. Sci: USA 91:10685-10689, 1994.
11. Benito, A., Grillot, D., Nunez, G. and Fernandez-Luna, J.L.: Regulation and function of Bcl-2 during differentiation-induced cell death in HL-60 promyelocytic cells. Am. J. Pathol. 146:481-490, 1995.
12. Wrone-Smith, T., Johnson, T., Nelson, B., Boise, L.H., Thompson, C., Nunez, G. and Nickoloff, B.J.: Discordant expression of Bcl-x and Bcl-2 by keratinocytes *in vitro* and psoriatic keratinocytes i*n vivo*. Am. J. Pathol. 146:1079-1088, 1995.
13. Dole, M.G., Jasty, R., Cooper, M., Thompson, C.B., Nunez, G. and Castle, V.P.: Bcl-Xl is expressed in neuroblastoma cells andmodulates chemotherapy induced apoptosis. Cancer Research 55:2576-2582, 1995.

14. Sunantran, V.N., Ealovega, M.W., Nunez, G., Clarke, M.F. and Wicha, M.S.: Overexpression of Bcl-xs sensitizes MCF-7 cells to chemotherapy-induced apoptosis. Cancer Research 55:2507-2510, 1995.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Merchant, A.K., Persels, L.A., Wagner, L.M., Merino, R., Nunez, G., Maybaum, J.: Bcl-2 attenuates fluorodeoxyuridine-induced cytotoxicity and DNA damage in non-apoptotic human tumor cells Carcinogenesis, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Ding, L., Kenny, J., Horton, K., Korsmeyer, S.J. and Nuñez ,G.: Prevention of apoptosis in M167-id^{+} B cells by overexpression of bcl-2 in M167 μk transgenic mice. Submitted.
2. Nuñez, G. and Clarke, M.: The bcl-2 family of proteins: Regulations of cell death and survival. Submitted.
3. Gonzalez-Garcia, M., Ding, L., Garcia, I., Boise, L.H., Thompson, C.B. and Nuñez, N.: Regulation of neuronal cell death by bcl-x proteins. Submitted.
4. Perez, G., Grillot, D., Nunez, G. and Fernandez-Luna, J.L.: Regulation of programmed cell death in myeloid cell lines by bcl-2. Submitted.

HAROLD A. OBERMAN, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Director, Blood Bank and Transfusion Service, University Hospitals.
B. Diagnosis of surgical specimens from University Hospital patients.
C. Diagnosis of surgical specimens from M-Labs.
D. Diagnosis of consultation breast cases from pathologists elsewhere in the United States.
E. Medical coverage of Transfusion Service.
F. Medical coverage of Necropsy Service (Quality Control Review).
G. Member, University of Michigan Breast Care Center.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Lectures on breast pathology and transfusion medicine to sophomore class (five contact hours).
B. Laboratory Course for sophomore medical students (Pathology 600) six hours (two weeks).
C. Daily case review with pathology house officer assigned to Blood Bank.
D. Weekly lecture/discussion with Pathology, Hematology and Pediatric Hematology house officers.
E. Lecture-Discussion (two) on Transfusion Medicine to senior student elective course in Laboratory Medicine.
F. Postgraduate Course, "Current Topics in Blood Banking", Planning Committee.
G. Lectures on Transfusion Medicine presented to Pathology and Hematology/Oncology House Officers.
H. Seminars and lectures on Pathology of Breast to Pathology House Officers.
I. Lectures on Transfusion Medicine to Pharmacology and Therapeutics senior student elective course. February 10, 1995.
J. Planning committee for curriculum in hematology for sophomore medical students.
K. Lecture, Pathology of the Breast, to Dental Pathology Course.
L. Presentation of consultation slide conferences (four) on pathology of the breast to pathology house officers.
M. Presentation of Clinical Pathology Grand Rounds. Medical-legal issues in transfusion medicine. April 28, 1995.

UNIVERSITY:

A. Doctoral committee for Midori Koga, candidate for Doctor of Musical Arts in Piano, School of Music.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Rapid 4D MRI of Gad-DTPA enhancement for breast lesion characterization (Grant DAMD 17-94-J-4381 from U.S. Army medical research acquisition activity ($605,849/4 years) (T. Chenevert, Principal Investigator, with members of Department of Radiology).
B. New Ultrasound Methods for Cancer Diagnosis and Treatment (3-5 years at 5% effort).
C. Microvascular and Structural Imaging of Breast Cancer (3-5 years at 3% effort).
D. Mucinous Carcinoma of the Breast: Correlation of Mammographic Appearance with Histopathology (with M. Helvie and T. Wilson).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Transfusion Medicine Program.
B. Director, Training Program in Blood Banking/Transfusion Medicine.

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

A. Transfusion Committee, Chairman.
B. Breast Care Center.
C. Bone Marrow Homotransplantation Task Force.
D. AIDS Task Force.
E. Hospital Quality Assurance Committee.
F. Task Force on Medical Center Governance, Medical Center Clinicians' Group.
G. Hematology Sequence Advisory Committee, M-2 year.
H. Medical School Grievance Review Committee.
I. University of Michigan Senate Assembly.

REGIONAL AND NATIONAL:

A. American Association of Blood Banks:
   1. Transfusion Practices Committee.
   2. Institutional Dues Structure Committee.
   3. Transfusion Medicine Research Strategies Committee.
B. American Society of Clinical Pathologists.
C. College of American Pathologists:
   1. Task Force on Breast Cancer, Chairman.
D. United States and Canadian Academy of Pathology:
   1. Abstract Review Board.
E. Michigan Society of Pathologists.
F. Southeastern Michigan Region Red Cross Blood Program:
   1. Board of Directors.
   2. Medical Advisory Committee.
G. Consultant, Veterans Administration Hospital, Ann Arbor.
H. 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. Reviewer, Cancer.
F. Reviewer, Journal of the American Medical Association.
G. Reviewer, Blood.
H. Reviewer, Cancer Research.
I. Reviewer, Journal of Clinical Oncology.

INVITED LECTURES/PAPERS/SEMINARS:

1. Blood component therapy. Lecture to Section of Thoracic Surgery, University of Michigan Medical School, September 24, 1994.
2. Borderline Breast Lesions. Lecture and Workshop to 3rd annual M-Labs symposium, Department of Pathology, University of Michigan, October 1, 1994.
3. Diagnostic Problems in Surgical Pathology of the Breast. Course presented with S. Silverberg at annual meeting of the American Society of Clinical Pathologists, Orlando, Florida, October 20, 1994.
4. Transfusion practices in HIV-infected patients. Paper presentation to annual meeting of American Association of Blood Banks, San Diego, California, November 15, 1994.
5. Legal aspects of blood transfusion. Seminar presentation with E. Goldman to annual meeting of American Association of Blood Banks, San Diego, California, November 14, 1994.
6. Selected aspects of breast pathology. Seminar presented to Detroit Pathology Society, Detroit, Michigan, September 20, 1994.
7. Presentation of Grand Rounds on Transfusion Medicine to Department of Anesthesiology, February 2, 1995.
8. Presentation of Grand Rounds to Department of Radiology: Spiculated lesions of the breast, March 9, 1995.
9. Pathology of noninvasive breast cancer. Course: Multimodality of Treatment of Breast Cancer. Sponsored by the Department of Radiation Oncology, University of Michigan, (Pinehurst, North Carolina), April 7, 1995.
10. Pathology of invasive breast cancer. Course: Multimodality of Treatment of Breast Cancer. Sponsored by Department of Radiation Oncology, University of Michigan, (Pinehurst, North Carolina), April 7, 1995.
11. The role of the pathologist in assessing prognosis of breast cancer. Course: Multimodality Treatment of Breast Cancer. Sponsored by Department of Radiation Oncology, University of Michigan, (Pinehurst, North Carolina), April 9, 1995.
12. Wilson, T., Helvie, M., Oberman, H.A. and Joynt, L.K.: Mucinous carcinoma of the breast: mammographic appearance with histopathologic correlation. Roentgen Ray Society, May 3, 1995.
13. Problem solving in the blood bank. Workshop, Current Topics in Blood Banking, 22nd annual symposium, University of Michigan, May 31, 1995.
14. Oberman, H.A. and Goldman, E.B.: Legal aspects of transfusion medicine. Current Topics in Blood Banking. 22nd annual symposium, University of Michigan, June 1, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Butch, S.H., Judd, W.J., Steiner, E.A., Stoe, M. and Oberman, H.A.: Electronic verification of donor-recipient compatibility: the computer crossmatch. Transfusion 34:105-109, 1994.
2. McCullough, J., Aster, R.H., Bove, J.R., Garratty, G., Issitt, P., Oberman, H.A. and Perkins, H.: Statistics in articles published in Transfusion. 34:654-656, 1994.

3. Wilson, T., Helvie, M., Oberman, H.A. and Joynt, L.K.: Mucinous carcinoma of the breast: mammographic appearance with histopathologic correlation. Am J. Roentgenol., In Press.
4. Popovsky, M., Benson, K., Glassman, A., Hume, H., Oberman, H.A., Pisciotto, P. and Anderson, K.: Transfusion practices in HIV-infected patients. Transfusion, In Press.
5. Pierce, L.J., Oberman, H.A., Strawderman, M.S. and Lichter, A.S.: Microscopic extracapsular extension in the axilla: is this an indication for axillary radiotherapy? Int. J. Radiation Oncol., In Press.
6. Piscioto, P., Benson, K., Hume, H., Glassman, A.B., Oberman, H.A., Popovsky, M., Hines, D. and Anderson, K.: Prophylactic versus therapeutic platelet transfusion practices in hematology and/or oncology patients. Transfusion 35:498-502, 1995.

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

1. Oberman, H.A.: Scientific Basis of Transfusion Medicine, by Anderson and Ness. Arch. of Pathol. Lab. Med. 119:564, 1995.
2. Book Review Editor, American Journal of Surgical Pathology.

SEM H. PHAN, Ph.D., M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Autopsy Service.

II. TEACHING ACTIVITIES:

A. Hong-Yi Zhang, M.D., Ph.D., Postdoctoral Fellow.
B. Kai Zhang, M.D., Postdoctoral Fellow.
C. Jonathan Yang, Undergraduate Research Opportunities Program.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Mechanisms of pulmonary fibrosis", NIH, RO-1, HL 28737, (20% effort), 1991-1996 (years 09-13), (Total direct costs: $928,544).
B. Principal Investigator, "Myofibroblasts in pulmonary fibrosis", NIH, RO-1, HL 52285, (25% effort), 1994-1998 (years 01-04), (Total direct costs: $906,614).
C. Project Leader, Project IV, "Macrophage function in lung injury and fibrosis", (P.A. Ward, Principal Investigator), NIH, PO-1, HL 31963, (25% effort), 1984-1994, (Total direct costs: $512,859, Project IV only).
D. Co-investigator, "Regulation of IL-8 gene expression", (D. G. Remick, Principal Investigator), NIH, RO-1 DK 43455, (5% effort), 1995-1999, (Total direct costs: $839,199).
E. Co-investigator, Project 1, "Cytokine networks regulating inflammation of pulmonary fibrosis", (G. B. Toews, Principal Investigator), SCOR NIH, P-50 HL 46487, SCOR in Occupational and Immunologic Lung Diseases, Project 1, (5% effort), 1992-1996, (Total direct costs: $828,155).
F. Co-investigator, "Renal fibrosis", (R. Wiggins, Principal investigator), NIH, RO-1, DK 46469, (10% effort), 1993-1998, (Total Direct Costs: $599,644).

PROJECTS UNDER STUDY:

A. Lung macrophage/monocyte, recruitment and activation during lung injury and fibrosis.
B. Cytokine regulation of fibroblast function - in terms of chemotaxis, collagen metabolism and proliferation in fibrotic lesions of lung, kidney and skin.
C. Regulation of α-smooth muscle actin expression and myofibroblast phenotype.
D. Regulation of production of fibrogenic mediators and cytokines by pulmonary endothelial cells, fibroblasts and keratinocytes.
E. Production of monocyte chemotactic factors by alveolar macrophages and fibroblasts and endothelial cells, and its regulation by bleomycin and cytokines.
F. Regulation of cytokine gene expression in fibrotic tissues.
G. Mechanism of eosinophil recruitment and regulation of cytokine expression by this cell.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Member, Medical Scientist Training Program Operating Committee.

REGIONAL AND NATIONAL:

A. Member, Lung Biology and Pathology Study Section, National Institutes of Health.
B. Reviewer for the following journals:
   1. American Review of Respiratory Diseases.
   2. American Journal of Pathology.
   3. Chest.
   4. Circulation Research.
   5. Journal of Immunology.
   6. American Journal of Physiology.
   7. American Journal of Respiratory Cell and Molecular Biology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Seminar, "Cellular localization of lung collagen gene expression in pulmonary fibrosis", VIth International Pulmonary Fibrosis Colloquium, Dijon, France, 1994.
2. Lecture, "Myofibroblasts in pulmonary fibrosis", Renal Fibrosis Conference, Gottingen, Germany, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Smith, R.E., Strieter, R.M., Phan, S.H., Lukacs, N.W., Huffnagle, G.B., Wilkie, C.A., Burdick, M.D., Lincoln, P., Evanoff, H. and Kunkel, S.L.: Production and function of murine macrophage inflammatory protein-1α in bleomycin-induced lung injury. J. Immunol. 1994.
2. Zhang, K., Gharaee-Kermani, M., Jones, M.L., Warren, J.S. and Phan, S.H.: Monocyte chemoattractant protein-1 gene expression in bleomycin-induced pulmonary fibrosis. J. Immunol. 153:4733-4741, 1994.
3. Friedland, M., Karmiol, S., Phan, S.H., Rodriguez, J.L., Normolle, D., Smith, D. Jr. and Garner, W.L.: Fibroblast responses to cytokines are maintained during aging. Ann. Plastic Surg., In Press, 1994.
4. Zhang, K., Garner, W., Cohen, L., Rodriguez, J. and Phan, S.H.: Localization of type I, III, IV collagen and TGFβ-1 mRNA in hypertrophic scar by in situ hybridization. J. Invest. Dermatol. 104:750-754, 1995.
5. Hull, S., Meisler, N., Absher, M., Phan, S.H. and Cutroneo, K.: Glucocorticoid-induced down regulation of transforming growth factor-β1 in adult rat lung fibroblasts. Lung 173:71-78. 1995.
6. Zhang, K., Flanders, K.C., and Phan, S.H.: Cellular localization of transforming growth factor B expression in bleomycin-induced pulmonary fibrosis. Am. J. Pathol. In Press, 1995.

BOOKS/CHAPTERS IN BOOKS:

1. Phan, S.H.: Endothelial cells in pulmonary fibrosis, in, Phan, S. H. and Thrall, R.S. (eds), Pulmonary Fibrosis, Marcel Dekker, New York, Chapter 14, pp 481-510, 1995.
2. Phan, S.H.: New strategies for treatment of pulmonary fibrosis. Thorax. 50:415-421, 1995.
3. Smith, R.E., Strieter, R.M., Zhang, K., Phan, S.H., Standiford, T.J., Lukacs, N.W. and Kunkel, S.L.: A role for C-C chemokines in fibrotic lung disease. J. Leukocyte Biol. 57:782-787, 1994.

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

1. Garner, W.L., Freedland, M.H., Karmiol, S., Rodriguez, J.L., Normolle, D., Phan, S.H. and Smith, D.J.: Cytokine responses of dermal fibroblasts are maintained in the elderly. Wound Healing Society, San Francisco, California, 1994.
2. Gharaee-Kermani, M., McGarry, B., and Phan, S.H.: Lung transforming growth β_1, β_2, and β_3 expression in bleomycin-induced pulmonary fibrosis. FASEB J., 1995.
3. Zhang, K., McGarry, B. and Phan, S.H.: Cellular localization of transforming growth factor β_1 gene expression in pulmonary fibrosis. FASEB J., 1995.
4. Smith, R.E., Strieter, R.M., Phan, S.H., Lukacs, N.W. and Kunkel, S.L.: Macrophage inflammatory protein-1α mediates B-cell accumulation during bleomycin-induced lung injury. FASEB J., 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Associate Director, Clinical Microbiology/Virology Laboratories.
B. Director, UMMC Ypsilanti Pediatrics Health Care Center Laboratory.
C. Director, UMMC Ypsilanti Family Practice Health Care Center Laboratory.
D. Coordinator, Infectious Disease Microbiology Laboratory rounds.
E. Technical Consultant, M-Labs.

II. TEACHING ACTIVITIES:

A. Coordinator, Pathology House Officer Microbiology rotation.
B. Lecturer, Clinical Pathology Grand Rounds.
C. Lecturer, Pathology PTH CLNL - 101.
D. Coordinator, Clinical Microbiology In-Service Program.
E. Lecturer, M-Labs Educational Program.
F. Virology rotation for Ghada Khalife, M.D.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Candida Vaginosis Study", National Institutes of Health, Principal Investigator: Barbara Reed, Department of Family Practice.
B. "MRL Quinolone Study", MRL Reference Laboratory, Franklin, Tennessee.
C. "Viral Serology Study", Gull Laboratories, Salt Lake City, Utah.
D. "Timentin E-Test Evaluation", Smith Kline Beecham, King of Prussia, Pennsylvania.
E. "Synercid - Vancomycin-resistant enterococci", Rhone-Poulenc, Collegeville, Pennsylvania.
F. "Effect of Delayed Entry on Recovery of Blood Isolates", Organon Teknika, Durham, North Carolina.
G. Changes in the *In Vitro* Susceptibility of the *Bacteroides fragilis* Group", Merck, Sharp and Dohme, West Point, Pennsylvania.

PROJECTS UNDER STUDY:

A. PCR for detection of *Pneumocystis carinii.*

B. PCR for detection of herpes simplex virus in CSF.
C. PCR for detection of *Chlamydia trachomatis* in male urine.
D. Evaluation of the Gull/Omni Automated Serology System.
E. Detection of *Ureaplasma urealyticum* in lung aspirates from infants with chronic pulmonary disease.
F. Comparative evaluation of the E-Test for anaerobe susceptibility.
G. Evaluation of the Crystal System for identification of nonfermenters.
H. Epidemiology of vancomycin-resistant *Enterococcus faecium* using PFGE.
I. Recovery of bacteria from sterile body fluids using the BacT/Alert.
J. Effective selection of antimicrobics.
K. Effect of antifungal agents on the detection of yeasts in the BacT/Alert.
L. Recovery of non-tubercular AFB from patients with cystic fibrosis.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Clinical Pathology Laboratory Director's Committee.
B. Test Utilization Committee.
C. UMMC Health Care Centers Laboratory Committee.
D. Chair, Clinical Microbiology/Virology Senior Staff Meeting.

MEDICAL SCHOOL/HOSPITAL:

A. Hospital Infection Control Committee.
B. Pharmaceutical & Therapeutics Committee (antimicrobics).
C. Committee for Restricting Antimicrobial Usage (ad Hoc).

REGIONAL/NATIONAL:

A. President, Michigan Branch of the American Society for Microbiology.
B. Executive Board, South Central Association for Clinical Microbiology.
C. Co-Chair, Tri-County Clinical Microbiology Association.
D. Co-Chair, Michigan Microbiology Laboratory Director's Association.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

A. American Society for Microbiology.
B. European Congress for Clinical Microbiology and Infectious Diseases.
C. Infectious Disease Society of America.
D. Michigan Infectious Disease Society.
E. South Central Association for Clinical Microbiology.
F. Tri-County Microbiology Association.

INVITED LECTURES/SEMINARS:

1. "Emergence of penicillin-resistant *Streptococcus pneumoniae* and vancomycin-resistant entercocci at the University of Michigan", Michigan Infectious Disease Society, Lansing, Michigan.
2. "Application of Molecular Diagnostics in Clinical Microbiology", Michigan Pathology Society Annual Meeting, Ann Arbor, Michigan.
3. "Testing variables in antimicrobial susceptibility testing", Metropolitan Hospital In-service Program, Cleveland, Ohio.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. MacDonald, L.J., Pierson, C.L and Chenoweth, C.E.: Penicillin-resistant *Streptococcus pneumoniae* at a tertiary care center. Clin. Infect. Dis., In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Duggan, J.M., Goldstein, S.J., Chenoweth, C.E., Pierson, C.L. and Bradley S.F.: Antimicrobial susceptibilities of clinical isolates of Achromobactor xylosoxidans. Diag. Microbiol. Infect. Dis.
2. Eyler, A.E., Pierson, C.L. and Reed, B.D.: Improved diagnosis of Candida vulvovaginitis using Diamond's media modified. J of Women's Health.
3. Carver, P.L., Welage, L., Pierson, C.L. and Kauffman, C.: Alterations in gastric acidity in HIV-infected patients. Clin. Infect. Dis.

BOOK/CHAPTERS IN BOOKS:

None.

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

1. Blythe, L.K., Pierson, C.L., Jones, M.F. and Smith, T.F.: Comparison of five commercial kits for the detection of antibodies to *Mycoplasma pneumoniae* in clinical sera. Abstracts, Amer. Soc. for Microbiol. G14, pg 299.
2. Koczman, C.L., Young, C.L and Pierson, C.L.: Effect of delayed entry on seeded BacT/Alert and FAN bottles. Abstracts, Amer. Soc. for Microbiol. C14, pg 3.

RODOLFO F.H. RASCHE, M.D.
CLINICAL ASSISTANT PROFESSOR II IN PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

OVERVIEW:

I continued with the same level of activity (65%) towards the M-Labs Program. At the end of this period, we concluded our selection of four new people. We continue to see a steady growth of CP revenues from new and existing clients as well as from an increased activity in AP consults. The M-Labs Symposium for pathologists continues to be successful, the sixth coming up October 14, 1995. In order to get enough input into our outreach activities from our lab directors an advisory group was started in April. My M-Labs-related activities also include signing out PAP smears from our clients and a marketing plan was started jointly with the Cytopathology group in order to increase their number of outside cases. Outside of my M-Labs activities, I continue to help cover autopsies in the Department.

I. CLINICAL ACTIVITIES:

A. Reading surgicals for M-Labs' clients (Albion and Addison Hospitals and selected offices). This activity is predominantly performed by E.M. Silverman, M.D. Reporting on consultation cases from our clients.
B. Cytopathology: reviewing and verifying cases from the University of Michigan Health Service and other M-Labs clients.
C. Autopsy coverage at the University Hospitals five weeks a year and six week-ends a year.
D. Pathologist, on site coverage for Albion and Addison Community Hospitals.

II. TEACHING ACTIVITIES:

A. Read out autopsies with house officers.
B. Organize and lecture at the MLabs Symposium, a one day-long event with lectures and case presentations for pathologists. Discussions also include Managed Care and Utilization. Fifth symposium held on May 6, 1995.
C. In-service teaching to laboratory staffs at Albion Community Hospital and the University of Michigan Health Service.

III. RESEARCH ACTIVITIES:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Associate Director, M-Labs Program. Participate in planning, marketing and implementation.
B. Organize advisory group (directors of laboratories) to assist MLabs activities.
C. Problem solving with lab directors and supervisors.
D. Communication forums with laboratory staff.

OTHER:

A. Director of Laboratory, University of Michigan Health Service.
B. Medical staff member at Albion and Addison Hospitals.
C. Monthly colposcopy meeting with Gynecology staff at the University of Michigan Health Service.

V. OTHER RELEVANT ACTIVITIES:

A. Continued enhancement of the MLabs version of the Spectrum, a newsletter sent to our clients and their medical staff.
B. Inspector for College of American Pathologists Inspection and Accreditation Program.
C. Fellow, College of American Pathologists.
D. Started a QA program for pathologists with AP faculty approval.
E. Participated in a week-long conference on networking, managed care and legal issues, sponsored by the Mayo Clinic.

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

ANNUAL DEPARTMENTAL REPORT

1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Director, Autopsy Service.
B. Supervision of Autopsies (2.5 months).
C. Coordinator of Senior Staff Autopsy Call Schedule.
D. Deputy Medical Examiner for University Hospitals (16 weeks).
E. Forensic Pathology (16 weeks).
F. Director, Electron Microscopy Service.

II. TEACHING ACTIVITIES:

A. Coordinator, Biweekly Pathology Gross Conference.
B. Lectures to Pathology House Officers in Anatomic and Clinical Pathology.
C. Lecturer, Pathology 600 Course.
D. Pathology 600, Provided written critiques of student autopsy write-ups (200).
E. Laboratory Instructor, Histopathology Laboratory for M1 students.
F. Mentor - Fourth Year Medical Student Clerkship.
G. Transplant Journal Club, two presentations.
H. Directed research of Allan Olson, M.D. (Department of Pediatrics), Jorge Rodriguez, M.D. (Department of Surgery); House Officers - Devina Prakash (Pediatrics) Postdoctoral fellows, Gordon Wollenberg, D.V.M., Ph.D., Lorelie Villarete, Ph.D.; Graduate students - Jami Foreback, Medical Students - Sunir Garg.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Regulation of gene expression of soluble mediators of inflammation using the following models:
   1. Endotoxin-stimulated human whole blood.
   2. Endotoxin injection in mice.
   3. Cecal ligation and puncture.
B. Toxic effects of immunomodulators.
C. Pathophysiology of septic shock.
D. Quantitation of mediators in septic shock.

E. Cloning, sequencing, and expressing cytokines including mTNF, hTNF, mIL-6, hIL-8, MCP, JE.
F. Oxident regulation of IL-8 gene expression.
G. Mechanisms of nosocomial pneumonia, and association with IL-8.
H. Immunopathology of inflammatory bowel disease.

SPONSORED SUPPORT:

A. Principal Investigator, "The Role of Cytokines in Sepsis and Trauma", GM44918 $906,182, 1990-1996.
B. Principal Investigator, "The Effects of IL-10", $31,500, 1994-96.
C. Principal Investigator, "Hepatic Ischemia-Induced TNF and Multi-Organ Injury", DK42455.
D. Sponsor, Medical Research Council of Canada Training Fellowship, Gordon Wollenberg, D.V.M., Ph.D., recipient.
E. Principal Investigator, "Correlation of Cytokine Levels with APACHE III Scores", $3000, 1994.
F. Pricipal Investigator, "Regulation of IL-8 gene expression: four years, GM50401 $870,822, 1995-1999.
G. G. Burroughs Wellcome Travel Fund, $3,890.00, 1995.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director - Autopsy Service.
B. Director, Electron Microscopy Service.
C. Interviewer - Candidates for faculty, house officer, postdoctoral, and graduate student positions.
D. Funeral Director's Tea, January 1995.
E. Co-ordinator of call schedule, autopsy service.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Medical School Admissions Committee.
B. Member, Michigan Cancer Center.
C. Reviewer, Biomedical Research Council grants.
D. Reviewer, Department of Surgery grants.

REGIONAL AND NATIONAL:

A. Co-Chair, Michigan Department of Public Health Postmortem Examination Workgroup.
B. Member, Executive Committee, Dementia Subcommittee, Chronic Disease Advisory Committee to the Michigan Department of Public Health.

C. Member, Dementia Subcommittee, Chronic Disease Advisory Committee to the Michigan Department of Public Health.
D. Deputy Medical Examiner for Washtenaw County.
E. Member, Executive Committee, Michigan Association of Medical Examiners.
F. Secretary, Michigan Association of Medical Examiners.
G. Member, Michigan Association of Medical Examiners, Shock Society, American Association of Immunologists, A. James French Society, American Society of Investigative Pathologists, United States-Canadian Academy of Pathology.

V. OTHER RELEVANT ACTIVITIES

A. Reviewer, Veterans Administration Merit grants.
B. Editorial Board: Shock
C. Reviewer:
1. Laboratory Investigation.
2. Journal of Immunology.
3. Journal Leukocyte Biology.
4. American Journal of Pathology.
5. Immunology and Infectious Diseases.
6. Circulatory Shock.
7. Journal of Clinical Investigations.
8. Infection and Immunity.
9. Blood.
10. Shock.
11. American Journal of Physiology.
12. Journal of Immunology.
13. Journal of Gerontology.

INVITED LECTURES/SEMINARS

1. Invited speaker "Update on Cytokines", American Society of Clinical Pathology, October, 1994
2. Invited organizer and participant, Michigan Association of Medical Examiners Annual Meeting, Midland, Michigan, October 1994.
3. Invited speaker "Update on Cytokines", Clinical Pathology Grand Rounds, University of Michigan, November 1994.
4. Invited speaker "Cytokines and the Plastic Surgeon", Plastic Surgery Research Conference, March 1995.
5. Invited speaker "Measurement of Cytokines, Protein and mRNA", Michigan Society for Clinical Laboratory Science, April 1995.
6. Invited speaker "Strategies for Use of Cytokine Inhibitors", Deaconess Hospital Course, May 1995.
7. Invited speaker "Autopsies", University of Michigan, Summer Minority Students, June 1995.
8. Visiting professor "The Role of Cytokines in Infectious Disease", University of Illinois, June 1995.
9. Invited participant, Washtenaw County Medical Examiner's Roundtable Discussion.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Saravolatz, L.D., Wherry, J.C., Spooner, C., Markowitz, N., Allred, R., Remick, D., Fournel, M. and Pennington, J.E.: Clinical safety, tolerability, and pharmacytokinetics of murine monoclonal antibody to human tumor necrosis factor-α. J. Infec. Dis. 1994; 169:214.
2. Colletti, L.M., Remick, D.G. and Campbell, D.A., Jr.: LPS pretreatment protects from hepatic ischemia/reperfusion. J.Surg.Res. 57:337-334, 1994.
3. DeForge, L.E., Takeuchi, E., Nguyen, D.T. and Remick, D.G.: Immunological priming attenuates the in vivo pathophysiological response to lipopolysaccharide. Comparison of cytokine production, tissue injury, and lethality in complete Freund's adjuvant-primed mice and in unprimed mice. Am.J.Pathol. 599-611, 1994.
4. Doherty, J.F., Golden, M.H., Remick, D.G. and Griffin, G.E.: Production of interleukin-6 and tumour necrosis factor-alpha *in vitro* is reduced in whole blood of severely malnourished children. Clin.Sci(Colch). 86:347-351, 1994.
5. Garner, W.L., Rodriguez, J.L., Miller, C.G., Till, G.O., Rees, R.S., Smith, D.J. and Remick, D.G.: Acute skin injury releases neutrophil chemoattracttants. Surgery 116:42-48 1994.
6. Griffin, G.E., Negussie, Y., Fekade, D., Morlese, J., Forrester, T. and Remick, D.G.: The Jarisch-Herxheimer reaction: A paradigm of the cytokine cascade in man. Clinical Infectious Diseases 1:65-74, 1994.
7. Remick, D.G.: Cytokines and septic shock. Clinical Infectious Diseases 1:37-50, 1994.
8. Remick, D.G., Colletti, L.M., Scales, W.A., McCurry, K.R. and Campbell, D.A., Jr., Cytokines and extrahepatic sequelae of ischemia-reperfusion injury to the liver. Ann.N.Y.Acad.Sci. 723:271-283, 1994.
9. Waage, A., Remick, D.G., Steinshamm, S., DeForge, L. and Lamvik, J. Interleukin-8 in serum in granulocytopenic patients with infections. British Journal of Haematology 86:36-40, 1994.
10. Brieland J.K., Flory C.M., Jones M.L., Miller G.R., Remick D.G., Warren J.S. and Fantone J.C. Regulation of monocyte chemoattractant protein-1 gene expression and secretion in rat pulmonary alveolar macrophages by lipopolysaccharide, tumor necrosis factor-alpha, and interleukin-1 beta. Am. J. Respir. Cell. Mol. Biol. 12:104-9, 1995.
11. Hsi, E.D. and Remick, D.G.: Monocytes are the major producers of interleukin-1β in an ex vivo model of local cytokine production. J of Interferon and Cytokine Research 1, 1995.
12. Ulich T.R., Howard S.C., Remick D.G., Wittwer A., Yi E.S., Yin S., Guo K., Welply J.K. and Williams J.H..: Intratracheal administration of endotoxin and cytokines. VI. Antiserum to CINC inhibits acute inflammation. Am. J. Physiol. 268:L245-50, 1995.
13. Colletti L.M., Remick D.G. and Campbell D.A., Jr.: Desferal attenuates TNF release following hepatic ischemia/reperfusion. J. Surg. Res. 57:447-53, 1994.
14. Scales W.E., Campbell D.A., Jr., Green M.E. and Remick D.G.: Hepatic ischemia/reperfusion injury: importance of oxidant/tumor necrosis factor interactions. Am J Physiol 267:G1122-7, 1994.

15. Ulich T.R., Fann M.J., Patterson P.H., Williams J.H., Samal B., del Castillo J., Yin S,. Guo K. and Remick D.G.: Intratracheal injection of LPS and cytokines. V. LPS induces expression of LIF and LIF inhibits acute inflammation. Am. J. Physiol. 267:L442-6, 1994.
16. Ulich T.R., Howard S.C., Remick D.G,. Yi E.S., Collins T., Guo K., Yin S., Keene J.L., Schmuke J.J. and Steininger C.N., et al.: Intratracheal administration of endotoxin and cytokines: VIII. LPS induces E-selectin expression; anti-E-selectin and soluble E-selectin inhibit acute inflammation. Inflammation 18:389-98, 1994.

