

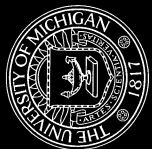
THE UNIVERSITY OF MICHIGAN

Department of Pathology

ANNUAL REPORT



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



1 July 1993 - 30 June 1994

THE UNIVERSITY OF MICHIGAN

Department Of Pathology

ANNUAL REPORT



1 July 1993 - 30 June 1994

LIST OF FACULTY

LIST OF FACULTY

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
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
Elnor, 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

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
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

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
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

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
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 Ophthalmology
- +++ Joint Appointment, Department of Surgery

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DEPARTMENTAL OVERVIEW

DEPARTMENTAL OVERVIEW

1993/1994

The academic year 1993-94 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 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology Services - four 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 Pathology Lab Sequence Director, Lecturer, Lab Instructor - 18 contact hours (six lectures, 12 labs).
- B. Sophomore Medical Class:
 - 1. Cardiovascular Sequence - four lecture hours.
 - 2. Cardiovascular Sequence - Pathology Lab Coordinator.
 - 3. Multidisciplinary Conferences - two contact hours.
- C. Hospital Conferences:
 - 1. Cardiovascular Pathology Conference - monthly.
 - 2. Internal Medicine CPC's - occasional.
 - 3. Internal Medicine Necropsy Review - monthly - occasional.
- D. House Officers:
 - 1. Training in Surgical and Necropsy Pathology.
- E. Invited Lectures:
 - 1. Freshman Orientation, August, 1993.
 - 2. Midwinter-Cardiovascular Update, February, 1994.
 - 3. Student Biomedical Research Program, June, 1994.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Evaluation of Cardiac Autonomic Innervation by PET. NIH 1-R01-HL 47543-1.

PROJECTS UNDER STUDY:

- A. Pathologic-Radiologic Correlation in Aortic Disease, with D. Williams.
- B. Pathologic Aspects of Cardiac Autonomic Innervation, with M. Schwiager.
- C. Pathogenesis of venous thrombosis, with T. Wakefield.
- D. Tissue reactions to implanted vena caval filters, with L. Greenfield.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Member, Pathology House Officer Selection Committee.

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Historical Center for the Health Sciences Liaison Committee.
- B. Member, Hospital Ethics Committee.
- C. Member, Component I Committee.
- D. Member, Curriculum Policy Committee.
- E. Director, Component II, Medical Curriculum.
- F. Ombudsperson, Medical Faculty
- G. Member, Medical School Advisory Committee on Appointments, Promotions and Titles.
- H. Member, School of Public Health Review Committee.
- I. Member, Medical Center Educational Space Advisory Committee.
- J. Member, ad hoc Committee to Review Appointment and Promotion Criteria in Clinical Track.
- K. Member, Executive Committee on Clinical Affairs.

REGIONAL AND NATIONAL:

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

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Williams, D.M., Joshi, A., Dake, M.D., Deeb, G.M., Miller, D.C. and Abrams, G.D.: Aortic cobwebs. An anatomic marker identifying the false lumen in aortic dissection. Imaging and Pathologic Correlation. Radiology 190:167-174,1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Medical Students:
 - 1. Course Director, Fundamentals of Laboratory Medicine (PTHCLNL.101) Component IV Medical School Curriculum.
 - 2. M1 Clerkship, Chemistry/Toxicology,
- B. House Officers:
 - 1. Lecturer, Clinical Pathology Grand Rounds.
 - 2. Lecturer, Clinical Pathology Didactic Lecture Series.
 - 3. Daily sign-out and interpretation of Laboratory Results.
 - 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.
- C. Pathology Associates.

MEDICAL SCHOOL/HOSPITAL:

- A. Pharmacokinetics Quality Improvement Team.

REGIONAL AND NATIONAL:

- A. National Awards Committee, American Association for Clinical Chemistry.
- B. Education Committee, Michigan Section, American Association for Clinical Chemistry.
- C. Board of Directors, American Board of Clinical Chemistry.
- D. Clinical Chemistry Examination Committee, American Board of Clinical Chemistry.
- E. Board of Directors, National Registry in Clinical Chemistry.
- F. Toxicology Examination Committee, National Registry in Clinical Chemistry.
- G. Credentials Committee, National Registry in Clinical Chemistry.
- H. Faculty, National Toxicology Review Course, American Association for Clinical Chemistry.
- I. Member, NCAA Drug Testing Team.
- J. Member, Academy of Clinical Laboratory Physicians and Scientists.
- K. Member, Clinical Ligand Assay Society.
- L. Member, American Association for Advancement of Sciences.
- M. Member, Association of Clinical Scientists.

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. "Anticonvulsant Drugs, Cardiac Drugs, Nicotine and Atropine", Professional Practice in Toxicology National Review Course, Cincinnati, Ohio, June, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Turgeon, D.K., Leichtman, A.B., Blake, D.S., Schmouder, R.L., Lown, K.S., Annesley, T.M. and Watkins, P.B.: Prediction of interpatient and inpatient variation in OG37-325 dosing requirements by the erythromycin breath test. *Transplantation* 57:1736-1741, 1994.
2. Annesley, T.M. and Clayton, L.T.: Determination of felbamate in human serum by high performance liquid chromatography. *Ther. Drug Monitor* In Press, 1994.
3. Shaw, L.M., Annesley, T., Gilmore, B. and Brayman, K.: Measurement of OG37-325 by high performance liquid chromatography. *Transplant. Proc.* In Press, 1994.

BOOKS/CHAPTERS IN BOOKS:

1. Annesley, T.M.: Overdoses and Poisonings, in, Warner, Hohnadel and Pesce (eds), *Anticonvulsant Drugs, Cardiac/Antiarrhythmic Drugs, Professional Practice in Toxicology: A Review*, AACCPress, pp. 129-172, 1994.
2. Annesley, T.M.: Preanalytical Test Variables, i, McClatchey, K.D. (ed), *Clinical Laboratory Medicine*, Williams and Wilkins, pp. 77-95, 1994.

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. *American Association of Pharmaceutical Scientists*, In Press.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. General surgical pathology - 4 1/2 months.
- B. Gastrointestinal and hepatic pathology consultation services - full time.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Medical Students:
 - 1. Pathology 600 - five full class lectures.
 - 2. Pathology 630 (dental) - two 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 - 4 1/2 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. Appendiceal epithelial neoplasia.
- C. Helicobacter-associated gastritis and non-ulcer dyspepsia with Grace Elta.
- D. The fate of the transplanted liver in chronic alcoholic patients with Michael Lucey and Kyle Carr.
- E. National Study of Thymosin Treatment of Chronic Hepatitis B with Milton Mutchnick.
- F. Chronic gastritis in Michigan with Paul Mazzara.
- G. Crohn's disease of the appendix with Jane Huang.

- H. Recurrent autoimmune hepatitis in the transplanted liver with Michael Lucey and Kyle Carr.
- I. Classification of gastric polyps with Priscilla Lindley.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITALS:

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

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. Lecturer, "Morphologic Expressions of Squamous Cell Carcinoma of the Esophagus; Diagnosis of Barrett's Mucosa Without Specialized Epithelium", presented at the 3rd International Polydisciplinary Congress of the International Organization for Statistical Studies on Diseases of the Esophagus, September 1-3, 1993, Paris, France.
- 2. Visiting Professor, Lectures on "Practical Approach to the Classification of Gastritis, the Role of the Pathologist in the Differential Diagnosis of Acute Infectious Colitis and Chronic Colitis, Dysplasia in Ulcerative Colitis, Development of Dysplasia and Carcinoma in Barrett's

- Esophagus, Pathology of Acute and Chronic Hepatitis, Pathology of Liver Transplantation", Department of Pathology, Mamara University, Istanbul, Turkey, September 6-7, 1993.
3. Lecturer, "Histopathology of the Esophagus and Stomach", American College of Gastroenterology, 1993 Annual Postgraduate Course, New York, New York, October 2, 1993.
 4. Lectures, "Pathologist's Role in IBD" and "Dysplasia in IBD", Inflammatory Bowel Disease Physicians Seminar presented by Crohn's and Colitis Foundation of America, Detroit Chapter, Sheraton Oaks Hotel, Novi, Michigan, October 16, 1993.
 5. Lecturer, "Dysplasia in IBD", Inflammatory Bowel Disease, New Orleans Update presented by Crohn's and Colitis Foundation of America, New Orleans Chapter, New Orleans Hilton Riverside, New Orleans, Louisiana, December 11, 1993.
 6. Lecturer, "The Role of the Pathologist in the Acutely Presenting Colitides", Colorado Society of Clinical Pathologists, Denver, Colorado, January 20, 1994.
 7. Visiting Professor, Lecture "Gut Lymphomas as Viewed by a Gut Pathologist; Is Hemotoxylin and Eosin a Useful Special Stain?", Department of Pathology, University of Colorado, Denver, Colorado, January 20, 1994.
 8. Lecturer, "Annoying Gut Biopsies", Annual Postgraduate Course, American Society for Gastrointestinal Endoscopy, Lake Buena Vista, Florida, February 11-13, 1994.
 9. Lecturer, "Neoplasms and Neoplastic-Like Disorders of the Vermiform Appendix", Gastrointestinal Pathology Society, San Francisco, California, March 13, 1994.
 10. Short Course, "Inflammatory Conditions of Esophagus, Stomach and Duodenum", with Donald Antonioli, United States and Canadian Academy of Pathology Annual Meeting, San Francisco, California, March, 1994.
 11. Lecturer, "The Pragmatist's Approach to Gastritis"; "Endoscopic Gastric Bumps, Neoplastic and Nonneoplastic Polyps and Mimics"; "Differential Diagnosis of the Acutely-Presenting Colitides", presented at the Tenth Annual Current Issues in Anatomic Pathology: 1994, The Department of Pathology, University of California School of Medicine, San Francisco, California, May 26-28, 1994.
 12. Seminar, "Neoplastic Diseases of Intestine", American Society of Clinical Pathologists, Monterey, California, June, 1994.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wu, G.D., Beer, D.G., Moore, J.H., Orringer, M.B., Appelman, H.D. and Traber, P.G.: Sucrase-isomaltase gene expression in Barrett's esophagus and adenocarcinoma. *Gastroenterol.* 105:837-844,1993.
2. Goldblum, J. and Appelman, H.D.: Achalasia. *Am. J. Surg. Path.* 18:327-337,1994.

CHAPTERS IN BOOKS:

1. Antonioli, D.A. and Appelman, H.D.: Anus and Perianal Area, Chapter 39, in, Sternberg, S. (ed.), Diagnostic Surgical Pathology, Second Edition, Raven Press, New York, New York, pp. 1613-1629, 1994.

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

1. Goldblum, J.R. and Appelman, H.D.: Stromal tumors of the duodenum: A clinicopathological study of 20 cases. *Mod. Pathol.* 7:60A,1994.
2. Huang, J.C. and Appelman, H.D.: Another look at isolated Crohn's disease of the appendix. *Mod. Pathol.* 7:61A,1994.
3. Carr, K.A., Ferrell, L.D., Wright, T.L., Lucey, M.R. and Appelman, H.D.: Post-transplant liver disease in patients transplanted for autoimmune chronic hepatitis. *Mod. Pathol.* 7:129A,1994.
4. Bilir, N., Sato, J., Appelman, H.D., Cherian, S. and Boland, C.R.: Sequential loss of tumor suppressor genes (TSGs) in the evolution of cancer in Barrett's esophagus. *Gastroenterol.* 106:A372,1994.
5. Kunz, K.R., DiTimasso, J., Appelman, H.D. and Boland, C.R.: The identification of a novel familial gastric cancer syndrome. *Gastroenterol.* 106:A406,1994.
6. Sato, J., Bilir, Sato, M., Appelman, H.D., Cherian, S. and Boland, C.R.: Analysis of genomic instability in multistep carcinogenesis in ulcerative colitis. *Gastroenterol.* 106:A437,1994.
7. Sato, J., Sato, M., Cherian, S., Chauhan, D.P, Appelman, H.D., Bresalier, R.S., Fukutomi, H. and Boland, C.R.: Mechanisms of genomic instability in gastrointestinal neoplasia, and their role in tumor progression. *Gastroenterol.* 106:A438,1994.
8. Sato, M., Sato, J., Cherian, S., Appelman, H.D., Fukutomi, H. and Boland, C.R.: Chromosomal losses and histopathology in human gastric cancer. *Gastroenterol.* 106:A438,1994.
9. Lucey, M.R., Carr, K., Fisher, L.R., Shieck, V., Brown, K.A., Beresford, T.P., Campbell, D.A. and Appelman, H.D.: Alcohol use and liver injury in alcoholics after liver transplantation - a long term follow-up study. *Gastroenterol.* 106:A935,1994.