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

1. Brieland, J.K., Freeman, P.T., Remick, D.G., Hurley, M.C., Fantone, J.C. and Engleberg, N.C. Endogenous tumor necrosis factor alpha (TNF-α) and gamma interferon (IFN-γ) *facilitate resolution of replicative legionella pneumophila* lung infection in A/J mice. Society for Leukocyte Biology 30th National Meeting, 1994.
2. Rodriguez, J.L., Cardellio, A.L., Corridore, M., Taheri, P.A., Garner, W.L., Gerndt, S.J. and Remick, D.G.: Human alveolar neutrophil dysfunction following trauma. Society of University Surgeons, 1994.
3. Cardellio, A.L., Remick, D.G. and Rodriguez, J.L. The upregulation of systemic cytokines in response to injury does not alter immune function. The American Association for the Surgery of Trauma, 1994.
4. Prakash, D. and Remick, D.G.: Reactive oxygen intermediates regulate chemokine production, Exp. Biol., 1995.
5. Wollenberg, G.K., Bolgos, G.L. and Remick, D.G.: Sepsis does not alter TNF, IL-6 and GRO alpha release by lung, Exp. Biol., 1995.
6. Preston, A.M. and Remick, D.G.: TNF soluble receptors and alpha TNF antibody block membrane bound TNF bioactivity, Exp. Biol., 1995.
7. Villarete, L. and Remick, D.G.: Nitric oxide regulation of cytokine gene expression, Exp Biol, 1995.
8. Bolgos, G.L., Wollenberg, G.K., Huie, T. and Remick, D.G.: Effects of high dose whole body radiation on cytokine response, Exp. Biol., 1995.
9. Remick, D.G., Manohar, P., Bolgos, G.L., Rodriguez, J., Moldawer, L. and Wollenberg, G.K. Anti-tumor necrosis factor antibody reduces LPS lethality, but not true sepsis, Exp. Biol., 1995
10. Yi, E.S., Lee, .S., Tang, W., Remick, D.G., Qi, M., Yin, S. and Ulich, T.R. Experimental model of angiitic form of pulmonary sarcoidosis, Exp. Biol., 1995.

BOOKS AND CHAPTERS IN BOOKS

1. Remick, D.G.: Macrophage-derived cytokines, in, van Oss, C.J. and van Regenmortel, M.H. (eds), Immunochemistry, Marcel Dekker, Inc. New York, NY, pp. 995-1016, 1994.
2. Remick, D.G. and DeForge L.E.: Cytokines and pulmonary fibrosis. Chapter 18, in, Phan, S.H. and Thrall, R.S. (eds), Pulmonary Fibrosis, Marcel Dekker, Inc, New York, NY, pp. 599-626, 1995.

CHARLES W. ROSS, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Director, Clinical Flow Cytometry Laboratory.
B. Diagnostic Surgical Pathology, Hematopathology.
C. Clinical Hematology Laboratory.
D. Clinical Molecular Diagnostics Laboratory.
E. Hematopathology Consultation Cases (including M-Labs and Veterans Administration Hospital).

II. TEACHING ACTIVITIES:

A. Medical Students and Dental Students:
   1. Lecturer, M2 Hematology Sequence.
   2. Laboratory Instructor, M2 Hematology Sequence.
   3. Lecturer, Dental School Pathology 630.
   4. Histopathology Laboratory Instructor, M1 Histology Course.
   5. Instructor, hematology portion of clinical pathology rotation, M4 clerkship in general pathology.
   6. Lecturer, Hematology Sequence, M4 clerkship in clinical pathology.
   7. Instructor, Hematology Sequence, summer program for minority M1 students.

B. House Officers:
   1. Sign-out of bone marrow biopsies, aspirates, blood smears, and body fluids in Hematology Laboratory.
   2. Sign-out of lymph node biopsies and review of hematopathology consultation material.
   3. Flow Cytometry sign-out.
   4. Molecular Diagnostics sign-out.
   5. Hematopathology case conferences/bimonthly.
   6. Hematopathology lecturer/bimonthly.

C. Hematopathology teaching:
   1. Leukemia conference/biweekly.
   2. Lymphoma conference/weekly.
   3. Molecular Diagnostics section conference/weekly.
   4. Cutaneous Lymphoma Conference/monthly.

D. Clinical Pathology Grand Rounds (two lectures).
E. Clinical Pathology Case Conference/weekly.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-investigator, "The role of stromal dendritic cells in cutaneous B cell lymphoma:, University of Michigan Cancer Center Grant, March 1, 1994 through February 28, 1995.

PROJECTS UNDER STUDY:

A. Immunophenotyping in acute and chronic leukemias.
B. Phenotyping and genotyping of lymphomas.
C. Detection of immunoglobulin gene rearrangements by the polymerase chain reaction.
D. Effects of radioimmunotherapy in B-cell lymphoma.
E. Detection of infectious agents in lymphoid lesions by polymerase chain reaction.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Clinical Flow Cytometry Laboratory.
B. Coordinator, CP resident teaching program.
C. Immunohistochemistry Utilization Committee.

REGIONAL/NATIONAL:

A. Member, Southwest Oncology Group Lymphoma Review Panel.
B. Ad hoc manuscript reviewer, American Society of Clinical Pathology.
C. Ad hoc manuscript reviewer, Blood.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Lecturer, "Molecular Diagnostics in Hematopathology", Michigan Society of Pathologists Annual Meeting, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ross, C.W., Schnitzer, B., Sheldon, S., Braun, D.K. and Hanson, C.A.: γ/δ T-cell post-transplant lymphoproliferative disorder presenting primarily in spleen. Am. J. Clin. Path. 102:310-315, 1994.
2. Krishnan, K., Ross, C.W., Adams, P.T., Pereira, A. and Roth, M.S.: Neural cell adhesion molecule (CD56) positive, t(8;21) acute myeloid leukemia (AML, M2) and granulocytic sarcoma. Ann. Hematol. 69:321-323, 1994.
3. Rysenga, E., Linden, M.D., Carey, J.L., Ross, C.W., Schnitzer, B., Sawdyk, M. and Maeda, K.: Peripheral T-cell non-Hodgkin's lymphoma following treatment of nodular lymphocyte predominance Hodgkin's disease. Arch. Pathol. Lab. Med. 119:88-91, 1995.
4. Alkan, S., Ross, C.W., Hanson, C.A. and Schnitzer, B.: Epstein-Barr virus and bcl-2 protein overexpression are not detected in the neoplastic cells of nodular lymphocyte predominant Hodgkin's disease. Mod. Pathol. 8:544-547, 1995.
5 Alkan, S., Morgan, M.B., Sandin, R.L., Moscinski, L.C. and Ross, C.W.: Dual role for Afipia felis and Rochalimaea henselae in cat-scratch disease. Lancet 345:385, 1995.
6. Alkan, S., Schnitzer, B., Thompson, J.L., Moscinski, L.C. and Ross, C.W.: Cyclin D1 protein expression in mantle cell lymphoma. Ann. Oncol., In Press.
7. Hoyer, J.D., Ross, C.W., Li, C.Y., Witzig, T.E., Gascoyne, R.A., Dewald, G.W. and Hanson, C.A . True T-cell chronic lymphocytic leukemia: a morphologic and immunophenotypic study of 25 cases. Blood, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Alkan, S., Ross, C.W., Siddiqui, J., Hanson ,C.A. and Schnitzer, B.: Whipple's disease in lymph nodes: Quick confirmation by polymerase chain reaction amplification.
2. Hsi, E.D., Greenson, J.K., Singleton, T.P., Siddiqui, J., Schnitzer, B. and Ross, C.W. Detection of immunoglobulin heavy chain (IgH) gene rearrangement by polymerase chain reaction (PCR) in chronic active gastritis associated with Helicobacter pylori (GAG-Hp).

BOOKS AND CHAPTERS IN BOOKS:

1. Hanson, C.A. and Ross, C.W.: Clinical applications of molecular biology: Hematopoietic disorders, in McClatchey K.D. (ed), Clinical Laboratory Medicine, Williams & Wilkins, Baltimore, Maryland, 1994.
2. Ross, C.W., Sadler, D.A. and Keren, D.F.: Flow cytometric evaluation of immunodeficiency diseases, in, Bauer, K.D., Duque, R.E. and Shankey, T.V. (eds), Flow Cytometry: Principles and Clinical Applications, Williams and Wilkins, In Press.

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

1. Alkan, S., Siddiqui, J., Ross, C.W., Hanson, C.A. and Schnitzer, B.: Molecular analysis of Whipple's disease presenting in lymph nodes. AJCP 100:342, 1993.
2. Ross, C.W.: Book review, "Tumors of the Hematopoietic S. system", Atlas of Tumor Pathology, Fascicle 28, by Lukes, R.J. and Collins, R.D . Am J Surg Pathol 18:114, 1994.
3. Hoyer, J.D., Ross, C.W., Li, C-Y, Witzig, T.E. and Hanson, C.A.: True T- (CD4+): A morphologic and immunophenotypic study of 18 cases. Mod Pathol 7:111A, 1994.
4. Hsi, E.D., Siddiqui, J., Alkan, S., Schnitzer, B. and Ross, C.W.: Analysis of immunoglobulin heavy chain (IgH) rearrangement in myoepithelial sialadenitis (MESA) by polymerase chain reaction (PCR). Mod Pathol 7:111A, 1994.
5. Utiger, C.A., Ross, C.W., Schnitzer, B. and Hanson, C.A.: Correlation of CD20 fluorescence intensity with morphologic parameters in B-cell chronic lymphoproliferative disorders. Mod Pathol 7:122A, 1994.
6. Kaminski, M.S., Zasadny, K.R., Milik, A.W., Ross, C.W., Francis, I.R., Burgess, J., Crawford, S., *et al*: Updated results of a phase I trial of 131-I-anti-B1 (anti-CD20) radioimmunotherapy (RIT) for refractory B-cell lymphoma. Blood 82:332A, 1993.
7. Rysenga, E., Linden, M.D., Carey, J.L., Ross, C.W., Schnitzer, B., Sawdyk, M. and Maeda, K.: Peripheral T-cell non-Hodgkin's lymphoma following treatment of nodular lymphocytic predominance Hodgkin's disease. Blood 82:577A, 1993.
8. Douglas V.K., Schnitzer B., Ross C.W. Plasma cell leukemia: clinical, laboratory, and morphologic findings. Am J Clin Pathol 102:545, 1994.
9. Alkan, S., Ross, C.W., Thompson, J.L. *et al.* Cyclin D1 protein expression in mantle cell lymphomas. Blood 84:449A, 1994.
10. Kaminski, M.S., Estes, J., Zasadny, K.R., Fenner, M., Francis, I.R., Milik, A.W., Ross, C.W. *et al.* Non-myeloablative radioimmunotherapy with 131-I-anti-B1 for refractory B-cell lymphoma: Phase I results. Blood 84:520A, 1994.
11. McCarthy C.J., Sheldon S., Ross C.W., McCune W.J. Cytogenetic abnormalities and hematologic malignancies associated with the use of alkylating agents in rheumatic diseases. American College of Rheumatology, 58th Annual Meeting, October, 1994.
12. Anderson, M.M., Sheldon, S., Singleton, T.P., Ross, C.W., and Schnitzer, B. Demonstration of a t(2;5) is important in the diagnosis of Ki-1 anaplastic large cell lymphoma (ALCL) with unusual features. Mod Pathol 8:105A, 1995.
13. Anderson, M.M., Singleton, T.P., Ross, C.W., Sheldon, S., and Schnitzer, B. Leukemic phase of mantle cell lymphoma, blastic variant. Mod Pathol 8:105A, 1995.

14. Cox, B., Anderson, M., Schnitzer, B., Ross, C., Sheldon, S. Anaplastic large cell lymphoma: Significance of the t(2;5). Applied Cytogenetics 21:107, 1995.
15. Hsi, E.D., Greenson, J.K., Singleton, T.P., Siddiqui, J., Schnitzer, B., Ross, C.W. Detection of immunoglobulin heavy chain (IgH) gene rearrangement by polymerase chain reaction (PCR) in chronic active gastritis associated with *Helicobacter pylori* (CAG-Hp). Mod Pathol 8:113A, 1995. Winner of Stowell-Orbison Award, US and Canadian Academy of Pathology, March 1995.
16. Alkan, S., Morgan, M.B., Sandin, R., Ross, C., Moscinski, L.C. Cat scratch disease: A dual etiologic role for *Afipia felis* and *Rochalimaea henselae*. Mod Pathol 8:125A, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

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

B. Interdepartmental:
   1. Oral Pathology, clinical consultations on an as needed basis, the University of Michigan School of Dentistry Clinics.
   2. Consultant to Veterans Administration Hospital, Ann Arbor, Michigan.

II. TEACHING ACTIVITIES:

FALL TERM, 1994:

A. Oral Pathology, Course 516, to Freshmen Dental Students (course director).
B. General Pathology Lab, Course 631, to Sophomore Dental Students.
C. Oral Pathology, Course 824, to Senior Dental Students.
D. Dental Hygiene, Course 220, to Sophomore Dental Hygiene Students.
E. Graduate Perio Seminar, to Graduate Periodontal Students.

WINTER TERM, 1995:

A. Oral Pathology, Course 624, to Sophomore Dental Students.
B. Oral Pathology, Course 625, to Sophomore Dental Students.
C. Dental Hygiene, Course 293, to Dental Hygiene Students.
D. Dental Hygiene, Course 313, to Dental Hygiene Students.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Project Director, "Oral Famciclovir in the Treatment of Experimentally Induced Herpes Simplex Labialis", (15%), SmithKline Beecham Pharmaceuticals, total direct costs $180,000.00, 12/01/92-01/01/95.

IV. ADMINISTRATIVE ACTIVITIES:

SCHOOL OF DENTISTRY COMMITTEES:

A. Human Subjects Committee, School of Dentistry.

REGIONAL, NATIONAL AND INTERNATIONAL COMMITTEES:

STATE OF MICHIGAN:

A. Member, Ad Hoc Committee on Regulated Medical Waste Training Standards, Michigan Department of Public Health.
B. Member, Mercury Pollution Prevention Task Force, Michigan Department of Natural Resources.
C. Member, Council of Michigan Dental Specialty Presidents.
D. Member, Specialty Ad Hoc Committee, Michigan Board of Dentistry.
E. Member, State of Michigan Dental Specialty Task Force.
F. President, Michigan Society of Oral Pathology.
G. Member, AIDS Speaker's Bureau, Michigan State Medical Society.
H. Member, Advisory Committee, Special Office on AIDS Prevention and the Disease Surveillance Section, Michigan Department of Public Health.
I. Member, Tobacco-Free Michigan Action Coalition, Michigan Department of Public Health.
J. Consultant, Committee on Cancer and Infection Control, Michigan Dental Association.
K. Member, Special Committee on Health and Hazard Regulation, Michigan Dental Association.
L. Member, Research Screening Committee, Delta Dental Fund.
M. Member, Michigan Coalition on Smoking or Health.
N. Member, Coalition for Access to Health Care.
O. Consultant in Oral Pathology, U.S. Veteran's Administration Hospitals.

NATIONAL:

A. Civilian Professor and Consultant, Office of the Surgeon General, United States Army.
B. Member, Science Information Committee, American Association for Dental Research.
C. Chairman, Council on Dental Therapeutics, American Dental Association.

INTERNATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Manuscript Consultant and Reviewer:
   1. Journal of the American Medical Association.
   2. Journal of Oral Pathology.
   3. Journal of the American Dental Association.
   4. Cancer.
   5. Journal of the Academy of General Dentistry.

HONORS AND AWARDS:

A. The William R. Mann Professor of Dentistry. Regents, The University of Michigan, 1994-1999.

CONTINUING EDUCATION:

A. "Diagnosis and Management of Soft Tissue Diseases", Macomb Dental Society, Warren, Michigan, February 1, 1995.
B. "Diagnosis and Management of Soft Tissue Diseases", Composite Study Club, Cleveland, Ohio, April, 13, 1995.
C. "Current Issues in Oral Pathology as They Relate to Dental Practice", Brighton Dental Study Club, Brighton, Michigan, April 27, 1995.
D. "Oral Complications of Infectious Diseases: Update in Therapy", American Academy of Oral Medicine (49th Annual Meeting), Nashville, Tennessee, May 4, 1995.

VI. PUBLICATIONS:

None.

VII. MISCELLANEOUS:

PROFESSIONAL MEETINGS ATTENDED:

A. American Dental Association Annual Meeting, New Orleans, Louisiana, October 22-25, 1994.
B. "Waste Management in the Dental Office", American Dental Association, New Orleans, Louisiana, October 24, 1994.
C. "An Update on Pharmacology and Therapeutics for the General Practitioner", Delta Dental. Fund and The University of Michigan, Ann Arbor, Michigan, January 11, 1995.
D. "Implementing OSHA Standards in Your Office", Michigan Dental Association, Lansing, Michigan, January 27, 1995.
E. American Academy of Oral Medicine, Nashville, Tennessee, May 2-5, 1995.
F. American Academy of Oral Pathology, Colorado Springs, Colorado, May 7-10, 1995.
G. Various component Dental Societies, Michigan and Ohio.

VII. OFFICES IN PROFESSIONAL SOCIETIES:

Chairman, Council on Dental Therapeutics, American Dental Association, 1992-1994.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Director, Clinical Hematology Laboratory.
B. Director, University of Michigan Health Services Laboratories.
C. Diagnostic Surgical Pathology, Hematopathology (12 months).
D. Diagnostic Hematopathology Consultant, Veterans Administration Hospital.
E. Diagnostic Hematopathology of M-Labs clients.
F. Consultant for external and transfer Hematopathology cases.
G. Review of Southwest Oncology Group (SWOG) cases (circa 150/year).
H. Review of lymphoma cases entered into Children's Cancer Study Group protocols.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITALS:

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

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARD:

A. Human Pathology. Designated reviewer.

INVITED LECTURES/SEMINARS:

1. "Hodgkin's Disease: Diagnosis and Differential Diagnosis", ASCP Workshop, Washington, D.C., October, 1994.
2. "A Practical Approach to the Diagnosis and Differential Diagnosis of Extranodal Lymphomas", ASCP Workshop, Washington, D.C., October, 1994.
3. "A Practical Approach to Diagnostic Hematological Problems", ASCP Educational Course, Lectures given included: a) Non-Hodgkin's Lymphomas; b) Hodgkin's Disease; c) A Practical Approach to the Diagnosis and Classification of Lymphomas and Leukemias by Flow Cytometry, and Electron Microscopy; d) Extranodal lymphomas; and e) Acute Lymphoblastic Leukemias, Orlando, Florida, November, 1994.
4. "Reactive Lymphadenopathies", Hematopathology Tutorial (Sponsored by the University of Minnesota). San Diego, California, February, 1995.
5. "Acute Lymphoproliferative Disorders", ASCP Workshop, Orlando, FL, April, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Rysenga, E., Linden, M.D., Carey, J.L., Ross, C.W., Schnitzer, B., Sawdyk,M. and Maeda, K.: Peripheral T-cell non-Hodgkin's lymphoma following treatment of nodular lymphocyte predominance Hodgkin's disease. Arch. Pathol. Lab. Med. 119:88-91, 1995.
2. Alkan, S., Ross, C.W., Hanson, C.A. and Schnitzer, B.: Epstein-Barr virus and bcl-2 protein overexpression are not detected in the neoplastic cells of nodular lymphocyte predominance Hodgkin's disease. Mod. Pathol. 8:544-547, 1995.

BOOKS AND CHAPTERS IN BOOKS:

1. Schnitzer, B.: Reactive lymphoid hyperplasia, in, Jaffe, E.S. (ed), Surgical Pathology of the Lymph Nodes and Related Organs, 2nd Edition, W.B. Saunders Co., 1994.

2. Schnitzer, B., Chan, W. and Weiss, L: Pathology of lymph nodes, in, Anderson's Pathology, 10th Edition, Mosby, 1995.

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

1. Douglas, V.K., Schnitzer, B. and Ross, C.W.: Plasma cell leukemia. Clinical, laboratory, and morphologic findings. Am. J. Clin. Pathol. 102:545, 1994.
2. Alkan, S., Ross, C.W., Thompson, J.L., Moscinski, L.C. and Schnitzer, B.: Cyclin D1 protein expression in mantle cell lymphomas. Blood 84:449a, 1994.
3. Cox, B., Anderson, M., Ross, C.W., Schnitzer, B. and Sheldon, S.: The significance of the t(2;5) in Ki-1 lymphoma. Applied Cytogen, 1995.
4. Anderson, M.M., Sheldon, S., Singleton, T.P., Ross, C.W. and Schnitzer, B.: Demonstration of a t(2;5) is important in the diagnosis of Ki-1 anaplastic large cell lymphoma (ALCL) with unusual histologic features. Modern Pathol. 8:105A, 1995.
5. Anderson, M.M., Singleton, T.P., Ross, C.W. and Schnitzer, B.: Leukemic phase of mantle cell lymphoma, blastic variant. Modern Pathol. 8:105A, 1995.
6. Hsi, E.D., Greenson, J.K., Singleton, T.P., Sidiqui, J., Schnitzer, B. and Ross, C.W.: Detection of Immunoglobulin heavy chain gene rearrangement by polymerase chain reaction (PCR) in chronic active gastritis associated with helicobacter pylori. Modern Pathol. 8:113A, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994- 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Cytopathology - Six months.
B. Gynecologic Pathology (transfer cases) - 12 months.
C. Consultation service, Department of Pathology:
    1. Cytopathology and Gynecologic Pathology - 12 months.
D. Necropsy Service - One week.

II. TEACHING ACTIVITIES:

A. Medical Students:
    1. Pathology laboratory instructor, September- May, 1994-1995.
    2. Reproductive sequence lecture: Gynecologic Pathology, April 6, 1995.
B. Residents and Cytopathology Fellow:
    1. Sign-out; gynecologic and non-gynecologic cytology cases.
    2. Instruction in the performance and interpretation of fine needle aspirates.
    3. Monthly Cytopathology Conference.
    4. Lecture-Obstetric/Gynecologic Pathology- one hour.
    5. Consult Case Conference - 1/year.
C. Other Education Activities:
    1. Cytotechnologists-Cytopathology conferences - three/year.
    2. Gynecologic Oncology Tumor Board Conference-bimonthly.
    3. Obstetric/Gynecologic Colposcopy/Pathology Conference-monthly.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Cervical atypia in women with SLE treated with intravenous Cyclophosphamide (in conjunction with Dr. J. McCune, Dept. of Internal Medicine/Rheumatology).
B. Genital infections as risk factors for low grade squamous intraepithelial lesion progression (in conjunction with Dr. Barbara Reed, Dept. of Family Practice).
C. The significance of annual vaginal smears in females post hysterectomy for benign gynecologic disease (in conjunction with Dr. Micheal Fetters, Department of Family Practice.)

D. Cytologic features of atypical glandular cells of undetermined significance (AGUS) on cervical smears.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Co-Director, Cytopathology Laboratory.
B. Member, Resident Selection Committee.
C. Member, Internal Departmental Review Committee.
D. Member, Laboratory Services Program Planning Group, East Medical Campus.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Quality Assurance/Quality Control Committee.
B. Member, M II Curriculum Committee-Reproduction Sequence.

REGIONAL AND NATIONAL:

A. Reviewer, Diagnostic Cytopathology.
B. Member, Cytopathology Committee, College of American Pathologists.
C. Member, Standards of Practice Committee, Papanicolaou Society of Cytopathology.
D. Member, Ovarian Cancer Task Force Committee, College of American Pathologists.
E. Member, Cervical Cancer Advisory Committee, Michigan Department of Public Health, Lansing, Michigan.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Squamous and Glandular Cell Atypia of Undetermined Significance, Guest Speaker; School of Cytotechnology, Henry Ford Hospital and Wayne State University, Detroit, Michigan, October 25, 1994.
2. Cytopathology workshop; Fine Needle Aspiration Cytology of Cystic Ovarian Lesions in Conjunction with Peritoneal Washing Cytology, Forty-second Annual Scientific Meeting of the American Society of Cytology, Chicago, Illinois, November 6, 1994.
3. Fine Needle Aspiration Cytology of Cystic Ovarian Lesions, Guest speaker; School of Cytotechnology, Henry Ford Hospital and Wayne State University, Detroit, Michigan, November 30, 1994.
4. Peritoneal Washing Cytology and Fine Needle Aspiration Cytology of Cystic Ovarian Lesions, Guest Speaker; Wisconsin Society of Cytology, Milwaukee, Wisconsin, April 1, 1995.
5. ASCUS and Pitfalls in the Cytologic Diagnosis of Squamous Lesions of the Cervix, Guest Speaker; The Delaware Valley Society of Cytology, Wayne, Pennsylvania, April 22, 1995.
6. Microglandular Hyperplasia and Adenocarcinoma In-situ of the Endocervix, Guest Speaker; Michigan Society of Cytology, Traverse City, Michigan, May 20, 1995.

7. The Role of Fine Needle Aspiration Biopsy in the Evaluation of Ovarian Lesions and the Significance of ASCUS and AGUS Cells in Cervical Smears, Guest Speaker; Fifteenth Annual Cancer Conference and Slide Seminar, University of South Florida College of Medicine and the H. Lee Moffitt Cancer Center, Longboat Key, Florida, June 17, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Selvaggi, S.M.: Cytologic features of squamous cell carcinoma-*in-situ* involving endocervical glands in endocervical cytobrush specimens. Acta Cytol. 38:687-692, 1994.
2. Patterson-Keels, L.M., Selvaggi, S.M., Haefner, H.K. and Randolph, J.F.: Morphologic assessment of endometrium overlying submucosal leiomyomas. J. Reprod. Med. 39:579-584, 1994.
3. Wojcik, E.M. and Selvaggi, S.M.: Fine needle aspiration cytology of cystic ovarian lesions. Diagn. Cytopathol. 11:9-14, 1994.
4. Selvaggi, S.M.: Small cell carcinoma of the ovary in peritoneal fluid. Diagn. Cytopathol. 11:266-270, 1994.
5. Selvaggi, S.M., Haefner, H.K., Lelle, R.J., Pearl, M.K. and Roberts, J.A.: Neovaginal cytology following total pelvic exenteration for gynecologic malignancies. Diagn. Cytolpathol., In Press.
6. Selvaggi, S.M. and Haefner, H.K.: Reporting of ASCUS on cervical smears: Is it significant? Diagn. Cytopathol., In Press.
7. Selvaggi, S.M. and Haefner, H.K.: Microglandular endocervical hyperplasia and tubal metaplasia: Pitfalls in the diagnosis of adenocarcinoma on cervical smears. Submitted to Diagn. Cytopathol.
8. Mikhail, A.A., H.K. and Selvaggi, S.M.: Endocervical polyps as a source of ASCUS and AGUS on cervical smears. Submitted to Diagn. Cytopathol.

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

1. Selvaggi, S.M.: Book Review: Fine Needle Aspiration of Palpable Masses. Stanley, M.W., Lowenhagen, T., Butterworth - Heinmann, 1993; Arch. Pathol. Lab. Med. 118:852, 1994.
2 Lindley, P. and Selvaggi, S.M.: Book Review: Benign to Malignant Progression in Cervical Squamous Epithelium. Ehrmann, R.L., Igaku-Shoin, 1994; Am. J. Surg. Pathol. 18:1272, 1994.
3. Selvaggi, S.M.: Book Review: Malignant Effusions; A Multimodal Approach to Cytologic Diagnosis. Bedrossian, C.W.M., Igaku-Shoin, 1994; Am. J. Surg. Pathol. 19:243, 1995.
4. Selvaggi, S.M., Haefner, H.K.: Reporting of ASCUS on Cervical Smears: Is it Significant? Acta. Cytol. 38:815, 1995.
5. Selvaggi, S.M.: Microglandular endocervical hyperplasia and tubal metaplasia: Pitfalls in the diagnosis of adenocarcinoma on cervical smears. Mod. Pathol. 8:44A, 1995.
6. Mikhail, A.A., Haefner, H.K. and Selvaggi, S.M.: Endocervical polyps as a source of ASCUS and AGUS on cervical smears. Mod. Pathol. 8:42A, 1995.

7. Greenebaum, E., Selvaggi, S.M and Lerner, J.: Fine needle aspiration of cystic ovarian lesions: Detection, cytologic analysis, ancillary techniques, in, Schmidt W.A., Miller, T.R., Cytopathology Annual. ASCP Press, In Press.
8. Selvaggi, S.M. and Lawrence, W.D.: Cytopathology of the uterine cervix, in Jordan, J.A., Blackledge, G.R.P. (eds), Textbook of Gynecologic Oncology, W.B. Saunders Co., In Press.

JACOB N. SHANBERGE, M.D.
CLINICAL PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Chief, Hemostasis and Coagulation Laboratory, William Beaumont Hospital, Royal Oak, Michigan.
B. Hematopathology, Bone Marrow Service, William Beaumont Hospital, Royal Oak, Michigan.
C. Clinical Consultant, Problems in Bleeding and Thrombosis, William Beaumont Hospital, Royal Oak, Michigan.

II. TEACHING ACTIVITIES:

A. Daily "plasma" rounds, monitoring blood component usage, William Beaumont Hospital.
B. Periodic lectures to ICU residents on blood component therapy, William Beaumont Hospital.
C. Clinical Pathology Grand Rounds, Vascular Abnormalities, University of Michigan.
D. Coagulation conferences for pathology residents, William Beaumont Hospital.
E. Seven lectures for Medical Technology Students - Coagulation and Hemostasis, William Beaumont Hospital.
F. Participated in Clinical Pathology Elective for Senior Medical Students - three didactic lectures on Approach to Bleeding Disorders plus case presentations and discussions, University of Michigan.
G. Weekly conferences on Coagulation, Thrombosis and Component Therapy for Blood Bank Residents, University of Michigan.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-Investigator, "Protamine filter for extracorporeal heparin removal," University of Michigan College of Pharmacy, NIH-NHLBI HL-38353 (5%), $204,000, 01/01/95-12/31/95.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Administrator, Afternoon and Night Shifts of Clinical Laboratories, William Beaumont Hospital.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

A. College of American Pathologists, Member of FFP, Platelet and Cryoprecipitate Administration Practice Guideline Development Task Force.

B. Member, Transfusion Committee, William Beaumont Hospital.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Shanberge, J.N.: Hemangioma of the uterus associated with hereditary hemorrhagic telangiectasia. Obstet. Gynecol. 84:708-710, 1994.
2. Shanberge, J.N. and Kajiwara, Y., Quattrociocchi-Longe: Effect of aspirin on adhesion of platelets to intact endothelium *in vivo*. J. Lab. Clin. Med. 125:96-101, 1995.
3. Shanberge, J.N.: Improvement in the tip of a jamshedi needle for use in hard bone. Amer. J. Hematol. 49:263, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Clinical Cytogenetics Laboratory.

II. TEACHING ACTIVITIES:

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

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

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

D. Clinical Pathology Grand Rounds, two lectures.
E. Pediatric Genetics Rounds, weekly participant, one lecture.
F. Leukemia Conference, biweekly.
G. Genetic Counseling graduate students:
   1. Two lectures.
   2. Individual tutorials.

H. Clinical Pathology M4 elective: eight hour lecture/laboratory.
I. Pathology Graduate Course, two lectures.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Role of the use of growth factors and mitogens for cytogenetic examination of hematologic malignancies in a clinical laboratory.
B. Use of growth factors to elaborate expression of a Philadelphia chromosome.
C. Use of intercalating agents to enhance resolution of chromosome bands.
D. Correlation of ploidy with expression of differential function.
E. Role of chromosome abnormalities in eosinophilia.
F. Fluorescence *in situ* hybridization for identification of marker chromosomes.
G. Fluorescence *in situ* hybridization as "interphase cytogenetics".

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Clinical Cytogenetics Laboratory.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Krishnan, K., Adams, P., Silveria, S., Sheldon, S. and Dabich, L.: Therapy-related AML following immunosuppression with azathioprine. Clin. Lab. Hematol., In Press.

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

1. McCarthy, C., Sheldon, S., Ross, C.W. and McCune, J.: Myelodysplastic syndromes in rheumatic diseases after immunosuppressive therapy: a cytogenetic study; presented at the American Rheumatological Society Meeting, Toronto, 1994.
2. Su, L., Sheldon, S. and Weiss, S.: Inflammatory myofibroblastic tumor: evidence for neoplasia. Abstr. USCAP, 1995.
3. Anderson, M., Sheldon, S., Singleton, T., Ross, C.W. and Schnitzer, B.: Demonstration of a t(2;5) is important in the diagnosis of Ki-1 anaplastic large cell lymphoma with unusual features. Abstr. USCAP,1995.
4. Anderson, M., Singleton, T., Ross, C.W., Sheldon, S. and Schnitzer, B.: Leukemic phase of mantle cell lymphoma, blastic variant. Abstr. USCAP, 1995.
5. Cox ,B., Anderson, M., Ross, C.W., Schnitzer, B. and Sheldon, S.: The significance of the t(2;5) in large cell anaplastic lymphoma. Applied Cytogenet. 21:109, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Coverage of M-Labs cases, including most cases from:
   1. Albion Community Hospital, Albion, Michigan (including frozen sections).
   2. University of Michigan Health Service, non-dermatology cases, Ann Arbor, Michigan.
   3. Addison Community Hospital, Addison, Michigan.
   4. Other various clients including numerous satellite sites and University acquired practices.

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

C. Rotation with other staff pathologists:
   1. Coverage at the University Hospitals of weekend and weekday autopsy call.

D. Perform bone marrow aspiration and biopsies at Albion Community Hospital, Albion, Michigan.

E. Review peripheral blood smears at Albion and Addison Community Hospitals.

F. Clinical Pathology consults at Albion and Addison Community Hospitals and other M-Labs clients.

G. Surgical Pathology "Quickie" Anatomic Pathology consults for a growing list of pathologists at M-Labs client hospitals.

II. TEACHING ACTIVITIES:

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

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

C. In-service teaching to laboratory staffs at Addison and Albion Community Hospitals.

III. RESEARCH ACTIVITIES:

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

B. Investigation of malacoplakia of the endometrium and vasitis nodose.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, M-Labs:
   1. Participate in planning, marketing, and implementation of M-Labs programs.
   2. Prepared plan for M-Labs expansion for presentation to University Hospitals. Planned and executed implementation of the expansion upon funding.
   3. M-Labs has experienced a 22% increase in net revenues from billings to clients for clinical pathology services and a 100% increase in net revenues from billings to patients for clinical pathology services. The number of M-Labs surgical

pathology cases has also increased by 22% . And, we will get another major client hospital beginning September, 1995.

4. Worked with a group of Michigan hospital laboratories to form GreatLakes Laboratory Network, which will have the capability to negotiate for statewide and, eventually, regional managed care contracts for laboratory services. M-Labs personnel now work in key committees of this group.
5. Developed a plan for provision of outpatient laboratory services by M-Labs to M-Care, employing a network of hospital laboratories. The network will distribute capitated revenues based on the relative volumes and complexities of testing of participant providers. Developed knowledge (through attendance at conferences and reading) in managed care with assistance from a medical technologist from our department. We have analyzed M-Care's historical outpatient laboratory utilization data and compared them with the Department of Pathology's costs to estimate an appropriate capitation rate. We have developed a listing of patient centers for the proposed M-Labs/M-Care Network of laboratory providers. This network will include M-Labs client hospitals currently in the proposed service area as well as other M-Care participating hospitals. Negotiations are currently underway with M-Care regarding service and quality issues as well as preliminary financial discussions.

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. Director of Laboratories, Addison Community Hospital, Addison, Michigan.
F. Chair, Tissue Transfusion and Infection Control Committees, Addison Community Hospital, Addison, Michigan, 9/92 -.
G. Plan and review Laboratory QA and CQI at Albion and Addison Community Hospitals.
H. Review Quality Control of Clinical Pathology tests at Albion and Addison Community Hospitals.

V. OTHER RELEVANT ACTIVITIES:

None

VI. PUBLICATIONS:

1. Silverman, E.M., Sapala, J.A. and Appelman, H.D.: Regression of hepatic steatosis in morbidly obese persons after gastric bypass. Am. J. Clin. Pathol. 104:23-31, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

I. CLINICAL ACTIVITIES:

A. 33% Neuropathology Service.

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Neuropathology 858 - six hours.
      b. CME accredited Conferences.
         Brain Conference - 40 hours.
         Neuromuscular Conference - 12 hours.
         Neuropath Conference for house staff - 16 hours.
   2. Andrew Merry: Pfizer Clinical Research Fellowship, $32,000, 5/1/94-4/30/95.

B. Undergraduate students:
   1. Neuropathology (NSB 600) - 12 hours.

C. Fellows:
   1. Hiroshi Ito: Pfizer Clinical Research Fellowship, $32,000, 5/1/94-4/30/95.
   2. Kenji Yamamoto: Pfizer Clinical Research Fellowship, $32,000, 5/1/94-4/30/95.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Sima, A.A.F. (PI, 40% effort), Tennekoon, G. and Rutkowski J.L., "Pathology of the Node of Ranview in Diabetic Neuropathy", RO1-DK 43884-04, National Institutes of Health, $1,472,882 for five years, 4/1/91-3/31/96.

B. Sima, A.A.F.(Co-Investigator, 5% effort), "Molecular Elements, Neurocircuits and Mental Illness", Watson, S. (PI), National Institute of Mental Health. $5,166,343 for five years, 12/1/91-11/30/96.

C. Co-Investigator, (5% effort), "Luteotrophic Actions of Insulin-like Growth Factor I", Keyes, L. (PI), National Institutes of Health, $404,922, 7/1/92-6/30/95.

D. Sima, A.A.F. (Co-Investigator, 10% effort), Greene, D.A. (PI), Michigan Diabetes Research and Training Center, National Institutes of Health, $1,250,000/annual, 5P60 DK20572-17, 12/1/92-11/30/97.

E. Sima, A.A.F., "The Effect of WAY-121,509 on the Development of Diabetic Neuropathy", Wyeth Ayerst, $80,000, 4/1/92-3/31/94.

F. Sima, A.A.F. (Neuropathologist, 5% effort), Gilman, S., (PI), Michigan Alzheimer's Disease Research Center, National Institutes of Health, $1,232,260/year, 10/1/89-5/31/94.

G. Sima, A.A.F. (Co-Investigator, 20% effort), Gilman, S., PI, Michigan Alzheimer's Disease Research Center, National Institutes of Health, $16,133,663, 06/01/94-05/31/99.

H. Sima, A.A.F. (Principal Investigator, 20% effort), Neuropathology Core, Michigan Alzheimer's Disease Research Center, National Institutes of Health, $225,027/year, 10/01/94-09/30/99.

I. Sima, A.A.F. (Principal Investigator, 10% effort), "Diffuse Lewy Body Disease (DLBD)", Michigan Alzheimer's Disease Research Center, National Institutes of Health, $105,600/year, 10/01/94-09/30/99.

J. Sima, A.A.F. (Principal Investigator), "Morphometric and NCV Evaluation of the Effect of Nimodipine on Diabetic Neuropathy in the Spontaneously Diabetic BB/W Rat", Miles Research, $50,000, 11/01/93-10/31/95.

K. Sima, A.A.F. (Co-Investigator, 5% effort), Project III "Histological Visualization and Assessment", of "Center for Neural Communication Technology", Anderson, D.J. (PI), National Institutes of Health, $204,280/year, 04/01/94-03/31/99.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. CERAD representative, Michigan Dementia Program.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Executive Committee, Michigan DRTC.
B. Director, Image Analysis Core, Michigan DRTC.
C. Director, Animal Core, Michigan DRTC.
D. Director, Neuropathology Core, MADRC.
E. Member, Executive Committee, MADRC.

REGIONAL/NATIONAL, INTERNATIONAL:

A. Member, Medical Advisory Board, Juvenile Diabetes Foundation International, New York, New York.
B. Executive Committee, Lessons from Animal Diabetes, Jerusalem, Israel.
C. Member, Council on Diabetic Complications, American Diabetes Association, New York, New York.
D. Abstract Review Board, American Diabetes Association, Alexandria, Virginia.
E Member, Specialty Committee Neuropathology, Royal College of Physicians and Surgeons of Canada, Ottawa, Canada.
F. Scientific Advisor, Wyeth-Ayerst Radon, Pennsylvania.
G. Scientific Advisor, Endocrinology Section FDA, Rockville, Maryland.
H. Member, Executive Committee, Wyeth Ayerst Inc.
I. Member, Executive Committee, Pfizer Pharmaceuticals.
J. Awards Committee, American Association of Neuropathologists.
K. Scientific Advisor, Hoffman-LaRoche, Basel, Switzerland.
L. NIH Committee, BB/W-rat Colony, Arthur Like, Worcester, Massachusetts.
M. Member, Executive Committee, International Diabetes Federation, Neuropathy Symposia, Kobe, Japan.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Diabetes Research and Clinical Practice.
B. Lessons from Animal Diabetes.
C. International Diabetes News.
D. International Journal of Diabetes (Regional Editor, North America).
E. Journal of Diabetic Complications.
F. Diabetes/Metabolism Review, Consulting Editor.
G. Ad hoc Reviewer for 29 journals (Neuropathology and Diabetes).
H. Study sections:
    1. Medical Research Council of Canada.
    2. Juvenile Diabetes Foundation International.
    3. American Diabetes Association.

VI. INVITED LECTURES/SEMINARS:

1. University of Erlangen, Germany, 1993.
2. Royal College of Physicians, London, England, 1993.
3. Gauss Symposium, Munich, Germany, 1993.
4. Neurodiab, Istanbul, Turkey, 1993.
5. Tokyo Metropolitan Diabetes Center, Tokyo, 1993.
6. Department of Neurology, University of Hirosaki, Hirosaki, Japan, 1994.
7. US-Japan Polyol Pathway Workshop, Kona, Hawaii, 1994.
8. Japanese Diabetes Association Annual Meeting, Tokushima, Japan, 1994.
9. Department of Medicine, Jikei University, Tokyo, Japan, 1994.
10. Department of Medicine, Shiga University, Shiga, Japan, 1994.
11. Department of Medicine, University of Buenos Aires, Argentina, 1994.
12. Department of Medicine, University of Oslo, Oslo, Norway, 1994.
13. Sumitomo Pharmaceutical Company, Osaka, Japan.
14. Department of Medicine, University of Nagasaki, Nagasaki, Japan, 1994.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Chakrabarti, S., Cherian, P.V. and Sima, A.A.F.: The effect of acarbose on diabetes- and age-related basement membrane thickening in retinal capillaries of the BB/W-rat. Diabetes Research and Clinical Practice 20:123-128, 1993.
2. Sima, A.A.F.: Diabetic neuropathy - The presence and future of a common but silent disorder. Modern Pathology, Editorials 399-401, 1993.
3. Kamijo, M., Cherian, P.V. and Sima, A.A.F.: The preventive effect of aldose reductase inhibition on diabetic optic neuropathy in the BB/w-Rat. Diabetologia 36:893-898, 1993.
4. Sima, A.A.F., Caplan, M.J., D'Amato, C.J., Pevzner, M. and Furlong, J.W.: Fulminant multiple system atrophy in a young adult presenting as motor neuron disease. Neurology 43:2031-2035, 1993.

5. Murray, F.T., Beyer-Mears, A., Johnson, R.D., Sima A.A.F., Cameron, D.F., Sninsky, C.A. and Selawry, H.: Assessment of proteinuria and neuropathy in the nonimmunosuppressed BB diabetic rat following abdominal intratesticular islet transplantation. Transplantation 56:680-686, 1993.
6. Yorek, M.A., Wiese, T.J., Davidson, E.P., Dunlap, J.A., Stefani, M.R., Conner, C.E., Kamijo, M., Sima, A.A.F. and Greene, D.A.: Reduced motor nerve conduction velocity and Na^+/K^+ ATPase in rats maintained on a diet containing L-fucose: Reversal by myo-inositol supplementation. Diabetes 42:1401-1406, 1993.
7. Greene, D.A., Sima, A.A.F., Stevens, M., Feldman, E., Killen, P., Henry, D., Thomas, T., Dannenberg, J. and Lattimer, S.A.: Aldose reductase inhibitors: An approach to the treatment of the nerve damage of diabetic neuropathy. Diabetes/Metabolism Reviews 9:189-217, 1993.
8. Liang, B.C., Albers, J.W., Sima, A.A.F. and Nostrant, T.T.: Case of the month: Paraneoplastic pseudo-obstruction, mononeuropathy multiplex and sensory neuronopathy. Muscle and Nerve 17:91-96, 1994.
9. Paro, M., Prashar, A., Prosdocimi, M., Cherian, P.V., Fiori, M.G. and Sima, A.A.F.: Urinary bladder dysfunction in the BB/W rat: Effect of ganglioside treatment on fuctional and structural alterations. J. Urology 151:781-786, 1994.
10. Peacock, M.L., Murman, D.L., Sima, A.A.F., Warren, J.T., Jr., Roses, A.D. and Fink, J.L.: Novel amyloid precursor protein gene mutation (codon 665 ^{Asp}) in a patient with late-onset Alzheimer's disease. Ann. Neurol 35:432-438, 1994.
11. Linstrom, P., Brismar, T. and Sima, A.A.F.: Impaired recovery in diabetic rat following anoxic conduction block. Exp. Neurology, In Press.
12. Felice, K.J., Fratkin, J.D., Feldman, E.L. and Sima, A.A.F.: Phrenic nerve involvement in Dejerine-Sottas disease: A Clincopathological case study. Pediatric Pathology, In Press.
13. Kamijo, M., Basso, M., Cherian, P.V./, Hohman, T.C. and Sima, A.A.F.: Galactosemia produces ARI-preventable nodal changes similar to those of diabetic neuropathy. Diab. Res. Clin. Prac., In Press.
14. Lynch, T., Sano, M., Marder, K.S., Bell, K.L., Foster, N.L., Defendini, R.F., Sima, A.A.F., Keohane, C., Hygaard, T.G., Fahn, S., Mayeux, R. Rowland, L.P. and Wilhelmsen, K.C.: Moynihan disease: Autosomal dominant front.
15. Stevens, M.J., Dananberg, J., Feldman, E.L., Lattimer, S.A., Kamijo, M., Thomas, T.P., Sima, A.A.F. and Greene, D.A.: The linked roles of aldose reductase, nitric oxide and Na/K-ATPase in experimental diabetic neuropathy. J. Clin. Invest., In Press.
16. Sima, A.A.F.: The effect of age and diabetes on peripheral nerve function and structure. Editorial. International Journal of Diabetes, In Press.
17. Sima, A.A.F.: Where is the water in diabetic nerve hydration? Editorial. J. Lab. & Clin. Med., In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Sima, A.A.F. and Greene, D.A.: Incidence and treatment of diabetic neuropathy in the elderly. Submitted for publication.
2. Sima, A.A.F., Kamijo, M., Merry, A., Cherian, P.V., Lattimer, S.A., Stevens, M.J. and Green, D.A.: The effect of acetyl-L-carnitine on nerve function and structure in the diabetic BB/W-rat. Submitted for publication.
3. Cherian, P.V., Kamijo, M., Angelides, K.J. and Sima, A.A.F.: Nodal Na^+-channel migration facilitated by axo-glial dysjunction accounts for nerve conduction slowing in diabetic BB/W-rat: Prevention by an aldose reductase inhibitor. Submitted for publication.
4. Kamijo, M., Merry, A.C., Cherian, P.V., Akdas, G. and Sima, A.A.F.: Nerve fibre regeneration following axotomy in the diabetic BB/W-rat: The effect of ARI-treatment. Submitted for publication.
5. Rosenblatt, D.E., Murphy, S. and Sima, A.A.F.: Comparison of protease mexin 1 immunolabelling of neuritic plaques with other staining methodologies. Submitted for publication.

6. Magnani, P., Cherian, P.V., Thomas, T.P., Tennekoon, G., Sima, A.A.F., DeVries, G.H., Greene, D.A. and Brosius III, F.C.: Localization and regulation of glucose transporters in native and cultured Schwann cells. Submitted for publication.
7. Takahashi, T., Kojima, Y., Tsunoda, Y., Beyer, L.A., Kamijo, M., Sima, A.A.F. and Owyang, C.: Impaired intracellular signal tranduction in gastric smooth muscle of diabetic BB/W rats.. Submitted for publication.
8. Lynch, T., Sano, M., Marder, K.S., Bell, K.L., Foster, N.L., Defendini, R.F., Sima, A.A.F., Keohane, C., Nygaard, T.G., Fahn, S., Mayeux, R., Rowland, L.P. and Wilhelmsen, K.C.: Clinical characteristics of a family with chromosome 17-linked disinhibition-dementia-Parksinsonism-amyotrophy-complex (DDAPAC). Submitted for publication.
9. Gilman, S., Sima, A.A.F., Junck, L., Kluin, K.J., Koeppe, R.A., Lohman, M.E. and Little, R.: Dominantly inherited multiple system atrophy. Submitted for publication.

BOOKS/CHAPTERS IN BOOKS:

1. Sima, A.A.F.: Diabetic neuropathy: pathogenesis, natual history and therapeutic potentials, in, Vasselli, J.R., Maggio, C.A. and Scriabine, A. (eds), Drugs In Development, Vol. I, a-Glucosideae Inhibition: Potential Use in Diabetes., Neva Press, Bradford, Connecticut, pp. 201-209, 1993.
2. Chakrabarti, S. and Sima, A.A.F.: The effect of acarbose on reinal microangiopathy in the BB/W or rat, in, Vasselli, J.R., Maggio, C.A. and Scriabine, A. (eds), Drugs In Development, Vol. I, a-Glucosidease Inhibition: Potentil Use in Diabetes, Neva Press, Bradord, Connecticut, pp. 227-235, 1993.
3. Sima, A.A.F. and Chakrabarti, S.: Acarbose slows the progression of diabetic neuropathy in the diabetic BB/W rats, in, Vasselli, J.R., Maggio, C.A. and Scriabine, A. (eds), Drugs In Development, Vol. I, a-Glucosidease Inhibition: Potential Use in Diabetes, Neva Press, Bradford, Connecticut, pp. 219-225, 1993.
4. Greene, D.A., Hohman, T., Raskin, P. and Sima, A.A.F.: Measurement of aldose reductase inhibition in humans, in, Mogensen, C.E. and Standl, E. (eds), Diabetes Forum Series V: Research Methodologies in Human Diabetes, Walter de Gruyter & Co., Berlin, In Press.
5. Greene, D.A., Sima, A.A.F. and Bron, M.: Conducting clinical trials in diabetic neural diseases, including poser analysis, in, Mogensen, C.E. and Standl, E. (eds), Diabetes Forum Series V: Research Methodologies in Human Diabtes, Walter de Gruyter & Co., Berline, In Press.
6. Sima, A.A.F. and Greene, D.A.: Nerve morphometry - a valuable tool in the assessment of natural history and electrophysiological correlates in diabetic neuropathy, in, Ghista, D.N. (ed), Biomedical Physics Horizons, Verlag Vieeg Publishers., In Press.
7. Greene, D.A. Sima, A.A.F., Feldman, E.L. and Stevens, M.J.: Diabetic neuropathy, in, Rifkin, H., Porte, D. and Sherwin, R. (eds), Ellenberg and Rifkin Diabetes Mellitus, 5th Edition, Appleton & Lange, In Press.

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

1. Sima, A.A.F. and Greene, D.A.: Nerve morphometry a valuable tool in the assessment of natural history and electrophysiological correlates in diabetic neuropathy. Abstract/Invited Lecture, 2nd Gauss Symposium, Munich, Germany, August, 1993.
2. Sima, A.A.F., Alberts, J.W., Cherian, P.V., Greene, D.A., Hohman T.C., Beg, M. and the Tolrestat Study Group: Correlations between structure and function in sural nerve biopsies from 336 diabetic patients. Diabetologia 36:A73, 1993.
3. Stevens, M.J., Feldman, E.L., Dananberg, J. Kamijo, M. Lattimer, S.A., Sima, A.A.F. and Greene, D.A.: Nitric oxide deficiency mediates nerve conduction slowing in expeimental diabetic neuropathy. Diabetologia 36:A52, 1993.

4. Hohman, T.C., Sima, A.A.F., Cherian, P.V., Greene, D.A., Albers, J.W., Gonen, B., Beg, M. and the Tolrestat Study Group: Effects of glucose on the sequestered polyol pathway in sural nerves from 336 diabetic patients. Diabetologia 36:A56, 1993.
5. Sima, A.A.F.: Morphometic evaluation of nerve histology - longitudinal studies. State of the Art Lecture. Proc. Neurodiab., Istanbul, Turkey, 1993.
6. Cherian, P.V., Kamijo, M. and Sima, A.A.F.: Quantification and ultrastructural localization of redistributed nodal sodium channels in the diabetic BB/W-rat. Proc. Neurodiab. Meeting, Istanbul, Turkey, 1993.
7. Kamijo, M., Cherian, P.V., Bossa, M., Hohman, T.C. and Sima, A.A.F.: Activation of the polyol-pathway in diabetic BB/W-rat optic nerve is prevented by aldose reductase inhibition. Proc. Neurodiab. Meeting, Istanbul, Turkey, 1993.
8. Kamijo, M., Cherian, P.V., Merry, A. and Sima, A.A.F.: The effect of ARI-treatment on nerve fiber regeneration and nodal maturation in diabetic BB/W-rats. Proc. Neuodiab. Meeting, Istanbul, Turkey, 1993.
9. Cherian, P.V. and Sima, A.A.F.: Redistribution of nodal sodium channels in diabetic neuropathy of the BB/W-rat. Internal Medicine Research Day, Ann Arbor, Michigan, 1993.
10. Kamijo, M., Preston, J. and Sima, A.A.F.: Impaired nerve fiber regeneration in the BB/W rat is restored to supranormal values following ARI-treatment. Internal Medicine Research Day, Ann Arbor, Michigan, 1993.
11. Kim, B., Chenevert, T.L., Sunkara, P.S., McCarthy, J.R., Sima, A.A.F. and Ross, B.D.: ^{1}H MRS and MRI studies of the antitumor activity of (E)-2'-fluoromethylene-2'-deoxycytidine (FMdc, MDL 101,731) on experimental intracranial gliomas. Society of Magnetic Resonance in Medicine 12th Annual Scientific Meeting, New York, New York, August, 1993.
12. Sima, A.A.F., Kamijo, M., Lattimer, S., Stevens, M. and Greene, D.A.: Acety-1-carnitine prevents diabetic neuropathy in the spontaneously diabetic rat. Michigan Neuropathy Day, 1993.
13. Homeister, J., D'Amato, C.J. and Sima, A.A.F.: The diverse pathology of Huntington's Disease. Michigan Neuropathology Day, 1993.
14. Sima, A.A.F., Albers, J.W., Cherian, P.V., Greene, D.A., Hohman T.C. and Beg, M.: Structural-functional relationships in diabetic neuropathy. US-Japan Aldose Reductase Workshop, Kona, Hawaii, February, 1994.
15. Sima, A.A.F., Cherian, P.V., Brosius, F.C. and Greene, D.A.: The effect of ARI treatment on immunocytochemical localization and semi-quantification of glucose transporters 1 and 3 in diabetic nerve. US-Japan Aldose Reductase Workshop, Kona, Hawaii, February, 1994.
16. Cherian, P.V., Kamijo, M. and Sima, A.A.F.: Immunocytochemical and quantitative localization of redistributed nodal sodium channels in the diabetic BB/W-rat. US-Japan Aldose Reductase Workshop, Kona, Hawaii, February, 1994.
17. Kamijo, M., Basso, M., Hohman, T.C. and Sima, A.A.F.: Long-term galactosemia produces a diabetes-like neuropathy prevented by ARI treatment. US-Japan Aldose Reductase Workshop, Kona, Hawaii, February, 1994.
18. Stevens, M., Dananberg, J., Lattimer, S., Kamijo, M., Sima, A.A.F and Greene, D.A.: Nitric oxide (NO) deficiency mediaes aldose reductase inhibitor (ARI) sensitive nerve conduction slowing in streptozotocin-induced diabetic (STZ-D) rats. US-Japan Aldose Reductase Workshop, Kona, Hawaii, February, 1994.
19. Sima, A.A.F., Kamijo, M., Cherian, P.V., Lattimer, S.A., Stevens, M.J. and Greene, D.A.: Diabetic neuropathy in the BB/W-rat is prevented by acetyl-1-carnitine treatment. Muscle & Nerve Suppl 1:S246, 1994.
20. Kamijo, M., Basso, M., Hohman, T.C. and Sima, A.A.F.: Long-term galactose feeding to rats produces ARI-preventable nodal changes similar to those of diabetic neuropathy. Muscle & Nerve Suppl 1:S246, 1994.
21. Kamijo, M., Cherian, P.V., Merry, A. and Sima, A.A.F.: Nerve fiber regeneraton and nodal maturation in diabetic BB/W-rats following axotomy and the effect of ARI-treatment. Muscle & Nerve Suppl 1:S194, 1994.

22. Healy, D.J., Sima, A.A.F, Tapp, A. Watson, S.J. and Meador-Woodruff, J.H.: Characterization of a schizophrenic brain collection. Annual Meeting of the Society of Biological Psychiatry, 1994.
23. Kojima, Y., Takahashi, T., Tsunoda, Y., Owyang, C., Kamijo, M. and Sima, A.A.F.: Evidence for altered intracellular signal randuction in diabetic gastric myopathy. American Gastroenterological Association, New Orleans, Louisiana, May, 1994.
24. Merry, A.C., Kamijo, M., Lattimer, S.A., Ristic, H. and Sima, A.A.F.: Long term prevention and intervention effects of acetyl-L-Carnitine on diabetic neuropathy in BB/W-Rats. Diabetes 43:108A, 1994.
25. Sima, A.A.F, Merry, A.C., Kamijo, M., Basso, M. and Hohman, T.C.: Aldose reductase inhibitors have a second site of action. Diabetes 43:17A, 1994.
26. Kamijo, M., Lattimer, S.A., Stevens, M.J., Greene, D.A. and Sima, A.A.F.: Acetyl-1-carnitine prevents diabetic neuropathy in the BB/W-rat. Japan Diabetes Society, Tokushima, Japan, May, 1994.
27. Kamijo, M., Cherian, P.V. and Sima, A.A.F.: Impaired nerve fiber regeneration in the BB/W-rat is restored to supranormal values following ARI-treatment. Japan Diabetes Society, Tokushima, Japan, May, 1994.
28. Sima, A.A.F.: Diabetic neuropathy -- Underlying mechanisms and potential therapies. Japanese Diabetes Association Annual Meeting, Tokushima, Japan, May, 1994.
29. Sima, A.A.F., Merry, A.C., Kamijo, M., Basso, M. and Hohman, T.C.: A comparative study of three aldose reductase inhibitors in the STZ diaetic rat. Peripheral Nerve Society, St. Paul, Minnesota, June, 1994.

TIMOTHY P. SINGLETON, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 AUGUST 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Sign-out hematologic biopsies, peripheral blood smears and body fluids that are sent for differential counts.
B. Quality control in immunohistochemistry laboratory.
C. Review of biopsies for weekly lymphoma conference and biweekly leukemia conference.

II. TEACHING ACTIVITIES:

A. Medical students, first two years:
   1. Lecture, Lymphoprolifertive Disorders.
   2. Laboratory, Hematology.

B. Medical students, last two years:
   1. Elective in pathology, laboratory session.
   2. Elective in pathology, review biopsies at sign-out.

C. Residents and fellows in pathology and other departments:
   1. Review of biopsies at sign-out.
   2. Bimonthly unknown conference in hematopathology.
   3. Bimonthly conference in immunohistochemistry.
   4. Grand Rounds Lecture, Myelodysplastic Syndromes.

D. Pathologists:
   1. M-Labs Symposium, Lecture: Immunohistochemistry for the surgical pathologist.

III. RESEARCH ACTIVITIES:

A. Directing research immunohistochemistry.

IV. ADMINISTRATIVE ACTIVITIES:

A. Assistant Director, Hematology Laboratory.
B. Assistant Director, Immunohistochemistry Laboratory.

V. PUBLICATIONS:

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

1. Hsi, E., Greenson, J., Singleton, T., Siddiqui, J., Schnitzer, B. and Ross,C.: Detection of immunoglobulin heavy chain (IgH) gene rearrangement by polymerase chain reaction (PCR) in chronic active gastritis associated with Helicobactor pylori (CAG-Hp). (Presented at International Academy of Pathology, 1995).

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

1. Anderson, M., Singleton, T., Ross, C., Sheldon, S.and Schnitzer, B.: Leukemic phase of mantle cell lymphoma, blastic variant. Presented at International Academy of Pathology, 1995.
2. Hsi, E., Greenson, J., Singleton, T., Siddiqui, J., Schnitzer, B. and Ross, C.: Detection of immunoglobulin heavy chain (IgH) gene rearrangement by polymerase chain reaction (PCR) in chronic active gastritis associated with Helicobactor pylori (CAG-Hp). Presented at International Academy of Pathology, 1995.
3. Anderson, M., Sheldon, S., Singleton, T., Ross, C. and Schnitzer, B.: DemonstRation of a t(2;5) is important in the diagnosis of Ki-1 anaplastic large cell lymphoma (ALCA) with unusual features. Presented at International Academy of Pathology, 1995.
4. Stevens, S., Cooper, K., Wahl, R., Ross, C., Singleton, T. and Kaminski, M.: Radioimmunotherapy of cutaneous B-cell lymphoma with [^{131}]-antiB1 (anti-CD20) antibody induces a novel cutaneous reaction pattern associated with complete remission of cutaneous disease. Presented at Society for Investigative Dermatology, 1995.
5. Cohen, L. and Singleton, T.: Increased TGF-beta imunologicalization in unhealed burn wounds. Presented at Meeting of Plastic Surgeons, 1995.

JAMES E. SMOLEN, PH.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Pathology 850 - Spring Term.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

PROJECTS UNDER STUDY:

A. Degranulations and Fusion in Neutrophils.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Admissions Committee.

REGIONAL AND NATIONAL:

A. Member, New York Academy of Sciences.
B. Member, American Society for Cell Biology.
C. Member, American Federation for Clinical Research.
D. Member, American Association of Pathologists.
E. Member, American Society of Hematologists.
F. Member, American Association for the Advancement of Science.
G. Veterans Administration - Infectious Diseases Merit Review Board.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Reviewer:
   1. Biochemical Pharmacology.
   2. Blood.
   3 European Journal of Hematology.
   4. Journal of Biological Chemistry.

5. Journal of Immunology.
6. Life Sciences.
7. Nature.
8. The Journal of Clinical Investigation.
9. Journal of Infectious Diseases.
10. Biochemical et Biophysica Acta.
11. Cancer Research.
12. Infection and Immunity.
13. Journal of Cellular Physiology.
14. Journal of Leukocyte Biology.
15. Molecular Pharmacology.
16. Pharmacology and Toxicology.
17. American Journal of Pathology.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REVIEWED JOURNALS:

1. Brock, T.G., Nagaprakash, K., Margolis, D.I. and Smolen, J.E.: Modeling neutrophil degranulation with liposomes: Effect of increasing the complexity of lipid composition on membrane fusion. J. Memb. Biol., In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

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. Autopsy service.

II. TEACHING ACTIVITIES:

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

1. Francis Wolber, Ph.D. candidate in Experimental Pathology (July, 1992 - present) - Ms. Wolber's thesis project focuses on the role of adhesion receptors in the recruitment of mononuclear leukocytes during the development of angiocentric pneumonitis in a murine model of chronic inflammation. Her study is based on *in vitro* modeling from this laboratory showing, for the first time, that the β1-integrin VLA-4 initiates the binding of lymphocytes to activated endothelium at physiologic levels of linear-shear stress without assistance from other adhesion receptors. This finding challenged the prevailing view that members of the selectin family must initiate contact before the integrins can act.
2. Vennay Reddy (Sept. 1992 - Aug. 1995) and Jan Lui (Sept. 1994-Aug. 1995), undergraduate students- projects focus on development of basic and advanced laboratory skills including immunostaining, operation of flow cytometer, data analysis and automated morphometric analysis. My laboratory provides instruction to one-two undergraduates/year willing to commit summers and five-ten hours per week during the school year. Eight undergraduate students have participated over the last eight years. These students enter the lab with no experience in bench research. They concentrate on development of laboratory skills and work together with the senior staff on ongoing projects. All graduates have either gone on to medical school or begun careers in research laboratories.
3. Neil Faulkner (summer, 1995), MD., Ph.D. student- Mr. Faulkner's project is based on recently completed studies by Randall Knibbs (see below) which identified the enzyme (fucosyl transferase) which regulates the synthesis of ligands for the selectins on the surface of T-cells. These ligands are essential for the recruitment of T-cells into sites of inflammation particularly in the skin. As a consequence, inhibition of synthesis may provide a novel, T-cell sparing approach to immunosuppression. Mr. Faulkner will determine whether the function of the enzyme, and thus the induced synthesis of selectin ligands, can be blocked through anti-sense inhibition of translation in an in vitro model system.
4. Randall Knibbs, Ph.D., Research Scientist (January, 1994-present) - Dr. Knibbs recently completed studies on the molecular regulation of selectin-ligand synthesis in T-cell. This investigation identified a member of the fucosyl-transferase family, termed Fuc-T7, as the rate limiting step in the synthesis of selectin ligands during antigen-driven T-cell proliferation. The selectin ligands

are essential for the recruitment of T-cells into sites of chronic inflammation thus contribute to the pathophysiology of numerous chronic inflammatory diseases. T-cells are unique in that these ligands are synthesized only in response to antigen-driven proliferation. As a consequence, the discovery of a rate limiting enzyme provides a novel target for T-cell sparing immunosuppression. Dr. Knibbs will next focus on the structure of the carbohydrate portion of the selectin ligands on T-cells.

B. Co-director, Hematology Sequence in Component II - designed/administered pathology component of sequence and co-directed course with Roland Hiss, M.D. (Department of Internal Medicine). Fall, 1993 was the inaugural flight of this sequence. As a consequence, the co-directors devoted many hours to extensive revision of content, structure, laboratories and examinations. The sequence received one of the highest ratings (both student and faculty) for any sequence in Component II.

C. Laboratory Instructor, Component II - joined group of ten pathology instructors as permanent faculty in the course. We are currently the only instructors in any department with teaching activities throughout the entire 2nd year curriculum. The group provides sequence-specific laboratory instruction, general reviews at intervals throughout the year and quality-control for laboratory examinations in all sequences.

D. Section leader, Hematopathology Section of Component II - several sequences use specialists to cover pertinent laboratories. This is in addition to serving as an instructor in the general pathology laboratories of Component II.

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

F. Daily sign-out of cases in flow cytometry and hematopathology with pathology residents and medical students (one week per month).

G. Attending, Autopsy Service (one week per year).

H. Preceptor, Senior medical student (M4) elective in Pathology (one month).

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT (80% of allowed salary):

A. Principal Investigator, project 4- "Leukocyte-Microvascular Adhesive Interactions in Rheumatoid Arthritis", NIH, P50AR41703 (SCOR in Rheumatoid Arthritis; Josi Holoshitz, M.D., program director), 25% effort, $398,269; 30 September 1992 - 31 August 1995.

B. Principal Investigator, project 3- "Selectin Binding Sites on Leukocytes and Inflamed Venules", NIH, PO1AI33189 (Oligosaccharides as Anti-inflammatory Agents; PA Ward, Program Director), 20% effort, $347,950; 1 September 1992- 31 August 1996.

C. Co-Principal Investigator, (J. Curtis, Principal Investigator), project 4- "Mechanisms of Lymphocyte Recruitment to the Lungs", NIH, P50HL46487 (SCOR in Pulmonary Fibrosis; G. Toews, M.D., Program Director), 15% effort, $650,000; 1 December 1991 - 31 November 1996.