**JAMES R. BAKER, JR., M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DIRECTOR, TISSUE TYPING LABORATORY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 June 1994**

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 Jennifer Johnson, Jeremy Janssen and undergraduate students in research.
G. Supervisor for Drs. Marc S. McMorris and Greg Gilmet (Allergy Fellows); Ali Motani and Richard Shen (Postdoctoral Fellows) Research Projects; and Sasha Krupnick (Medical Student) Independent Study.
H. Internal Medicine Grand Rounds.
I. Director, Allergy Training Program.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. "Characterization of Thyroid Autoantibodies and Antigens", National Institutes of Health-National Institute of Allergy and Infectious Disease, R29-AI 30501, May 1, 1993 - April 30, 1994, \$70,000/year.
B. "Immune Response to Thyroid Peroxidase in Thyroid Cancer", John E. Fogarty International Center, National Institutes of Health, 1 RO3 TW00192-01, April 1, 1993 - March 31, 1994, \$20,000/year.
C. Core Co-Director, "University of Michigan-MAC: Hybridoma Core", National Institutes of Health, 2 P60 AR20557-15, January 1, 1994 - December 31, 1994, \$42,853/year.
D. Core Co-Director, "MDRTC: Hybridoma Core", National Institutes of Health, 5 P60 DK20572-16, December 1, 1993 - November 30, 1994, \$171,413/year.
E. Cystic Fibrosis Foundation: Research Development Program, October 1, 1993 - September 30, 1994, \$29,456/year.
F. "Long-Term Effects of Mycophenolate Mofetil in Renal Transplants", Syntex Corporation (Study ICM MYC/1880/USA), July 1, 1993 - June 30, 1994, \$53,904/year.
G. "Randomized, Controlled, Dose Ranging Study of Mycophenolate Mofetil", Syntex Corporation (Study IID 2176), August 12, 1993 - August 11, 1994, \$75,765/year.
H. "Dendrimers and Gene Transfer", Michigan Molecular Institute, March 1, 1994 - February 28, 1996, \$200,000/year.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Planning Committee, Advances in Internal Medicine, University of Michigan Medical School, 1990-1994.
- B. Executive Board, Michigan Diabetes Research and Training Center.
- C. Dean's Committee on Restructuring Immunology.
- D. Chief, Division of Allergy, Department of Medicine..

REGIONAL AND NATIONAL:

- A. Histocompatibility Committee, Organ Procurement Agency of Michigan.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. Boots Pharmaceuticals Grand Rounds, Chicago, Illinois, September, 1993.
- 2. EPID 520 Fundamental Mechanisms of Pathogenesis, School of Public Health, University of Michigan, Ann Arbor, Michigan, September, 1993.
- 3. Immune Deficiency Foundation of Michigan, Ann Arbor, Michigan, November, 1993.
- 4. Schering Pharmaceuticals, Dearborn, Michigan, May, 1994.
- 5. "Histocompatibility and the Immune Response", Plenary Presentation, National Meeting of the American Academy of Allergy and Immunology, Anaheim, California, March, 1994.
- 6. "The Immune Response in Autoimmune Thyroid Disease", American Thyroid Association Annual Meeting, Tampa, Florida, November, 1993.

SCIENTIFIC ACTIVITIES:

- A. Editorial Board, 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, Journal of New England Journal of Medicine.
- K. Reviewer, Journal of Endocrinological Investigation.
- L. Consultant Director, HLA Laboratory, Walter Reed Army Medical Center, Washington, DC.
- M. Director, Hybridoma Core, University of Michigan Medical School.
- N. Regional Accreditation Commissioner, American Society for Histocompatibility and Immunogenetics.
- O. Endocrine Diseases Study Section, Ad Hoc Member, National Institutes of Health.
- P. Immunologic Sciences Study Section, Ad Hoc Member, National Institutes of Health.

WORKSHOPS/PANEL DISCUSSIONS:

- 1. Michigan Diabetes Research and Training Course Summer Student Program, Ann Arbor, Michigan, University of Michigan, July and August, 1993.
- 2. American Thyroid Association Annual Meeting, Tampa, Florida, November, 1993.

3. Boots Pharmaceuticals, Thyroid Research Advisory Council, Green Lake, Wisconsin, July and October, 1993, and October, 1993, and February, 1994.
4. Syntex Laboratories, Ketorolac Advisory Board, Palo Alto, California, February, 1994.
5. American Academy of Allergy and Immunology Annual Meeting, Anaheim, California, March, 1994.
6. American Association for Cancer Research, San Francisco, California, April, 1994.
7. Clinical Research Meeting, Baltimore, Maryland, April, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

1. Peele, M.E., Carr, F.E., Baker, J.R., Jr., Wartofsky, L. and Burman, K.D.: TSH beta subunit gene expression in human lymphocytes. *Am. J. Med. Sci.* 305:1-7,1993.
2. Baker, J.R., Jr: Editorial: Dissecting the immune response to the thyrotropin receptor in autoimmune thyroid disease. *J. Clin. Endo. Metab.* 77:16-18,1993.
3. Ross, P.V., Koenig, R.J., Arscott, P., Ludgate, M., Waier, M., Nelson, C.C., Kaplan, M.M. and Baker, J.R., Jr.: Tissue specificity and serologic reactivity of an autoantigen associated with autoimmune thyroid disease. *J. Clin. Endo. Metab.* 77:433-438,1993.
4. Bermann, M., Magee, M., Koenig, R.J., Kaplan, M.M., Arscott, P., Maastricht, J., Johnson, J. and Baker, J.R., Jr: Differential autoantibody responses to thyroid peroxidase in patients with Graves' disease and Hashimoto's thyroiditis. *J. Clin. Endo. Metab.* 77:1098-1101,1993.
5. Baker, J.R., Jr and Fosso, C.K.: Immunological aspects of cancers arising from thyroid follicular cells. *Endocr. Rev.* 14:729-746,1993.
6. Baker, J.R., Jr, Arscott, P.A. and Johnson, J.: An analysis of the structure and antigenicity of different forms of human thyroid peroxidase. *Thyroid* 4:173-178,1994.
7. Hennessey, L.R., Pek, S.B., Gupta, T., Shu, S. and Baker, J.R., Jr: Permanent reversal of diabetes in NOD mice treated with *Bacillus Calmette-Guerin* or bacterial superantigen. *Vaccine Research*, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Sack, J., Zilberstein, D., Geinski, P., Baker, J.R., Jr., Wartofsky, L. and Burman, K.D.: Thyrotropin binding sites in *Yersina Enterocolitica*. Submitted for publication.
2. Salazar, R.O., Arscott, P., Klapper, D., Burge, H.B., Solomon, W.R. and Baker, J.R., Jr.: Detection and quantitation of airborne ragweed pollen using an immunoblotting technique. Submitted for publication.
3. Schaudies, R.P., Djuh, Y.-Y., La Rocca, R.V., Wartofsky, L., Rhooms, P., Carr, F., Nicholson, D., D'Avis, J., Baker, J.R., Jr. and Burman, K.D.: Epidermal growth factor receptor gene in normal and pathologic tissue in patients with autoimmune thyroid disease, cancer and multinodular goiter: Correlation of unique genetic hybridization pattern with cellular responsiveness. Submitted for publication.
4. McClain, J.B., Col, MC, Bharati, J., Baker, J.R., Jr. and Cross, A., Col, MC: Alternative pathway complement activity to *E. Coli* K1 and 25922 contrasted to *Leptospira interrogans* and *Leptospira biflexa*. Submitted for publication.
5. Baker, J.R., Jr and Arscott, P.L.: Reversal of diabetes in NOD mice. Submitted for publication.

BOOKS AND CHAPTERS IN BOOKS:

1. Hennessey, L. and Baker, J.R., Jr.: Immunomodulators, in, Stites, D.P. and Terr, A. (eds), *Basic and Clinical Immunology*, Appleton and Lange, Norwalk, Connecticut/San Mateo, California, 1994.

2. Baker, J.R., Jr.: Endocrine diseases, in, Stites, D.P. and Terr, A. (eds), Basic and Clinical Immunology, Appleton and Lange, Norwalk, Connecticut/San Mateo, California, 1994.

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

1. Hennessey, L.R., Pek, S.B., Shu, S. and Baker, J.R., Jr.: Differential effect of immunization with bacillus calmette-guerin (BCG) on the incidence of diabetes mellitus (DM) and thyroiditis in non-obese diabetic (NOD) mice. Poster presentation, Endocrine Society Annual Meeting, Las Vegas, Nevada, June, 1993.
2. Arscott, P.L., Johnson, J., Magee, M. and Baker, J.R., Jr.: Native thyroid peroxidase is a disulfide-linked dimer. Poster presentation, American Thyroid Association 67th Annual Meeting, Tampa, Florida, November, 1993.
3. Baker, J.R., Jr, Magee, M., Shen, M.R., Kaplan, M., Koenig, R.J. and Arscott, P.L.: Identification of localized autoantibody epitopes in the amino acid 513-633 (TPO 513-633) region of thyroid peroxidase (TPO). Oral presentation, American Thyroid Association 67th Annual Meeting, Tampa, Florida, November, 1993.
4. Fosso, C.K., Arscott, P.L., Thompson, N.W., Sisson J.C., Shu, S. and Baker, J.R., Jr.: The induction of thyroid peroxidase (TPO) immune responses in patients with thyroid cancer (TC). Poster presentation, American Academy of Allergy and Immunology Annual Meeting, Anaheim, California, March, 1994.
5. McMorris, M.S., Lebedovych, L., Ward, P.A., Johnson, K.J. and Baker, J.R., Jr.: Variables altering cutaneous and pulmonary infiltrates in an *in vivo* model of delayed-phase allergic inflammation. Poster presentation, American Academy of Allergy and Immunology Annual Meeting, Anaheim, California, March, 1994.
6. Baker, J.R., Jr, Fosso, C.K., Arscott, P.L., Thompson, N.W., Sisson, J.C. and Shu, S.: The induction of thyroid peroxidase (TPO) immune responses in patients with thyroid cancer (TC). Poster presentation, American Association for Cancer Research, San Francisco, California, April, 1994.
7. Baker, J.R., Jr, Hennessey, L.R., Pek, S.B., Gupta, T. and Shu, S.: Permanent reversal of diabetes but not thyroiditis in NOD mice treated with Bacillus Calmette-Guerin (BCG) or bacterial superantigens. Poster presentation, Clinical Research Meeting, Baltimore, Maryland, April, 1994.
8. McMorris, M.S., Lebedovych, L., Ward, P.A., Johnson, K.J. and Baker, J.R., Jr: The induction of cutaneous and pulmonary delayed-phase allergic inflammation in an *in vivo* rat model. Poster presentation, Clinical Research Meeting, Baltimore, Maryland, April, 1994.
9. Janssen, J., Arscott, P., Smallridge, R. and Baker, J.R., Jr.: Characteristics of the immune response to thyroid peroxidase in patients with post-partum thyroiditis. Abstract submitted to the American thyroid Association, Chicago, Illinois, September, 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. Diagnostic Electron Microscopy, Veterans Affairs Medical Center, Director of Electron Microscopy Center of Excellence.
- B. Cytopathology, Veterans Affairs Medical Center, Director Center of Excellence.
- C. Coordinator of Decentralized Hospital Computer Program in Pathology and Laboratory Medicine Service, Veterans Affairs Medical Center.
- D. Fine Needle Aspiration, Veterans Affairs Medical Center.
- E. Surgical/Autopsy Pathology, Veterans Affairs Medical Center.
- F. National Chief Surgical and Cytopathology, Department of Veterans Affairs.
- G. Tumor Board, Veterans Affairs Medical Center.
- H. Deputy Washtenaw County Medical Examiner.
- I. 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. Pathology Lab Section, M-2 Year
- E. Graduate School doctoral thesis committee.
- F. 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. Acinic cell carcinoma of the parotid gland, predictors of clinical behavior. (with K. M. Stenson)
- I. 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 Affairs Medical Center.
- B. Invasive Procedures Review Committee, Veterans Affairs Medical Center.
- C. Electron Microscopy Committee, Chair, Veterans Affairs Medical Center.
- D. Medical Records Review Committee, Veterans Affairs Medical Center.
- E. Automated Data Processing Committee, Veterans Affairs Medical Center.
- F. Medical School Admissions Committee.

REGIONAL AND NATIONAL:

- A. Association of Veterans Affairs Pathologists, Secretary-Treasurer.
- B. Department of Veterans Affairs, Central Office Electron Microscopy Review Group.
- C. Armed Forces Institute of Pathology, Scientific Advisory Board.
- D. Association of Pathology Chairs, Veterans Affairs Committee, Consultant.
- E. American Society of Clinical Pathologists, Quality Management Cytology Committee.
- F. College of American Pathologists, Cytopathology Committee.
- G. Reviewer: Gastroenterology, Biotechnic and Histochemistry, Diagnostic Cytopathology, Acta Cytologica.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Diagnostic Problems in Cytopathology (Department of Internal Medicine, Pulmonary Conference Series).
2. Ultrastructural Abnormalities in Cilia (Department of Internal Medicine, Pulmonary Conference Series).
3. Electron Microscopy as an Aid to Diagnostic Cytopathology, Henry Ford Medical Center, Detroit, Michigan.
4. Short course, "Closed Lung Biopsy Interpretation", with A. Flint, USCAP, San Francisco, California, March, 1994.
5. Cytology Proficiency Testing in the Department of Veterans Affairs. National Symposium: Cytology Proficiency Testing, Atlanta, Georgia, November, 1993.
6. In Situ Hybridization: Review of Ultrastructural Techniques. Great Lakes Electron Microscopy Affiliates Conference, Indianapolis, Indiana, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Hinshaw, D.B., Burger, J.M., Miller, M.T., Adams, J.A., Beals, T.F. and Omann, G.M.: ATP depletion induces an increase in the assembly of a labile pool of polymerized actin in endothelial cells. *Am. J. Physiol.* 264 (Cell Physiol 33):C1171-C1179,1993.
2. Hinshaw, D.B., Miller, M.T., Omann G.M., Beals, T.F. and Hyslop, P.A.: A cellular model of oxidant-mediated neuronal injury. *Brain Res.* 615:13-26,1993.
3. Gregg, C.M., Beals, T.F., McClatchey, K.D., Fisher, S.G. and Wolf, G.T.: DNA content and tumor response to induction chemotherapy in patients with advanced laryngeal squamous cell carcinoma. *Otolaryngol. Head and Neck Surg.* 108:731-737,1993.
4. Beals, T.F. and Travers, E.M.: The Cytopathology proficiency program of the Department of Veterans Affairs. *Lab. Med.* 25:234-236,1994.
5. 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.
6. Goldblum, J.R., Beals, T.F. and Weiss, S.W.: Neuroblastoma-like neurilemoma. *Am. J. Surg. Pathol.* 18:266-273,1994.