D. Principal Investigator, project 5- "Mononuclear Leukocyte Adhesion and Recruitment in Chronic Inflammatory Disease" - NIH, P01, HL31963 (Inflammatory Cells and Lung Injury; PA Ward, M.D., Program Director), 20% effort, $500,000; 1 February 1994 - 29 January 1999.

PROJECTS UNDER STUDY:

A. Inhibition of selectin-ligand synthesis during T-cell activation: This projects builds on the discovery of a rate limiting enzyme in the synthesis of selectin ligands on T-cells.

Anti-sense approaches will be tested for their ability to inhibit this enzyme's activity and thus the synthesis of selectin ligands. In addition, proximal regulatory steps in the induction of enzyme activity will be identified. These studies will identify pathways critical to the recruitment of T-lymphocytes into sites of chronic inflammation thus potential targets for novel anti-inflammatory therapy.

B. Identification and structural characterization of selectin ligands on T-cells: Studies in this area have been hampered by the difficulty of collecting sufficient starting material for structural studies on authentic ligands. We have overcome this obstacle through the development of a growth protocol which allows the production of $>10^{11}$ human T-cells expressing high levels of functional ligands for the selectins. Viable lymphocytes from any source can be used with a 100-1000 fold increase in cell number achieved over two weeks. These ligands are indistinguishable from those on circulating T-cells. This growth protocol will permit, for the first time, detailed structural analysis of selectin ligands on human T-cells.

C. Utilization of endothelial adhesion receptors during recruitment of adoptively-transferred, *ex vivo* expanded lymphocytes into host tumors: This project builds on the discovery that the protocols used to expand vaccine-derived and tumor-infiltrating lymphocytes prior to infusion into patients dramatically alter the prevalence and function of adhesion receptors used by the infused cells to gain access into tissues. We have now determined that current protocols generate cells which require expression of adhesion molecules in the selectin family for optimal recruitment. However, studies in animal models show virtually no induction of these molecules in the vascular beds of experimental tumors. If this is true in human neoplasms then a "mismatch" between the adhesion molecules on the infused cells and the adhesion molecules expressed on the vasculature in the tumor bed may account for the poor recruitment of cells into tumors during adoptive immunotherapy. Future studies will determine the expression of adhesion molecules in the vasculature of human tumors and use animal models to determine whether augmentation of selectin expression in the tumor bed will enhance recruitment of adoptively transferred cells.

IV. ADMINISTRATIVE ACTIVITIES:

A. Co-Director Flow Cytometry Laboratory - manage the development and maintenance of the analytic systems. This system was designed to meet the needs of both the clinical laboratories and research investigators.

B. Co-Director, Hematology Sequence in Component II - responsible for design and implementation of pathology component of this sequence.

C. Co-Chair, Selectin Workshop, International Congress of Immunology, San Francisco, California, 1995.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Lymphoblast-endothelial interactions under shear-stress in adoptive immunotherapy (AI)", Experimental Biology, Atlanta, Georgia, 1995.
2. "Pathophysiology of leukocyte recruitment in chronic inflammatory diseases", Plenary lecture, XIIIth European Congress of Rheumatology, Amsterdam, The Netherlands, 1995.
3. "α4-integrins on lymphoblasts mediate selectin-independent arrest on VCAM under shear: implications for recruitment into the brain", Integrin Workshop, International Congress of Immunology San Francisco, California, 1995.
4. "Control of selectin ligand expression on human T-cells", Selectin Workshop, International Congress of Immunology San Francisco, California, 1995.

EDITORIAL BOARDS:

A. Journal of Clinical Investigation.
B. Journal of Laboratory Investigation.
C. American Journal of Pathology.
D. Journal of Immunology (Associate Editor).
E. Journal of Experimental Medicine.
F. Journal of Biological Chemistry.
G. Nature.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Kaldjian, E. and Stoolman, L.M.: Regulation of L-selectin mRNA in Jurkat cells: Opposing influences of calcium- and protein kinase C-dependent signaling pathways. J. Immunol. 22:4351-4362, 1995.
2. Ley, K., Zakrzewicz, A., Hanski, C., , Stoolman, L.M. and G.S. Kansas.: Sialylated mucins and L-selectin on neutrophils sequentially mediate rolling *in vivo*. Blood 85:3727-3735, 1995.

MANUSCRIPTS SUBMITTED/IN PREPARATION FOR PUBLICATION:

1. Stoolman, L.M., Craig, R.A., Wolber, F., Abbassi, O., Smith, C.W., McIntire, L.V. and Ballew, J.R: Requirements for optimal selectin-independent tethering through the α4-integrins on endothelium under flow conditions: implications for lymphoblast trafficking. 1995.
2. Knibbs, R.N., Craig, R.A., Natsuka, S., Cameron, M., Lowe, J.B., Stoolman, L.M.: The fucosyltransferase FTVII regulates expression of selectin ligands in human T-cells. 1995.
3. Stoolman, L.M., Craig, R.A., Knibbs, R.N., Lowe, J.B., Cameron, M., Thall, A. and Malle, P.: Knock-out of the fucosyltransferase FTVII but not FTIV prevents selectin-ligand synthesis by murine T-cells. 1995.
4. Stoolman, L.M., Craig, R., Cameron, M., Reddy, V., Liu, J. Ballew, J. and Chang, A.E.: *Ex vivo* expansion of lymphocytes for adoptive-immunotherapy alters the prevalence and function of adhesion receptors involved in recruitment into tissues.
5. Wolber, F., Curtis, J., Kim, S. and Stoolman, L.M.: Expression of endothelial adhesion receptors on the vasculature in a murine model of chronic angiocentric pneumonitis.

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

1. Knibbs, R.N., Craig, R.A., Natsuka, S., Thall, A., Cameron, M., Lowe, J.B. and Stoolman, L.M.: Fucosyltransferases in the synthesis of selectin ligands on T-cells. Experimental Biology Atlanta, Georgia, 1995.
2. Stoolman, L.M., Craig, R.A., Cameron, M.J., Chang, A.E. and Ballew, J.R.: Lymphoblast-endothelial interactions under shear-stress in adoptive immunotherapy (AI). Experimental Biology, Atlanta, Georgia, 1995.

3. Stoolman, L.M., Craig, R.A., Cameron, M., Chang, A. and Ballew, J.: α4-integrins on lymphoblasts mediate selectin-independent arrest on VCAM under shear: implications for recruitment into the brain. International Congress of Immunology, San Francisco, California, 1995.
4. Wolber, F.M., Sonstein, J., Fields, K., Ballew, J., Kim, S., Vestweber, D., Curtis, J. and Stoolman, L.M.: Endothelial adhesion molecules and lymphocyte recruitment in a murine model of lung inflammation. International Congress of Immunology 1995, San Francisco, California, 1995.
5. Stoolman, L.M.: Pathophysiology of leukocyte recruitment in chronic inflammatory diseases. Rheumatology Highlights, The Proceedings Book of the EULAR Congress 1995, Amsterdam.

DENISE SULAVIK, M.D.
LECTURER
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Diagnostic Surgical Pathology, Hematopathology.
B. Clinical Hematology Laboratory.
C. Clinical Flow Cytometry Laboratory.
D. Hematopathology Consultation Cases (including M-Labs).

II. TEACHING ACTIVITIES:

A. House Officers:
   1. Sign-out of bone marrow biopsies, aspirates, blood smears and body fluids in Hematology Laboratory.
   2. Sign-out of lymph node biopsies and review of hematopathology consultation material.
   3. Flow Cytometry sign-out.

B. Medical Students:
   1. Laboratory instructor, M4 Clerkship in Clinical Pathology.

C. Hematopathology Teaching:
   1. Lymphoma conference/weekly.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Histomorphologic, flow cytometric and cytogenetic variances of blasts in a treated acute lymphoblastic leukemia.

IV. ADMINISTRATIVE ACTIVITIES:

None.

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. General Pathology for Dental Students and Graduate Students (Lecture Path 630/580). Lectures on inflammation and wound healing.
B. Aresh Monem - Pharm. D. - Research.
C. Hagen Schmal - Medical Student - Research.
D. Dorothy Pao - Undergraduate Student - Research.
E. Minh Nguyen - Undergraduate Student - Research.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Role of Cytokines and Adhesion Molecules in Thermal Injury", (NIH GM-48477), Principal Investigator.
B. "Lung Injury Produced by Oxygen Metabolites", (NIH GM-29507), Co-Principal Investigator with Dr. P.A. Ward.
C. "The Effect of Bradykinin Antagonists on CVF-Induced Lung Injury", Scios Nova Inc., Palo Alto, California, Principal Investigator.

PENDING SUPPORT:

A. None.

PROJECTS UNDER STUDY:

A. Role of leukocytes, inflammatory mediators, and adhesion molecules in thermal trauma-related cell and tissue injury.
B. Pathomechanisms of ocular ischemia-reperfusion injury.
C. Functional responses of retinal pigment epithelial (RPE) cells *in vitro*.
D. Role of bradykinin in experimental acute lung injury.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interviewed candidates for faculty and postdoctoral positions.
B. Interviewed candidates for Medical Scientist Training Program.
C. Participation in undergraduate research program.

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. Member of the Honors and Awards Committee of the American Shock Society.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Member Editorial Advisory Board Immunobiology.
B. Reviewer for the following scientific journals:
    1. American Journal of Pathology.
    2. American Journal of Physiology.
    3. Cardiovascular Research.
    4. Circulation.
    5. Free Radical Biology and Medicine.
    6. Journal of Biological Chemistry.
    7. Journal of Cataract and Refractive Surgery.
    8. Journal of Leukocyte Biology.
    9. Laboratory Investigation.
    10. Shock.

INVITED LECTURES/SEMINARS:

1. Invited speaker at the Fifth International Workshop on Intensive Care and Emergency Medicine, Schloss Wilhelminenberg, Vienna, Austria, December 8-10, 1994.
2. Invited speaker at the Fifth Vienna Shock Forum, Vienna, Austria, May 7-11, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Murphy, H.S., Maroughi, M., Till, G.O. and Ward, P.A.: Phorbol-stimulated influx of extracellular calcium in rat pulmonary artery endothelial cells. Am. J. Physiol. 267:L145-51,1994.
2. Garner, W.L., Rodriguez, J.L., Miller, C.G., Till, G.O., Rees, R.S., Smith, D.J. and Remick, D.G.: Acute skin injury releases neutrophil chemoattractants. Surgery 116:42-48, 1994.
3. Mulligan, M.S., Till, G.O., Smith, C.W., Anderson, D.C., Miyasaka, M., Tamatani, T., Todd, R.F., 3rd, Issekutz, T.B. and Ward, P.A.: Role of leukocyte adhesion molecules in lung and dermal vascular injury after thermal trauma of skin. Am. J. Pathol. 144:1008-1015,1994.
4. Colton, D.M., Hirschl, R.B., Johnson, K.J., Till, G.O., Dean, S.B. and Bartlett, R.H.: Neutrophil infiltration is reduced during partial perfluorocarbon liquid ventilation in the setting of lung injury. Surg. Forum 45:668-670, 1994.
5. Liu, Z., Giudice, G.J., Swartz, S.J., Fairley, J.A., Till, G.O., Troy, J.L. and Diaz, L.A.: The role of complement in experimental bullous pemphigoid. J. Clin. Invest. 95:1539-44, 1995.
6. Colton, D.M., Hirschl, R.B., Till, G.O., Johnson, K.J., Dean, S.B., Patel, S. and Bartlett, R.H.: Neutrophil infiltration is reduced during liquid ventilation. I. *In vivo* analysis. Am. J. Resp. Crit. Care Med., In Press.
7. Rodriguez, J.L., Kelty, L., Miller, C.G., Garner, W.L., Smith, D.J., Till, G.O. and Remick, D.G.: Interleukin-8 (IL-8) and acute burn injury. Surgery, In Press.
8. Winn, W.C., Davis, G.S., Durda, J.P. and Till, G.O.: The effect of neutropenia on experimental Legionella pneumonia. Infec. Immun., In Press.
9. Seekamp, A., Schmal, H., Friedl, H.P., Hultquist, D.E., Ward, P.A. and Till, G.O.: Protection by vitamin B2 against oxidant-mediated acute lung injury. Free Radic. Biol. Med., In Press.

BOOKS AND CHAPTERS IN BOOKS:

1. Marak, G.E., Schmal, H., Foreman, K.E., Friedl, H.P., Ward, P.A. and Till, G.O.: Anti-inflammatory properties of xanthine oxidase inhibitors, in, Nussenblatt, R.B., Whitcup, S.M., Caspi, R.R. and Gery, I. (eds), Advances in Ocular Immunology, Elsevier Science B.V., Amsterdam, pp. 241-243, 1994.
2. Till, G.O.: Chemotaxis, in, Rother K. O., Till G. O., Haensch G. M. (eds), The Complement System; Springer-Verlag, Berlin Heidelberg, In Press.
3. Till, G.O.: Role of complement in trauma, shock and thermal injury, in, Rother K.O., Till, G.O., Haensch, G.M. (eds), The Complement System,. Springer-Verlag, Berlin Heidelberg, In Press.
4. Rother, K.O., Till, G.O. and Haensch, G.M.: The complement system, Springer-Verlag, Berlin Heidelberg, In Press.
5. Morganroth, M.L., Till, G.O. and Ward, P.A.: Pathophysiology of ischemia-reperfusion lung injury, in, Das, D.K. (ed), Pathophysiology of Reperfusion Injury, CRC Press, Inc., In Press.
6. Ward, P.A., Warren, J.S., Till, G.O., Varani, J. and Johnson, K.J.: Free radicals in lung disease, in, Rice-Evans, C. (ed),. Proceedings on Free Radicals, Diseased States and Anti-Radical Interventions, The Richelieu Press, London, In Press.

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

1. Foreman, K.E., Till, G.O., Johnson, K.J. and Ward, P.A.: Complement activation, endothelial cell P-selectin and the role of C5b-C9. FASEB J. 9:A34, 1995.
2. Colton, D.M., Hirschl, R.B., Till, G.O., Johnson, K.J., Wilkins, A., Compton, C. and Bartlett, R.H.: Partial liquid ventilation (PLV) decreases neutrophil infiltration when initiated before induction of lung injury. Chest, 1994.
3. Till, G.O.: Anti-adherence measures in experimental lung injury. Shock 3:A7, 1995.
4. Colton, D.M., Hirschl, R.B., Till, G.O., Johnson, K.J., Ichiba, S., Plato, C.C. and Bartlett, R.H.: Lung vascular permeability is reduced during partial liquid ventilation (PLV) in the setting of respiratory failure. Am. J. Resp. Crit. Care Med., 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Lecturer, Pathology 581.
B. Member, Dissertation Committee of Douglas F. Gibbs (Pathology).
C. Member and Co-mentor, Dissertation Committee of Mr. Zwehi Song (Biological Chemistry).
D. Member, Dissertation Committee of Mike Model (Biophysics).
E. Member, Dissertation Committee of Mr. Todd Kroll (Pharmacology - M.D./Ph.D.).
F. Mentor for students who worked in my laboratory over the past year including one post-doctoral fellows, five undergraduate students, two graduate students and one high school student.
G. Mentor, 1993 Minority Student Research Opportunities Program.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Small Bead Microcarriers", NIH CA61616, 7/1/93-12/31/93.
B. Principal Investigator, "Peptide-coated Microcarrier for Enhanced Adhesion", NIH, CA58154, 9/1/92-3/30/95.
C. Co-Investigator, "Protease-Oxidant Interactions in Lung Inflammation", NIH HL42607, 7/1/89-6/30/94.
D. Principal Investigator on Project 10, "Retinoic Acid and Cells of the Skin", Johnson and Johnson Corporation, 7/1/91-6/30/2001.
E. Principal Investigator, "Perfluorocarbon and Acute Lung Injury", Alliance Pharmaceutical Co., 7/1/94 -

PROJECTS UNDER STUDY:

A. The development of substrates for optimum growth of cells in large-scale culture.
C. The role of thrombospondin in the biology of human squamous carcinoma cells.
D. Influence of retinoic acid on proliferation and matrix production by dermal fibroblasts and epidermal keratinocytes in monolayer culture and organ culture.
E. Mechanisms of vascular cell injury in lung inflammation and kidney inflammation.
F. Role of terminal α-galactosyl residues in cancer metastasis.
G. Mechanisms of squamous epithelial cell invasion.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member, Department of Pathology Advisory Committee on Appointments, Promotions and Tenure.
B. Member, Department of Pathology Space and Research Committee.
C. Member, Department of Pathology Graduate Program Committee.
D. Member, Department of Pathology Human Resource Committee.
E. Member, Department of Pathology Graduate Program Comprehensive Exam Committee.
F. Director, Pathology Research Seminar Series.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Medical School Committee on Summer Research Opportunities.
B. Program Director, University of Michigan Cancer Center Program on Tumor Cell Metastasis and the Extracellular Matrix.
C. Member, University of Michigan Cancer Center Basic Research Committee.
D. Member, Cancer Biology Research Training Grant Scientific Steering Committee.
E. Member, Department of Dermatology Research Training Grant Steering Committee.

REGIONAL AND NATIONAL:

A. Editorial Board of Invasion and Metastasis.
B. Manuscript Reviewer for:
    1. American Journal of Pathology.
    2. Cancer Research.
    3. Clinical and Experimental Metastasis.
    4. Cancer.
    5. Experimental Cell Research.
    6. International Journal of Cancer.
    7. Journal of Immunology.
    8. Journal of Investigative Dermatology.
    9. Journal of Leukocyte Biology.
    10 Laboratory Investigation.
    11. Invasion and Metastasis.
    12. Science.
    13. Proceedings of the National Academy of Sciences.
C. Grant reviewer for:
    1. The Medical Research Council of Canada.
    2. Veterans Administration.
    3. The Johns Hopkins Center for Alternatives to Animal Research.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Speaker, Department of Microbiology and Immunology University of North Dakota, Grand Forks, North Dakota, September 15, 1993.
2. Invited Speaker, First International Conference on Advanced Pharmaceutical Substance Screening, Vienna, Austria, November 29-December 3, 1993.
3. Invited Speaker, Division of Hematology and Oncology, Department of Medicine, Emory University, February 8, 1994.

4. Invited Speaker, Symposium on Tissue Engineering, American Chemical Society Annual Meeting, San Diego, California, March 13, 1994.
5. Invited Speaker, Symposium on Epithelial-Mesenchymal Interactions, Experimental Biology, 1994, Anaheim, California, April 27, 1994.
6. Invited Speaker, Symposium on Leukocyte-Endothelial Cell Interactions, Shock Society Annual Meeting, Big Sky, Missouri, June 7, 1994.
7. Invited Speaker, Johnson & Johnson Symposium on Retinoids and Skin, Peddler's Village, Pennsylvania, June 2, 1994.
8. Invited Speaker, Symposium on Retinoids in Psoriasis, 6th International Psoriasis Meeting, Chicago, Illinois, July 21,1994.
9. Invited Speaker, Fourth Research Workshop on the Biology, Prevention and Treatment of Head and Neck Cancer, Arlington, Virginia, September 8, 1994.

PATENTS:

1. Combination Peptide Microcarriers for Enhanced Cell Attachment, Pending.
2. Organ-Cultured Skin for Assessment of Toxicological/Pharmacological Effects, Pending.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Varani, J., Larson, B.K., Perone, P., Inman, D.R., Fligiel, S.E.G. and Voorhees, J.J.: All-trans retinoic acid and extracellular Ca^{2+} differentially influence extracellular matrix production by human skin in organ culture. Am. J. Pathol. 142:1813-1822,1993.
2. Varani, J., Fligiel, S.E.G., Perone, P., Inman, D.R. and Voorhees, J.J.: Effects of sodium lauryl sulfate on human skin in organ culture: Comparison with all-trans retinoic acid and epidermal growth factor. Dermatology 187:19-26,1993.
3. Schuger, L., Mitra, R., Varani, J. and Gilbride, K.: Effect of retinoic acid on mouse lung branching activity. Develop. Biol. 159:462-473,1993.
4. Taylor, C.G., Dame, M.K., Murphy, H., Ward, P.A. and Varani, J.: Spontaneous injury of human umbilical vein endothelial cells is prevented by protein kinase activation. Lab. Invest. 70:822-831,1994.
5 Varani, J. and Ward, P.A.: Mechanisms of endothelial cell injury. Biological Signals 3:1-14,1994.
6. Varani, J. and Taylor, C.: Further studies on the mechanism of mesangial cell killing by activated neutrophils. Euro. J. Biochem., In Press.
7. Song, Z., Varani, J. and Goldstein, I.J.: Carbohydrate epitopes on Ehrlich tumor cells adapted for growth as solid or ascites tumors. Int. J. Cancer 55:1029-1035,1993.
8. Mulligan, M.S., Desrochers, P.E., Chinnaiyan, A.M., Gibbs, D.F., Varani, J., Johnson, K.J. and Weiss, S.J.: *In vivo* suppression of immune complex-induced alveolitis by secretary leukoproteinase inhibitor and tissue inhibitor of metalloproteinases-2. Proc. Nat. Acad. Sci. USA 90:11523-11527,1993.
9 Varani, J., Inman, D.R., Perone, P., Fligiel, S.E.G. and Voorhees, J.J.: Retinoid toxicity for fibroblasts and epithelial cells is independent of growth promoting activity and is inhibited by phosphatidylcholine. J. Invest. Dermatol. 101:839-842,1993.

10. Shumaker, D.K., Sklar, M.D., Prochownik, E.V. and Varani, J.: Increased cell-substrate adhesion accompanies conditional reversion to the normal phenotype in ras-oncogene-transformed NIH-3T3 cell. Exp Cell Res., In Press.
11. Huang, S., Varani, J. and Chakrabarty, S.: Control of cellular phenotype by fibronectin and its receptor in AKR fibroblasts: Down-modulation of fibronectin and its receptor by antisense fibronectin RNA expression. J. Cell Physiol., In Press.
12. Varani, J., Perone, P., Griffith, C.E.M., Inman, D.R., Fligiel, S.E.G.and Voorhees, J.J.: All-trans retinoic acid (RA) stimulates events in organ cultured human skin that underlie repair. J. Clin. Invest., In Press.
13. Varani, J., Burmeister, B., Sitrin, R.G., Schollenberger, S.B., Inman, D.R., Fligiel, S.E.G., Gibbs, D.F. and Johnson, K.J.: Expression of serine and metalloproteinases in organ-cultured human skin: Altered levels in the presence of retinoic acid. Amer. J. Pathol., In Press.
14. Fligiel, S.E.G. and Varani, J.: *In situ* epithelial cell invasion in organ culture. Invasion & Metastasis, In Press.
15. Ginsburg, I., Mitra, R. Jr., Gibbs, D.F., Varani, J. and Kohen, R.: Killing of endothelial cells and release of arachidonic acid. Inflammation 17:295-319,1993.
16. Ginsburg, I., Misgav, R., Gibbs, D.F., Varani, J. and Kohen, R.: Chemiluminescence in activated human neutrophils: Role of buffers and scavengers. Inflammation 17:227-243,1993.
17. Mulligan, M.S., Wilson, G.P., Todd, R.F., Smith, C.W., Anderson, D.C., Varani, J., Myasaka, M., Vaporciyan, A. and Ward, P.A.: Role of β_1 and β_2 intergrins and ICAM-1 in lung injury after deposition of IgG and IgA immune complexes. J. Immunol. 150:2407-2417,1993.
18. vanEckhout, M., Wright, S.M., Varani, J. and Kelleher, J.J.: Effects of diet on herpes simplex virus, type I infection in mice. Nutrition Res. 14:545-552,1994.
19. Nickoloff, B.J., Mitra, R.S., Varani, J., Dixit, V.M. and Polverini, P.J.: Aberrant production of interleukin-8 and thrombospondin-1 by psoriatic keratinocytes mediates angiogenesis. Am. J. Pathol. 144:820-828,1994.
20. Varani, J., Perone, P., Fligiel, S.E.G., Inman, D.R. and Voorhees, J.J.: All-trans retinoic acid preserves viability of keratinocytes and fibroblasts in full-thickness human skin and fibroblasts isolated dermis in organ culture. Arch. Dermatol. Res., In Press.
21. Varani, J., Inman, D.R., Fligiel, S.E.G. and Hillegas, W.J.: Use of recombinant and synthetic peptides as attachment factors for cells on peptides. Cytotechnology 13:89-98,1994.
22. Varani, J. and Ward, P.A.: Endothelial cell injury in acute inflammation. Shock, In Press.

BOOKS AND CHAPTERS IN BOOKS:

1. Varani, J.: Non-collagenous glycoprotein components of the extracellular matrix in pulmonary fibrosis, in, Thrall, R. and Phan, S.H. (eds), Pulmonary Fibrosis, Series Title: Lung Biology in Health and Disease, Marcel Dekker, Inc., New York, New York, In Press.
2. Ginsburg, I., Varani, J., Ligumski, M. and Kohen, R.: Destruction of tissues at inflammatory sites, Proceedings of 5th World Congress on Inflammation. Antirheumatic, Analgesic and Immunomodulators, Bioscience Ediprint. Inc., Geneva, Switzerland, 1994, In Press.
3. Hillegas, W.J. and Varani, J.: Peptides as a coating for cells on Microcarriers, Proceedings of Japanese Society for Cell Technology Symposium on Large Scale Culture of Anchorage-Dependent Cells, Tokyo, Japan, 1994, In Press.

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

1. Varani, J., Taylor, C.G., Dame, M.K. and Murphy, H.: Age-related injury to human umbilical vein endothelial cells. J. Cell. Biochem. Suppl. 18A:335.
2. Gibbs, D.F., Burmeister, B., Varani, J. and Johnson, K.J.: Characterization of serine and metalloproteinases from stimulated rat neutrophils and rat alveolar macrophages. J. Cell Biochem. Suppl. 18B:143.
3. Varani, J., Burmeister, B., Sitrin, R.S., Schollenberger, S., Gibbs, D.F. and Johnson, K.J.: Serine and metalloproteinases in human skin: Relation to loss of epidermal cohesion in retinoic acid-treated organ-cultured skin. J. Cell Biochem. Suppl. 18B:148.
4. Burmeister, W., Sitrin, R.G., Schollenberger, S., Johnson, K.J. and Varani, J.: Proteolytic enzymes elaborated by human skin maintained in organ culture. FASEB J. 8:5057,1994.
5. Varani, J., Perone, P., Zouboulis, C. and Tavakkol, A.: Epithelial-stromal interactions in maintenance of human skin in organ culture. FASEB J. 8:3854,1994.
6. Inman, D.R., Varani, J. and Fligiel, S.E.G.: Squamous epithelial cell invasion under *in situ* conditions. FASEB J. 8:677,1994.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Beatrice Beck-Schimmer, M.D., Postdoctoral Fellow.
      b. Michael J. Eppinger, M.D., Postdoctoral Fellow.
      c. Hangjun Duan, Pathology Graduate Student.
      d. Kimberly E. Foreman, Ph.D.
      e. Jami Foreback, Pathology Graduate Program Student (MSTP student) (mentor).
      f. Teletha Gipson, Ph.D., Postdoctoral Fellow.
      g. Elizabeth Schmid, M.D., Postdoctoral Fellow.
      h. Ralph C. Schimmer, M.D., Postdoctoral Fellow.
      i. Hagen Schmal, M.D., Postdoctoral Fellow.
      j. Thomas Shanley, M.D.. Postdoctoral Fellow.
      k. Roscoe Warner, Ph.D., Postdoctoral Fellow.
      l. UROP Undergraduate Students.
      m. Morgan Althoen, Medical Student.
      n. Ankit Patel, Medical Student.
      o. Gregory S. Shannon, Honors Student.
   2. Indirect supervision of four Research Scientists.
   3. Gross Autopsy Conference, 25 hours.
   4. Clinical Pathology Grand Rounds Lecture, Reflections on the Pathology Board Examination.
B. Undergraduate students:
   1. Lecture, College Honors Seminar 250, March 29, 1994, three hours.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Lung Immunopathology" (Training Grant), NHLBI-NIH-HL-07517 (5%), $288,584/year ($2,693,183/ten years), June 1, 1986 -May 31, 1996.
B. Principal Investigator, "Lung Injury by Oxygen Metabolites", NIGMS-NIH-5-R37-GM-29507 (20%), $234,056/year ($1,271,378/five years), July 1, 1992 - June 30, 1997.
C. Principal Investigator, "Inflammatory Cells and Lung Injury", NHLBI-HL-31963 (29%), Section I - $183,141, Core A -$36,462/year ($1,010,734/five years), March 1, 1989-February 28, 1994.

D. Co-Investigator, "Mechanisms of Glomerular and Tubular Injury" (R. Wiggins, Principal Investigator), NIADDK-NIH-DK-39255 (5%), Section 1 - $47,174/year, August 1, 1993 - July 31, 1993.
E. Principal Investigator, "Oligosaccharides as Inflammatory Agents" NIH-AI33189-01 (Core - 10%; Administrative Core - 5%), $449,661/year ($2,192,155/four years), September 1, 1992-June 30, 1996.

PENDING:

A. Co-Investigator, "The Role of Cytokines and Adhesion Molecules in Thermal Injury", (5%), $178,772/year ($1,384,651/five years).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Dean's Cabinet, 1993--.
B. Advisory Committee for the Howard Hughes Medical Institute, 1984--.
C. Clinical Council, 1993--.
D. Conflict of Interest Committee, 1993--.
E. Dean's Advisory Council, 1985--.
F. Geriatric Center Executive Committee.
G. Howard Hughes Medical Institute Dean's Advisory Committee.
H. Internal Medicine Advisory Committee for the University of Michigan George M. O'Brien Renal and Urologic Center, 1991--.
I. Michigan Eye Bank Research Review Committee, 1980--.
J. Presidential Initiatives Fund, The University of Michigan, March, 1987--.
K. Undergraduate Research Opportunity Program, University of Michigan, 1992--.
L. University of Michigan Cancer Center Executive Committee.

REGIONAL AND NATIONAL:

A. American Association for Advancement of Science.
B. American Association of Immunologists.
C. American Association of Pathologists.
    1. Nominating Committee, 1985-present.
    2. Executive Committee, Intersociety Pathology Council and Universities Associated for Research and Education in Pathology, Inc.
    3. Representative to the Universities Associated for Research and Education in Pathology, 1988-89.
    4. Steering Committee for the Federal Demonstration Project, 1990-1992.
    5. Future Directions Committee, 1989--.
D. American Board of Pathology, effective January 1, 1988:
    1. Vice-President, 1995
    2. Trustee, 1980--.
    3. Immunopathology Test Committee, 1980-85, 1988--. Vice-Chairman.
    4. Anatomic Pathology Examination Committee, 1988--.

5. By-Laws Committee, 1988--.
6. Examination Evaluation Committee, 1988--.
7. Professional Qualification/Competence Committee, 1988--.
8. ABP/ABPRF Research Committee, 1989--.
9. Residency Review Committee for Pathology.
10. Building Committee, 1992--.
11. Planning and Development Committee, 1992--.
12. Test Committee for Molecular Pathology, 1993--.

E. American Federation for Clinical Research.
F. American Heart Association, Cardiopulmonary Division.
G. American Lung Association.
H. American Society for Clinical Investigation.
I. American Pathology Foundation.
J. American Thoracic Society.
K. Association of American Physicians.
L. Association of Pathology Chairmen.
M. Center for Alternatives to Animal Testing, Johns Hopkins University.
N. A. James French Society of Pathologists, 1988--.
O. Health Policy Agenda for the Amerian People, Advisory Committee.
P. Institute of Medicine, July 1, 1990.
Q. United States and Canadian Academy of Pathology, Inc.
1. Council Member, April 1, 1986-1989.
2. Member, Finance Committee, April 1, 1986-1990.
3. Vice-President, 1990.
4. President-Elect, 1991.
5. President, 1992.
6. Past-President, 1993.

R. Michigan Society of Pathologists.
S. Michigan Thoracic Society, 1988--.
T. National Research Council
1. Institute of Laboratory Animal Resources.
2. Committee on Human Rights, Correspondent.

U. The Oxygen Society, 1988--.
V. Phi Rho Sigma, President, The University of Michigan Chapter, September, 1988.
W. Society of Medical Consultants to the Armed Forces:
1. President, 1988.

X. Universities Associated for Research and Education in Pathology, Inc., Board of Directors.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. American Journal of Pathology, Editorial Board, 1982--.
B. American Review of Respiratory Diseases, Consulting Editor, 1977--.
C. Archives of Pathology and Laboratory Medicine, Reviewer, 1973--.
D. Arthritis and Rheumatism, Consulting Editor, 1975--.
E. Biological Signals, Consulting Editor.
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 Critical Care, Editorial Board.
O. Journal of Experimental Cell Research, Consulting Editor.
P. Journal of Experimental Lung Research, Consulting Editor.
Q. Journal of Experimental Pathology, 1986--.
R. Journal of the Reticuloendothelial Society, Consulting Editor.
S. Laboratory Investigation, Editorial Board, 1981--.
T. Toxicologic Pathology, Editorial Board, 1988--.

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, "Mechanisms of Airway Injury: Cellular and Molecular Interaction", NHLBI Conference on Mechanisms of Airway Injury: Cellular and Molecular Interactions, Groβhansdorf, Germany, July 6-10, 1994.
2. Invited Lecturer, "Cytokines, Adhesion Molecules and Inflammatory Injury", Ninth Annual Symposium on Mechanisms of Immunotoxicity, Virginia Beach, Virginia, August 31-September 1, 1994.
3. Invited Lecturer, "Cytokines, Adhesion Molecules and Inflammatory Injury", Searle Corporation, Skokie, Illinois, September 15, 1994.
4. Invited Lecturer, "Defining the *In Vivo* Role of Cytokines in Inflammation", IBC Business Communications Meeting, "Chemotactic Cytokines', Washington, D.C., September 18-19, 1994.
5. Visiting Lecturer, "Cytokines, Adhesion Molecules and Lung Injury", COR Therapeutics, Inc., South San Francisco, California, September 21-23, 1994.
6. Invited Lecturer, "Selectins, Cytokines and Lung Injury", Postgraduate Course on Inflammation and Disease", Amsterdam Leiden Institute for Immunology, Leiden, Netherlands, October 4-7, 1994.
7. Invited Keynote Speaker, "The Cellular Basis of Ischemic Injury", Second Chicago Symposium on Advances in CPR Research and Utstein III: Setting Guidelines on Laboratory Research, The Drake Hotel, Chicago, Illinois, October 16-17, 1994.
8. Invited Lecturer, "Role of Selectins in Intrapulmonary Inflammation", 2nd International Congress of Physiology, Kyoto, Japan, November 19-21, 1994.
9. Invited Lecturer, "Regulation of Cytokine and Adhesion Molecule-Dependent Inflammation", Ono Pharmaceutical Company, Osaka, Japan, November 22-23, 1994.
10. Invited Lecturer, "Cytokines, Adhesion Molecules and Inflammatory Lung Injury", Osaka University Medical School, Osaka, Japan, November 22-23, 1994.
11. Invited Lecturer, "Cytokines, Adhesion Molecules and Lung Injury", Institut Pasteur First Euro Conference on Adhesion Proteins, Paris, France, November 26-30, 1994.
12. Invited Lecturer, "Cytokines, Adhesion Molecules and Lung Injury", Selectin Meeting, Bristol-Myers Squibb Company, Seattle, Washington, December 3, 1994.
13. Invited Lecturer, "Regulatory Pathways of Cytokine and Lung Inflammation", ICOS Corporation, Bothell, Washington, December 9, 1994.
14. Invited Lecturer, "Novel Agents that Block *In Vivo* Selectin-Dependent Inflammmatory Reactions", in the Glycobiology of Inflammation Session, The Biochemical Society Meeting No. 653, University of Sussex, Sussex, England, December 12-14, 1994.
15. Invited Lecturer, "Cytokines, Adhesion Molecules and Lung Injury", Zeneca Pharmaceuticals, Macclesfield, England, December 14-16, 1994.
16. Invited Lecturer, "Mechanisms of Oxidant-Mediated Endothelial Cell Injury", American Heart Association Conference on The Functional and Structural Aspects of the Vascular Wall, Snowbird, Utah, February 2, 1995.
17. Visiting Professor, "Regulation of Lung Inflammation", Department of Pathology Research Seminar, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, March 24, 1995.

18. Co-Chair Symposium with Dr. Charles N. Serhan, "The Role of Reactive Lipids and Nitrogen Metabolites in Inflammation", at the Experimental Biology '95 Meeting in Atlanta, Georgia, April 12, 1995.
19. 1995 Ecker Lecturer, "Role of Complement and Cytokines in Endothelial Injury", Department of Pathology, Case Western Reserve University, Cleveland, Ohio, April 18, 1995.
20. Invited Lecturer, "Mechanisms of Ischemia Reperfusion Injury of Lung", Ischemia-Reperfusion Seminar Series, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, April 28, 1995.
21. Visiting Scientist, "Regulation of Lung Inflammatory Responses", NexStar Pharmaceuticals, Inc., Boulder, Colorado, May 4, 1995.
22. Invited Lecturer, "Cytokines in Pulmonary Inflammation", Cystic Fibrosis Foundation Williamsburg Conference on Gene Therapy, Williamsburg, Virginia, June 5-7, 1995.
23. Invited Lecturer, "The Networking of Cytokines in Lung Inflammatory Injury", Cytokines and Adhesion Molecules in Lung Inflammation Symposium, Institut Pasteur, Paris, France, June 22, 1995.
24. Co-Chair Session, "Adhesion Molecules", with Dr. Roy Lobb, Cytokines and Adhesion Molecules in Lung Inflammation Symposium, Institut Pasteur, Paris, France, June 22, 1995.
25. Invited Lecturer, "Roles of Chemokines and Regulatory Cytokines in Lung Injury", Institute de Recherches Internationales Servier, I.R.I.S., Suresnes, France, June 23, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Eppinger, M.J., Jones, M.L., Deeb, G.M., Bolling, S.F. and Ward, P.A.: The role of tumor necrosis factor-alpha in a rat lung model of ischemia-reperfusion injury. Surg. Forum. 45:297-300, 1994.
2. Foreman, K.E., Vaporciyan, A.A., Bonish, B.K., Jones, M.L., Johnson, K.J., Glovsky, M.M., Eddy, S.M. and Ward, P.A.: C5a-induced expression of P-selectin in endothelial cells. J. Clin. Invest. 94:1147-1155, 1994.
3. Kim, J.S., Gautam, S.C., Chopp, M., Zaloga, C., Jones, M.L., Ward, P.A. and Welch, K.M.A.: Expression of monocyte chemoattractant protein-1 and macrophage inflammatory protein-1 after focal cerebral ischemia in the rat. J. Neuroimmunol. 56:127-134, 1994.
4. Murphy, H.S., Maroughi, M., Till, G.O. and Ward, P.A.: Phorbol-stimulated influx of extracellular calcium in rat pulmonary artery endothelial cells. Amer. J. Physiol. 267:L145-L151, 1994.
5. Taylor, C.G., Dame, M.K., Murphy, H.S., Ward, P.A. and Varani, J.: Spontaneous injury to human umbilical vein endothelial cells increases during *in vitro* culture and is blocked by protein kinase C activation. Lab. Invest. 70:822-829, 1994.
6. Ward, P.A.: Oxygen radicals, cytokines, adhesion molecules, and lung injury. Environ. Health Perspect. 102:13-16, 1994.
7. Ward, P.A. and Mulligan, M.S.: Blocking of adhesion molecules *in vivo* as anti-inflammatory therapy. Therapeutic Immunol. 1:165-171, 1994.
8. Zhang, R.L., Chopp, M., Li, Y., Zaloga, C., Jiang, N., Jones, M., Miyasaka, M. and Ward, P.A.: Anti-ICAM-1 antibody reduces ischemic cell damage after transient middle cerebral artery occlusion in the rat. Neurology 44:1747-1751, 1994.
9. Eppinger, M.J., Jones, M.L., Deeb, M., Bolling, S.F. and Ward, P.A.: Pattern of injury and the role of neutrophils in reperfusion injury in rat lung. J. Surg. Res. 58:713-718, 1995.
10. Kilgore, K.S., Shen, J.P., Miller, B.F., Ward, P.A. and Warren, J.S.: Enhancement by the complement membrane attack complex of tumor necrosis factor-α induced endothelial cell expression of E-selectin and ICAM-1. J. Immunol. 155:1434-1441, 1995.

11. Mulligan, M.S., Miyasaka, M., Suzuki, M., Kawashima, H., Lizuka, M., Hasegawa, A., Kiso, M., Warner, R.L. and Ward, P.A.: Anti-inflammatory effects of sulfatides in selectin-dependent acute lung injury. Inter. Immunol. 7:1107-1113, 1995.
12. Mulligan, M.S., Vaporciyan, A.A., Warner, R.L., Jones, M.L., Foreman, K.E., Miyasaka, M., Todd, R.F., III and Ward, P.A.: Compartmentalized roles for leukocytic adhesion molecules in lung inflammatory injury. J. Immunol. 154:1350-1363, 1995.
23. Shanley, T.P., Schmal, H., Friedl, H.P., Jones, M.L. and Ward, P.A.: Regulatory effects of intrinsic IL-10 in IgG immune complex-induced lung injury. J. Immunol. 154:3454-3460, 1995.
24. Shanley, T.P., Schmal, H., Friedl, H.P., Jones, M.L. and Ward, P.A.: Role of macrophage inflammatory protein-1α (MIP-1α) in acute lung injury in rats. J. Immuno1. 54:4793-4802, 1995.
25. Vaporciyan, A.A., Mulligan, M.S., Warren, J.S., Barton, P.A., Miyasaka, M. and Ward, P.A.: Up-regulation of lung vascular ICAM-1 in rats is complement dependent. J. Immunol. 155:1442-1449, 1995.
26. Ward, P.A.: Adhesion molecule knockouts: One step forward and one step backward. (Editorial) J. Clin. Invest. 95:1425, 1995.
27. Warner, R.L., Paine, R., III, Christensen, P.J., Marletta, M.A., Richards, M.K., Wilcoxen S.E. and Ward, P.A.: Lung sources and cytokine requirements for *in vivo* expression of inducible nitric oxide synthase. Amer. J. Resp. Cell and Molec. Biol. 12:649-661, 1995.
28. Eppinger, M.J., Ward, P.A., Jones, M.L., Bolling, S.F. and Deeb, G.M.: Disparate effects of nitric oxide on lung ischemia-reperfusion injury.
29. Foreman, K.E., Glovsky, M.M., Warner, R.L., Horvath, S.J. and Ward, P.A.: Comparative effect of C3a and C5a on adhesion molecule expression on neutrophils and endothelial cells. Inflammation, In Press.
30. Jones, M.L., Vaporciyan, A.A. and Ward, P.A.: A new fluorescent method for quantitative assessment of neutrophil monocyte chemotaxis. J. Immunol. Methods.
31. Jones, M.L., Vaporciyan, A.A. and Ward, P.A.: A new fluorescent method for quantitative assessment of neutrophil and monocyte chemotaxis. Submitted to J. Immunol. Methods.
32. Lebedovych, L., Johnson, K.J., McMorris, M., Andrews, A., Hirschl, R. and Ward, P.A.: The induction of late allergic responses in rats passively sensitized with monoclonal IgE antibodies.
33. Lebedovych, L., Johnson, K.J., McMorris, M.S., Gilardy, A.K., Hirschl, R.B., Ward, P.A. and Baker, J.R., Jr.: Characteristics of late allergic responses in rats passively sensitized with monoclonal IgE antibodies. Submitted to J. Clin. Invest.
34. Mulligan, M.S., Johnson, K.J., Smith, C.W., Todd, R.F., Miyasaka, M., Tamatani, T., Issekutz, T.B., Anderson, D.C. and Ward, P.A.: Role of β2 integrins, VLA-4 and ICAM-1 in nephrotoxic nephritis. J. Clin. Invest., In Press.
35. Mulligan, M.S., Jones, M.L. and Ward, P.A.: Roles of IL-4 and IL-10 in immune complex injury of lung. Submitted to J. Clin. Invest.
36. Mulligan, M.S., Miyasaka, M., Suzuki, Y., Iizuka, M., Hasegawa, A., Kiso, M. and Ward, P.A.: Protective effects of sulfatides in selectin-dependent acute lung injury. Submitted to Science.
37. Mulligan, M.S., Miyasaka, M., Tamatani, T. and Ward, P.A.: TNFα regulates *in vivo* intrapulmonary expression of ICAM-1. Submitted to Amer. J. Pathol.
38. Mulligan, M.S., Miyasaka, M. and Ward, P.A.: Cytokine and adhesion molecule requirements for glycogen-induced peritoneal recruitment of neutrophils. Submitted to Amer. J. Pathol.
39. Mulligan, M.S., Polley, M.J., Paulsen, J.C. and Ward, P.A.: Evidence for a role of P-selectin in lung injury developing after systemic complement activation. J. Biol. Chem., In Press.
40. Mulligan, M.S., Shanley, T.P., Jones, M.L., Johnson, K.J., Bonish, B.K. and Ward, P.A.: Cytokine and adhesion molecule requirements in lung injury induced by anti-glomerular basement membrane antibody. J. Clin. Invest.
41. Mulligan, M.S., Smith, C.W., Anderson, D.C. and Ward, P.A.: *In vivo* recruitment of neutrophils: Consistent requirements for L-arginine and variable requirements for adhesion molecules. Submitted to Am. J. Pathol.
42. Mulligan, M.S., Sulavik, C., Ward, P.A., Kunkel, R.G. and Johnson, K.J.: The delayed phase of anti-GBM nephritis in deferoxamine sensitive but catalase-insensitive. Inflammation, In Press.

43. Mulligan, M.S., Sulavik, C., Bavorik, P.A., Ward, P.A. and Johnson, K.J.: Evidence for the role of oxygen radicals in autologous nephrotoxic nephritis. Submitted to Lab. Invest.
44. Mulligan, M.S., Warren, J.S., Smith, C.W., Anderson, D.C., Yeh, G., Rudolph, A. and Ward, P.A.: Lung injury following depositon of IgA immune complexes: Requirements for CD18 and L-arginine. Submitted to J. Immunol.
45. Mulligan, M.S., Warren, J.S., Till, G.O., Smith, C.W., Anderson, D.C., Todd, R.F., III and Ward, P.A.: Roles of rat homologues of CD11b and CD18 neutrophil adhesion molecules in complement- and oxygen radical-mediated acute inflammatory reactions. Submitted to J. Clin. Invest.
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47. Murphy, H.S., Seiler, A. and Ward, P.A.: Relationship of protein kinase C activity to 0_2^- production by rat pulmonary artery endothelial cells. Submitted to J.Cell Phys.
48. Murphy, H.S., Seiler, A. and Ward, P.A.: Protein kinase C activity in0_2^- producing endothelial cells. Submitted to Lab. Invest.
49. Murphy, H.S., Seiler, A. and Ward, P.A.: Distinct patterns or protein kinase C activity in stimulated endothelial cells: Effects of phorbol ester, C5a, bradykinin and TNFα. Submitted to J. Bio. Chem.
50. Murphy, H.S., Shayman, J.A., Till, G.O., Mahrougui, M., Owens, C.B., Ryan, U.S. and Ward, P.A.: Superoxide responses of endothelial cells to C5a and TNFa: Divergent signal transduction pathways. Submitted to Amer. J. Phys.
51. Schmal, H., Shanley, T.P., Jones, M.L., Friedl, H.P. and Ward, P.A.: Role for macrophage inflammatory protein-2 (MIP-2) in LPS-induced lung injury in rats. J. Immunol.
52. Schmal, H., Shanley, T.P., Schrier, D.G., Flory, C.M., Friedl, H.P., Ward, P.A. and Jones, M.L.: Transciptional characterization of IgG immune complex-mediated lung injury by Northern blot and quantitative PCR analysis. J. Immunol.
53. Seekamp, A., Hultquist, D.E., Xu, F., Ward, P.A. and Till, G.O.: Protection by vitamin B2 against oxidant-mediated acute lung injury. Free Rad. Biol. Med., In Press.
54. Seekamp, A., Mulligan, M.S., Till, G.O. and Ward, P.A.: Role of oxygen radicals, nitric oxide and complement in ischemia reperfusion injury. Submitted to the Amer. J. of Path.
55. Seekamp, A. and Ward, P.A.: Ischemia - reperfusion injury. Agents in Actions (Supplement), In Press.
56. Shanley, T.P., Miyasaka, M., Suzuki, Y., Kawashima, H., Iizuka, M., Suzuki, T., Hasegawa, A., Kiso, M. and Ward, P.A.: Sulfatides as novel anti-inflammatory compound in selectin-dependent acute lung injury. Science, In Press.
57. Shanley, T.P., Warner, R.L., Kapur, V., Ward, P.A., Musser, J.M. and Jones, M.L.: Augmentation of lipopolysaccharide-induced lung injury in rats by streptococcal extracellular cystine protease. Submitted to J. Clin. Invest.
58. Shanley, T.P., Warner, R.L. and Ward, P.A.: The role of cytokines and adhesion molecules in the development of inflammatory injury. Mol. Med. Today, In Press.
59. Till, G.O., Friedl, H.P. and Ward, P.A.: Role for histamine and xanthine oxidase in complement- and oxidant-mediated acute lung injury. Free Rad. Biol. Med., In Press.
60. Till, G.O., Lee, S., Mulligan, M.S., Wolter, J.R., Smith, C.W., Ward, P.A. and Marak, G.E.: Adhesion molecules in experimental phacoanaphylactic endophthalmitis. Invest. Ophthalmol. Vis. Sci., In Press.
61. Till, G.O. and Ward, P.A.: Immunologic and phagocytic cell defects in thermally injured patients. J. Crit. Care Med., In Press.
62. Vaporciyan, A.A. and Ward, P.A.: Induction by C5a of P-selectin dependent endothelial adhesiveness for neutrophils. J. Immunol., In Press.
63. Varani, J., Gibbs, D.F., Johnson, K.J., Weinberg, J.M., Ryan, U.S., Ginsburg, I. and Ward, P.A.: Hydrogen peroxide-induced cell and tissue injury: Protective effects of Mn^{2+}. Submitted for publication.
64. Varani, J., Ginsburg, I., Johnson, K.J., Gibbs, D.F., Weinberg, J.M. and Ward, P.A.: Amino acids and metal ions protect endothelial cells from lethal injury. FASEB J., In Press.

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66. Ward, P.A.: The wound environment - Local and systemic perturbations: Inflammation and the burn wound. J. Burn Care & Rehab, In Press.
67. 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.
68. Ward, P.A.: Oxidant damage. Submitted to the Task Force on Allergy and Immunology, National Institutes of Health.
69. Ward, P.A. and Johnson, K.J.: Lung inflammatory mechanisms. J. Human Path., In Press.
70. Ward, P.A., Johnson, K.J. and Till, G.O.: Mechanisms of lung injury. Prax. Klin. Pneumonol., In Press.
71. Ward, P.A. and Marks, R.M.: The acute inflammatory reaction. Current Opinion on Immunol.
72. 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.
73. Ward, P.A., Till, G.O., Varani, J., Todd, R.F. and Warren, J.S.: Role of rat CD11b neutrophil adhesion molecule in complement and oxygen radical-mediated inflammatory reactions. Submitted to J. Clin. Invest.
74. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: PAF, cytokines, toxic oxygen products and cell injury. Submitted for publication.
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BOOKS/CHAPTERS IN BOOKS:

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3. Ward, P.A.: Interventional approaches *in vivo* for selectin-dependent inflammatory injury, in, Seiss, W., Lorenz, R. and Weber, P.C. (eds), Topics in Molecular Medicine, Volume 1, Adhesion Molecules and Cell Signaling: Biology and Clinical Applications, Raven Press, Ltd., New York, New York, pp. 243-249, 1995.
4. Ward,P.A.: Overview, in Kinney, J.M. and Tucker, H.N. (eds), Organ Metabolism and Nutrition: Ideas for Future Critical Care, Raven Press, Ltd., New York, New York, pp. 497-510, 1994.
5. Kunkel, S.L., Driscoll, K.E., Ward, P.A., Nickoloff, B. and Strieter, R.M.: Immunopathology of environmental and occupational disease, Chapter 24, in, Craighead, J.E. (ed), The Pathology of Human Environmental and Occupational Disease, Mosby Yearbook, St. Louis, Missouri, pp. 385-395.
6. Ward, P.A. and Mulligan, M.S.: Role of adherence molecules in lung inflammation, Chapter 16, Granger, D.N. and Schmid-Schonbein, G.W. (eds), Physiology and Pathophysiology of Leukocyte Adhesion, Oxford University Press, New York, New York, pp. 313-322, 1995.
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8. Fantone, J.C. and Ward, P.A.: Mechanisms of inflammation, in, Cohen, A.S. (ed), Rheumatology and Immunology, Grune and Stratton, In Press.
9. 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, Second Edition, J.B. Lippincott Inc., New York, New York, In Press.
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12. Maderazo, E.G., Woronick, C.L. and Ward, P.A.: Inhibitors of chemotaxis, in, Methods in Enzymology, Academic Press, Orlando, Florida, In Press.
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14. Mulligan, M.S. and Ward, P.A.: Inflammatory mechanisms of cellular and tissue damage, in, Cooper, G., Dudley, H.A.F., Gann, D.S., Little, R.A. and Maynard, R.L. (eds), Mechanisms of Cellular Damage for the Volume on Scientific Foundations of Trauma, Heinemann Medical Books, London, England, In Press.
15. Mulligan, M.S. and Ward, P.A.: Molecular Mechanisms in Acute Lung Injury", in, August, J.T., Anders, M.W. and Murad, F. (eds), Advances in Pharmacology, Volume 24, Academic Press, Orlando, Florida, In Press.
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18 Till, G.O. and Ward, P.A.: Role of complement and neutrophils in experimental acute lung injury, in, Nuki, G. and Zvaifler, N. (eds) The Lungs and Rheumatic Disease, Butterworths International Medical Reviews, Rheumatology 3, Butterworth and Co., England, In Press.
19. Till, G.O. and Ward, P.A.: The lung and rheumatic disease: Role of complement. Butterworth's International Medical Reviews, Rheumatology 3, In Press.
20. Till, G.O. and Ward, P.A.: Thermal injury and lung tissue damage, in, Critical Topics in Pulmonary Pharmacology and Toxicology, In Press.
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23. Varani, J., McCoy, J.P. and Ward, P.A.: The attraction of wandering metastatic cells, Kaiser, H. (ed), Progressive Stages of Neoplastic Growth, In Press.
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32. Ward, P.A., Johnson, K.J. and Sulavik, M.D.: Lung injury produced by oxygen derived free radicals from leukocytes, In, Mechanisms of Lung Injury Symposium, given at the Graduate Hospital, Philadelphia, Pennsylvania, 1986, In Press.
33. Ward, P.A., Johnson, K.J. and Till, G.O.: Tissue injury as a consequence of oxygen radicals produced by phagocytic cells, in Proceedings of Symposium by Comparative Respiratory Society, Anaheim, California, In Press.
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41. Ward, P.A., Warren, J.S., Till, G.O., Varani, J. and Johnson, K.J.: Modification of disease by preventing free radical formation: A new concept in pharmacologic intervention, Hershko, C. (ed), Iron Chelating Therapy, Bailliere Tindall Limited, Harcourt Brace Jovanovich, Publishers, London, England, In Press.
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43. Ward, P.A. and Mulligan, M.S.: Role of products of L-arginine in inflammatory lung damage, Moncada, S., Nistico, G. and Higgs, E.A. (eds), Nitric Oxide: Brain and Immune System, Portland Press, London, England, In Press.
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51. Warren, J.S., Ward, P.A. and Johnson, K.J.: Oxygen radicals as "Mediators of Inflammation", Volume 6, in, Hensom, P.M. (ed), The Handbook of Inflammation, Elsevier Biomedical Division, Amsterdam, The Netherlands, In Press.
52. Warren, J.S., Ward, P.A. and Johnson, K.J.: The respiratory burst and mechanisms of oxygen radical mediated tissue injury, in, Sbarra, A.J. and Strauss, R.P. (eds), The Respiratory Burst and its Physiological Significance in Medicine, Plenum Press, New York, New York, In Press.

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

1. Marak, G.E., Schmal, H., Foreman, K.E., Friedl, H.P., Ward, P.A. and Till, G.O.: Anti-inflammatory properties of xanthine oxidase inhibitors. Proceedings of the 6th International Symposium on the Immunology and Immunopathology of the Eye, Washington, D.C., June 22-24, 1994, Advances in Ocular Immunology, 1994.
2. Varani, J. and Ward, P.A.: Editorial Review: Mechanisms of endothelial cell injury in acute inflammation. Shock 1994;5:_____, 1995.
3. Ward, P.A.: Effects of prolonged exposure to low doses of nitric oxide or nitrogen dioxide on alveolar septa of the adult rat lung, by Mercer, R. et al. (Editorial). Lab. Invest. In Press.
4. Ward, P.A.: Adhesion molecule knockouts: One step foward and one step backward (Editorial). J. Clin. Invest. 95:1425, 1995.
5. Ward, P.A.: Book Review, in, Das, D.K.: Cellular, Biochemical and Molecular Aspects of Reperfusion Injury. Ann. N.Y. Acad. Sciences, Volume 723, 1994, pp. 506. Res. Comm. Molecular Pathol. Pharmacol. 87:371, 1995.
6. Ward, P.A.: The Vanishing Lung (Editorial). Lab. Invest. 1-2, 1995.
7. Eppinger, M.J., Jones, M.L., Deeb, G.M., Bolling, S.F. and Ward, P.A.: Appearance of adhesion molecules in a rat lung model of ischemia-reperfusion. J. Leukocyte Biol. (Suppl.):53, 1994.
8. Beck, B., Jones, M.L., Schimmer, R.C., Schmal, H., Friedl, H.P. and Ward, P.A.: Cloning and expression of rat intercellular adhesion molecule-1 (ICAM-1) in the pET and baculovirus systems. FASEB J. 9;A37, 1995.
9. Doyle, N.A., Quinlan, W.M., Bullard, D.C., Vestweber, D., Jones, M.L., Ward, P.A., Beudet, A.L. and Doerschuk, C.M.: P-selectin and ICAM-1 in cobra venom factor-induced lung injury: Anti-adhesion molecule antibodies and mutant mice. Amer. J. Resp. & Critic. Care Med. 151:A455, 1995.
10. Eppinger, M.J., Jones, M.L., Deeb, G.M., Bolling,. S.F. and Ward, P.A.: Acute phase lung ischemia-reperfusion injury is macrophage mediated. FASEB J. 9;A961, 1995.
11. Eppinger, M.J., Ward, P.A., Jones, M.L., Bolling, S.F. and Deeb, G.M.: Inhaled nitric oxide reduces lung ischemia-reperfusion injury. Soc. Thoracic Surgeons, January, 1995.
12. Foreman, K.E., Till, G.O., Johnson, K.J. and Ward, P.A.: Complement activation, endothelial cell P-selectin and the role of C5b-C9. FASEB J. 9;A34, 1995.
13. Gipson, T.S., Shanley, T.P., Jones, M.L., Ward, P.A. and Johnson, K.J.: Molecular cloning and *in vivo* transcriptional expression of rat TIMP-2 in lung inflammation. FASEB J. 9;A748, 1995.
14. Kubo, H., Quinlan, W.M., Doyle, N.A., Kutkoski, G., Jones, M.L., Ward, P.A., Dinauer, M.C. and Doerschuk, C.M.: Cobra venom factor-induced injury in mice with chronic granulomatous disease. Amer. J. Resp. & Crit. Care Med. 151:454, 1995.
15. Schimmer, R.C., Schrier, D.J., Flory, C.M., Conroy, M.C., Metz, A., Beck, B., Friedl, H.P., Jones, M.L. and Ward, P.A.: The role of the VLA-4/VCAM-1 adhesion pathway in SCW-induced monarthritis in rats. FASEB J. 9;A270, 1995.
16. Shanley, T.P., Schmal, H., Friedl, H.P., Jones, M.L. and Ward, P.A.: Regulatory effects of intrinsic IL-10 in IgG immune complex-induced lung injury. FASEB J. 9;A960, 1995.
17. Warner, R.L., Paine, III, R., Christensen, P.J., Marletta M.A., Richards, M.K., Wilcoxen, S.E. and Ward, P.A.: *In vivo* sources and regulation of iNOS in rat lung. FASEB J. 9;A853, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Director, Division of Clinical Pathology/Clinical Laboratories, May 1993-present.
B. Director, Clinical Immunopathology Laboratory; September 1989-present.

II. TEACHING ACTIVITIES:

A. "Current Topics in Immunopathology" series: pathology residents, M4 students; (25 contact hours).
B. Clinical Pathology Grand Rounds:
   1. "The Inflammatory Response" (1/6/95).
C. Immunopathology journal club: EMU medical technology students, medical technologists, pathology residents (one hour; biweekly, September-June).
D. Immunopathology signout: pathology residents, M-4 medical students, EMU medical technology students (3x/week; 26 weeks/year).
E. M-4 Laboratory Medicine Elective; 4th year medical students, four week block; (eight contact hours).
F. M-1 Histopathology sequence; 1st year medical students; (12 contact hours).
G. Supervision of Research activities for:
   1. Kenneth Kilgore, Ph.D. (postdoctoral fellow); (1/1/94-present) (supported by American Heart Association of Michigan Fellowship).
   2. Joseph Shen (interflex student); (5/10/93-7/30/93) (sponsored by American Heart Association of Michigan summer fellowship); (5/10/94-8/15/94) (sponsored in Student Biomedical Research Program).
   3. Brigitt Casselman (Undergraduate, University of Michigan); (5/1/94 - 4/30/95).
   4. Anu Malani (Undergraduate, University of Michigan); (9/1/94-5/30/95).
   5. Kirk Wahtera (Undergraduate, University of Michigan); (10/1/94-4/30/95).
   6. Joseph Stratton (Undergraduate, University of Michigan); (12/15/94-4/30/95).
   7. Douglas Allen (Undergraduate, University of Michigan); (9/1/94-present).
   8. Valary Evans (Undergraduate, University of Michigan); (9/1/94-present), (sponsored in Howard Hughes Medical Institute Student Fellowship Program).
   9. Jennifer Beyer (Undergraduate, Texas Technical University); (5/1/95-present).
   10. Vipul Maheswara (Undergraduate, University of Michigan); (6/15/95-present).
H. Preliminary Examination Committees:
   1. Michael Gralinski, Department of Pharmacology, University of Michigan Medical School (9/15/94).
   2. James Park, Department of Pharmacology, University of Michigan Medical School (6/2/95).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Monocyte Chemoattractant Protein 1 in Pulmonary Granulomatosis", NIH (RO1-HL48287), (40% effort), $470,623; direct costs, 4/1/92-

3/31/95. (Competing Continuation resubmitted 3/1/95 for 12/1/95-11/30/99, $693,465; direct cost).

B. Co-Investigator, "Monocyte Chemoattractant Protein 1 in Corpus Luteum", NIH (RO1-HD33478), (10% effort), $651,215; direct costs. Landis Keyes, Ph.D., Department of Physiology, University of Michigan, Principal Investigator (Submitted 7/1/95).

PROJECTS UNDER STUDY:

A. Pathogenesis of endotoxic shock in mice with homozygous C5 deficiency.
B. Role of neutrophil-derived mediators in MCP-1-mediated pulmonary granulomatous vasculitis.
C. Modulation of proinflammatory endothelial cell functions by the membrane attack complex (MAC).
D. Monocyte activation by ANCA.
E. Role of MCP-1 in luteolysis (collaboration with Landis Keyes, Ph.D., Department of Physiology, University of Michigan Medical School).
F. Role of MCP-1 in PAN-induced interstitial nephritis (collaboration with Allison Eddy, M.D., Department of Pediatrics, University of Toronto, Canada).
G. Pathogenesis of extrinsic allergic enephalomyelitis (collaboration with Joan Berman, Ph.D., Department of Neurology, Albert Einstein, NY).
H. Ischemia-reperfusion injury in perinatal rat brain (collaboration with Faye Silverstein, M.D., Departments of Pediatrics and Neurology, University of Michigan Medical School).
I. Role of MCP-1 in cutaneous delayed type hypersensitivity (collaboration with Douglas Ringler, V.M.D., LeukoSite, Inc., Cambridge, MA).
J. MCP-1 in arterialized vein grafts (collaboration with John Hoch, M.D., Department of Surgery, University of Wisconsin, Madison, WI).
K. P-selectin antagonists in glucan-induced granulomatous vasculitis (collaboration with Mark Anderson, Ph.D., GlycoMed Corp., Alameda, CA).
L. MCP-1 antagonists in granulomatous vasculitis (collaboration with Kurt Jarnagin, Ph.D, Roche Bioscience, Palo Alto, CA).
M. Role of MCP-1 in peripheral nerve regeneration (collaboration with Marina Mata, M.D., Department of Neurology, University of Pittsburgh, PA).

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

A. Northeast Ann Arbor (East Medical Campus) Facility Planning Committee, 1994-1995.
B. Chairman, East Medical Campus Laboratory Program Planning Committee, 1994-1995.
C. Clinical Contracting Strategic Advisory Group, University of Michigan Medical Center, 1994-present.
D. Dean's Advisory Committee (ad hoc substitute for Dr. Ward), 1994-present.
E. Incentive Task Group, advisory to Medical Service Plan Executive Committee, 1995-present.

DEPARTMENTAL:

A. Interviewer of Pathology Residency Candidates, 1989-present.
B. Interviewer of Pathology Graduate Program Candidates, 1990-present.
C. Selection Committee for Pathology Residents, 1991-present.
D. Coordinator for Revised Resident Training in Clinical Pathology, 1992-present.
E. Preclinical Advisory Program, 1992-present.
F. Chairman, Laboratories Communications Committee, 1993-present.

G. Chairman's Advisory Committee, 1993-present.
H. Eastern Michigan University Medical Technology Advisory Committee, 1993-present.
I. Chairman, Department of Pathology Quality Assurance Committee, 1993-present.
J. Chairman, Utilization Management Committee, Department of Pathology, 1995-present.

REGIONAL AND NATIONAL:

A. Ad hoc referee for:
1. American Journal of Pathology.
2. Laboratory Investigation.
3. Human Pathology.
4. Journal of Applied Physiology.
5. Lung.
6. Blood.
7. Journal of Laboratory and Clinical Medicine.
8. Pediatric Research.
9. Journal of Leukocyte Biology.
10. American Review of Respiratory Disease.
11. Chest.
12. Journal of Pharmacology and Experimental Therapeutics.
13. Circulation.
14. Ophthalmology.
15. American Journal of Respiratory Cell and Molecular Biology.
16. Clinical Immunology and Immunopathology.
17. Circulation Research.
18. Journal of Immunology.
19. Surgery.
20. Reviews of Infectious Diseases.
21. Infection and Immunity.
22. Experimental Lung Research.
23. Journal of Rheumatology.
24. Clinical Infectious Diseases.
25. Journal of Clinical Investigation.
26. Cytometry.
27. Biological Signals.
28. Metabolism.