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

1. Wideroff, L., Schottenfeld, D., Carey, T., Beals, T., Fu, G., Sakr, W., Sarkar, F., Schork, T., Grossman, H. and Shaw, M.: Human papilloma virus DNA in malignant and hyperplastic prostate tissue of black and white males. *National Human Papilloma Virus Conference*, 1993.
2. Stenson, K.M., Bradford, C.R., Wolf, G.T., Poore, J. and Beals, T.F.: The expression of proliferating cell nuclear antigen in acinic cell carcinoma of the parotid gland. *Am. Soc. Head and Neck Surgeons, Palm Beach*, 1994.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

I. CLINICAL ACTIVITIES:

- A. Eight months of Neuropathology Service.
- B. Five weeks of Autopsy Service.
- C. Muscle and nerve biopsies referred by other hospitals in- and out-of-state throughout the year.
- D. Consultations on brain biopsies and rheumatology cases.
- E. Skin and rectal biopsies for storage disorders.

II. TEACHING ACTIVITIES:

- A. Taught residents, fellows and staff in Neurology, Rheumatology and Pediatrics and medical students on muscle and nerve biopsies.
- B. Taught Pathology Residents how to perform and read-out autopsies.
- C. Lectured on muscle, nerve and brain pathology to residents in Pathology and Neurology.
- D. 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. Skeletal muscle and spinal cord in MND mice models.
- B. Histochemistry and morphometry of skeletal muscle in patients with hypertension and diabetes. With Hypertension Clinic and Sweden.
- C. Histology and histochemistry of orbicularis muscle, normal, aging, diseased.
- D. Histochemistry, morphometry and EM of levator palatini muscle in children with cleft palate.
- E. Histology of animal models of rheumatoid arthritis with Arthritis and Rheumatology Section.
- F. 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. Member, American Association of Neuropathologists, IAP, and AAN.
- C. Attended IAP, American Association of Neuropathologists and Peripheral Neuropathy Association 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., and Physics*, accepted for publication.
2. Meyer, J.R., Gebarski, S.S. and Blaivas, M.: Cerebello-pontine angle invase papillary cystadenoma of endolymphatic sac origin with temporal bone involvement. *Amer. J. R. N.* 14:1319-1321,1993.
3. Simmons, Z., Blaivas, M., Aquilera, A., Feldman, E.L., Bromberg, M.D. and Javad Towfighi: Low diagnostic yield of sural nerve biopsy in patients with peripheral neuropathy and primary amyloidosis. *J. Neurological Sci.* 120:60-63,1993.
4. O'Rourke, K.S., Blaivas, M. and Ike, R.W.: Utility of needle muscle biopsy in a university rheumatology practice. *J. Rheumatol.* 21:413-424,1994.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Colon, G.P., Quint, D.J., Blaivas, M. and McGuillicuddy, J.E.: Cardiac sarcoma metastatic to the brain. Submitted to *J. Neurosurg.*

2. Blaivas, M. and Nelson, C.C.: Aging changes in human orbicularis oculi muscle. Resubmitted to Investigative Ophthalmology and Visual Science.

BOOKS/CHAPTERS IN BOOKS:

1. McKeever, P.E. and Blaivas, M.: The Brain, Spinal Cord, and Meninges (Chapter 10), in, Sternberg, S.S. (ed.), Diagnostic Surgical Pathology, Second Edition. Raven Press, Ltd., New York, New York, pp. 409-492, 1994.

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

1. Robertson, W., Cornblath, W., Blaivas, M., Gebarski, S. and DiNome, M.: The eyes have it. Presented at the 26th Annual Frank B. Walsh meeting in Chicago, Illinois, April 9-10, 1994.
2. Wald, J., Crisco, L.V., Blaivas, M., Martinez, F.L. and Poole, R.M.: Mitochondrial NADH-dehydrogenase (complex I) deficiency and carnitine myopathy presenting as adult respiratory failure partially responsive to carnitine supplementation. Presented at VIII NMD meeting in Kyoto, Japan, July 10-15, 1994.
3. 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. To be presented at the meeting Cold Spring Harbor Lab, August 31-September 4, 1994.
4. 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. Accepted in the International Journal of Radiation Oncology, Biology, and Physics. Presented at the 35th Annual Meeting of the American Society for Therapeutic Radiology and Oncology in New Orleans, 1993.
5. Gebarski, S.S. and Blaivas, M.: Imaging of normal leptomeningeal melanin. To be presented at the annual Radiology Society of North America meeting in November 1994, Chicago.
6. Meyer, J.R., Gebarski, S.S., Deveikis, J. and Blaivas, M.: Cerebellopontine angle endolymphatic sac carcinoma with temporal bone involvement. Presented at joint annual meeting of German and North American Skull Case Societies, 1994.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

I. CLINICAL ACTIVITIES:

- A. Attending Staff, University of Michigan Autopsy Service.

II. TEACHING ACTIVITIES:

- A. Graduate Students, John Germiller (MSTP), Karl Jepsen (Mechanical Engineering, Bioengineering), Jeffrey Rouleau (Bioengineering), Robert Guldberg (Bioengineering), Mark Richards (MSTP) and Kuo-Fung Tseng (Bioengineering).
- B. Postdoctoral Fellows, Wushan Yin, M.D., Jianming Fang, M.D., Maria Moalli, D.V.M. and Laura Senunas (Medical Student).
- C. Undergraduate Students, Rebecca Brown (Marion Parker Scholars Program) and Dana Dumont (Kalamazoo College).
- D. Courses:
1. Pathology 600 - Laboratory Instructor.
 2. Molecular Cell Biology - Section Head.
 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, 1993.
 2. "Gene Transfer Into Osteogenic Cells *In Vivo*", University of Michigan, Department of Pathology Seminar Series, February 16, 1994.
 3. "Direct Gene Transfer Into Skeletal Tissues", Samuel Higby Camp Biomechanics Day, April 21, 1994.
 4. "Direct Gene Transfer Into Skeletal Tissues", Moses Gunn Conference, May 26, 1994.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Transgenic Mouse Model of Osteogenesis Imperfecta Type I", NIAMSD, National Institutes of Health, AR40679 (25% effort), \$162,679/year direct costs, \$462,843/three years, 1991-1994.

- B. Principal Investigator, "Direct Gene Transfer into Osteogenic Cells *In Vivo*", OVPR, \$15,000, 1994.

PROJECTS UNDER STUDY:

- A. Molecular cloning of microfibril constituents.
- B. Direct gene transfer into skeletal tissues.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

- A. Member, Pre-clinical Advisory Program, 1988 - present.
- B. Biomechanics Core Steering Committee, Multipurpose Arthritis and Musculoskeletal Diseases Center, 1991 - present.

DEPARTMENTAL:

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

V. OTHER RELEVANT ACTIVITIES:

- A. Ad-hoc Reviewer:
 - 1. The Journal of Clinical Investigation.
 - 2. The Journal of Biological Chemistry.
 - 3. American Journal of Human Genetics.
 - 4. Genomics.
- B. Consultant Editor:
 - 1. European Journal of Experimental Musculoskeletal Research 1991-present.
- C. Study Section:
 - 1. National Institutes of Health, NIAMS (SCOR Supplements), April 2, 1994.
 - 2. National Institutes of Health, NIDR (Special Emphasis Panel, Small Grant Program), July 6, 1994.
- D. Member:
 - 1. University of Michigan Multipurpose Arthritis Center.
 - 2. Michigan Cancer Center.
 - 3. University of Michigan Program Bioengineering Program.
- E. Patent:
 - 1. "Direct Gene Transfer Into Osteogenic Cells *In Vivo*." Patent application filed, February 18, 1994. Co-discoverer: Steven A. Goldstein, Ph.D., University of Michigan. Patent application is pending.

V. INVITED LECTURES/SEMINARS:

1. "Structure and Expression Pattern of the Murine *Magp* Gene", Annual meeting of the National Marfan Foundation, Portland, Oregon, August 22-23, 1993.
2. "Molecular Cloning of a Novel Fibrillin-like cDNA", Annual Meeting of the National Marfan Foundation, Portland, Oregon, August 20-22, 1993.
3. "Primary Structure and Developmental Expression of Mouse *Fbn-1*: Further Evidence of the Tissue-Specific Expression of 10nm Microfibril Components", Annual Meeting of the National Marfan Foundation, Portland, Oregon, August 20-22, 1993.
4. "Gene Transfer Into Osteogenic Cells *In Vivo*", Merck and Co., West Point, Pennsylvania, December 14, 1993.
5. "Structure-Function Relationships in Long Bone: The Results of Studies Using Transgenic Mice", Fifth International Conference on Osteogenesis Imperfecta, Oxford, United Kingdom, September 27-30, 1993.
6. "Direct Gene Transfer Into Regenerating Achilles' Tendon", 40th Annual Meeting, Orthopaedic Research Society, New Orleans, Louisiana, February 21-24, 1994.
7. "Expression Pattern of Fibrillin in Developing Mouse Embryos", Invited Lecture, Cardiac Morphogenesis and Development (National Institutes of Health Grantees Meeting), Charleston, South Carolina, March 23-24, 1994.
8. "Gene Therapy", Invited Lecture, Plenary Session, 1994, Clinical Ligand Assay Society Annual Meeting, Orlando, Florida, April 26-30, 1994.
9. "Molecular Biology of Wound Healing", Invited Lecture, Plastic Surgery Research Council Annual Meeting, Molecular Biology Symposium, Ann Arbor, Michigan, June 3, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Bonadio, J., Jepsen, K., Mansoura, M.K., Kuhn, J. L., Goldstein, S.A. and Jaenisch, R.: An adaptive response by murine skeletal tissues that significantly increases the mechanical properties of cortical bone: Implications for the treatment of skeletal fragility. *J. Clin. Invest.* 92:1697-1705,1993.
2. Chen, Y., Faraco, J., Yin, W., Germiller, J., Francke, U. and Bonadio J.: Structure, chromosomal localization and expression pattern of the murine *Magp* gene. *J. Biol. Chem.* 268:27381-27389,1993.
3. Lewsi, D.B., Liggitt, H.D., Effmann, E.L., Motley, S.T., Teitelbaum, S.L., Jepsen, K.J., Bonadio, J., Goldstein, S.A., Carpenter, J. and Perlmtter, R.M.: Osteoporosis induced in mice by overproduction of interleukin-4. *Proc. Natl. Acad. Sci. U.S.A.* 90:11618-11622,1993.
4. Li, X., Pereira, L., Zhang, H., Sanguineti, C., Ramirez, F., Bonadio, J. and Francke, U.: Conserved chromosomal synteny between the mouse and human genes coding for fibrillin (Fib15 and Fib5) proteins. *Genomics* 18:667-672,1993.
5. Zhang, H., Apfelroth, S.D., Hu, H., Davis, E.C., Sanguineti, C., Bonadio, J., Mecham, R.P. and Ramirez, F.: Structure and expression of fibrillin-2, a novel microfibrillar component preferentially located in elastic matrices. *J. Cell Biol.* 124:855-863,1994.

6. Yin, W., Germiller, J., Sanguineti, C., Smiley, E., Pangilinan, T., Pereira, L., Ramirez, F. and Bonadio, J.: Primary structure and developmental expression of *Fbn-1*, the mouse fibrillin gene. *J. Biol. Chem.*, In Press.
7. Li, X., Yin, W., Perez-Jurado, L., Bonadio, J. and Francke, U.: Mapping of human and murine genes or latent TGF- β binding protein-2 (LTBP2). *Mammalian Genome*, In Press.