B. Preparation of Immunopathology Subspecialty Board Exam Questions, 1990-present.
C. Preparation of Clinical Pathology Board Exam Questions, 1991-present.
D. Ad hoc reviewer: Special Emphasis Panel; Request for Applications "Mechanisms of Post Bone Marrow Transplantation Injury"; National Institutes of Health (NHLBI); Bethesda, MD; April 5-6, 1995.

V. INVITED LECTURES/SEMINARS:

1. "Update in Immunopathology", Intercellular Adhesion Molecules in Inflammation." ASCP Workshops, Seattle, Washington, October 14, 1994.
2. "Antinuclear Antibody Testing and Autoimmune diseases", ASCP Workshops, Seattle, Washington, October 15, 1994.
3. "Immunopathology of Inflammation", Indiana University, Indianapolis, Indiana, December 5, 1994.
4. "Clinical Immunopathology Laboratory Assays", Rheumatology Division, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, December 17, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Grande, J.P., Jones, M.L., Swenson, C.L., Killen, P.D. and Warren, J.S.: Lipopolysaccharide induces monocyte chemoattractant protein-1 production by rat mesangial cells. J. Lab. Clin. Med. 124:112-117,1994.
2. Markey, B.M. and Warren, J.S.: Use of antineutrophil cytoplasmic antibody to distinguish between vasculitic disease activity and complications of immunosuppressive therapy. Am. J. Clin. Pathol. 102:589-594,1994.
3. Zhang, K., Gharaee-Kermani, M., Jones, M.L., Warren, J.S. and Phan, S.H.: Lung monocyte chemoattractant protein-1 gene expression in bleomycin-induced pulmonary fibrosis. J. Immunol. 153:4733-4741,1994.
4. Flory, C.M., Miller, B.F. and Warren J.S.: Regulatory roles of tumor necrosis factor-α and interleukin 1β in monocyte chemoattractant protein-1-mediated pulmonary granuloma formation in the rat. Am. J. Pathol. 146:450-462,1995.
5. Su, L., Keren, D.F. and Warren, J.S.: Failure of anti-lambda immunofixation reagent mimics alpha heavy chain disease. Clin. Chem. 41:121-123,1995.
6. Brieland, J.K., Flory, C.M., Jones, M.L., Miller, G.R., Remick, D.G., Warren. J.S. and Fantone. J.C.: Regulation of monocyte chemoattractant protein 1 gene expression and secretion in rat pulmonary alveolar macrophages by lipopolysaccharide, tumor necrosis factor-α, and interleukin-1β. Am. J. Respir. Cell Molec. Biol. 12:104-109,1995.
7. Vaporciyan, A.A., Mulligan, M.S., Warren, J.S., Barton, P.A., Miyasaka, M. and Ward, P.A.: Upregulation of lung vascular ICAM-1 in rats is complement-dependent. J Immunol, In Press.
8. Kilgore, K.S., Shen J.P., Miller B.F., Ward P.A. and Warren J.S.: Enhancement by the complement membrane attack complex of tumor necrosis factor-α induced endothelial cell expression of E-selectin and ICAM-1. J. Immunol., In Press.
9. Casselman, B., Kilgore, K.S., Miller, B.F. and Warren, J.S.: Antibodies to neutrophil cytoplasmic antigens induce monocyte chemoattracta protein-1 (MCP-1) secretion from human monocytes. J. Clin. and Lab. Med., In Press.
10. Barton, P.A., Imlay, M.M., Flory, C.M. and Warren, J.S.: Role of intercellular adhesion molecular-1 (ICAM-1) in glucan-induced pulmonary granulomatosis in the rat. J. Lab. Clin., In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Eddy, A. and Warren, J.S.: Expression and function of monocyte chemoattractant protein-1 in experimental nephrotic syndrome. Submitted to Am. J. Pathol.
2. Pearson, J.P. and Warren, J.S.: Mechanisms of neutrophil-dependent anti-neutrophil cytoplasmic antibody-mediated endothelial cell injury. An *in vitro* analysis. Submitted to Lab Invest.
3. Kilgore, K.S., Miller, B.F. and Warren, J.S.: Neutrophil adhesion to human endothelial cells is induced by the membrane attack complex: the roles of P-selectin and platelet activating factor. Submitted to Am. J. Pathol.
4. Townson, D.H., Naftalin, D.M., Flory, C.M., Warren, J.S. and Keyes, P.L.: Expression of monocyte chemoattractant protein-1 (MCP-1) in the corpus luteum of the rat. Submitted to Biol. Reproduction.
5. Szaflarski, J., Liu, X-H, Warren, J.S. and Silverstein, F.S.: Treatment with antibody to monocyte chemoattractant protein-1 attenuates excitotoxic brain injury in perinatal rats. Submitted to J. Neuroscience (abstract).
6. Kilgore, K.S., Miller, B.F. and Warren, J.S.: The membrane attack complex of complement selectively induces the secretion of monocyte chemoattractant protein-1 and interleukin-8 but not GROα and RANTES from human umbilical vein endothelial cells. Submitted to J Immunol.

7. Kilgore, K.S., Imlay, M.M., Szaflarski, J.P., Silverstein, F.S., Malani, A.N. and Warren, J.S.: Neutrophil and reactive oxygen intermediates mediate glucan-induced granuloma formation through the local induction of MCP-1. Submitted to J. Clin. Invest.

BOOKS/CHAPTERS IN BOOKS:

1. Warren, J.S.: Immunodeficiency disease, in, McClatchey, K.D. (ed), Clinical Laboratory Medicine, Williams and Wilkins, Baltimore, Maryland, pp. 1579-1598, 1994.
2. Warren, J.S., and Ward, P.A.: Immunoglobulin and complement mediated immune injury, in, Crystal, R.G. and West, J.B. (eds), The Lung: Scientific Foundations, Second Edition, Raven Press, New York, New York, In Press.
3. Warren, J.S. and Ward, P.A.: Consequences of oxidant injury, in, Crystal, R.G. and West J.B. (eds), The Lung: Scientific Foundations, Second Edition, Raven Press, New York, New York, In Press.

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

1. Kilgore, K.S., Imlay, M.M., Miller, B.F. and Warren, J.S.: P-selectin-dependent neutrophil adhesion to human endothelial cells is induced by the membrane attack complex (MAC). Cardiovascular Research Forum, American Heart Association of Michigan, Ann Arbor, Michigan, September 20, 1994 (abstract).
2. Shen, J., Alrawi, A.M., Flory, C.M. and Warren, J.S.: Locally produced monocyte chemoattractant protein-1 (MCP-1) mediates monocyte-endothelial adhesive and killing interactions. Cardiovascular Research Forum, American Heart Association of Michigan, East Lansing, Michigan, September 20, 1994 (abstract).
3. Alrawi, A.M., Shen, J., Flory, C.M. and Warren, J.S.: Monocyte chemoattractant protein-1 induced platelet activating factor (PAF) synthesis and secretion by monocytes. Cardiovascular Research Forum, American Heart Association of Michigan, East Lansing, Michigan, September 20, 1994 (abstract).
4. Kilgore, K.S., Imlay, M.M., Miller, B.F. and Warren, J.S.: P-selectin-dependent neutrophil adhesion to human endothelial cells is induced by the membrane attack complex (MAC). Colloguium on the Role of Adhesion Molecules in Cardiovascular Pharmacology (sponsored by the American Society for Pharmacology and Experimental Therapeutics), Ann Arbor, Michigan, June 27, 1994.
5. Shen, J.P., Kilgore, K.S., Miller, B.F. and Warren, J.S.: Tumor necrosis factor (TNF) and the membrane attack complex (MAC) synergistically promote neutrophil adhesion to endothelial cells. University of Michigan Student Biomedical Research Forum 1994 (abstract).
6. Townson, D.H., Naftalin, D.M., Warren, J.S. and Keyes, P.L.: Immunolocalization of monocyte chemoattractant protein-1 (MCP-1) in corpora lutea of the rat ovary. University of Michigan Reproductive Sciences Program Forum, Ann Arbor, Michigan, October 14, 1994 (abstract).
7. Casselman, B., Miller, B.F., Kilgore, K.S. and Warren, J.S.. Anti-neutrophil cytoplasmic antibodies (ANCA) induce MCP-1 release from human monocytes. Experimental Biology, Atlanta, Georgia, April 9-13, 1995 (abstract).
8. Kilgore, K.S., Miller, B.F., Imlay, M.M. and Warren, J.S.: P-selectin and PAF-dependent neutrophil adhesion to endothelial cells is induced by the membrane attack complex (MAC). Experimental Biology, Atlanta, Georgia, April 9-13, 1995 (abstract).

9. Imlay, M.M., Kilgore, K.S., Malani, A. and Warren, J.S.: Role of neutrophils in the development of monocyte/macrophage - rich angiocentric granulomas. Experimental Biology, Atlanta, Georgia, April 9-13, 1995 (abstract).
10. Ivacko, J., Szaflarski, J., Warren, J.S. and Silverstein, F.S.: Hypoxic-ischemic (HI) injury induces monocyte chemoattractant protein-1 (MCP) mRNA expression in perinatal rat brain. Society for Pediatric Research (abstract).
11. Townson, D.H., Naftalin, D.M., Flory, C.M., Warren, J.S. and Keyes, P.L.: Localization of monocyte chemoattractant protein-1 (MCP-1) in corpora lutea of the rat ovary. Society for the Study of Reproduction (abstract).
12. Schemmel, M.T., Haefner, H.K., Warren, J.S. and Hurd, W.W.: Comparison of the harmonic scalpel to CO_2 laser and electrocautery in terms of tissue injury and adhesion formation in a rabbit model. American Society for Reproductive Medicine (abstract).
13. Szaflarski, J., Liu, X.H., Warren, J.S. and Silverstein, F.S.: Systemic administration of anti-monocyte chemoattractant protein-1 (MCP) antibody attenuates excitotoxic brain injury in perinatal rodents. Neuroscience (abstract).
14. Ringler, D.J., Rand, M., Newman, W. and Warren, J.S.: Inhibition of T cell recruitment in vivo with neutralizing antibodies to MCP-1. Inflammation (abstract).
15. Tang, W.W., Qi, M. and Warren, J.S.: The role of monocyte chemoattractant protein-1 (MCP-1) in ANTI-GBM AB GN. Effect of IL-1ra on MCP-1 expression. Submitted to ASN (abstract).
16. Su, L., Keren, D.F. and Warren, J.S.: Immunoselection vs. immunofixation for light chain typing. Clin Chem 41: 947-948, 1995 (Letter to editor).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Chief, Pathology and Laboratory Medicine Service, Department of Veterans Affairs Medical Center, Ann Arbor, Michigan, and Outpatient Clinic, Toledo, Ohio.
B. Surgical Pathology, Department of Veterans Affairs Medical Center.
C. Autopsy Pathology, Department of Veterans Affairs Medical Center.
D. Cytopathology - occasional coverage, Department of Veterans Affairs Medical Center.

II. TEACHING ACTIVITIES:

A. Director of program for house officers at Department of Veterans Affairs Medical Center in surgical pathology, autopsy pathology, and electives.
B. Clinicopathologic conference - monthly, Department of Veterans Affairs Medical Center.
C. Department of Veterans Affairs Medical Center Tumor Board - weekly.
D. Dental Student lectures (three) in bone pathology.
E. Medical student - second year pathology laboratory.
F. Medical student - fourth year rotation at the Department of Veterans Affairs Medical Center.
H. Gross pathology seminar for house officers at University of Michigan.
I. Bone pathology seminars, University of Michigan.
J. Medical student - Musculoskeletal Sequence Coordinator, University of Michigan.

III. RESEARCH ACTIVITIES:

COOPERATIVE STUDIES:

A. Ongoing: With Environmental Epidemiology Service, Department of Veterans Affairs, Agent Orange and non-Hodgkin's lymphoma and Hodgkin's disease.

SPONSORED SUPPORT:

None.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/VETERANS AFFAIRS MEDICAL CENTER:

A. Overall responsibility for Department of Veterans Affairs Medical Center Pathology and Laboratory Medicine and for the laboratory at Department of Veterans Affairs 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, Department of Veterans Affairs Medical Center.
E. Dean's Committee, Department of Veterans Affairs representative.

F. Quality Assurance Board, Department of Veterans Affairs Medical Center.
G. Professional Standards Board, Department of Veterans Affairs Medical Center.
H. Radiation Safety Committee, Department of Veterans Affairs Medical Center.
I. Pharmacy and Therapeutic Committee, Department of Veterans Affairs Medical Center.
J. Resident Selection Committee, University of Michigan Department of Pathology.

REGIONAL AND NATIONAL:

A. Red Cross Medical Advisory Board, Southeastern Michigan Region.

V. OTHER RELEVANT ACTIVITIES:

A. Inspector for College of American Pathologists Inspection and Accreditation Program.
B. Deputy Medical Examiner, Washtenaw County.
C. Fellow, College of American Pathologists.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Organizer and discussion leader of seminar on Ethics in Science -Cellular and Molecular Biology Training Program.
B. Supervision of three postdoctoral fellows and one graduate student.
C. Member, Program Committee - Cellular and Molecular Biology Training Program.
D. Program Committee, Graduate Program in Pathology.
E. Chairman, Examination Committee, Graduate Program in Pathology.
F. Member, dissertation committees for two graduate students.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Prevention and Repair of DNA Damage in Bacteria", National Science Foundation, DMB-8922562.
B. Principal Investigator, "Endonuclease V of *Escherichia coli*", National Institutes of Health, NIEHS, RO1 ES06047.

PROJECTS UNDER STUDY:

A. Alternate pathways of thymidylate metabolism.
B. A superoxide response regulation of *Escherichia coli.*
C. A DNA repair endonuclease of *Escherichia coli.*

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Co-director, Graduate Training Program in Pathology.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A.. Referee for the following journals:
1. Molecular and General Genetics.
2. Biochemistry.
3. Journal of Biological Chemistry
4. Molecular Microbiology.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wu, J., Dunham, W.R. and Weiss, B.: Overproduction and physical characterization of SoxR, a [2Fe-2S] protein that governs an oxidative response regulon in *Escherichia coli*. J. Biol. Chem. 270:10323-10327,1995.

SHARON W. WEISS, M.D.
PROFESSOR OF PATHOLOGY
DIRECTOR OF ANATOMIC PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Service - 3.5 months.
B. Consultant for Bone and Soft Tissue - 12 months.
C. Secondary Consultant for Breast Pathology - 12 months.
D. M-Labs Surgical Pathology Service - as needed.

II. TEACHING ACTIVITIES

A. Sophomore Medical Class:
   1. Pathology 600 - lecture - two contact hours.
   2. Pathology 600 - laboratory section - 26 hours
B. House Officers:
   1. Training in Surgical Pathology.
   2. Lectures - five hours.
   3. Surgical Pathology Consultation Conference - six hours.
C. Hospital Conferences:
   1. Sarcoma Conference - monthly.
   2. Correlative Radiologic/Pathologic Bone Conference - bimonthly.
D. Graduate Student:
   1. Responsible for training of Dr. Melanie Griem, February-March, 1995; Dr. Gerson Paull, June, 1995.
E. Medical Student Advisor:
   1. Responsible for mentoring of Anneli Bowen (M4) and Stephen Mauger (M4).

III. RESEARCH ACTIVITIES

PROJECTS UNDER STUDY:

A. Epithelioid smooth muscle tumors of soft tissue.
B. Borderline vascular tumors.
C. Typical and atypical giant cell tumors.
D. Needle biopsy in the diagnosis of soft tissue tumors.
E. Fibromatosis and well-differentiated fibrosarcoma.
F. Angiosarcoma in children.

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL:

A. Director, Division of Anatomic Pathology.
B. Chief, Surgical Pathology.
C. Member, Divisional Directors' Committee.
D. Member, Photography Committee.
E. Member, Program Committee, Residency Training Program.
F. Co-Director, Surgical Pathology Fellowship Program.

UNIVERSITY:

A. Member, Neurofibromatosis Center.
B. Member, University of Michigan Cancer Center
C. Member, Tissue and Invasive Procedures Committee.
D. Member, Musculoskeletal Core, Year II Curriculum.
E. Member, Operating Room Committee.
F. Member, Curriculum Policy Committee.
G. Member, Curriculum Policy Advisory Committee.
H. Member, Academic Appointments, Promotions, and Tenure Committee.

REGIONAL AND NATIONAL:

A. Chairman, WHO Committee for Classification of Soft Tissue Tumors.
B. US-Canadian Academy of Pathology:
    1. Director, US-CAP Diagnostic Pathology Course.
    2. Vice-President Elect.
C. Anatomic Pathology Test Writing Committee, American Board of Pathology.
D. Association of Directors of Anatomic Pathology.
E. Consultant in Pathology, National Institutes of Health.
F. Member, Michigan Society of Pathologists.
G. Member, Arthur Purdy Stout Society of Surgical Pathologists.
H. Ad hoc reviewer, Laboratory Investigation.
I. Ad hoc reviewer, American Journal of Pathology.
J. Editorial consultant, Human Pathology.

V. OTHER RELEVANT ACTIVITIES

EDITORIAL BOARDS:

A. Editorial Board, American Journal of Surgical Pathology.
B. Editorial Board, American Journal of Clinical Pathology.
C. Editorial Board, Seminars in Diagnostic Pathology.

D. Editorial Board, International Surgical Pathology.
E. Editorial Board, AFIP Fascicles (3rd Series).
F. Editorial Board, Modern Pathology.

INVITED LECTURES:

1. Speaker, "Lipomatous Tumors of the Skin," German Society of Dermatology, Munich, Germany, July, 1994.
2. Speaker, "Fibrohistiocytic Tumors of the Skin," German Society of Dermatology, Munich, Germany, July, 1994.
3. Speaker, "Borderline Vascular Tumors," German Society of Dermatology, Munich, Germany, July, 1994.
4. Speaker, "Fibroblastic Tumors of Childhood," German Society of Dermatology, Munich, Germany, July, 1994.
5. Faculty, "Diagnostic Pathology 1994," United States and Canadian Academy of Pathology, Colorado Springs, Colorado, August, 1994.
6. Faculty, "Soft Tissue Tumors," Penrose Cancer Conference, Colorado Springs, Colorado, September, 1994.
7. Speaker, "Soft Tissue Tumors: Clinical and Pathological Correlations," Royal Canadian Society of Medicine, Toronto, Ontario, Canada, September, 1994.
8. Speaker, "Borderline Vascular Tumors," Long Course, International Academy of Pathology, Hong Kong, October, 1994.
9. Speaker, Soft Tissue Slide Seminar, International Academy of Pathology, Hong Kong, October, 1994.
10. Visiting Professor, Kyushu University, Fukuoka, Japan.
11. Faculty, "Vascular Tumors," Soft Tissue Tumors Course, Memorial Sloan-Kettering Cancer Center, New York, New York, November, 1994.
12. Faculty, "Malignant Fibrous Histiocytoma," Soft Tissue Tumor Course, Memorial Sloan-Kettering Cancer Center, New York, New York, November, 1994.
13. Speaker, "Malignant Fibrous Histiocytoma: A Historical Perspective," Washington Society of Pathologists, Washington, D.C., November, 1994.
14. Speaker, Robert S. Totten Memorial Lecture, University of Pittsburgh, Pittsburgh, Pennsylvania, November, 1994.
15. Visiting Professor, Slide Seminar, University of Pittsburgh, Pittsburgh, Pennsylvania, November, 1994.
16. Speaker, Ohio Society of Pathologists, Columbus, Ohio, January, 1995.
17. Visiting Professor, "Fibrohistiocytic Tumors," Emory University School of Medicine, February, 1995.
18. Speaker, Soft Tissue Slide Seminar, Emory University School of Medicine, February, 1995.
19. Long Course Director, 1995 USCAP Long Course on Soft Tissue Tumors, Toronto, Ontario, Canada, March, 1995.
20. Panelist, Bone and Soft Tissue Specialty Conference, USCAP Annual Meeting, Toronto, Ontario, Canada, March, 1995.
21. Speaker, Soft Tissue Slide Seminar, Indiana Association of Pathologists, May, 1995.

22. Speaker, Soft Tissue Slide Seminar, Ontario Association of Pathologists, Montebello, Ontario, Canada, June, 1995.
23. Speaker, "An Approach to the Diagnosis of Soft Tissue Tumors," South Bay Pathology Society, Monterey, California, June, 1995.
24. Speaker, Soft Tissue Slide Seminar, South Bay Pathology Society, Monterey, California, June, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Fisher, C.R., Chappel, M.E. and Weiss, S.W.: Neuroblastoma-like epithelioid schwannoma. Histopathol.
2. Fisher, C.R., Hedges, M. and Weiss, S.W.: Ossifying fibromyxoid tumor of soft parts with stromal cyst formation and ribosome-lamella complexes. Ultrastruct. Pathol. 18:593,1994.
3. Robertson, J., Lawrence, T., Weiss, S.W., Sondak, V.K. and Chang, A.E.: IUDR and radiotherapy for retroperitoneal sarcomas. Int. J. Rad. Oncol. Biol. Phys. 31:87,1995.
4. Goldblum, J.R., Frank, T.S., Poy, E. and Weiss, S.W.: p53 mutations and histologic progression in well-differentiated liposarcoma and dermatofibrosarcoma protuberans. Int. J. Surg. Pathol. 3:35,1995.
5. Gross, A.S., Louis, D.S., Carr, K.A. and Weiss, S.W.: Carpal tunnel syndrome: A clinicopathologic study. J. Occup. Med. 37:437,1995.
6. Flint, A., Weiss, S.W.: CD-34 and cytokeratin distinguishes solitary fibrous tumor from desmoplastic malignant mesothelioma. Hum. Pathol. 26:428,1995.
7. Smith, M.E.F., Fisher, C. and Weiss, S.W.: Pleomorphic hyalinizing angiectatic tumor of soft parts: A low grade neoplasm resembling neurilemoma. Am. J. Surg. Pathol, In Press.
8. Weiss, S.W., Willis, J., Jansen, J.F., Goldblum, J.R. and Greenfield, L.J.: Frozen section consultation: Utilization patterns and knowledge base of surgical faculty at a university hospital. Am. J. Clin. Pathol., In Press.
9. Harada, M., Shimada, M., Fukayama, M., Kaneko, T., Kitazume, K. and Weiss, S.W.: Crystal-storing histiocytosis associated with lymphoplasmacytic lymphoma mimicking Weber-Christian disease: Immunohistochemical, ultrastructural and gene-rearrangement studies. Hum. Pathol., In Press.
10. Chung, K.C., Berger, Weiss, S.W., J., and Kuzon, W.M.: Multifocal congenital hemangiopericytoma associated with Kasabach-Merritt syndrome. Br. J. Plast. Surg. 48:240,1995.

SUBMITTED FOR PUBLICATION:

1. Pearson, J.P., Weiss, S.W. and Headington, J.T.: Malignant cutaneous melanocytic neoplasm arising in rare and unique benign neuromelanocytic (neurocristic) hamartoma. Submitted to Am J Surg Pathol.

BOOKS AND CHAPTERS IN BOOKS:

1. Enzinger, F.M., Weiss, S.W., Soft Tissue Tumors, 3rd Edition, C.V. Mosby, St. Louis, Missouri, 1995.
2. Montgomery, L.A., Kraybill, W.G., Weiss, S.W., Soft tissue tumors, in, Pathology for the Surgeon, W.B. Saunders, New York, In Press.
3. Miettinen, M., Weiss, S.W., Soft tissue tumors, in, Anderson's Pathology, 10th ed., C.V. Mosby, St. Louis, In Press.

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

1. Su, L., Sheldon, S. and Weiss, S.W.: Inflammatory myofibroblastic tumor: Cytogenetic evidence supporting clonal origin. Mod. Pathol., 1995.
2. Henricks, W., Goldblum, J.R. and Weiss, S.W.: Dedifferentiated liposarcoma: A clinicopathologic analysis of 155 cases. Mod. Pathol., 1995.

KIRK J. WOJNO, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 AUGUST 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Services-four months.
B. Surgical Pathology On-call-six weeks.
C. Immunoperoxidase Service-six months.
D. Consultant for Genitourinary Pathology.
E. Back-up Consultant for Endocrine Pathology.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Sophomore Medical Class:
   1. Reproductive sequence - one lecture hour.
B. House Officers:
   1. Pathology Consult Conference - Occasional.
   2. Pathology Resident Series - Occasional.
C. Interdepartmental:
   1. GU Grand Rounds - Weekly.
   2. GU Pathology - Monthly.
   3. Peds Urologic Pathology/Radiology - Occasional.
   4. GU Oncology Conference - Weekly.
   5. GU Journal Club - Weekly.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-investigator, Analysis of 8P loss in Human Prostate Cancer, Principal Investigator, Jill Macoska, Ph.D. (5% effort).
B. Co-Investigator, Loss of Heterozygosity Involving Chromosome 13q14.3 in Sporadic Prostate Cancer. Small Grant Program, University of Michigan. $7500.

PROJECTS UNDER STUDY:

A. Evaluation of surrogate and point biomarkers as prognostic indicators in prostate cancer . (Bcl2, Her2nu, P53, Angiogenesis. PP32, Ki67, PC-2, Pth-LP, Tib-166, Gp78, etc.)
B. Fractal analysis in prostate cancer.
C. Precursor lesions in prostate cancer, PIN, AAH.
D. Role of chromosome 13 and 17 loss in prostate cancer prognosis with Kathleen Cooney, M.D.
E. Role of Chromosome 8 and 10 loss in prostate cancer progression with Jill Macoska, Ph.D.
F. Role of BRCA-1 in prostate cancer progression with Kathleen Cooney, M.D.
G. Hereditary prostate cancer with K. Cooney.
H. Significance of free PSA measurements with Drs. England, Giacherio, and Oesterling.
I. Significance and utility of reverse transcriptase PSA PCR with Drs. Killen, Oesterling and Montie.
J. Significance of PSA glycotypes with Dr. Robbins.
K. Effects of "TUNA" on prostate tissue. Sponsored by Vita Med with Drs. Oesterling and Issa.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Co-Director, Immunoperoxidase Laboratory.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Prostate Needle Biopsy, Borderline Lesions. 4th M-Labs Symposium, Ann Arbor, Michigan, January 21, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wojno K.J., Vogalsang G.B., Beschorner W.E.and Santos G.W.: Pulmonary hemorrhage as a cause of death in allogeneic bone marrow recipients with severe acute graft-vs-host disease. Transplantation 57: 88-92,1994.
2. Wojno K.J., Olson J.L. and Sherman M.E.: Cytopathology of pleural effusions following radiotherapy. Acta Cytologica 38: 1-8,1994.

3. Wojno K.J. and McCarthy E.F.: Fibro-osseous lesions of the face and skull with aneurysmal bone cyst formation. Skeletal Radiology 23:15-18,1994.
4. Sola J.E., Wojno K.J., Dooley W.C. and Colombani P.M.: P-glycoprotein status of favorable histology Wilms' tumor predicts treatment outcome. J. Pediatric Surg. 29:1080-1084,1994.
5. Wholey M.H. and Wojno K.J.: Case Report: Pediatric hepatic mesenchymal hamartoma. Pediatric Radiol. 24:143-4,1994.
6. Thuluvath P., Wojno K.J., Yardley J.H. and Mezey E.: Effects of helicobacter pylori infection and gastritis on gastric alcohol dehydrogenase activity. Alcoholism: Clinical and Experimental Research, 18:795,1994.
7. Batsacky S.I., Wojno K.J., Carmichael M.J., Walsh P.C. and Epstein J.I.: Pathologic features of hereditary prostate cancer. J. Urology 153:987-992,1995.
8. Wojno K.J. and Epstein J.I.: The utility of basal cell specific cytokeratin antibody (34bE12) in the diagnosis of prostate cancer: A review of 228 cases. Amer. J. Surg. Path. 19:251-260,1995.
9. Rozansky, T., Wojno, K.J. and Bloom, D.: Remnant orchiectomy: Analysis of fifty cases. J. Urol., In Press.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Macoska, J.A., Trybus, T.M., Benson, P.D., Saki, W.A., Grignon, D.J., Wojno, K.D. and Powell, I.J.: Evidence for three tumor suppressor gene loci on chromosome 8p in human prostate cancer. Cancer Research, Submitted April, 1995.
2. Chang, A.K., Michels, V., Poland, G.A., King, B.F., Wojno, K.J. and Oesterling, J.E.: Neurofibromatosis with involvement of the prostate gland. Urology, submitted May 1995.
3. Cohan, R.H., Wilson, T., Wojno, K.J. and Korobkin, M.: Cystic renal masses: Accuracy of the Bosnial classification system revisited Submitted for publication Amer J Radiol., July 1995.
4. Cooney, K.A., Wetzel, J., Merjaver, S.D., Macoska and Wojno, K.J. Loss of heterozygosity involving chromosome 13q14.3 in sporadic prostate cancer. Submitted for publication, Cancer Research, July 1995.

BOOK CHAPTERS

1. Wojno, K.J.: Testicular tumors in current urogenital cancer surgery, in, Williams and Wilkins, Baltimore, Maryland 2nd Edition, Submitted July 1995.
2. Wojno, K.J.: New pathologic techniques for diagnosing GU malignancies in cancer treatment and research, Kluwer Academic Publishers, in preparation July 1995.

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

1. Batsacky S.I., Wojno K.J., CarMichael M.J., Walsh P.C. and Epstein J.I.: Pathologic features of hereditary, familial and sporadic forms of prostate adenocarcinoma. (Presented at the 1994 USCAP and AUA meetings.) Modern Pathol., 7:69A,1994; J. Urol, 151:277A,1994.

2. Wojno, K.J. and Epstein, J.I.: The utility of basal cell specific keratin antibody (34ßE12) in the diagnosis of prostate cancer: A review of 228 cases over 4.25 years. (Presented at the 1994 Fall American Society of Clinical Pathology meeting.) Amer. J. Clin. Pathol. 102:537.
3. Renedo, D.E, Poy, E.L., Oesterling, J.E. and Wojno, K.J.: Clinical significance and distinction of adenosis from low grade adenocarcinoma of the prostate on TURP (Presented at the USCAP meeting in Toronto, Ont, May 1995.) (Accepted for publication Modern Pathol.)
4. Gaudin, P., Wojno, K.J., Oesterling, J.E. and Epstein, J.I.: The significance of high-grade PIN on TURP without adenocarcinoma. (To be presented at the USCAP meeting in Toronto, Ont, May 1995.) (Accepted for publication Modern Pathol.)
5. Cohan, R.H., Wilson, T., Wojno, K.J. and Korobkin, M.: Cystic renal masses: Accuracy of the Bosnial classification system revisited (To be presented at the 43rd UAR meeting, San Diego, CA, April 1995.) (Submitted for publication Amer J Radiol.)
6. Rozansky, T., Wojno, K.J. and Bloom, D.: Remnant orchiectomy analysis of fifty cases. (To be presented at the AUA 1995 Annual Meeting, Las Vegas, NV, April 1995.) (Submitted for publication Amer J. Urol.)
7. Cooney, K.A., Wetzel, J., Merjaver, S.D., Macoska and Wojno, K.J.: Loss of heterozygosity involving chromosome 13q14.3 in sporadic prostate cancer. (Submitted for publication, (Presented at American Cancer Society, April 1995.)
8. Strohbehn, K., Quint, L.E., Prince, M.R., Wojno, K.J.. Ashton-Miller, J.A. and DeLancey, J.O.L.: MRI anatomy of the urethra: Comparative histology. (To be presented at the American Urogynecologic Society Annual Meeting, Seattle, Washington,October 12-15, 1995.)
9. Reviewer, Solid Organ Transplantation Pathology, Vol. 30, Major Problems in Pathology, W.B. Saunders Co., Philadelphia, PA, Amer J Surg Pathol, 1995

SECTION REPORTS

DIVISION OF ANATOMIC PATHOLOGY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

The past year witnessed many changes in our faculty. Most significantly, Dr. Bernard Naylor, Director of Cytopathology, retired after 40 years of service to the Department. Recruited to this Department during the tenure of Dr. A. James French, Dr. Naylor was the consummate diagnostic pathologist and teacher. Although his special areas of expertise were cytopathology and pulmonary pathology, his microscopic skills were so extraordinary that he often served as "the pathologist's pathologist" on any difficult or problematic case in the Department. His lectures and papers served as models of the quality to which we all aspire. Our Division thanks him for his years of inimitable service and the enrichment he brought to our professional lives. We are pleased that Dr. Suzanne Selvaggi has accepted the position as the new Director of Cytopathology and will be assisted in the Cytopathology Laboratory by Dr. Claire Michael (University of South Alabama). Our surgical pathology service reached its full complement of staff with the additions of Dr. Kenneth Devaney (Brown University), Kirk Wojno (Johns Hopkins Hospital), and Tom Giordano (Memorial Sloan-Kettering).

We remain committed to our educational and academic mission within the Division. Our faculty participates actively in both M-2 and M-4 teaching and was greatly honored when Dr. Andrew Flint won the Kaiser Permanente Award for preclinical teaching. Seven residents presented papers/posters at the annual USCAP meeting in conjunction with our faculty and one was singled out for the Stowell Orbison Award (Eric Hsi). Dr. Wally Henricks and Eric Hsi were also designated as winners of the first Murray Abell Award for resident research done in conjunction with anatomic pathology faculty. The Division hosted three visiting professors during this year. Dr. Ross Zumwalt (University of New Mexico) discussed the Hanta virus outbreak, while Dr. Victor Reuter (Memorial Sloan-Kettering) presented a lecture on bladder neoplasia and a slide seminar on testicular pathology. Dr. Karel Geboes, internationally known liver pathologist, joined us in the spring for both formal lectures and microscopic tutorials. Several trainees and pathologists joined us for periods of training: Dr. Gerson Paull (Emory University), Melanie Griem (University of Chicago), and Rose-Marie Caduff (Switzerland).