ABSTRACTS:

1. Yin, W., Germiller, J. and Bonadio, J.: Molecular cloning and expression of a novel Fib15-like cDNA. Elastin Gordon Conference, Meridian, New Hampshire, August 8-13, 1993.
2. Zhang, H., Bonadio, J., Mehan, R. and Ramirez, F.: Characterization of Fib5, a novel component of elastic fibers. Elastin Gordon Conference, Meridian, new Hampshire, August 8-13, 1993.
3. Chen, Y., Yin, W., Germiller, J. and Bonadio, J.: Structure and expression pattern of the murine *Magp* gene. Annual Meeting of the National Marfan Foundation, Portland, Oregon, August 20-22, 1993.
4. Yin, W., Germiller, J. and Bonadio, J.: Molecular cloning of a novel fibrillin-like cDNA. Annual Meeting of the National Marfan Foundation, Portland, Oregon, August 20-22, 1993.
5. Yin, W., Germiller, Pangilinan, T., Sanguineti, C., Pereira, L., Ramirez, F. and Bonadio, J.: Primary structure and development expression of mouse *Fbn-1*: Further evidence of the tissue-specific expression of 10nm microfibril components. Annual Meeting of the National Marfan Foundation, Portland, Oregon, August 20-22, 1993.
6. Bonadio, J., Jepsen, K.J., Tseng, K-F. and Goldstein, S.A.: Structure-function relationships in long bone: The results of studies using transgenic mice. Fifth International Conference on Osteogenesis Imperfecta, Oxford, United Kingdom, September 27-30, 1993.
7. Germiller, J.A., Yin, W., Chen, Y. and Bonadio, J.: Patterns of microfibril gene expression in developing musculoskeletal and connective tissues. 40th Annual Meeting, Orthopaedic Research Foundation, New Orleans, Louisiana, February 21-24, 1994.
8. Yin, W., Rouleau, J., Goldstein, S.A. and Bonadio, J.: Molecular cloning of a novel fibrillin-like cDNA: Expression in callus tissue as alternatively spliced transcripts. 40th Annual Meeting, Orthopaedic Research Foundation, New Orleans, Louisiana, February 21-24, 1994.
9. Zhu, Y.Y., Voytik, S.L., Bradylak, S.F. and Bonadio, J.: Direct gene transfer into regenerating achilles' tendon. 40th Annual Meeting, Orthopaedic Research Foundation, New Orleans, Louisiana, February 21-24, 1994.
10. Waanders, N.A., Senunas, L.A., Steen, H., Goulet, J.A., Bonadio, J. and Goldstein, S.A.: Bone formation in distraction osteogenesis: Histologic and immunohistochemical findings. 40th Annual Meeting, Orthopaedic Research Foundtion, New Orleans, Louisiana, February 21, 24, 1994.
11. Jepsen, K.J., Schaffler, M.B., Gibson, G.J., Bonadio, J. and Goldstein, S.A.: Type I collagen mutation leads to altered structure, composition, and mechanical function in Mov long bone. 40th Annual Meeting, Orthopaedic Research Foundtion, New Orleans, Louisiana, February 21, 24, 1994.
12. Tseng, K-F., Bonadio, J., Stewart, T.A. and Goldstein, S.A.: The effects of local expression of growth hormone and mechanical properties of murine cortical bone. 40th Annual Meeting, Orthopaedic Research Foundtion, New Orleans, Louisiana, February 21, 24, 1994.

13. Germiller, J.A., Wong, M., Bonadio, J. and Goldstein, S.A.: 1993 ASME Bioengineering Conference, Breckenridge, Colorado, June 25-29, 1993.
14. Goldstein, S.A., Hollister, S.J., Guldborg, R.E., Germiller, J., Richards, M. and Bonadio, J.: Mechanical influences on bone adaptation. Second World Congress of Biomechanics, Amsterdam, The Netherlands, July 10-15, 1994.
15. Waanders, N.A., Senunas, L.E., Steen, H., Goulet, J.A., Bonadio, J. and Goldstein, S.A.: The influence of fixator stiffness on bone formation in distraction osteogenesis. Association for the Study and Application of the Methods of Ilizarov, Annual Meeting, New Orleans, Louisiana, February 23, 1994.
16. Tseng, K-F., Goldstein, S.A. and Bonadio, J.: The effects of system over-secretion of growth hormone on murine cortical bone - A hierarchical approach. 1994 ASME Bioengineering Conference, Chicago, Illinois, November 6-11, 1994.
17. Roessler, B.J., Kerrick, G.P., Goldstein, S.A. and Bonadio, J. Focal transduction of adult osteogenic cells *in vivo*. 1994 American College of Rheumatology 58th Annual Scientific Meeting, Minneapolis, Minnesota, October 23-27, 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 AUGUST 1993 - 30 JUNE 1994**

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: Forensic Pathology and Death Certification (3.5 hours; two sessions).
- B. Anatomic Pathology Conference Presentation (Seminars in Molecular Pathology): "Forensic Molecular Pathology".
- C. Presentation to fourth year medical students, Laboratory Medicine elective, Forensic Pathology and Toxicology.
- D. Presentation to high school students, "Introduction to Forensic Pathology".
- E. Presentations to medical students, fourth year Medical Student Courtship, "Basic Principles of Forensic Pathology and Death Certification".
- F. Presentation to Pathology House Officers, kodachrome review of Forensic Pathology for ASCP Pathology Resident In-Service Examination.
- G. Presentation to Michigan Funeral Director's Association, Medicolegal Death Investigations in Washtenaw County.

III. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Medicolegal Autopsies (Forensic Pathology).
- B. Interview candidates for Pathology House Officer positions.
- C. Director/Coordinator, Deputy Medical Examiner System for In-Hospital deaths, University of Michigan Hospitals.

IV. INVITED LECTURES AND SEMINARS:

1. "Ruptured Diaphragmatic Varices as the Probable Fatal Mechanism in Spontaneous Hemoperitoneum Complicating Cirrhosis of the Liver", American Academy of Forensic Sciences Annual Meeting, San Antonio, Texas, February, 1994.

ABSTRACTS:

1. Caplan, M.J.: Ruptured diaphragmatic varices as the probably fatal mechanism in spontaneous hemoperitoneum complicating cirrhosis of the liver. American Academy of Forensic Sciences Annual Meeting, San Antonio, Texas, February, 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. Director, Clinical Laboratories, Veterans Affairs Medical Center, responsibilities include, new equipment and methodology evaluation, review and consultation regarding quality management programs, personnel counseling and grievance procedures.
- B. Hematology/Coagulation, daily evaluation of pathologist referred blood smears, bone marrow smears and interpretation of special coagulation studies (12 months/year), Veterans Affairs Medical Center.
- C. Surgical/Frozen Section Diagnosis, (four months/year, approximately 2200 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 570, four lecture hours.
- C. Graduate course, Epidemiology 520, two lecture hours.
- D. Pathology house officers, Surgical Pathology/Autopsy supervision and instruction, (four months/year).
- E. Technologists and technicians, ongoing instruction on clinical laboratory topics.
- F. Graduate students, research training toward doctoral degrees.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

PROJECTS UNDER STUDY:

- A. Analysis of cytokine orchestration in TH1 and TH2 mediated forms of 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 evaluation.
- 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.
- B. Inspector, College of American Pathologists.
- C. Medical Advisory Committee, American Red Cross, SMBSR.

V. INVITED LECTURES/SEMINARS:

- 1. Invited lecturer, Symposium on Immunology of Schistosomiasis, American Society of Parasitology and the American Society of Tropical Medicine and Hygiene Joint Meeting, Atlanta, Georgia, November 1, 1993.
- 2. The Invited lecturer and chairperson, Minisymposium on Immunopathology of Infections, FASEB, Anaheim, California, April 24-28, 1994.
- 3. Invited lecturer, Pulmonary Medicine seminar series.
- 4. Case presentations at Tumor Board and Morbidity and Mortality Conferences.
- 5. Tissue evaluation for clinical researchers.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Lukacs, N.W., Kunkel, S.L., Strieter, R.M. and Chensue S.W.: The role of chemokines in *Schistosoma mansoni* granuloma formation. *Parasitol. Today* 10:322-324, 1994.
- 2. Spengler R.N., Chensue, S.W., Giacherio, D.A., Blenk, N. and Kunkel, S.L.: Endogenous norepineprine regulates tumor necrosis factor-alpha production from macrophages *in vitro*. *J. Immunol.* 152:3024-3031, 1994.
- 3. Lukacs, N.W., Chensue, S.W., Smith, R.E., Strieter, R.M., Warmington, K.S., Wilke, C. and Kunkel, S.L.: Production of monocyte chemoattractant protein-1 and macrophage inflammatory protein 1a by inflammatory granuloma fibroblasts. *Am. J. Pathol.* 144:711-718, 1994.

4. Lukacs, N.W., Chensue, S.W., Strieter, R.M., Warmington K.S. and Kunkel, S.L.: Inflammatory granuloma formation is mediated by TNF- α inducible intercellular adhesion molecule-1. *J. Immunol.* 152:5883-5889, 1994.
5. 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.*, In Press.

BOOKS/CHAPTERS IN BOOKS:

1. 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 International Congress on the Immune Consequences of Trauma Shock and Sepsis*, Munich, Germany.

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

1. Chensue, S.W., Ruth, J., Warmington, K.S., Lincoln, P. and Kunkel, S.L.: Demonstration of IL-10 and gamma IN cross regulation during schistosome egg-induced granuloma formation. *FASEB J.* 8:A266, 1994.
2. Kunkel, S.L., Strieter, R.M., Chensue, S.W., Evanoff, H.I. and Lukacs, N.W.: The interaction of TNF and ICAM-1 in pulmonary granuloma formation. *FASEB J.* 8:A802, 1994.
3. Bash, J.A., Paulus, S., Kirpalani, A. and Chensue, S.W.: The central role of polymorphonuclear neutrophils (PMN) in IL-6 mediated cachexia induced by a GM-CSF secreting murine adenocarcinoma line C-26c. *The 1994 UCI Symposium in Cancer Research "cytokines in Disease and Therapy"*, March 17-19, 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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. Plan and conduct weekly Brain Cutting Conference for house officers, students and staff, for gross diagnosis and demonstrations of diagnostic methods, and teaching.
- E. Plan and present gross and microscopic Neuropathology 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.

II. TEACHING ACTIVITIES:

- A. Neuroscience Sequence, Neuropathology for Second Year Medical Students, one hour lecture, ten hours laboratory.
- 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.
- C. Growth, spread and antigenicity of ENU-induced gliomas in rats, in collaboration with Paul E. McKeever, M.D., Ph.D.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Anatomic Pathology Committee.
- B. Coordinator, Neurpathology 858 Course.

MEDICAL SCHOOL/HOSPITAL:

- A. Co-coordinator for the Neuroscience Sequence (new curriculum).
- B. Neuroscience Curriculum Committee.
- C. Coordinator for Neuropathology, Neuroscience Sequence.
- D. Neuroscience Examination Committee.
- 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:

- 1. Member, Dementia Subcommittee of the Chronic Disease Advisory Committee (State of Michigan).
- 2. Member, Executive Committee of the Postmortem Examination Work group of the Dementia Subcommittee (State of Michigan).
- 3.. Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Committee.
- 4. Presentation, "Alzheimer's Disease and Other Dementias", Alzheimer Association, Catherine McCauley Health Center, Ann Arbor, Michigan, January, 1994.
- 5. Presentation, "Brain Autopsy-Just the Facts", Michigan Autopsy Education Workshop: Towards a Greater Understanding." Kellogg Center, E. Lansing, Michigan, March, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Lloyd, R.V., D'Amato, C.J., Thiny, M.T., Jin, L., Hicks, S.P. and Chandler, W.F.: Corticotroph (basophil) invasion of the pons nervosa in the human pituitary: localization of proopiomelanocortin peptides, galanin and peptidyl glycine α -amidating monooxygenase-like immunoreactivities. *Endocrine Pathol.* 4:86-94,1993.
- 2. Sima, A.A.F., Caplan, M., D'Amato, C.J., Pevzner, M. and Furlong, J.W: Fulminant multiple systems atrophy in a young adult presenting as motor neuron disease. *Neurol.* 43:2031-2035,1993.

3. Sima, A.A.F., Douglas, V. and D'Amato, C.J.: A case of early diffuse lewy body disease suggests degeneration of mesocortical dopaminergic afferents. Submitted for publication in *Neurology*, April 1994.

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

1. Homeister, J., D'Amato, C.J. and Sima, A.A.F.: The diverse pathology of Huntington's disease. Presented at the 1993 Neuropathology Day, October 1993, Beaumont Hospital, Detroit, Michigan.
2. Sima, A.A.F., D'Amato, C., Defendini, R.F., Jones, M.Z., Foster, N.L., Lynch, T. and Wilhelmsen, K.C.: Primary limbic lobe gliosis; familial and sporadic cases. XIIth International Congress of Neuropathology, September, 1994, Toronto.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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. "Blood Component Therapy", Surgical Intensive Care Unit Grand Rounds, August 12, 1993.
- D. "Statistics", Department of Pathology Resident Teaching Conference, December 16, 1993.
- E. "Blood Component Therapy", Orthopedic Surgery Grand Rounds, December 23, 1993.
- F. Transfusion Medicine sequence, Course in Clinical Pathology for Medical Students, May, 1994.
- G. Department of Pathology, Clinical Pathology Grand Rounds, May 20, 1994.
- H. "Case Studies in Transfusion Medicine", workshop in continuing medical education course: Current Topics in Blood Banking, June 1, 1994.

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 Interval Review Committee.

V. OTHER RELEVANT ACTIVITIES:

- A. Reviewer, Chest.
- B. Reviewer, Transfusion.
- C. Reviewer, American Journal of Clinical Pathology.
- D. Program committee, Michigan Association of Blood Banks

INVITED LECTURES AND SEMINARS:

1. Invited speaker, "Role of Interleukins in the Pathogenesis of Hemolytic Transfusion Reactions", Symposium on: The Role of Biological Response Modifiers in Molecular and Clinical Transfusion Medicine, Arlington, Virginia, September, 1993.
2. Invited speaker, "The Role of Cytokines in Hemolytic Transfusion Reactions", Michigan Association of Blood Banks, Troy, Michigan, September, 1993.
3. Invited Speaker, "Cytokine Roles in Hemolytic Transfusion Reactions", Council of Hospital Blood Bank Directors of the Greater New York Region. New York, New York, October, 1993.
4. Invited speaker, "Blood Component Therapy", Update on Pediatric Hematology/Oncology in the Primary Care Office, Ann Arbor, Michigan, March 1994.
5. Invited speaker, "The Immunosuppressive Effect of Blood Transfusion", Michigan Society of Medical Technologists, Romulus, Michigan, April, 1994.
6. Invited speaker, "The Role of Cytokines in Hemolytic Transfusion Reactions", 12th International Convocation on Immunology, Buffalo, New York, May, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Goldblum, J. R., Shannon, R., Kaldjian, E. P., Thiny, M., Davenport, R., Thompson, N. and Lloyd, R.V.: Immunohistochemical assessment of proliferative activity in adrenocortical neoplasms. *Mod. Pathol.* 6:663-668,1993.
2. 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.
3. Davenport, R. and D., Kunkel, S. L.: Cytokine roles in hemolytic and nonhemolytic transfusion reactions. *Transfus. Med. Rev.*, In Press.
4. 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.
5. Davenport, R. D.: The role of cytokines in hemolytic transfusion reactions. *Immunol. Invest.*, In Press.
6. Davenport, R. D., Polak, T.J. and Kunkel, S.L.: Leukocyte associated procoagulant activity induced by ABO incompatibility. *Transfusion.*, In Press.
7. Davenport, R. D.: Cytokines and red cell incompatibility. *Cur. Opin. Hematol.*, In Press.

BOOKS/CHAPTERS IN BOOKS

1. Davenport, R. D.: Can leukocyte depletion of blood components prevent transfusion-associated graft-versus-host disease?, in, Anderson, K.C. and Leitman, S., (eds.), *Transfusion-Associated Graft-versus-Host Disease*, 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. None.

II. TEACHING ACTIVITIES:

- A. Graduate students:
1. Responsible during the current academic year for the following activities:
 - a. Course Instructor: "Fundamentals in Electron Microscopy".
 - b. Student Training and Doctoral Committees.
 - c. Joint Student Training in Pharmacology and Toxicology with Florida A&M School of Pharmacy, Toxicology Program.
 - d. 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 developing 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, Joint University of Michigan and Parke-Davis 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, Toxicology.
- C. Editorial Board Member, Toxicologic Pathology.

VI. INVITED LECTURES/SEMINARS:

- 1. "Unaltered Nucleotide Sequences in Ki-Ras Genes from Rat Acinar Cell Pancreatic Tumors Induced by Gabapentin", American Epilepsy Society, Orlando, Florida, November, 1993.
- 2. "Pancreatic Acinar Cell Tumors in Wistar Rats Treated with Gabapentin", American Epilepsy Society, Orlando, Florida, October 1993.
- 3. "Histopathologic Findings in Rodents Treated Two Years with the Angiotensin Converting Enzyme Inhibitor, Quinapril Hydrochloride", 12th International Symposium, Society of Toxicologic Pathologists, Alexandria, Virginia, June, 1993.
- 4. "Carcinogenicity Studies in Rodents with the Benzothiazine Derivative Isoxicam", Society of Toxicology, Dallas, Texas, March, 1994.
- 5. "Studies in Peroxisome Biogenesis, ILSI Conference on Research Update on Peroxisome Proliferation", ILSI Risk Science Institute and Environmental Protection Agency, Dallas, Texas, March, 1994.
- 6. "Gross and Histologic Findings Following Intravenous Administration of Recombinant Human Epidermal Growth Factor 1-48 for 2 Weeks in Cynomolgus Monkeys", 13th International Symposium, Society of Toxicologic Pathologists, Charleston, South Carolina, June, 1994.
- 7. "Multisystemic Cellular Hyperplasia in Wistar Rats Induced by Continuous IV Infusion of Human Recombinant Epidermal Growth Factor 1-48", 13th International Symposium, Society of Toxicologic Pathologists, Charleston, South Carolina, June, 1994.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Bleavins, M.R. and de la Iglesia, F.A.: Delayed-type hypersensitivity in cynomolgus monkeys. *Fund. Appl. Toxicol.*, In Press.
- 2. Sigler, R.E., Gough, A.W. and de la Iglesia, F.A.: Pancreatic acinar cell neoplasia in male Wistar rats following two years of gabapentin exposure. *Toxicology*, In Press.
- 3. Feuer, G., Dhami, M.S.I. and de la Iglesia, F.A.: Changes by progesterone derivatives in fatty acids from phosphatidylcholine and phosphatidylethanolamine fractions in rat liver endoplasmic reticulum. *Exp. Toxicol. Pathol.*, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

- 1. 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.
- 2. Bleavins, M.R., de la Iglesia, F.A., McCay, White, K.L. and Munson, A.E.: Immunotoxicologic studies with CI-959, a novel benzothiophene cell activation inhibitor. Submitted for publication.
- 3. Fowler, M.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. Submitted for publication.

4. de la Iglesia, F.A., Martin, R.A., Walker, R.M. and Feuer, G.: Metabolic effects of antiinfective agents on the liver of common marmosets (*Callithrix jacchus*). Submitted for publication.
5. McGuire, E.J. and de la Iglesia, F.A.: Hypolipidemic effects on rat liver mitochondria studied by quantitative microscopy. Submitted for publication.

BOOKS/CHAPTERS IN BOOKS:

1. Welling, P.G. and de la Iglesia, F.A. (eds): Drug Toxicokinetics, M. Dekker, New York, 1993.
2. Cameron, R., Feuer, G and de la Iglesia, F.A. (eds): Drug Induced Hepatotoxicity, Handbook of Experimental Pharmacology, Springer Verlag Publishers, 1994.
3. Feuer, G. and de la Iglesia, F.A., Cameron, R., Feuer, G. and de la Iglesia (eds), Biochemical and Morphological Correlates in Experimental Models of Hepatotoxicity, Drug Induced Hepatotoxicity, Springer Verlag Publishers, 1994.

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

1. Lalwani, N.D., Fowler, M.L., Sigler, R.E. and de la Iglesia, F.A.: Unaltered nucleotide sequences in ki-ras genes from rat acinar cell pancreatic tumors induced by gabapentin. *Epilepsia* 34:14, 1993.
2. Gough, A.W., Sigler, R., Walker R. and de la Iglesia, F.A.: Pancreatic acinar cell tumors in Wistar rats treated with gabapentin. *Epilepsia* 34:14-15, 1993.
3. Gough, A.W., Reindel, J.F., McGuire, E.J. and de la Iglesia, F.A.: Histopathologic findings in rodents treated two years with the angiotensin converting enzyme inhibitor, Quinapril Hydrochloride. *Toxicologic Pathol.* 21:594, 1993.
4. McGuire, E.J., Rothwell, C.E., Herman J.R. and de la Iglesia, F.A.: Carcinogenicity studies in rodents with the Benzothiazin Derivative Isoxicam. *The Toxicologist* 14:65, 1994.
5. de la Iglesia, F.A., McGuire, E.J., Haskins, J.R. and Lalwani, N.D.: Studies on peroxisome biogenesis, Proceedings, ILSI Conference on Research Update on Peroxisome Proliferation, ILSI Risk Science Institute and Environmental Protection Agency, 1994.
6. Reindel, J.F., Pilcher, G.D., Walsh, K.M., Gough, A.W. and de la Iglesia, F.A.: Gross and histologic findings following intravenous administration of recombinant human epidermal growth factor 1-48 for 2 weeks in cynomolgus monkeys. *Toxicol. Pathol.*, In Press.
7. Breider, M., Bleavins, M.R., Reindel, J.F., Gough, A.W. and de la Iglesia, F.A.: Multisystemic cellular hyperplasia in Wistar rats induced by continuous IV infusion of human recombinant epidermal growth factory 1-48. *Toxicol. Pathol.*, In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

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, Donna Osterhout, Aziz Qabar, Zhi Zheng.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Structure and Function of Thrombospondin", #89-217, American Heart Association Established Investigatorship Award, Budget \$35,000 annually, \$175,000 Total, 07/01/89-06/31/94.
- B. 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.
- C. Principal Investigator, "Novel Thrombospondin Receptors on Squamous Carcinoma Cells", NIH-CA51888, 20% effort, Budget \$97,454 current year, \$304,211 Total, 02/01/91 - 01/31/94.
- D. 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.
- E. 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.
- F. 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.
- G. Principal Investigator, "Role of *Eck* in Murine Lung Development", Amgen Contract, Budget \$100,000 current year, \$230,000 Total, 07/01/93 - 06/31/95.
- H. 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. Structure/function relationships in thrombospondin.
- B. Mechanisms of action of tumor necrosis factor.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Interview prospective graduate students for a) Molecular and Cell Biology Program, and b) Medical Scientist Training Program.
- B. 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. American Heart Association Study Section.
- C. Pathology A Study Section (Ad-hoc).

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Invited Speaker, FASEB, New Orleans, Louisiana, 1993.
2. Invited Speaker, Parke Davis, Ann Arbor, Michigan, 1993.
3. Invited Speaker, Scripps Research Institute, La Jolla, California, 1993.
4. Invited Speaker, Northwestern University, Evanston, Illinois, 1993.
5. Invited Speaker, Southwestern Medical Center, University of Texas, San Antonio, Texas, 1993.
6. Invited Speaker, AMGEN, Thousand Oaks, California, 1993.
7. Invited Speaker, AHA, Lathrop Village, Michigan, 1994.
8. Invited Speaker, Keystone Symposia, Silverthorne, Colorado, 1994.
9. Invited Speaker, Thomas Jefferson University, Philadelphia, Pennsylvania, 1994.
10. Invited Speaker, New York University, New York, New York, 1994.
11. Invited Speaker, XIV Washington International Symposium, Washington, DC, 1994.
12. Invited Speaker, Gordon Research Conference, Meriden, New Hampshire, 1994.
13. Invited Speaker, Mayo Clinic, Scottsdale, Arizona, 1994.
14. Invited Speaker, AMGEN, Thousand Oaks, California, 1994.

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

1. Castle, V.P., Ou, X., O'Rourke, K. and Dixit, V.M.: Thrombospondin 1 expression confers serum and anchorage independent growth. *J. Biol. Chem.* 268:2899-2903, 1993.
2. Laherty, C.D., Perkins, N.D. and Dixit, V.M.: HTLV-I TAX and PMA induce expression of the A20 zinc finger protein by distinct mechanisms involving NF- κ B. *J. Biol. Chem.* 268:5032-5039, 1993.
3. Wolf, F.W., Sarma, V., Seldin, M., Drake, S., Suchard, S.J., Shao, H., O'Shea, K.S. and Dixit, V.M.: B94, a primary response gene inducible by tumor necrosis factor- α , is expressed in developing hematopoietic tissues and the sperm acrosome. *J. Biol. Chem.* 269:3633-3640, 1993.
4. 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.
5. 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.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Qabar, A., Derrick, 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.*
2. Hong, M.H., Boguski, M.S. and Dixit, V.M.: A novel RING finger protein interacts with the cytoplasmic domain of CD40. *Nature.*
3. Zhiwu, L., Perkins, N.D. and Dixit, V.M.: NF- κ B mediated stimulation of B94 expression is precisely regulated by TNF induced repression of AP-2. *Mol. Cell. Biol.*

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

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. Postdoctoral Mentor for Hamed Benghuzzi, Ph.D.
D. Participant, Clinical Pathology Grand Rounds.
E. 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) P30 HD18258: Center for the Study of Reproduction, Co-Director, Standards and Reagents Core Facility, \$348,320/year, 1989-1994.
C. 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. Roundtable Presenter: Annual Meeting, Clinical Ligand Assay Society. Estradiol Calibration. What's Right?

VI. INVITED LECTURES AND SEMINARS:

1. Benghuzzi, H.A., Possley, R. and England, B.G.: Pulsatile delivery of progesterone and estradiol to mimic the ovulatory surge in adult ewes by means of TCPL implants. Proceedings of the 31st Annual Meeting of the Rocky Mountain Bioengineering Symposium, Kansas City, Kansas, April 22-23, 1994.
2. Benghuzzi, H.A., Praphulla, K., Bajpai, P.K. and England, B.G.: Pathophysiological evaluation associated with sustained delivery of danazol and dihydrotestosterone in adult male rodents. Proceedings of the 31st Annual Meeting of the Rocky Mountain Bioengineering Symposium, Kansas City, Kansas, April 22-23, 1994.
3. Benghuzzi, H.A., Possley, R. and England, B.G.: The use of tricalcium-phosphate-lysine implants to deliver estrogen at a sustained level for one year in adult castrated rams. Proceedings of the 13th Southern Biomedical Engineering Conference, Washington, D.C., April 16-17, 1994.
4. 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 Engineering Conference, Washington, D.C., April 16-17, 1994.
5. 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 Engineering Conference, Washington, D.C., April 16-17, 1994.
6. Benghuzzi, H.A., Praphulla, K., Bajpai, P.K. and England, B.G.: Pathological evaluation of the reproductive organs of adult male rodents exposed to long-term sustained delivery of danazol plus dihydrotestosterone. Annual Meeting of Scanning Electron Microscopy: Cells and Materials, Toronto, Canada, May 7-12, 1994.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. I'Anson, H., Quint, E.H., Wood, R.I., England, B.F. and Foster, D.A.: Adrenal axis and hypogonadotropism in the growth-restricted female lamb. *Biology of Reproduction* 50:137-143, 1994.
2. Benghuzzi, H.A., England, B.G., Bajpai, P.K. and Giffin, B.F.: Successful antidote of multiple lethal infections using sustained delivery of difluoromethylornithine by means of ceramic drug delivery devices. *Journal of Clinical Materials* 15:151-160, 1994.
3. Benghuzzi, H.A., Possley, R. and England, B.G.: Pulsatile delivery of progesterone and estradiol to mimic the ovulatory surge in adult ewes by means of TCPL implants. *Biomedical Sciences Instrumentation* 19:187-196, 1994.
4. Benghuzzi, H.A., Bajpai, P.K. and England, B.G.: Pathophysiological evaluation associated with sustained delivery of danazol and dihydrotestosterone in adult male rodents. *Biomedical Sciences Instrumentation* 29:197-204, 1994.
5. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: The effects of density of the ceramic delivery devices on sustained release of androgens in castrated rats. *J. of Clinical Materials*, In Press.