Our fellowship experiences continue to draw on both excellent internal and external candidates. Drs. Eric Hsi, Jeffrey Pearson, David Renedo, and Kathryn Lane distinguished themselves as surgical pathology fellows, while Dr. Akmal Mikhail performed in an outstanding fashion as the cytopathology fellow. As we enter into a new health care milieu and seek new ways to reduce expenditures, we are exploring new ways to format our fellowship experience.

Our faculty has renewed its efforts to improve our laboratory efficiency. Under the capable direction of Dr. Thomas Frank and assisted by Drs. Timothy Singleton and Kirk Wojno, the immunohistochemistry laboratory has completed its automation and has instituted a daily quality control process. It now provides the faculty with 24-48 hour turn-around-times. Aided by a computer support group with substantial contribution of time by Dr. Paul Killen, automatic re-queuing has finally been

realized for all anatomic pathology report verifications. Over the next year we will place a great deal on test utilization by ourselves and our clinical colleagues. We look upon this as a process which requires no only monitoring but, more importantly, education and consensus building as we devise practice guidelines.

Lastly, our Division and, indeed, entire Department was saddened by the death of Dr. Hendrix who succumbed in June to leukemia. "Sheriff Bob", as he was known to his friends and colleagues, had spent over 40 years in the Department and for many years directed the Autopsy Service. He was for many years the mainstay of our forensic expertise in the Department and provided invaluable assistance to Drs. Remick and Caplan in formalizing this program. The residents will remember him for his advice on court conduct and how brevity in speech is often an asset in this milieu. We all cherish the years he spent amidst us.

Sharon W. Weiss, M.D.
Division Director

AUTOPSY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. TIMELY COMPLETION OF AUTOPSY REPORTS:

Autopsies are still not completed in a timely fashion, and this has resulted in a citation during the most recent CAP inspection. The evaluation of turn-around time for calendar year 1994 showed that the average time to completion of a case was 161 days, with 77% of cases requiring more than 90 days to completion and 39% requiring more than 180 days. Several steps have been implemented in order to decrease the turnaround time, and these will be closely followed. This represents the most frequent complaint about the autopsy service, and one that is being addressed in a most vigorous manner.

II. MORGUE RENOVATIONS:

We have examined several options for the renovation of the morgue, and the hospital has approved replacement of the entire cooler system. This will increase the storage capacity from 8 bodies to 15 bodies, and will help to relieve the congestion frequently observed in the morgue. The additional renovations for the morgue, including the establishment of a grieving room, has not yet been approved.

III STATISTICS:

	1991/92	1992/93	1993/94	1994/95
Total U of M cases	322	420	488	499
M-Labs cases	8	5	3	
Brain only on U of M patient				
brain harvested at outside hospital				18
Medical Examiner's Cases	58	101	159	211
In hospital	24	47	63	66
Outside cases	34	54	74	145
External examination only			24	38
Autopsy rate (includes tetralogy)	35%	39%	47%	35%

Over half of the medical examiner cases from the hospital also include permission from the family for the performance of the autopsy.

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

CYTOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

This past year has brought several new developments to the division of Cytopathology. With the announcement of Dr. Naylor's retirement, an active search was conducted for a cytopathologist. Dr. Claire W. Michael an Assistant Professor from the University of South Alabama accepted the position and, in conjunction with Dr. Suzanne M. Selvaggi, will run the Cytopathology Laboratory. We extend a warm welcome to her.

An on-site review of the cytopathology fellowship program was conducted by the Accreditation Council for Graduate Medical Education. Our program was approved for three years and for two fellows, an increase over our usual one fellow per year. In the ninth year of our cytopathology fellowship, Dr. Akmal Mikhail completed his training with distinction and is eligible to take the examination for the Special Qualification in Cytopathology. Dr. Robert Stern is the new fellow.

Our recent laboratory inspection by the College of American Pathologists was a success. The CAP checklist for inspection of cytopathology laboratories was extensively modified to comply with the Federal regulations. Our laboratory staff under the direction of Ms. Belinda Davis did an excellent job in compiling the data needed for our review.

The division has continued to refine its computer program for the reporting of cervicovaginal cytology and will begin to develop a software package for non-gynecologic cytology in conjunction with Pathology Data Systems. Ms. Belinda Davis is working with representatives from Cerner to develop a working quality assurance/quality control software program for cervicovaginal cytology.

The cytotechnologists have been actively involved in the regional cytology society. Ms. Belinda Davis is the current President of the Michigan Society of Cytology and serves as a screener for the College of American Pathologists Cytopathology Committee. Drs. Naylor and Selvaggi continue to participate in a joint lecture series for the Wayne State University and Henry Ford Hospital programs of Cytotechnology and have presented several workshops and papers at various national meetings and cytology societies.

Gynecologic specimens numbered 31,913 and non-gynecologic specimens 5,603 of which 30% were fine needle aspirates. The increasing number of aspirates represents the main area of growth in cytopathology. It is anticipated that the demand for aspirates will continue to increase in the new health care era and with the opening of the Cancer Center.

Suzanne M. Selvaggi, M.D.
Director, Cytopathology Laboratory

DERMATOPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

The Dermatopathology Service receives diagnostic case material from six different sources: (1) UMMC (ID) cases; (2) outside contractual (MD) cases; (3) personal consultations (HE and NI) cases; (4) outside slides reviewed for referred patients (TD) cases; (5) miscellaneous intramural referrals (IE, IF, IS, ME, SC, TS) cases; (6) and informal consultations (intramural, VAH and MU)..

Work load volume is as follows:

	1991-1992	1992-1993	1993-1994	1994-1995
HE	731	981	694	569
ID	5651	4255	4791	4759
MD	--	1347	1663	2240
TD	--	550	709	553
Misc.	--	--	71	218
Informal	300	225	254	106

Total Cases were 8,445. HE and NI cases declined slightly. ID cases remained the same. MD cases increased by about 25%. TD cases declined slightly but were representative of a much higher volume of difficult pigmented lesions. Miscellaneous lesions increased due to inclusion of routine diagnosis of eyelid lesions.

As noted for the previous year the workload in the Dermatopathology service continues to be significantly impacted by the growth of Cutaneous Oncology services. The number of patients being seen in the Melanoma Clinic increased this year to almost 400 and bi-weekly conferences including 15 to 20 patients or more are not exceptional. The Otolaryngology and Plastic Surgery services have also been contributing complex cases for microscopic study.

Dermatopathology teaching in the Department of Dermatology remains unchanged.

Correlative activities include participation in the Pigmented Lesion Clinics (bi-weekly), Cutaneous Lymphoma Conference (monthly), and Dermatology Grand Rounds (weekly).

Formal presentations were made to both the medical and dental students.

John T. Headington, M.D.,
Director, Dermatopathology Service

ELECTRON MICROSCOPY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

The electron microscopy service continues to provide important diagnostic services to the University of Michigan. The facility provides high quality diagnostic work for the nephropathologists, neuropathologists, hematopathologists, and the general pathologists.

This past year there has been a continuing major effort to decrease the turnaround time required to complete specimens. Using the successfull changes implemented last year, the turnaround time has consistently been within departmental guidelines (7 days for completion of prints for kidney, 14 days for all other cases).

The aging Zeiss microscope is in the process of being replaced. Funds have been requested from the hospital in order to purchase a new scope. The new electron microscope will have a digitizing camera interfaced with the scope, and a laser printer. This will further decrease turnaround time since most cases will be capable of analysis using the laser prints, rather than using the labor intensive process of printing the film images. The EM staff have already evaluated several electron microscopes, and have found the quality to be very satisfactory.

This following table is the analysis of the work volume in the EM laboratory for the 1994/1995 year. During the previous year, there were 472 biopsies processed, including 218 renal biopsies. Thus, we have had an increase of 59 total biopsies, and 38 renal biopsies.

	All Cases	Outside	Inside
Total cases	531	227	304
Brain	26	4	22
Buffy Coat	3	4	7
Kidney	133	123	256
Muscle	64	109	173
Nerve	18	28	46
Other	5	18	23

Daniel G. Remick, M.D.
Director, Electron Microscopy Service

NEUROPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

The Laboratory of Neuropathology continues to have three interrelated functions: Laboratory diagnostic service, teaching and research. Dr. Samuel P. Hicks was on Active Emeritus status, and made significant contributions to the Autopsy Neuropathology Service. Dr. Mila Blaivas, Ms. Constance J. D'Amato, Dr. Paul E. McKeever, and Dr. Anders A.F. Sima also contributed to the Neuropathology Service.

CLINICAL ACTIVITIES:

The following examinations were completed with the support of our neurohistology, electron microscopy, general histology, immunohistology, and secretarial staff.

1. There were 744 neurosurgical cases including CNS, pituitary, muscle and nerve examined this year. 79 of these cases were from outside hospitals in consultation. A portion of these were part of an interdepartmental study of PET/BUDR and neuropathology funded by NIH. Approximately 300 surgical specimens required special neurohistologic procedures.
2. There were 395 brains histologically processed out of 499 autopsies. (Of the 395 brain cases, which is 79% of all autopsies, 61 ADRC and Michigan Dementia Network Program cases were processed in the Neuropathology Core Laboratory of the MADRC, plus an additional 12 received from other institutions.) An additional 16 brains were histologically processed from other institutions and hospitals. In addition to these a few cases were examined as outside consults on slides prepared elsewhere.
3. There were 242 muscle biopsies, nearly all with histochemistry, 173 with electron microscopy. There were 45 (27 internal, 18 external) peripheral nerve biopsies. There were 26 teased fiber preparations, 22 thick plastic sections and 48 had electron microscopy performed. The combination of nerve teasing, muscle histochemistry, electron microscopy and morphometry make the service regionally competitive for diagnostic consultation.
4. Faculty interpreted 257 cases in semithin or thin section from electron microscopy. The majority of these cases were nerve, pediatric muscle, and neurosurgical biopsy cases.
5. The ceroid service, buffy coat division, reported 1 case.
6. The Brain Tumor Board of the University of Michigan Cancer Center and Hospitals, supported weekly by a neuropathologist, reviewed neuropathology and clinical aspects of more than 130 difficult neuro-oncology cases.
7. One brain was examined for research purposes.
8. There are two neuropathology quality assurance meetings each month. Attendees include neuropathologists from nearby institutions.

TEACHING ACTIVITIES:

1. Medical Students: This year the neuropathology faculty taught in the eight week neuroscience sequence of our new 2nd year curriculum. There were ten hours of neuropathology taught: six hours of lecture and four hours in the laboratory.
2. House Officers, Graduate Students, Postgraduate and other students and faculty: These include periodic conferences with Neurology; twice monthly Continuing Medical Education (CME) accredited conferences where all biopsies are presented and interpreted; a weekly conference where abnormal brains are examined with all clinicians invited; monthly nerve and muscle biopsy conferences accredited for CME; individual instruction on autopsies and biopsy material;

Neuropathology 858, an 18 hour laboratory-lecture course; bimonthly conferences with Neuroradiology, conferences for neuromuscular disease and bi-weekly Neuropathology seminars for Neurosurgery and Neuroradiology House staff. Weekly seminars are provided to neurological and neurosurgical house staff on clinico-pathological correlations.

3. Two Neuromuscular fellows were instructed at conferences held weekly.
4. Electives: Two Pathology Residents, one Neurosurgery and one Neurology Resident chose elective rotations on the Neuropathology Service.

RESEARCH ACTIVITIES:

1. Dr. Hicks and Ms. D'Amato provided neuropathologic support for MADRC. Ms. D'Amato is Core Coordinator of the Diagnostic Neuropathology Unit of the Neuropathology Core of the MADRC. Ms. D'Amato is also Co-Investigator with Dr. Anders Sima on the MADRC Project: The Pathology of Diffuse Lewy Body Disease.
2. Dr. Blaivas and associates investigate: 1) ocular muscle (aging and botulinum effect), 2) musculature related to cleft palates in children 3) histology of animal model of rheumatoid arthritis, 4) histochemistry and morphometry of muscle in patients with hypertension and diabetes.
3. Dr. Sima's laboratory is investigating pathogenetic mechanisms involved in experimental and human diabetic neuropathies. In particular, the laboratory is focusing on the molecular, structural, and functional abnormalities of the nodal apparatus of myelinated fibers in diabetic nerve. The laboratory is also investigating trophic and immunological factors governing nerve fiber regeneration in diabetes. The Morphometric Imaging Core, directed by Dr. Sima, serves as an international reading laboratory for nerve biopsies obtained from several ongoing multicenter clinical trails of drugs designed to ameliorate and halt the progression of diabetic neuropathy.
4. Dr. McKeever and associates are determining the extent and cause of differences in gene product expression in brain tumor tissue versus cells in culture. These differences may result from a separate population of cells within brain tumors or from genetic instability in neoplastic cells. They are assessing the prognostic value of DNA content, specific chromosomal markers by *in situ* hibridization, and Ki-67, PCNA and BUdR labeling indices in brain tumor specimens *in vivo* and *in vitro*. He is studying receptor-ligand interactions and neuropathology of epilepsy with colleagues in Neurology.
5. Groups of the University of Michigan Cancer Center faculty and staff with clinical research interests in brain tumors, met and generated a number of project considerations from Pathology, Neurosurgery, Nuclear Medicine, Neuropathology, Neurology and Neuroradiology collaborations.
6. Collaboration with Neurology, Michigan State University, The State of Michigan Department of Public Health, the Alzheimer's Association, Henry Ford Hospital, and Beaumont Hospital has established a registry for Alzheimer's disease and other dementias and degenerative diseases.

Paul E. McKeever, M.D., Ph.D.
Chief
Neuropathology Section

IMMUNOHISTOLOGY AND MOLECULAR ANALYSIS LABORATORIES

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
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The Immunohistology Laboratory offered over 75 different immunohistochemical stains for paraffin and frozen tissues and performed approximately 900 tests each month, or over 10,000 during the year. The laboratory has undergone several major changes in order to provide technically consistent service in a timely fashion. The requisition form and ordering procedures were completely revised to eliminate the need for separate requests for unstained slides and immunologic stains and to streamline billing. The number of unstained slides prepared by the hospital-based histology laboratory was standardized, eliminating substantial redundant effort. Most importantly, a policy was instituted that guaranteed a two-day turnaround time for all requests submitted by an early afternoon cut-off, reducing turnaround time and improving diagnostic test reporting.An increasingly diverse array of diagnostic tests was made available through increased utilization of programmable automated immunostainers, two of which are now located in the Immunohistology Laboratory. Several technical modifications were also instituted this year to improve service and efficiency. Analysis of estrogen and progesterone status in breast carcinomas was switched from a cumbersome technique performed weekly to a semi-automated method performed on a daily basis. Tissue freezing methods were revised to reduce artifact, and tissue pre-treatments were modified and standardized to improve efficiency and reduce error. Computerization finally arrived to the lab as well, as all records pertaining to antibody clones, titers, and methodologies were transferred to an active database. Weekly laboratory meetings were instituted to faciliate the many changes instituted this year and will continue to be held, and when of general interest the minutes of these meetings will be distributed by electronic mail.

In the future the Immunohistology Laboratory will seek to improve cost-effectiveness by reducing redundancy in its menu and further modifying the requisition to encourage efficient test ordering. The need for increased diagnostic frugality will be balanced with department's academic mission through the establishment of a separate automated facility for the performance of projects, supported jointly by the Department of Pathology and the University of Michigan Comprehensive Cancer Center and co-directed by Drs. Frank and Singleton. In addition, we will seek to integrate nucleic acid analyses into the existing diagnostic laboratory. Such tests have been offered in a separate Molecular Analysis Laboratory, chiefly for investigation. This year the Molecular Analysis Laboratory supported several housestaff projects that were presented at national meetings and published in peer-reviewed journals. In addition, this laboratory performed almost fifty technically demanding, specialized nucleic acid analyses for diagnostic purposes on paraffin-embedded tissues including identification of DNA and RNA viruses (EBV, hepatitis B and hepatitis C, parvovirus, CMV), species determination of

mycobacteria, and resolution of suspected specimen mislabeling by genetic "fingerprinting" of paraffin embedded tissues. In the future we will seek to integrate these molecular diagnostic methods with existing immunohistologic testing.

Tom S. Frank, M.D.
Director
Immunohistology And Molecular Analysis Laboratories

Timothy P. Singleton, M.D. and Kirk J. Wojno, M.D.
Assistant Directors
Immunohistology Laboratory

SURGICAL PATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
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The surgical pathology service remains an active University service despite the fact that growth has stabilized in recent years. Intramural accessions numbered 27,878 and intramural (personal) consultations 5,402 for a total volume of 33,280 representing a 1% increase over last year. Approximately 4,000 intraoperative (frozen section) consultations are provided yearly with an accuracy of over 98%. Several hundred STAT biopsies, largely on transplant patients, are requested requiring rapid turn-around-time and immediate interpretation by our faculty. Our service continues to administer the Tissue Procurement Core for the Cancer Center which annually distributes over 1,400 specimens to investigators throughout the Medical Center. This activity will soon occupy dedicated space within the Cancer Center with its impending opening in the next year.

Our service reached full staffing with the successful recruitment of Drs. Kenneth Devaney (Brown University), Tom Giordano (Memorial Sloan-Kettering), and Kirk Wojno (Johns Hopkins University) to provide expertise in orthopedic/otolaryngic, endocrine, and genitourinary pathology respectively. Four surgical pathology fellows completed their training: Drs. Eric Hsi, Jeffrey Pearson, Kathryn Lane (Duke Medical Center), and David Renedo (University of Vermont). This program continues to draw not only on our own residents but on an excellent pool of external candidates. We believe the strength of this program resides in the autonomy granted our fellows on the frozen section service, the exceptional instruction obtained on the various consultation services, and the opportunity to engage in a variety of research projects with the faculty. We were especially gratified that one of our surgical pathology fellows (Dr. Eric Hsi) won the Stowell Orbison Award for outstanding resident research for his clonality work on Helicobacter gastritis done in conjunction with Drs. Joel Greenson and Charlie Ross. Surgical pathology is an important part of the M-4 clerk rotation and the pathology elective for under-represented minority students. Our educational activities also include a daily Staff Consensus Conference which features discussions of problematic or interesting cases. A multiheaded scope linked to a video monitor offers the opportunity for all residents as well as visiting scientists to participate in this activity.

We continue to strive for ways to improve our efficiency in the surgical pathology laboratory. Important changes which have occurred in the past year relate to an expansion of template reporting for surgical pathology reports and automatic re-queuing of reports so that a pathologist can verify all his/her reports from a single screen rather than searching through several screens. We continue to explore the possibility of consolidating our histopathology function and automate slide check-out and tracking. A major initiative of the coming year will be a study of utilization patterns by our clinical colleagues and

faculty. Through the formation of a number of working committees we will analyze the utilization and turn-around-times of frozen sections, multiple biopsies, immunohistochemical stains, and specimen blocking in an effort to devise more efficient means of processing cases.

Sharon W. Weiss, M.D.
Director, Surgical Pathology Service

DIVISION OF CLINICAL PATHOLOGY

DEPARTMENT OF PATHOLOGY
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1 JULY 1994 - 30 JUNE 1995

Despite a continuing, institution-wide mandate to maintain a stable budget, the Clinical Laboratories continued to provide excellent, full-spectrum service. The virtually flat cost per unit of activity provided by the Clinical Labs, in the face of rising overall health care costs, is a testimony to the professionalism of the staff and the management capabilities of the laboratory directors and senior laboratory personnel. In 1994-95 the Clinical Labs performed 3.2 million billable analyses. The Clinical Laboratories successfully completed the biannual on-site College of American Pathologists (CAP) inspection and, with the oversight of Clinical Laboratory personnel, the UMMC - acquired physician office practices and satellite facilities received COLA certification. The Divisional Quality Assurance Program, as a component of the Departmental Quality Assurance Program, continues to be at the forefront both within the University of Michigan Medical Center and among Clinical Laboratories located in tertiary care facilities throughout the United States. Maintenance of the delicate balance among quality service, cost effective testing, utilization control, and the research and development which characterizes an academic institution, will be a continuing challenge.

1994-95 was marked by three major initiatives. First, an organizational and funding framework was developed, in conjunction with the Division of Molecular Medicine (Internal Medicine), to provide for expanded activities in the area of molecular diagnostics. The clinical component of this bipartite laboratory, the Clinical Molecular Diagnostics Laboratory, is directed by Anthony A. Killeen, M.D., Ph.D., who joined the Department of Pathology faculty as Director of the Clinical Chemistry Section (Chemistry, Ligand Assay, Drug Analysis and Toxicology, Immunopathology, and Clinical Molecular Diagnostics) in September, 1993. Second, the Clinical Laboratories successfully garnered the resources necessary to meet the marked increase in bone marrow transplantation activity experienced in 1994-95. Integral to the programmatic demand was implementation of DNA-based high resolution class II antigen typing as a clinical assay. Augmentation of the capabilities of the Blood Bank, Tissue Typing, and Cytogenetics Laboratories was contributory to the approval of UMMC as a participant in the National Allogeneic Bone Marrow Transplantation Program. Finally, the Clinical Laboratories have responded to the institutional initiative to acquire broader primary care capabilities within the region. Specifically, nine medical practices and two UMMC satellite facilities that maintain on-site laboratory testing were added to the overall UMMC laboratory network. This activity was coupled with a robust expansion of on-site point-of-care testing and data handling activities. In preparation for the future, the Clinical Laboratories continue to support the growing M-Labs outreach program, forge strong collaborative relationships with local reference laboratories, and intensify our role in institutional utilization management.

Faculty and laboratory staff participated in a wide variety of intramural and extramural educational programs during 1994-95. For instance, the 26th annual Blood Bank/Transfusion Medicine course and the Laboratory Information Systems course were each attended by more than 200 registrants

making them among the most visible courses of their kind in the United States. These courses, along with the M-Labs educational programs, are prominent examples of outreach activities. Evaluations from senior medical students enrolled in the third M4 Laboratory Medicine course were highly laudatory. The revised clinical pathology residency training format (July, 1993) which organizes pathology residents into teams that rotate through three blocks of clinical laboratories that are grouped according to relatedness of discipline, continues to meet with critical success. The continued high quality of trainees in the Hematopathology Fellowship program has enhanced the service, educational, and academic missions of the Hematopathology group and the Department. Certification of a Clinical Chemistry Fellowship was received from the ACGME. This fellowship will further enhance the service, academic, and educational missions of the Department.

The academic achievements of faculty members within the Clinical Pathology Division have been outstanding. As a group. the CP faculty had over 100 articles published in peer-reviewed journals. Most faculty members played highly visible leadership roles in national organizations, courses, symposia, as well as on editorial boards, examining committees, and research review study sections; an illustration of their high levels of recognition throughout the United States (see individual reports). Numerous faculty members received extramural funding that supported a variety of scholarly activities (see individual reports).

The Clinical Pathology Division is faced with numerous challenges in the future. In addition to its ongoing academic enterprises, educational issues, faculty diversity initiatives, leadership and development in quality assurance, and laboratory resource utilization in the context of the hospital cost efficiency program, the Division plans to greatly expand its clinical molecular diagnostics program, and, in cooperation with the M-Labs program, to optimize its position in the regional clinical laboratory market. Achievement of these objectives will require the continued commitment, professionalism, and hard work of the faculty, laboratory staff, administration, and house officers.

Jeffrey S. Warren, M.D.
Director, Clinical Pathology Division

UNIVERSITY HOSPITALS BLOOD BANK AND TRANSFUSION SERVICE

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1994 - 30 JUNE 1995

PATIENT CARE:

Although efforts to contain blood utilization in University Hospital were intensified, the laboratory continued to experience increased activity. This related to modification of our patient population. The institution has mounted new programs which require large volumes of blood. These programs include liver and bone marrow transplantation, thoraco-abdominal aneurysmectomy, and thoracic aortic aneurysm repair. In addition, the institution now has a Level 1 Trauma Center, and the extracorporeal membrane oxygenation service has been extended to include adult patients.

These programs, in large measure, have accounted for a 13 per cent increase in Red Blood Cell transfusions during the past year and a comparable increase in transfusion of other blood components. This increase in utilization has occurred in spite of pretransfusion monitoring of many requests for platelet concentrate transfusions and auditing of selected Red Blood Cell transfusions. In addition, monthly review of blood transfusion associated with open-heart surgery has resulted in a progressive decrease in blood utilization for those procedures. The latter is exemplified by a reduction in donor exposures for patients undergoing CABG operations from an average of 14.4 units in 1990 to an average of 6.7 units in 1995.

The Transfusion and Apheresis area experienced the usual peaks and valleys of activity during the year. A pressing problem has been an inability to respond to requests for increased collection of peripheral blood progenitor cells for bone marrow transplantation. The space available in the laboratory has precluded collection of more than two patients per day. It is hoped that the introduction of the Cancer Center will allow relocation of some of the outpatient transfusion activity, thereby freeing up additional space for progenitor cell collections.

Members of the staff played an integral role in support of specialized clinical activities. Mrs. Hoffman worked closely with the Bone Marrow Transplantation Program and also coordinated orders for HLA-matched Single Donor Platelets from our blood suppliers. Ms. Steiner supported the Department of Obstetrics and Gynecology, attending their weekly high-risk pregnancy conference, and playing a vital role in PUBS procedures. Ms. Butch led the Quality Management program of the clinical laboratories of the Department of Pathology and Mrs. Stoe chaired the Department's Laboratory Safety Committee.

EDUCATIONAL ACTIVITIES:

As in previous years, the medical, technical and nursing staffs of the Blood Bank/Transfusion Service were active in providing educational programs within the institution and at regional and national meetings. The long-standing two-week Blood Bank orientation program for House Officers at University Hospital was presented on two occasions during the year, related to modification in the training program schedule. In addition, the Blood Bank portion of the Laboratory Medicine course for senior medical students was well received. Three hours of lecture were provided for the sophomore medical class in the context of the Department of Pathology course, and a presentation on Transfusion Medicine was provided for the medical student senior elective course in Pharmacology and Therapeutics.

Lectures on Transfusion Medicine were given to clinical departments in University Hospital, including the Section of Thoracic Surgery and the Departments of Anesthesiology and Pediatrics.

The 22nd annual postgraduate course, "Current Topics in Blood Banking", was held on May 31, June 1 and 2, 1995. The course, under the direction of Mr. Judd, attracted 170 technologists and physicians from throughout the United States. It continues to be one of the most popular postgraduate courses in the country devoted to blood bank topics. Members of the Blood Bank and Transfusion Service staff presented Workshops on a variety of topics, and Ms. Steiner, Ms. Butch, Mr. Judd and Dr. Oberman participated in the plenary sessions of the symposium.

Members of the Blood Bank and Transfusion Service faculty and staff participated in the annual meeting of the American Association of Blood Banks, providing poster presentations and lectures covering a variety of topics. In addition, members of the laboratory, including Mr. Judd, Ms. Butch, Mrs. Stoe, Ms. Steiner and Drs. Davenport and Oberman, presented invited lectures to a variety of regional and national blood banking organizations and state societies.

Aside from the lectures and presentations noted in the individual faculty reports of Mr. Judd and Drs. Davenport and Oberman, Mrs. Stoe lectured to the Michigan Association of Blood Banks, including presenting the annual Loring seminar, and Ms. Butch provided numerous invited lectures throughout the country. She also authored chapters in three books and presented a poster at the annual meeting of the American Association of Blood Banks. Mrs. Knafl was active in organization of the MABB spring meeting. Ms. Steiner lectured in Chicago and Toledo, as well as at the annual meeting of the American Association of Blood Banks.

PROFESSIONAL ACTIVITIES:

Members of the Blood Bank and Transfusion Service medical and technical staffs were active at the regional and national levels. Dr. Oberman served as Associate Editor of TRANSFUSION and was a member of the Transfusion Practices Committee of the American Association of Blood Banks. Ms. Butch served on the Standards Committee of the American Association of Blood Banks. Ms. Butch also served on the Information Systems Committee and on the Chief Technologist's Forum of the American Association of Blood Banks. Ms. Steiner served as chairperson of the AABB Committee on Reference Laboratories and Rare Donor File, co-edited the newsletter of the Michigan Association of Blood Banks

and chaired the By-laws and Policy Manual Committee of the MABB. In addition, members of the technical staff participated in the Inspection and Accreditation program of the American Association of Blood Banks. Dr. Oberman's, Dr. Davenport's, and Mr. Judd's activities are further noted in their individual faculty reports.

RESEARCH ACTIVITIES:

The individual reports of Drs. Oberman, Davenport and a Mr. Judd record their publications and investigative efforts related to blood banking and Transfusion Medicine. In addition, Ms. Butch and Mrs. Knafl participated in a study of adult extracorporeal membrane oxygenation with Drs. Oberman and Bartlett.

Harold A. Oberman, M.D.
Director, Blood Bank and Transfusion Service

CHEMICAL PATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
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The Chemical Pathology Laboratory completed another hectic but overall very successful year. Cross training of technologists from Chemistry, Ligand Assay, and Immunology Labs continued through the year, allowing for greater flexibility in scheduling. The Chemistry Laboratory experienced an approximate 5% increase in test volume for the year. The lab performed nearly 3.2 million tests this past fiscal year. The laboratory is projecting that it will likely finish several percent under budget for this same time period.

The laboratory undertook a major beta-site evaluation of the new Ektachem 950 IRC automated chemistry analyzer. Sue Stern, supervisor of automated chemistry, was the principle operator for this four month long extensive evaluation of the accuracy and precision of over 50 serum, urine, and CSF tests of the Ektachem 950 analyzer. In addition, Dr. Giacherio, Sue Stern, and Keith Matz performed a more detailed comparison study of serum digoxin and phenytoin assays on the E-950 analyzer. These evaluations gave the laboratory an excellent overview of the capabilities and potential advantages of this new analyzer.

The laboratory has continued its major commitment to the expansion of point of care testing. In collaboration with PDS, we implemented new interfaces to the blood gas/ electrolyte analyzers in the Emergency Department and the operating rooms of Mott and Main Hospitals. These satellite labs are supervised and maintained by Chemistry lab staff, with most of the actual testing being performed by unit based personnel. The interface makes it possible to capture all pertinent data from these remote sites in the laboratory information system and make it a part of the permanent medical record. The lab would like to acknowledge the contributions of the late Bob Cohn to making this project a success.

As part of a multi-departmental initiative to reduce blood product utilization, Chemistry personnel were responsible for the evaluation, implementation, and ongoing management of a program that will bring rapid delivery of platelet counts, prothrombin time, and APTT to the operating rooms. A small Coulter MD8 hematology analyzer and portable Coagucheck Plus whole blood coagulation analyzers have been placed in the operating rooms. Testing is performed by Anesthesiology Department staff, with Chemistry Lab personnel doing all the training, quality control evaluation, and ongoing competency assessment of all operators.

The lab has continued its active role in the supervision of bedside blood glucose monitoring programs at University Hospitals. The maintains quality control, linearity, and proficiency testing records on 75 whole blood glucose meters stationed throughout the institution. Several new glucose meters are being evaluated by the Point of Care Testing group, and the Chemistry Lab continues to actively pursue options for the computerized collection and analysis of quality control data from these meters.

The Point of Care group in Chemistry has implemented a number of other smaller projects. Pregnancy tests are being performed in Mott OR and in the OB/GYN Clinic, with results collected and entered into Pathnet by Chemistry personnel. Cholesterol testing is being performed on select patients at the MedSport Clinic, and Hemoglobin A_{1c} is being performed in the Diabetes Clinic. In both of these programs, clinic personnel perform the tests, and Chemistry Lab staff are responsible for training, quality assurance, and proficiency testing. Other sites being considered for Point of Care testing include the Cardiac Catheterization Lab and the Medical Procedures Unit.

The Lab's role in managing small laboratories at off-site clinics has also continued to grow. The seven U of M health care clinic labs supervised by Chemistry personnel all passed inspections and received accreditation from COLA. Small laboratories are also managed at an acquired physician office practice in Chelsea and the U of M Livonia Surgical Center.

Finally, the Chemistry Lab and its Point-of Care Testing services passed a CAP inspection with no citations or deficiencies. Martha Thiessen, the Chief Technologist, and all the laboratory staff deserve credit for making sure the lab was in compliance with the changing regulations.

CLINICAL FLOW CYTOMETRY LABORATORY

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The Clinical Flow Cytometry Laboratory processed approximately 3100 immunophenotyping specimens, a volume increase of 15% from the previous year. This included approximately 700 specimens submitted for leukemia/lymphoma immunophenotyping, over 1000 specimens for monitoring of acquired and inherited immunodeficiencies, and over 600 specimens for T-cell subset monitoring in organ transplant recipients. Anti-platelet and anti-neutrophil antibody assays were performed on approximately 300 specimens. In addition, the laboratory processed about 2800 specimens of peripheral blood for flow cytometric reticulocyte analysis.

The laboratory has continued to increase its volume of work through the M-Labs Program. The comprehensive hematopathology consultation service provided by the laboratory has helped to attract this enlarging referral base. For the past year, M-Labs referrals comprised 36% of all acute leukemia immunophenotyping panels, 45% of all chronic leukemia/lymphoma profiles, and 38% of all non-transplant immunodeficiency monitoring.

The laboratory works in close cooperation with clinical services to enhance efficiency and control costs. For example, a collaborative study with the solid organ transplant service was aimed at improving T-cell subset monitoring in patients on the drug OKT3. The study resulted in a streamlined reagent panel (fewer antibodies, at lower cost) and a modified patient report. The impact of these changes on utilization of this expensive drug will be monitored over the coming year. Working in conjunction with the bone marrow transplant service, the laboratory now provides same-day reports of stem cell quantitation from apheresis products.