6. 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, In Press.
7. 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, In Press.
8. 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, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Benghuzzi, H.A., Bajpai, P.K. and England, B.G.: Ceramic drug delivery system: density effects on the delivery of androgens in male rats. Submitted for publication.

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

1. Benghuzzi, H.A., Possley, R., Brownlee, B. and England, B.G.: The relationship between danazol, antioxidants and lipoprotein profiles in adult female mice. *Experimental Biology* 94, Anaheim, California, April 25-28, 1994. *FASEB Journal* 8:A577, 1994.
2. England, B.G. and Benghuzzi, H.A.: High-density lipoprotein response to long-term sustained delivery of androgens in castrated rams. *Experimental Biology* 94, Anaheim, California, April 25-28, 1994. *FASEB Journal* 8:A576, 1994.
3. Benghuzzi, H.A., Possley, R. and England, B.G.: The effectiveness of TCPL implants to deliver dihydrotestosterone and its role on gonadotropin secretion using wethers as a model. Annual Meeting of Endocrine Society, Anaheim, California, June 12-15, 1994 (Abstract #1187, p. 496).

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. Autopsy Service.

II. TEACHING ACTIVITIES:

- A. Director, Resident Training Program.
- B. Graduate Program Committee (Chairman).
- C. Course Director - Teaching Laboratories.
- D. Director - Component I: Medical Student Curriculum.
- E. Laboratory Instructor, M1 Histopathology Sequence
- F. Lecturer, M1 Host Defense Sequence.
- G. Lecturer - Microbiology and Immunology 624.
- H. Coordinator, Department of Pathology Summer Clinical Program for Minority Medical Students.
- I. Pulmonary Pathology Conference (six per year to Pulmonary Division, Department of Internal Medicine).
- J. Graduate Student Ph.D. Thesis Committee (three).
- K. 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, "Mechanisms and Genetic Regulation of Pulmonary Fibrosis", (S.H. Phan; Principal Investigator), NIH-5-R01-HL-28737.
- C. Co-Investigator, "Pharmacologic Studies on the Ischemic Heart", (B. Lucchesi, Principal Investigator), NIH-R01-HL-19782.

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 Harrassment Contact Person.

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

- A. NIH Site Visit, SCOR: Myocardial Injury, Washington, D.C., 1994.
- B. AHA of Michigan, Grant Review Committee, 1994.
- C. USMLE, Pathophysiology Test Group.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Editorial Board, Infection and Immunity.
- B. Editorial Board, Laboratory Investigation.
- C. Editorial Board, Biological Signals.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Brieland, J.K., Jones, M.L., Flory, C.M., Miller, G.R., Warren, J.S., Phan, S.H. and Fantone, J.C.: Expression of monocyte chemoattractant protein-1 (MCP-1) by rat alveolar macrophages during chronic lung injury. *Am. J. Respir. Cell. Mol. Biol.* 9:300-305, 1993.
2. 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. *Amer. J. Respir. Cell Mol. Biol.* Accepted for Publication, 1994.

3. Brieland, J.K., Freeman, P., Kunkel, R., Chrisp, C., Hurley, M., Fantone, J.C. and Engleberg, C.: Replicative *Legionella pneumophila* lung infection in intratracheally inoculated A/J mice: A murine model of human Legionnaires' disease. Amer. J. Path. Accepted for Publication, 1994.
4. Crockett-Torabi, E., Smith, C.W. and Fantone, J.C.: Activation of human neutrophils through L-selectin and Mac-1 molecules. Submitted for Publication, J. Immunol.

BOOK CHAPTERS:

1. Fantone, J.C. and Ward, P.A.: Inflammation, in, Rubin, E. and Farber, J., (eds.), Textbook of Pathology. 2nd Edition, Lippincott Co., Publishers, 1993.
2. Brieland, J. and Fantone, J.C.: Neutrophils and Pulmonary Fibrosis, in, Phan, S. and Thrall, R., (eds.) Pulmonary Fibrosis. Mercel Dekker, Publishers, In Press.

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

1. Brieland, J.K., Tsai, P., Engleberg, N.C., Remick and D.G. and Fantone, J.C.: Differential effects of *Legionella pneumophila* virulence on mononuclear phagocytic cell cytokine production. Soc. Leuk. Biol., 1993.
2. Brieland J.K., Freeman, P.T., Remick, D.G., Hurley, M.C., Fantone, J.C. and Engleberg, N.C.: Endogenous tumor necrosis factor alpha and gamma interferon facilitate resolution of relocalitive *Legionella pneumophila* lung infection in A/J mice. Soc. Leuk. Biol., 1994.
3. Crockett-Torabi, E. and Fanton, J.C.: Crosslinking of L-selectin molecules induced charges in intracellular calcium in human neutrophils. FASEB, Anaheim, California, April 24-28, 1994.
4. Fantone, J.C. and Crokett-Torabi, E.: MAC-1 adhesion molecules induce human neutrophil activation through Ca²⁺ dependent and Ca²⁺ independent pathways. FASEB, Anaheim California, April 24-28, 1994.
5. Robins, L.S., Fantone, J.C., Alexander, G.L., Wolf, F.M., Oh, M.S. and Davis, W.K.: The impact of curricular change on student satisfaction with the educational process and the overall learning environment. 32nd Annual Research in Medical Education Conference, Washington, D.C., November 5-11, 1993.
6. Robins, L.S., Fantone, J.C., Alexander, G.L., Oh, M.S. and Davis, W.K.: The impact of pass/fail grading on student performance and satisfaction with the evaluation/exam system. 32nd Annual Research in Medical Education Conference, Washington, D.C., November 5-11, 1993.
7. Robins, L.S., Davis, W.K., Shalfer, M., Alexander, G.L., Oh, Mary S., Davis, W.K. and Fantone, J.C.: The impact of curricular change on student perceptions o the medical School learning environment. 33rd Annual Research in Medical Education Conference, Boston, Massachusetts October 28-November, 3, 1994.
8. Robins, L.S., Davis, W.K., Anderson, R.M. and Fantone, J.C.: The influence of gender and ethnicity of student perceptions on the medical school learning environment. 24th Annual Meeting of the Association for the Behavioral Sciences and Medical Education.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology Rotations, July (1/4), August (2/4), September (2/4), October (2/4), November (2/4), February (2/4), March (4/4), April (2/4), June (2/4).
- B. Estrogen and progesterone receptor analysis of paraffin embedded breast carcinomas by image analysis 97 samples.

II. TEACHING ACTIVITIES:

- A. Pathology 600 Lectures:
 - 1. Obstructive and Interstitial Diseases, November 10, 1993.
 - 2. Neoplasms and Anomalies, November 16, 1993.
 - 3. Pathology of ARDS, November 16, 1993.
 - 4. Vascular Diseases, November 17, 1993.
 - 5. Laboratory Instructor, October, 1993 - January, 1994.
 - 6. Student question and answer sessions, afternoons and evenings, November, 1993 - January, 1994.
- B. Pathology 630:
 - 1. Respiratory Disease I, October 29, 1993.
 - 2. Respiratory Disease II, November 1, 1993.
- C. Residency Training:
 - 1. Diseases of the Chest I, November 16, 1993.
 - 2. Diseases of the Chest II, November 23, 1993.
 - 3. Diseases of the Chest III, November 30, 1993.
 - 4. Surgical Pathology Consultant's Conference, December, 1993; April, 1994.
- D. Other educational activities:
 - 1. M4 student elective mentor, August, 1993.
 - 2. Center for Research on Learning and Teaching Workshop: Presenting Lectures, October 7, 1993.
 - 3. Member, M-2 Respiratory Sequence Committee, 1993-1994.
 - 4. Course Director, M-4 Student Pathology Clerkships.
 - 5. Pathology Resident Mentor.
 - 6. Participant, Thoracic Surgery Residents Core Curriculum.
 - 7. Facilitator, Pathology for High School Students, Community High School, March, 1993.

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. Quantitation of immunochemically-determined estrogen and progesterone receptors of breast carcinoma.
- B. Interstitial lung disease: The influence of biopsy site on diagnosis.
- C. Regional expression of Ki-67 activity in colonic polyps.
- D. Analysis of TGF- β and its binding protein, decorin, in lung tissue of ARDS patients.
- E. Histologic predictors of obliterative bronchiolitis in lung transplant patients.
- F. Overexpression of Glut-1 glucose transporter in human lung cancer.
- G. Ploidy analysis of urothelial carcinoma.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Interviewed House Officer Candidates (September, 1993-January, 1994).
- B. Director, Surgical Pathology Fellowship Program.
- C. Member Credentials Committee, University Hospital .Member Bylaws Committee of the Arthur Purdy Stout Society, 1992- present

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Reviewer, American Journal of Pathology.
- B. Reviewer, American Review of Respiratory and Critical Care Medicine (formerly the American Review of Respiratory Disease).

INVITED LECTURES/SEMINARS:

1. Guest Pathologist, Tri-State Thoracic Society, Perdido Beach, Alabama, January, 1994.
2. Visiting Professor, the University of Alabama at Birmingham, Birmingham, Alabama, November, 1993.
3. "Interpretation of Closed Lung Biopsy Samples", Alabama Association of Pathologists, Birmingham, Alabama, November, 1993.
4. "Closed Lung Biopsy Interpretation", short course, , Annual Meeting, San Francisco, California, March, 1994

VI. PUBLICATIONS:

1. Flint, A. and Frank, T.S: Cytomegalovirus detection in lung transplant biopsy samples by polymerase chain reaction. *J. Heart Lung Transplant.* 13:38-42, 1994.
2. Flint, A. and Weiss S.W.: CD-34 and keratin expression distinguishes solitary fibrous tumor (fibrous mesothelioma) of pleura from desmoplastic mesothelioma. *Hum. Pathol.*, In Press.
3. Martinez, F., Orens, J.B., Deeb, M., Flint, A. and Lynch, J.P., III: Recurrence of sarcoidosis following bilateral allogenic lung transplantation: A case report. *Chest*, In Press.
4. Becker, F.S., Martinez, F.J., Brunsting, L.A., Deeb, G.M., Flint, A. and Lynch, J.P., III: Limitations of spirometry in detecting rejection following single lung transplantation. *Amer. Rev. Resp. Critical Care*, In Press.
5. Park, J., Shinohara, N., Liebert, M., Noto, L., Flint, A. and Grossman, H.B: P-glycoprotein expression in bladder cancer. *J. Urol.* In Press.
6. Mizukami, I.F., Garni-Wagner, B.A., DeAngelo, L.M., Liebert, M., Flint, A., Lawrence, D.A., Cohen, R.B. and Todd, R.F.: Serologic detection of the cellular receptor for urokinase plasminogen activator. *Clin. Immunol. Immunopathol.* In Press.

SUBMITTED PUBLICATIONS:

1. Orens, J.B., Kazerooni, E.A., Curtis, J.L., Martinez, F.J., Gross, B.H., Whyte, R.I., Flint, A. and Lynch, J.P., III: Normal high resolution computed tomographic scans in interstitial lung disease: Report of two cases. *Ann. Intern. Med.*
2. Cherniack, R.M., Colby, T.B., Flint, A., Thurlbeck, W., Waldron, J.A., Jr., Ackerson L, Schwarz, M.I. and King, T.E., Jr.: Correlation of structure and function in idiopathic pulmonary fibrosis. *Amer. Rev. Resp. Critical Care.*

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

1. Martinez, F., Hampton, J., Becker, F., Orens, J., Flint, A., Toews, G. and Lynch, J.P., III: Mortality in idiopathic pulmonary fibrosis (IPF): Predictors prior to high dose corticosteroid therapy. *American Lung Association/American Thoracic Society Annual Meeting*, 1994.
2. Orens, J.B., Becker, F.S., Flint, A., Toews, G.B., Hampton, J., Whyte, R.I., Lynch, J.P., III and Martinez, F.J.: Incremental cardiopulmonary exercise testing in patients with idiopathic

- pulmonary fibrosis correlates with pathologic score of open lung biopsy. American Lung Association/American Thoracic Society Annual meeting, 1994.
3. Liebert, M., Wedemeyer, G., Washington, R., Hubbel, A., Brozovich, M., Flint, A., Faerber, G. and Grossman, H.B.: Loss of urothelial differentiation antigens in interstitial cystitis: Role in urothelial activation. ICA/NIDDK Interstitial Cystitis Scientific Workshop.
 4. Grossman, H.B., Washington, R., Flint, A., Bromberg, J., Kintner, H. and Liebert, M.: Reduced survival in bladder cancer patients with increased expression of the alpha6beta4 integrin. American Urological Association Annual Meeting, San Francisco, California, 1994.
 5. Liebert, M., Wedemeyer, G., Washington, R., Hubbel, A., Brozovich, M., Flint, A., Faerber, G. and Grossman, H.B.: Loss of urothelial differentiation antigens in interstitial cystitis: Role in urothelial activation. American Urological Association Annual Meeting, San Francisco, California, 1994.
 6. Lee, C., Liebert, M., Hubbel, A., Washington, R., Wedemeyer, G., Flint, A. and Grossman, H.B.: Expression of MUC1 antigens in human prostate cancer. American Urological Association Annual Meeting, San Francisco, California, 1994.

**THOMAS FRANK, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. General surgical pathology: approximately 2000 cases.
- B. Gynecologic pathology consultations: approximately 200 cases.
- C. Molecular Diagnostics for Anatomic Pathology.
- D. Weekly interdisciplinary Gynecologic Oncology Tumor Board Review.

II. TEACHING ACTIVITIES:

- A. Sequence coordinator, Oncology course (M2).
- B. M2 medical student lectures:
 - 1. Neoplasia (five hours), January 1994.
 - 2. Gynecology (three hours), March 1994.
- E. Lecturer, three Anatomic Pathology Didactic Conferences.
- F. Monthly Pathology-Gynecology teaching conference for house officers in Obstetrics/Gynecology.

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. Linkage and Mapping of Breast Cancer to Chromosome 17, NIH Grant RO1 CA57601-01, 7/1/91-6/30/97, (5% effort).
- C. Genetic Markers In Gynecologic Malignancy, Harris Foundation, 1/1/92-6/30/95.
- D. 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, 3% effort.
- E. Director, Tissue Procurement Core, 5% effort.

PROJECTS UNDER STUDY:

- A. Genetic alterations in epithelial malignancies of endometrium and ovary (with Rosmarie Caduff, M.D. Visiting Scientist and Carolyn Johnston, M.D., Dept. of Obstetrics and Gynecology).

- B. Analysis 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 the polymerase chain reaction.

IV. **ADMINISTRATIVE ACTIVITIES:**

DEPARTMENTAL:

- A. Director, Preserved Tissue Analysis (Molecular Diagnostics for Anatomic Pathology Specimens).
- B. Surgical Pathology quality assurance/quality control.

UNIVERSITY:

- A. Member, University of Michigan Comprehensive Cancer Center and Director of Tissue Procurement Core.
- 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. Organizer, Annual Symposium: Molecular Diagnostics in Pathology, sponsored by Universities Associated for Research and Education in Pathology, Inc. (UAREP).
- D. Member, American Association for the Advancement of Science.
- E. Member, American Society of Clinical Pathologists.
- F. Member, A. James French Society.

V. **INVITED LECTURES/SEMINARS:**

1. Short course, "Diagnostic Molecular Pathology," with Carolyn Mies M.D., US-CAP, San Francisco, California, March, 1994.
2. Visiting professor, "p53 in Human Neoplasia" Lecture, Medical College of Wisconsin, Milwaukee, Wisconsin, December, 1993.
3. Lecturer, "PCR in Surgical Pathology", Workshop on Molecular Diagnostics in Pathology (Sponsored by Universities Associated for Research and Education in Pathology), Bethesda, Maryland, November, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Goldblum, J.R., Bartos, R.E., Carr, K.A. and Frank, T.S.: Hepatitis B and alterations of the p53 tumor suppressor gene in hepatocellular carcinoma. *Amer. J. Surg. Pathol.* 17:1244-1251, 1993.
2. Ikeda, D.M., Helvie, M.A., Frank, T.S., Chapel, K.L., Andersson, I.T., Linell, F. and Adler, D.D.: Paget's disease of the nipple: Radiologic/pathologic correlation. *Radiol.* 189:89-94, 1993.
3. Perosio, P.M. and Frank, T.S.: Detection of mycobacteria in paraffin-embedded lung biopsies by the polymerase chain reaction. *Amer. J. Clin. Pathol.* 100:643-647, 1993.
4. Elson, B.C., Helvie, M.A., Frank, T.S., Wilson, T.E. and Adler, M.D.: Tubular carcinoma of the breast: mode of presentation, mammographic appearance, and frequency of nodal metastases. *Amer. J. Roentgenol.* 161:1173-1176, 1993.
5. Pearl, M.L., Johnston, C.J., Frank, T.S. and Roberts, J.A.: Synchronous dual primary ovarian and endometrial carcinomas. *Int. J. Gynaecol. Obstet.* 43:305-312, 1993.
6. Mahacek, M.L., Beer, D., Frank, T.S. and Ethier, S.P.: Finite proliferative lifespan *in vitro* of a human breast cancer cell strain isolated from a metastatic lymph node. *Cancer Res. and Treatment* 28:267-276, 1993.
7. Frank, T.S., Bartos, R.E., Haefner, H.K., Roberts, J.A., Wilson, M.D. and Hubbell, G.P.: Loss of heterozygosity and overexpression of the p53 gene in ovarian carcinoma. *Modern Pathology* 7:3-8, 1994.
8. Cook, S.M., Bartos, R.E., Pierson, C.L. and Frank, T.S.: Detection and characterization of atypical mycobacteria by the polymerase chain reaction. *Diagn. Molec. Pathol.* 3:53-58, 1994.
9. Flint, A. and Frank, T.S.: Polymerase chain reaction detection of cytomegalovirus in lung transplant biopsy samples. *J. Heart Lung Transplant.* 13:38-42, 1994.
10. Helm, C.W., Kinney, W.K., Keeney, G., Lawrence, W.D., Frank, T.S., Gore, H., Reynolds, R.K., Soong, S-J., Partridge, E.E., Roberts, J.A., Podratz, K.C. and Shingleton, H.M.: A matched study of surgically treated IB adenosquamous carcinoma and adenocarcinoma of the cervix. *Int. J. Gynecol. Ca.* 3:245-249, 1993.
11. 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.*, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Caduff, R.F., Johnston, C.M. and Frank, T.S.: Mutations of the *Ki-ras* oncogene in carcinoma of the endometrium.
2. Goldblum, J.R., Frank, T.S., Poy, E.L. and Weiss SW: p53 mutations and tumor progression in well-differentiated liposarcoma and dermatofibrosarcoma protuberans.
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.
4. Ikeda, D.M., Frank, T.S. and Marn, C.S.: Case report: Lymphoma of the breast.

5. Walling, D.M., Clark, N., Markovitz, D., Frank, T.S., Braun, D.K. and Raab-Traub, N: Epstein-Barr virus coinfection, replication, and recombination in non-HIV-associated oral hairy leukoplakia.
6. Weber, B.L., Abal, K.J., Couch, F.J., Merajver, S.D., Chandrasekharappa, S.C., Castilla, L., McKinley, D., Ho, P.P., Calzone, K., Frank, T.S., Xu, J., Brody, L.C. and Collins, F.S.: Progress toward isolation of a breast cancer susceptibility gene: BRCA1.

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

1. Frank, T.S., Johnston, C.M., Bartos, R.E. and Caduff, R.F.: Patterns of gene expression and loss in carcinomas of the endometrium vary with histologic subtype [platform presentation, United States-Canadian Academy of Pathology, 1994]. *Modern Pathol*, 7:88A, 1994.
2. Cook, S.M. and Frank, T.S.: Analysis of paraffin sections of Crohn's disease for Mycobacteria paratuberculosis using polymerase chain reaction [poster presentation, United States-Canadian Academy of Pathology, 1994]. *Modern Pathol*. 7:59A, 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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 laboratory section, Pathology 600.
- B. Teaching and supervision of five Pathology house officers participating in two-week Pathology Data Systems rotations throughout the year.

MEDICAL SCHOOL/HOSPITALS:

- A. Program Director of the Twelfth Annual Clinical Laboratory Computer Symposium at the Towsley and Power Centers, June 8-10, 1993. Symposium attracted 210 registrants and 36 vendors.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- 1. Development of a vendor-supported fax server, LIS-FAX, to distribute year-round information about laboratory information systems and LIS vendors to callers from around the country.
- 2. Grant of \$5,000 from the Ameritech Foundation through the Consortium for Research on Telecommunications Policy to study Community Health Information Networks with Professor Will Mitchell, Department of Corporate Strategy, University of Michigan Business School
- 3. Commitment to write a chapter on Community Health Information Networks for an upcoming book on telemedicine edited by Professor Rashid Bashshur of the School of Public Health.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Chairman, Internal Review Committee for the Department of Pathology.
- B. Clinical Laboratory Directors Committee.
- C. Quality Assurance Committee.

HOSPITAL:

- A. Chief Information Officer Management Team (CIOMT), University of Michigan Medical Center.

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 for Pathology Patterns, an upcoming supplement to the American Journal of Clinical Pathology on pathology informatics
- 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. Invited Lecturer, "Managing the Information Product of Pathology: A Tactical and Strategic Overview", a lecture presented to the house officers and staff of the Department of Pathology, the University of Alabama at Birmingham, Birmingham, Alabama, October 12, 1993.
2. "Integrating Medical Information in the 1990s", a workshop presented at the ASCP Fall Meeting, Orlando, Florida, October 20, 1993.
3. "Pathology Informatics: Means to an End of Dead End. Managing the Information Product of Pathology: A Tactical and Strategic Overview", two lectures delivered while a Visiting Professor at the Emory University School of Medicine, Atlanta, Georgia, November 8-9, 1993.
4. "Informatics in the Clinical Laboratory", a two-hour teleconference sponsored by the Catholic University of America as part of a graduate course in clinical laboratory management, April 21, 1994.

5. "Healthcare Reform and the Changing Role of the Phlebotomist", a lecture delivered at a symposium entitled "The Phlebotomy Team: Technical and Management Perspectives" presented at the University of Michigan Medical School, Ann Arbor, Michigan, April 22, 1994.
6. "Laboratory Information Processing in the year 2000", the keynote lecture delivered at the annual user group meeting of CHC, a vendor of a laboratory information system, Houston, Texas, April 24, 1994.
7. "Healthcare Reform: Implications for the Information Manager in the Clinical Laboratory", a lecture presented to the 12th Annual Laboratory Information System Symposium, Ann Arbor, Michigan, June 9, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Friedman, B.A. and Napolitan, E.J.: Selecting and managing a professional consultant to a clinical laboratory. Clin. Lab. Manage. Rev., In Press.
2. Friedman, B.A., Mitchell, W. and Singh, K.: Differentiating between marketing-driven and technology-driven vendors of medical information systems. Arch. Pathol. Lab. Med., In Press.
3. Friedman, B.A.: The laboratory information float, time-based competition, and point-of-care testing. Clin. Lab Manage. Rev., In Press.

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

1. Friedman, B.A. and Napolitan, E.J.: A second look at some clinical laboratory dogma. Med. Lab. Obs. (MLO) March: 53-55,1993.
2. Friedman, B.A.: Flounder factors and the laboratory information system. Vision March/April: 13-15,1993.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

I. CLINICAL ACTIVITIES:

- A. Director, General Chemistry Laboratory.
- B. Daily sign-out and interpretation of electrophoresis results.
- C. Direct operation of blood gas-electrolyte analyzers in 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. Other
 - 1. Dissertation Committee, Godwin Ogbonna, Department of Biochemistry, University of Windsor.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Evaluation of an assay for troponin T as an early marker for myocardial infarction.
- B. Development of an HPLC assay for iohexol and validation of plasma iohexol clearance as an indicator of glomerular filtration rate.
- C. Measurement of plasma concentration of atrial natriuretic factor in patients with congestive heart failure.
- D. Evaluation of portable instruments for the measurement of prothrombin time in a satellite clinic setting.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Quality Assurance Committee.
- B. Director, Chemistry Section.
- C. Coordinator, Chemistry Lab Supervisors Meetings.
- D. Coordinator, Clinical Chemistry In-Service Education Program.

MEDICAL SCHOOL/HOSPITAL:

- A. Glucose Monitoring/Bedside Testing Work Group.

REGIONAL AND NATIONAL:

- A. Past-Chair, Michigan Section, AACC.
- B. Editor, Michigan Section AACC Newsletter.
- C. Coordinator, College of American Pathologists Clinical Chemistry Standards Assay Laboratory.
- D. Lipids and Lipoproteins Division, AACC.
- E. Education Committee, Michigan Section, AACC.
- F. Member, Clinical Ligand Assay Society.
- G. Member, American Association of Pathologists.
- H. Manuscript Reviewer for "Clinical Chemistry"

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. "Improvements in Assays of Biochemical Markers for Myocardial Infarction", Michigan State Medical Technologist western region meeting. Kalamazoo, Michigan, October, 1993.
- 2. "Tumor Markers", Department of Chemistry and Biochemistry, University of Windsor, April, 1994.
- 3. "Apolipoproteins as Predictors of Risk for Coronary Disease", Michigan State Medical Technologists Annual Meeting, Romulus, Michigan, April, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Spengler, R.N., Chensue, S.W., Giacherio, D.A., Blenk, N. and Kunkel, S.L.: Endogenous norepinephrin regulates tumor necrosis factor-alpha production from macrophages in vitro. J. Immunol. 152:3024-3031, 1994.
- 2. O'Connell, T.D., Giacherio, D.A., Jarvis, A.K., and Simpson, R.U. Inhibition of cardiac myocyte maturation by 1,25 dihydroxyvitamin D₃. Endocrinology, Accepted for Publication.