Last year the laboratory implemented a simplified cell antigen profile for acquired immunodeficiency monitoring using three-color analysis. That change has resulted in a 50% cost savings (reagents plus labor costs) for this high-volume test. Another major area of utilization management continues to be the close monitoring of all requests for leukemia/lymphoma immunophenotyping. The hematopathologists staffing the laboratory must screen all requests for these extensive antigen profiles. Of the 700 specimens submitted for leukemia/lymphoma immunophenotyping, pathologist review led to cancellation of 300 of these requests.

Quality assurance conferences enable medical and technical staff to review leukemia/lymphoma cases reported by the laboratory. These meetings entail a comprehensive review of each case to assure such things as appropriateness of the test request, technical quality of the analysis, clerical quality of the reports, and consensus regarding final diagnoses. Teaching activities in the laboratory include daily case

sign-out with the residents and hematopathology fellow. Continuing medical education for the technologists and house staff is also offered at the biweekly leukemia conference, an interdisciplinary conference held in conjunction with the Division of Hematology, Internal Medicine.

Charles W. Ross, M.D.
Director

Lloyd M. Stoolman, M.D.
Co-director

CLINICAL CYTOGENETICS LABORATORY

DEPARTMENT OF PATHOLOGY
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The Clinical Cytogenetics Laboratory has continued to plateau in volume in some areas, while others have continued to expand. In the area of prenatal diagnosis, just over 900 amniotic fluid specimens, 70 chorionic villus biopsy, and 50 tissues were analyzed; this is approximately the same number as last year. Of interest is the increase in the number of cases that are seen solely for the purpose of growing fibroblasts with the ultimate aim of DNA or biochemical diagnosis; these cases are in addition to the 50 enumerated above. The bone marrow specimens continue to skyrocket, from under 400 two years ago, to 480 in the last year to 573 in the current fiscal year. These requests are scrutinized more carefully due to staffing problems, and the increased volume does not include the approximately 100 requests which were declined for one or more reasons. In addition, 504 peripheral blood specimens were analyzed, a ten percent increase from last year. Approximately 50 of these tests were for high resolution karyotypes. Most of the fragile X testing by cytogenetic analysis has been replaced by routine karyotyping and a specific DNA test (performed in the Molecular Diagnostics Laboratory).

Cytogenetic analysis of solid tumors has remained steady. Pediatric sarcomas and "small round, blue cell tumors" remain the specimens most commonly submitted. Although there are descriptions of various other tumors with specific cytogenetic abnormalities, often the clinical significance is unclear.

The demand for molecular Cytogenetic analysis has increased from one request a month to 2 or more per week. The Laboratory is currently offering a number of specific gene probes for fluorescence in situ hybridization on a research basis including those for Prader-Willi, Angelman's, Williams, and DiGeorge syndromes. Marker chromosomes are characterized. A probe for the so-called minor breakpoint cluster region in the bcr/abl gene rearrangement in CML and ALL are being developed as a potential supplement to cytogenetic analysis. In situ hybridization is performed on at least a weekly basis.

Again, the Laboratory is faced with space constraints, and the consequent staffing constraints. This is particularly worrisome as other Clinical Services are being encouraged to expand by the institution of a Clinical Delivery System. Cytogenetics technologists still require a minimum of one year to train, and several additional years to properly evaluate the more complex specimens which are being received at an increasingly frequent rate.

Susan Sheldon, Ph.D.
Director, Clinical Cytogenetics

CLINICAL HEMATOLOGY LABORATORY

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LABORATORY ACTIVITIES:

A. Implemented automated billing and electronic signature for professional component of pathologist review procedure.
B. Evaluated the Abbott Cell Dyne hematology instrument.
C. Acted as a beta site for testing of Coulter instrumentation.
D. Served as a reference lab to establish normal values for MAS urine controls.
E. Completed the normal value study for complete blood counts and differentials.
F. Several internal quality improvement teams dealt with such laboratory problems as work flow on different shifts, EMU students, implementation of new policies, etc.
G. Daily bone marrow and lymph node signout with House Officers, Hematology Fellows and Fellows from Adult and Pediatric Hematology/Oncology as well as visiting pathologists from other institutions.
H. Daily signout of in-house and UM clients' cases of abnormal smears and body and joint fluids takes place 7 days per week.

TEACHING ACTIVITIES:

A. Pathology House Officers and Hematopathology Fellows, Fellows from Pediatric and Adult Hematology/Oncology and visitors from other institutions (Dr. Hanny Adam, University of Zurich, Switzerland and Dr. Sun-Hee Kim from Korea) participated in the following activities:
   1. Daily review of abnormal blood smears, body fluids, joint fluids for crystals, bone marrow aspirates, smears 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 Dr. Schnitzer .
   4. Correlation of morphology with special studies (cytochemistry, flow cytometry, immunoperoxidase and occasionally electron microscopy).
   5. Daily review of abnormal blood smears from M-Labs clients.
   6. A formal teaching conference for House Officers has been continued.
   7. Weekly review of cases to be presented at Lymphoma Conference (Hematopathologists, Fellows, and house officers).
   8. Review of SWOG cases.
   9. Weekly Interdepartmental Lymphoma Conference.
   10. Biweekly Interdepartmental Leukemia Conference.
   11. Pediatric and Adult Hematology/Oncology Fellows participate in signouts.

B. Hematopathology Fellowship Program.
C. Continuing medical education for medical technologists - monthly.
D. Senior Student Clerkship Elective.
E. Summer Clinical/Research Program for Under-represented Minority Students.

FISCAL YEAR 1995/1996 GOALS:

A. Implement competency testing and competency based evaluations.
B. Implement reticulocyte counts using the Coulter STKS.
C. Continue as a beta site for Coulter Corp.
D. Prepare for the opening of the laboratory in the Cancer/Geriatric Center.
E. Continuation of cost-containment programs.
F. Continued review and development of laboratory utilization.
G. Implement limits on repetitive differential requests.
H. Continue to liberalize automated differential criteria.
I. Continue studies of limiting WBC requests from intensive care units.
J. Continue to enhance the overall efficiency of the laboratory operation..

Bertram Schnitzer, M.D.
Director
Clinical Hematology Laboratory

Timothy P. Singleton, M.D.
Assistant Director
Clinical Hematology Laboratory

CLINICAL IMMUNOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
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OVERVIEW:

The Immunopathology Laboratory experienced a 4% increase in overall test volume in 1994-95. Anthony A. Killeen, M.D., Ph.D., provided an invaluable service commitment to the laboratory in the interpretation of protein electrophoresis studies. Kent Johnson, M.D., and Kevin Cooper, M.D. (Dermatology) continued to signout tissue immunofluorescence studies under the auspices of the Anatomic Pathology Division. Paul Killen, M.D., Ph.D. and Dr. Johnson, also under the auspices of Anatomic Pathology, continued to enhance the Rnal Biopsy Service. Dr. Killen provided invaluable technical oversight of tissue immunofluorescence studies and leadership in the area of case-handling and tracking. Drs. Johnson and Killen also provided cross coverage of anti-neutrophil cytoplasmic antibody (ANCA) and anti-GBM studies.

CLINICAL SERVICES:

As the fiscal year approached its conclusion, the laboratory had experienced a modest increase in overall volume (approximately 4%). Particularly gratifying was the continued growth in several specialized assays; most notably the ANCA test and the anti-GBM indirect immunofluorescence test. Neutrophil cytoplasic antibody determinations increased from approximately 100/month to more than 125/month. More than 100 indirect immunofluorescence assays for anti-glomerular basement membrane antibodies were interpreted in 1994-95. New procedures were also implemented in the protein electophoresis area. We have recently evaluated and initiated a series of new utilization control measures in the laboratory. Most notable in this regard is sendout assays of circulating immune complexes, at a cost of $180/test. By instituting necessary approval by IP laboratory professional staff the number of these requests declined 5-fold, resulting in more than $12,000 saved. Finally, laboratory personnel continued cross-training programs with the Chemistry Laboratory. This was one of the chief goals of the 1992-93 Chemistry Section consolidation.

RESEARCH AND DEVELOPMENT:

The laboratory participated in an ongoing methods comparison study of microalbuminuria assays. This study is being conducted by Dr. Patricia Mueller at the Centers for Disease Control and Prevention in Atlanta. Involvement in this study was an outgrowth of our support of clinical studies of ambulatory diabetic patients that were carried out by Dr. William Herman (formerly of the Department of Medicine, University of Michigan) and Dr. Mindy Smith (Department of Family Practice, University of Michigan). We continued laboratory support of clinical studies of the effects of cytotoxic/immunosuppressive drugs on IgG, IgA and IgM as well as IgG subclass concentrations in lupus patients in conjunction with Dr. Joseph McCune (Department of Medicine, University of

Michigan). Finally, we recently added the capability of determining specific IgG and IgM anti-cardiolipin antibody concentrations. This assay has relevance to the "anti-phospholipid antibody syndrome" which has been associated with thrombosis, thrombocytopenia, and fetal wastage. Several commercially-financed methods evaluations were also carried out. These studies involved anti-streptolysin O and anti-cardiolipin antibody measurements.

QUALITY ASSURANCE:

The laboratory participated in two departmental QA projects. These related to a project that addressed transmission of laboratory testing data from point of order to medical record and the development of a department-wide utilization management database and activity plan.

TEACHING/PROFESSIONAL:

Residents, M4 medical students, and medical technology students from Eastern Michigan University rotated through the laboratory. Immunopathology journal club for medical technologists and on-service house officers was conducted biweekly during the academic year. Clinical Pathology Grand Rounds included immunopathology presentations by Dr. John Carey (Henry Ford Hospital, Detroit), Dr. Daniel Remick (Department of Pathology, University of Michigan), Dr. David Keren (Warde Medical Laboratory, Ann Arbor), and Dr. Jeffrey Warren (see individual faculty report). Dr. Keren was appointed as a Clinical Professor of Pathology and Drs. Warren and Keren continued the weekly series of didactic sessions entitled "Current Topics in Immunopathology". Other professional activities of faculty and staff in the laboratory are summarized under individual reports.

Jeffrey S. Warren, M.D.
Director, Clinical Immunopathology Laboratory

MICROBIOLOGY/VIROLOGY LABORATORY

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CLINICAL ACTIVITIES

The Clinical Microbiology section of the Microbiology/Virology laboratory has demonstrated a 7.99% increase in volume in the past year. The virology section has demonstrated a 12.5% increase in overall volume. Significant increases in volume were noted in: blood cultures, Chlamydia testing, antimicrobial sensitivity testing, and urine cultures. In the virology section of the laboratories CMV IGG antibody, CMV culture/shell vials, EBV antibody, miscellaneous IGG antibodies, rubeola, and rubella IGG antibody all demonstrated a significant increase in volume. The Microbiology/Virology laboratory continues to focus on utilization management in such areas as antimicrobic sensitivity correlations with the use of antimicrobics. In addition, studies of the appropriate use of blood cultures and the use of blood culture systems for specimens other than blood are ongoing.

The laboratory is an active participant in the U of M Hospitals Program for Excellence with a quality improvement team continuing to work on unacceptable sputum specimens. The Microbiology/Virology laboratory continues to improve the quality of correlative clinicopathologic laboratory data to our clinical colleagues in Infectious Disease and Infection Control. The clinicopathologic data is used in clinical laboratory rounds on a daily basis.

RESEARCH ACTIVITIES

The laboratory continues to focus on clinically applied research in such areas as viral serology, the effect of delayed bottle entry on recovery of blood isolates, and in vitro susceptibility studies including, for example; in vitro susceptibility of *Bacteroides fragilis.* The laboratory is an active collaborator in a National Institute of Health grant entitled "Candida Vaginosis Study." The principal investigator of the Candida Vaginosis Study is Dr. Barbara Reed in the Department of Family Practice.

In addition, the laboratory is focusing its applied research activities on PCR for the detection for organisms in various body sites. For example, under study at the present time are PCR methodologies for the detection of Pneumocystis carinii, Herpes simplex and Chlamydia trachomitis.

The laboratory also continues to evaluate data from two hospital small grants: 1) the possible over utilization of blood cultures on clinical services, and 2) monitoring of antimicrobic usage in intensive care settings with intervention where appropriate (an attempt to affect change in ordering patterns). These grants will be converted to ongoing monitors in the laboratory to support the hospital's utilization management initiative.

The result of interdepartmental collaboration has resulted in four papers accepted or submitted for publication as well as abstracts presented by staff at national Infectious Disease and Microbiology meetings.

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

Carl L. Pierson, Ph.D.
Associate Director

DRUG ANALYSIS AND TOXICOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

The Drug Analysis and Toxicology Laboratory continues to maintain its prominent role as an active, progressive, and vital contributor to the success of the Department of Pathology and the University of Michigan.

The laboratory continues to be certified by the College of American Pathologists for the forensic drug testing program. The laboratory successfully passed the 1995 inspection for recertification in this special area. The requirements and demands to achieve this recognition escalate each year. Support of the M-Labs program through involvement in this added certification process places a large burden of responsibility on the staff of the laboratory, and the technologists in the laboratory deserve special recognition for their efforts. The Drug Analysis Laboratory successfully passed the 1995 general clinical laboratory inspection by the College of American Pathologists and performed very well during the review.

The laboratory continued several ongoing quality assurance projects. These projects involve review of corrected reports, turnaround times, and accuracy of data entry. The laboratory maintained involvement in a pharmacokinetic Quality Improvement Team, headed by the Pharmacy Department, which is evaluating the appropriateness of serum drug requests. A document outlining specific outcomes and future strategic goals was submitted in May 1995 to hospital administration for implementation.

The Drug Analysis Laboratory has been actively involved in novel research and development projects. The laboratory supports a large number of institutional clinical projects through collaboration with the Departments of Surgery, Dermatology, Obstetrics and Gynecology, Pediatrics and Pharmacology. Dr. Patel has continued to be active in athletic substance abuse testing for the NCAA and IOC. Dr. Annesley was a co-investigator in a major funded Phase III clinical trial supported by the Sandoz Corporation which is investigating the clinical utility of a new immunosuppressant drug. This trial was terminated in February 1995. The laboratory has also been involved as a reference facility for several external commercial research projects.

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3. Annesley, T.M., Hunter, B.C., Fidler, D., and Giacherio, D.A.: Stability of tacrolimus (FK506) and cyclosporin G in whole blood. Ther. Drug Monitor., In Press, 1995.

4. Shaw, L.M., Annesley, T.M., Kaplan, B., and Brayman, K.L.: Analytical requirements for immunosuppressive drugs in clinical trials. Ther. Drug Monitor., In Press, 1995.
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8. Annesley, T.M.: Quality assurance and quality control in clinical toxicology. Ther. Drug Monitor. Clin Toxicol. News 10:2-3, 1995.
9. Welage, L., Mason, N., Hoffman, E., Odeh, R., Dombrouski, J., Patel, J., and Schwartz, R.: Influence of cellulose triacetate on vancomycin pharmacokinetics. J Am Soc Nephrology, 1995.

Thomas Annesley, Ph.D.
Drug Analysis and Toxicology Laboratory

PATHOLOGY DATA SYSTEMS

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
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The following are some of the major achievements of Pathology Data Systems (PDS) personnel during the past year:

- ❑ Extensive work on the STC interface engine (hub) including developing specifications for a Cerner HL7 interface to the hub; deployment of the HL7 interface anticipated for this Fall.

- ❑ Revision of the autopsy information system to allow on-line house officer editing of autopsy reports and searching of the autopsy database by diagnosis.

- ❑ Sponsorship of the 13th Annual Symposium June 7-9 on Automated Information Management in the Clinical Laboratories with 310 paid registrants and 41 vendors; two hours of programming presented as an audioconference for 53 pathology training programs in the U.S. and Canada.

- ❑ Improvements to the Anatomic Pathology module of PathNet with automatic requeueing to increase faculty efficiency (reassignment of finalized surgical pathology reports from the original workcenter to the queue of the surgical pathologist who signs out the case).

- ❑ MLabs information support with a test-ordering interface to Foote Hospital in Jackson, Michigan, using Eagle software, work in-progress on an HL7 interface to transmit parsed test results from PathNet to the Parke Davis laboratory management information systems (LIMS), work in progress on a hub-mediated host-to host interface from PathNet to the LIS at Mt. Clemens Hospital.

- ❑ Installing and interfacing a Coulter analytic instrument in the operating room for rapid TAT of hemoglobin, hematocrit, and platelet count, with anticipated favorable effects on the utilization of blood and blood products.

- ❑ Wireless access to PathNet by phlebotomists, allowing phlebotomists in Mott to enter point-of-care test results; this functionality will be expanded as soon as barcodes are printed on patient wrist bands to allow bedside identification of patients, positive pre-transfusion identification checks, and "specimen-drawn" notification to PathNet directly from patient care units.

- ❑ PCIS/TDS deployment planning with numerous task forces studying various aspects of system activation such as identification of the blood drawer for physician draws and a strategy for printing PathNet barcodes labels directly in patient care units.
- ❑ Reduction of scheduled and unscheduled system downtime to a four-year low for PDS (total down time now averaging 1-2% per month including scheduled daily and weekly maintenance).

- ❑ Deployment of new Help Desk software in PDS to track and document problems.

- ❑ Modification of the biweekly meeting of PDS personnel with a special focus on the priority list of ongoing PDS projects.

- ❑ Deployment of new PathNet software for non-gynecology cytology specimens including automatic diagnosis coding.

Bruce A. Friedman, M.D.
Laboratory Director

PHLEBOTOMY SERVICES AND CENTRAL DISTRIBUTION

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE1995

The following are major achievements for phlebotomy and central distribution during 1994-1995:

- Expansion of the resident phlebotomist program to all floors in University Hospital and Mott; the resident phlebotomist is assigned permanently to a patient care unit and is responsible for most of the blood drawing on that unit during daylight hours.

- Deploy antibiotic peak blood drawing services Monday through Friday during resident phlebotomy hours; this has been a much sought after service by house officers that also improves the quality of the antibiotic levels.

- Transfer of 28 messenger service FTEs to the phlebotomy service accompanied by the hiring and training all these new personnel; all blood specimens in the hospitals are now picked up by phlebotomy personnel, blood products are delivered by them, and "code" specimens are managed by the phlebotomy team in the Taubman Center, Mott, and University Hospital.

- Phlebotomists now enter point-of-care results into the PathNet database from the Mott ICU's using wireless laptop computers; this has been both a technically challenging project as well as being worthwhile from the perspective of ensuring the completeness of the pathology database.

- Management of the Death Registry land release of deceased patients to funeral directors by central distribution personnel; this is a service for the department that was not being optimally managed off-hours that central distribution was able to take over.

- Remote blood drawing services are now being managed by traveling phlebotomists for the Clozaril project and at the Hawthorne Center.

- Blood drawing services now being offered in the Radiology/Oncology unit once per week as a valuable service to patients who are too sick to comfortably come to the Taubman blood drawing stations.

- Planning for blood drawing services in connection with the PCIS/TDS project, in the Cancer/Geriatric Hospital, and in the East Medical Campus; these are complex planning projects that will have a major impact on the laboratory service load and through-put.

- Limited laboratory bench testing by phlebotomists now being offered at the Turner blood drawing station and also at the Briarwood Family Practice Center.

- Designed and implemented a plan with Dr. Dieter Roloff from the Holden Pediatric Center for reducing the amount of blood drawn from premature infants; this required close cooperation with the various laboratories in terms of the blood volume necessary for adequate testing, but the new policy has been effective in reducing test-related anemia in premature infants.

Bruce A. Friedman, M.D.
Laboratory Director

M-LABS

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
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This last year has been a multifaceted year of growth for M-Labs. We have experienced increases in net revenues from the clinical and anatomical pathology services. We began significant efforts in the area of managed care. We now participate in providing laboratory services for the growing list of newly acquired University of Michigan practices, and have begun efforts to expand our services to the pharmaceutical industry. Finally, we have seen an increase in the size of the M-Labs staff.

This last fiscal year has seen a 22% increase in net revenue from billings to clients for clinical pathology services and a 100% increase in net revenues from billings to patients for clinical pathology services. In anatomic pathology, the number of surgical pathology cases has increased by 22% to approximately 11,500 cases per year. Cytopathology cases have also increased. Although most of the increase in revenues has been through additional services rendered to existing clients, some has been due to the addition of 3 new physician office accounts, a group practice account, a home care account, and new accounts for dermatopathology, renal biopsy service (up to 21% in volume), flow cytometry, and muscle biopsies service. A new small hospital account has just been acquired and is not yet reflected in these numbers. One hospital contract for clinical pathology services was terminated. This was with a hospital which had been previously taken over by a larger hospital. Another hospital contract for both anatomic and clinical pathology services continues despite that hospital's recent affiliation with a larger institution.

We have begun our involvement in the area of managed care by exploring the opportunity to provide outpatient laboratory services to M Care. We propose to provide these services using the University of Michigan clinical laboratories in our own service area and using a network of hospital laboratories in areas outside of our service area. Such a network has the capablility of providing high quality laboratory services to M Care subscribers at a competitive price to M Care, and to help maintain the laboratory volume and reduce per-unit costs for the hospital laboratory network providers. Involvement in this network will also provide a significant marketing tool to M-Labs. We have analyzed M Care's historical outpatient laboratory utilization data and compared that with the Department of Pathology costs to estimate an appropriate capitation rate. We have developed a listing of patient centers for the proposed M-Labs/M Care network of laboratory providers. This network will include the M-Labs client hospitals currently in the proposed area of service as well as other M Care participating hospitals. Our new managed care representative, Deirdre Fidler, has done much work in preparing the ground work for negotiations with M Care. Discussions are currently underway with M Care regarding service and quality issues as well as preliminary financial discussions.

In the last year we have been active participants in the formation of a network of hospital laboratories being organized to bid for state-wide managed care contracts. Susan Valliere, the M-Labs manager, has assumed the chairmanship of the newly formed Marketing and Communication Committee for this network. Deirdre Fidler serves on the operations committee.

During the year Kent Johnson, M.D., has spearheaded an effort to expand our laboratory services for clinical phase drug testing for Parke-Davis Co. of Ann Arbor. This effort has resulted in a decision by Parke-Davis to send us more phase 1 clinical laboratory testing. In the future we expect to expand our efforts in this potentially lucrative market.

Dr. Rudolfo Rasche's effort at expanding our services to clients has resulted in some innovative and successful new programs. Three M-Labs symposia in the last year were well attended by client and

potential client pathologists. The presentations were by our Anatomical Pathology faculty and were well received. A symposium on rules-based control of utilization presented by the Pathology Data Services group was of great interest to our clients. Dr. Rasche's efforts and the support of the Anatomic Pathology faculty have resulted in our developing and providing an innovative quality assurance program for surgical pathology for client pathologists. These efforts in the last year have also resulted in a steadily growing number of surgical pathology and cytopathology "quick" consult cases, sent from pathologists at six hospitals.

The past year has seen the commitment of additional funds by the University Hospital for expansion of the M-Labs program. This has resulted in the promotion of Susan Valliere to manager of M-Labs, and in the addition of Debra Moss (operations), Melissa Brown (sales), and Kenneth Cartwright (information systems) to our staff. Competitive market forces now dictate that we be prepared to offer and deliver interfaces between the University of Michigan Pathnet system and client hospital laboratory information systems. Pathology Data Systems is now working towards the establishment of our first complete interface with Mount Clemens General Hospital, a project that we hope will be completed by November 1, 1995.

Impediments to the success of the M-Labs program persist, however. Clients complaints about the report format of many of our tests remain our biggest problem. Some billing problems persist, although there has been some improvement in this realm.

Mistakes in accessioning specimens have increased recently and, in my view, will require a double order entry system or other means of cross-checking of entries before specimens are tested until systems are in place to allow for order entry by clients at client sites.

Turnaround times for some of our services also do not meet current market expectations. We hope that through increased volume via our outreach efforts, and innovative test sharing with other local laboratories, improvements can be made in turnaround time.

We have recently submitted proposals for complete clinical laboratory testing to three potential client hospitals and we are optimistic that some of these proposals will be accepted. We are currently preparing a proposal for laboratory services to a nearby network of nine hospitals. Exploration is underway with a potential client hospital that previously rejected a proposal from us but is now reconsidering.

In the future, we must continue our efforts to meet the needs of our client hospitals and their physicians in various areas of surgical and clinical pathology. Some tasks will be to revise our requisitions and test panels and to establish reflex testing to help control utilization. We must explore the possibilities of increasing our market share in the potentially very rewarding area of laboratory testing for clinical phase drug trials.

Our new strengths are the addition of some bright new faces to the seasoned veterans of a dedicated, highly motivated M-Labs staff.

Our continuing strengths are the breadth of expertise of our faculty and staff and our positioning ourselves as allies to our client hospitals and their laboratory staffs in an increasingly competitive environment. The key to our success will be making this expertise available to our client hospitals, in assisting them with their outreach efforts, and in helping them, through networks of hospital laboratories, to remain players in the managed care arena.

EM Silverman, M.D.

DEPARTMENT OF VETERANS AFFAIRS MEDICAL CENTER
PATHOLOGY AND LABORATORY MEDICINE SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
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INTRODUCTION:

The Department of Veterans Affairs Medical Center (VAMC) is a Dean's Committee institution affiliated with the University of Michigan. The VAMC Pathology and Laboratory Medicine Service maintains a close relationship with the University Department of Pathology at every level. The pathologists in the Pathology and Laboratory Medicine Service have academic appointments and participate in University departmental activities in a manner similar to other sections. Recruitment efforts for pathologists are combined and candidates are selected on the basis of academic performance and potential as well as professional competence similar to any departmental candidate. There are four full-time pathology staff positions and these are presently filled. Three resident training positions have been maintained at the VAMC for university pathology residents who serve monthly rotations in Surgical Pathology, Autopsy Pathology, and a number of arranged electives including Electron Microscopy and special study programs in Surgical Pathology. The Chief, Pathology and Laboratory Medicine Service is a voting member of the Dean's Committee.

ANATOMIC PATHOLOGY:

A. Surgical Pathology: 4,733 surgical cases have been accessioned and reported during this period of time. This is a decrease of 468 cases over the past year. The resident assigned to surgical pathology, usually a first year resident, acts as coordinator of the section and in that capacity has the opportunity to examine all of the specimens grossly and microscopically under close one-to-one supervision by the staff pathologist. The resident interacts with the clinical staff, the medical students and other laboratory sections as appropriate to obtain a broad educational experience and to aid in providing high quality medical care. There is an extensive quality improvement program within Surgical Pathology including regular consultations with the Armed Forces Institute of Pathology, University of Michigan, and other outside consultants. There is extensive review and analysis of frozen sections, amended diagnoses and surgical appropriateness within the medical center.

B. Autopsy Pathology: 64 autopsies were performed during this year which is a rate of approximately 30% of deaths. Assigned residents perform the autopsies, prepare the pathologic diagnosis, and present the case in conference to the staff pathologists and other residents. The resident cuts and otherwise prepares the tissue for the preparation of slides and then reviews them and makes a microscopic diagnosis. These steps are supervised by staff pathologists who permit a gradual increase in independence for the resident with increased experience. During the year the residents presented the findings of selected autopsies at the Medicine Morbidity and

Mortality Conference with a total of 22 cases presented. Several autopsies performed at the VAMC were also presented at the extended Gross Conference at the University.

C. Cytology: 2,222 cases were examined and diagnosed during this period. Although there is not a formal rotation in cytology within the VAMC the cytologic material is readily available and is used as correlative information for surgical and autopsy pathology. This laboratory is a "Center of Excellence" in cytology and is the program center for the national VA quality improvement survey which was established and is directed by Dr. Beals.

D. Electron Microscopy: 328 electron microscopy cases were reported. An elective rotation is available for pathology residents in electron microscopy. In other rotations the electron microscope findings are used to complement surgical or cytopathology diagnoses. During the academic year Dr. Beals presents biweekly electron microscopy seminars at the University of Michigan. This VAMC is a "Center of Excellence" in electron microscopy and serves as consultant to other VA Medical Centers, to the University of Michigan Medical Center, and to other hospitals by contract.

CLINICAL PATHOLOGY:

During the last fiscal year (Fiscal Year 1994) 1,220,224 clinical pathology procedures were done in the laboratory. In Chemistry there were 708,227; in Hematology 122,707; in Microbiology 90,618, and in Blood Bank approximately 7,000 crossmatches. This represents raw data rather than weighted test numbers. There is not a formal clinical pathology rotation available for pathology residents at this time although the residents may participate or observe clinical pathology procedures when this activity is appropriate in relation to their other rotations. Dr. Chensue is director of clinical pathology and makes available interesting and pertinent clinical laboratory available to residents as desired. Clinical Pathology data is available to residents via computer for their information in surgical pathology, autopsy pathology, and elective rotations.

EDUCATION AND TEACHING:

In surgical pathology the staff pathologists provide one-to-one teaching during the surgical sign out time. In addition, there is a surgical pathology conference approximately every other week and an autopsy conference with the entire staff following each autopsy. Because of the closeness of various sections of the laboratory there is frequent consultation among the pathologists and the residents are involved throughout. Since the VAMC is relatively close to the University, the residents are permitted and expected to attend the appropriate teaching conferences at the University as well. The entire staff participates in the laboratory and lecture portions of the second year medical students at the University of Michigan. Lectures in bone pathology are also given to the dental students. The VA staff also participate in other ad hoc lectures and in a moderate number of seminars for the resident staff, most often given at the University of Michigan.

RESEARCH:

The specific efforts of the pathology staff are included on individual reports. Dr. Stephen Chensue has a strong funded research program that was renewed for four years in October, 1993. He also participates in cooperative studies with other investigators at the University of Michigan. Other staff participate in various clinical studies and collaborate with a variety of investigators. The laboratory in general serves the VAMC research program by providing considerable technical support for clinical research and in some cases for more basic research in both anatomic and clinical pathology. The staff also serves as consultants and advisors for a number of research programs. Dr. Peter Brawn continues his research in carcinoma of the prostate gland and has been a member of the VA Research and Development Committee since 1 July 1993.

ADMINISTRATION:

The staff pathologists at the VAMC serve in various capacities involving administrative tasks for the University of Michigan, such as the Resident Selection Committee, the Medical Student Admissions Committee, and the teaching faculty of the second year medical students. At VA Medical Center the pathology staff members serve on all major committees involved with institutional policies and procedures. Dr. Beals has been designated as the National Veterans Administration Office Representative to oversee anatomic pathology within Department of Veterans Affairs Medical Centers. He has been instrumental in developing policies and procedures related to anatomic pathology within the Department of Veterans Affairs. Late in 1994, Dr. Beals was appointed Acting Director of Pathology for the VA nationally and serves in that position at the time of this report.

SUMMARY:

The Department of Veterans Affairs Medical Center Pathology and Laboratory Medicine Service considers the practice of high quality medicine and the appropriate care of patients as its first and highest responsibility. There is close supervision of resident activities as they are involved with patient care. All staff members are privileged and evaluated in accordance with their training, experience, continuing education and participation in quality improvement activities. Within the service there is an extensive quality improvement program that integrates with that of the hospital as a whole. The Pathology and Laboratory Medicine Service has been accredited by the College of American Pathologists since the early 1960's. The Blood Bank is certified by the American Association of Blood Banks and is approved by the Federal Drug Administration. The association with the University of Michigan serves to strengthen and improve the quality of patient care. The teaching effort involving both residents and medical students is of mutual benefit to the two institutions. The physical plant of the VAMC Pathology and Laboratory Medicine Service is short of space but there has been considerable progress toward the VA Clinical Addition that will double the present space.

Lee Weatherbee, M.D.
Chief, Pathology and Laboratory Medicine Service
Ann Arbor VA Medical Center

WARNER-LAMBERT/PARKE-DAVIS/UNIVERSITY OF MICHIGAN JOINT PROGRAM

DEPARTMENT OF PATHOLOGY
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The Department of Pathology for several years has enjoyed a close professional relationship with the Department of Toxicology/Pathology at the Parke-Davis Pharmaceutical Research Division of Warner-Lambert Company which is located in Ann Arbor. This Department at Parke-Davis is headed by Dr. Felix De la Iglesia who also has a faculty appointment in the Department. Dr. De la Iglesia is a world expert on hepatic injury as well as morphometric analysis of cellular injury. For several years we have collaborated scientifically with Dr. De la Iglesia and his colleagues which has resulted in several publications.

In the past few years these collaborative interactions have been greatly expanded in the context of increased collaborations between the University and Parke-Davis. Parke-Davis and the University of Michigan, Department of Pathology have entered into an agreement with Dr. De la Iglesia and colleagues to enhance joint research interests. This includes combining positions for postdoctoral fellowship programs as well as providing research opportunities for individuals at both institutions. Currently, there is one Parke-Davis postdoctoral fellow in the Department and several fellows from the Department who collaborate with colleagues at Parke-Davis including working at the Parke-Davis Faculty. In terms of faculty interactions there are collaborations with faculty from Parke-Davis and the Pathology Department dealing with models of inflammation and the regulation of the inflammatory response. There are also collaborations dealing with the mechanisms of apoptosis and DNA alteration in diseases such as SLE as well as morphometric evaluation of tissue injury. These interactions are mutually beneficial and have provided both groups with expertise that is not otherwise available at only one of the two institutions. These collaborations have been mutually reinforcing as demonstrated by joint seminars between the two institutions and joint efforts in recruitment of postdoctoral fellows.

These interactions are expected to continue to increase in the future. This industrial-academic partnership represents an important model for collaborative experiment research that will be jointly beneficial. It also provides an important exposure for our fellows to needs of the pharmacuetical industry.

Felix A. de la Iglesia, M.D.