ABSTRACTS:

- 1. Giacherio, D.A., and Matz, K.: Evaluation of the BMD troponin T assay in the diagnosis of acute myocardial infarction. Michigan Section AACC Spring Symposium, May 20, Frankenmuth, Michigan.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology - Room I and Room II, eight weeks. 7/1-12/31/93.
- B. Diagnostic Electron Microscopy - share nephropathology work with Drs. Kent Johnson and Paul Killen. 7/1-12/31/93.
- C. Consultation service for Uropathology. 7/1-12/31/93.
- D. Conduct monthly conference in Urologic Pathology with Urology Section. 7/1-12/31/93.
- E. Participate in weekly Renal Biopsy Conference for Nephrology Section with Drs. Kent Johnson and Paul Killen. 7/1-12/31/93.
- F. Frozen Section "on call" Rotation, 30 days. 7/1-12/31/93.
- G. Consultant, Veterans Administration Hospital.

II. TEACHING ACTIVITIES:

- A. Renal and Urinary Tract Sequence for M-2 students. 20 hours, Fall Term 1993.
- B. Lecture on Urologic Pathology to Dental Pathology 630 students. Fall Term 1993.
- C. Pathology Resident Teaching. Lecture on Renal Disease Fall Term 1993.
- D. Pathology Lab Section for M-1 students. Winter term 1994.

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. NCAA, NFL, U.S. Olympic Committee, American Association Clinical Chemists and College of American Pathologists Committee on Sports Drug Testing Laboratory Accreditation.

- E. Chairman, Board of Directors, Public Citizen, Inc. (Ralph Nader, Initial Chairman and Founder).
- F. College of American Pathologists Laboratory Inspection Team.

V. **OTHER RELEVANT ACTIVITIES:**

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

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

None.

**DAVID GORDON, M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. Supervision of Autopsies (six weeks).
- B. Cardiovascular Pathology Consultation (Autopsy Service).
- C. Cardiovascular Surgical Pathology.

II. TEACHING ACTIVITIES:

- A. Lecturer, Biomedical Summer Research Program for Minority Students.
- B. Laboratory instructor for Pathology Laboratories for M2 curriculum.
- C. Atherosclerosis lecture: Cardiovascular Sequence (M2)

III. RESEARCH ACTIVITIES:

- A. Patterns of growth factor gene expression and cell proliferation in human atherosclerosis and transplant arteriosclerosis.
- B. Patterns of collagen type gene expression in human atherosclerosis and transplant arteriosclerosis.
- C. Evaluation of the effects of specific genes transferred into the artery wall (collaborative research with Gary and Elizabeth Nabel, Department of Internal Medicine).
- D. Immunosuppressive modifications of transplant rejection (collaborative research with Larry Turka and Hua Lin in Depts. of Internal Medicine and Surgery).
- E. The pathobiology of arterial stenting (collaborative research with David Muller, Division of Cardiology).
- F. Studies of the effects of pulmonary artery pressure on wall cell proliferation and collagen synthesis (collaboration with Dr. Thomas Kulik, Pediatric Cardiology).
- G. Studies of cell proliferation and collagen gene expression in allografted aortic valves in rats (collaboration with Dr. Mark Lupinetti, Thoracic Surgery).
- H. Studies of the interactions between leukocyte adhesion and intimal thickening in transplant arteriosclerosis (collaboration with Parke-Davis).
- I. Pathology support for ongoing melanoma gene transfer studies (Gary Nabel, P.I.).
- J. Organizer of the Vascular Biology Forum Journal Club.

SPONSORED SUPPORT:

- A. Principal Investigator, "Proliferation and Growth Factors in Atherosclerosis", National Institutes of Health, HL42119, five years, \$710,820, 1988-1993 (now in no cost extension).
- B. Principal Investigator (Michigan Subcontract), "Cells and Molecules Mediating Graft Atherosclerosis", HL43322, five years \$284,743, 1989-1994.
- C. Principal Investigator, "Vascular Biology Patterns of Collagen Gene Expression in Human Atherosclerosis", AHA 93013780, three years, \$120,000, 1993-1996.
- D. Principal Investigator, "The Patterns of Collagen Synthesis During Arterial Restenosis", AHA Michigan, one year, \$25,994. 1993-1994.

- E. Collaborating Investigator, 10% effort (Principal Investigator: Elizabeth G. Nabel, Cardiology), "Expression and Function of Recombinant TGF- β in Arteries.=", NIH DK42706, 1993-1998

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Interviewer - Candidates for faculty and house officer positions.

MEDICAL SCHOOL/HOSPITAL:

- A. Cardiovascular Research Center, Executive Committee.
B. Dean's Advisory Focus Group.
C. Dean's Diversity Advisory Group.

REGIONAL AND NATIONAL:

- A. National American Heart Association Grant-in-Aid review committee.
B. American Heart Association of Michigan Grant-in-Aid review committee.
C. United Network for Organ Sharing (UNOS) Minority Advisory Committee.

INVITED LECTURES/SEMINARS:

1. Poster session moderator, National American Heart Association meeting in Atlanta, 1993.
2. Invited speaker, "Cell proliferation in Human Atherosclerosis", University of Michigan Pediatric Cardiology division., Ann Arbor, Michigan, February, 1994.
3. Invited speaker, "Cell Proliferation and Collagen Gene Expression in Human Atherosclerosis", Cleveland Clinic Vascular Biology Group, Cleveland, Ohio, February, 1994 .
4. Invited speaker, "Cell Proliferation and Collagen Gene Expression in Human Atherosclerosis", University of Michigan Department of Pathology, February, 1994 .
5. Invited speaker, "Cell Proliferation and Collagen Gene Expression in Human Atherosclerosis", Society for Biomaterials, Boston, Massachusetts, April, 1994.
6. Invited speaker, "Cell Proliferation in Human Atherosclerosis", University of Michigan Pediatric Cardiology division, April, 1994 ("Collagen gene expression in human atherosclerosis.").
7. Invited speaker, "Cell Proliferation in Human Atherosclerosis", North American Vascular Biology Organization (NAVBO) meeting in Anaheim, California, April, 1994.
8. Invited speaker, "Cell Proliferation and Vlllgen Gene Expression in Human Atherosclerosis", University of Toronto, Toronto, Ontario, Canada, May 1994.
9. Invited speaker, "Cell Proliferation and Collagen Gene Expression in Human Atherosclerosis", University of Michigan Vascular Academic Medicine seminar series, Ann Arbor, Michigan, May, 1994.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Rekhter, M.D., Zhang, K., Narayanan, A.S., Phan, S., Schork, M.A. and Gordon, D.: Type I collagen gene expression in human atherosclerosis: Localization to specific plaque regions. *Am. J. Pathol.*, 143:1634-1648, 1993.
2. Nabel, G.J., Nabel, E.G., Yang, Z., Fox, B.A., Plautz, G.E., Gao, X., Huang, L., Shu, S., Gordon, D. and Chang, A.E.: Direct gene transfer with DNA-liposome complexes in melanoma:

- Expression, biologic activity, and lack of toxicity in humans. *Proc. Natl. Acad. Sci. USA* 90:11307-11311, 1993.
3. San, H., Yang, Z., Pompili, V.J., Jaffe, M.L., Plautz, G.E., Xu, L., Felgner, J.H., Wheeler, C.J., Felgner, P.L., Gao, X., Huang, L., Gordon, D., Nabel, G.J. and Nabel EG: Safety and short-term toxicity of a novel cationic lipid formulation for human gene therapy. *Human Gene Therapy* 4:781-788, 1993.
 4. Beach, K.W., Hatsukami, T., Detmer, P.R., Primozech, J.F., Ferguson, M.S., Gordon, D., Alpers, C.E., Burns, D.H., Thackray, B.D. and Strandness, D.E.: *Stroke*. 24, 314-319, 1993
 5. Zhang, K., Rekhter, M.D., Gordon, D. and Phan, S.H.: Myofibroblasts and their role in lung collagen gene expression during pulmonary fibrosis. *Am. J. Pathol.* 145:114-125, 1994.
 6. Muller, D.W.M., Golomb, G., Gordon, D. and Levy, R.J.: Site-specific dexamethasone delivery for the prevention of neointimal thickening after vascular stent implantation. *Coronary Artery Disease* 5:435-442, 1994.
 7. Gibran, N.S., Isik, F.F., Heimbach, D.M. and Gordon, D.: Basic fibroblast growth factor in the early human burn wound. *J. Surg. Res.* 56:226-234, 1994
 8. Rekhter, M.D. and Gordon, D.: Cell proliferation and collagen synthesis are two independent events in human atherosclerotic plaques. *J. Vasc. Res.*, In Press.
 9. Rekhter, M.D. and Gordon, D.: Does PDGF-A stimulate proliferation of arterial mesenchymal cells in human atherosclerotic plaques?, *Accepted Circ. Res.*, 1994).
 10. Ohno, T., Gordon, D., San, H., Pompili, V.J., Imperiale, M.J., Nabel, G.J. and Nabel, E.G.: Inhibition of vascular smooth muscle cell proliferation following arterial injury by genetic intervention. *Science*, In Press, 1994.

CHAPTERS:

1. Gordon, D. and Rekhter, M.D.: Chapter 11: Cell proliferation and collagen gene expression in human myointimal hyperplasia. in *myointimal hyperplasia*, in, Philip B. Dobrin (ed), copyright R.G. Landes Co., 1994, In Press.

ABSTRACTS:

1. Rekhter, M.D., Schwartz, S.M., O'Brien, E., Simpson, J.B. and Gordon, D.: Collagen I gene expression in human coronary lesions, primary atherosclerosis versus restenosis. *Circulation* 88(4):I-228a, 1993.

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

ANNUAL DEPARTMENTAL REPORT
1 AUGUST 1993 - 30 JUNE 1994

I. CLINICAL ACTIVITIES:

- A. General surgical pathology - three and one-half months.
- B. Gastrointestinal and hepatic pathology consultation services - six months.
- C. Liver transplant pathology - six months.
- D. Multidisciplinary GI tumor board - every other week.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Medical Students:
 - 1. Pathology 600 - one full class lecture (1 contact hour).
 - 2. Pathology Sequence Coordinator for endocrinology subunit (60 contact hours).
 - 3. One hour CPC on Whipple's disease, February, 1993.
- B. House Officers:
 - 1. Surgical pathology diagnosing room instruction for house officers - 3 1/2 months.
 - 2. Two didactic lectures on gastrointestinal pathology - May, 1993.
 - 3. Gastrointestinal and hepatic pathology tutoring - six months.
 - 4. Four consultation conferences.
- C. Interdepartmental:
 - 1. Liver biopsy conference - one hour per month.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

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 Moll 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, Henry Appelman, and Bob Merion from the Division of Transplantation Surgery.
- E. Treatment of ulcerative colitis with vitamin E derivatives with Grace Elta, Division of Gastroenterology.
- F. Histologic comparison of the effects of bowel preps on colonic biopsies with the Division of Gastroenterology.
- G. Study of MALT lymphomas arising in Helicobacter pylori gastritis with Eric Hsi, Henry Appelman, and Charlie Ross.
- H. Study of kinetics of gastric and duodenal mucosa after endoscopy with Jim Scheiman, Division of Gastroenterology and Tom Frank.
- I. Study of colorectal carcinoma metastases with collaborators at Ohio State University.
- J. Immunophenotypic analysis of hepatitis C and acute rejection in liver transplant allografts with collaborators at Ohio State University.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Co-Coordinator, Surgical Pathology Staff Service Rotations.
- B. Interviewed house officer candidates and surgical pathology fellowship candidates.

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. Panelist, Liver Pathology Specialty Conference, United States and Canadian Division of the International Academy of Pathology Meeting, San Francisco, California, March, 1994.
2. Lecturer, "Hepatitis C, An Iverview", Catherine McAuley Health Center, Department of Pathology, Ann Arbor, Michigan, June 2, 1994.
3. Guest Speaker, "AIDS Enteropathy", Seventh Annual Nathan B. Friedman Alumni Dinner and Lecture, Cedars-Sinai Medical Center, Los Angeles, California, June 9, 1994.
4. Guest Speaker, "The Differential Diagnosis of Colitis on Endoscopic Biopsy Specimens", M-Labs Symposium, Ann Arbor, Michigan, January, 1994.

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

1. Greenson, J.K., Isenhardt, C.E., Rice, R., Mojzisek, C., Houchens, D. and Martin, E.W., Jr: Identification of occult micrometastases in pericolic lymph nodes of Dukes' B colorectal cancer patients using monoclonal antibodies against cytokeratin and CC49: Correlation with long-term survival. *Cancer* 73:563-569, 1994.
2. Brainard, J.A., Greenson, J.K., Vesey, 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*, In Press.
3. 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.*, In Press.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. 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. Submitted to *Cancer*.
2. 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 ¹²⁵I-Radiolabeled Monoclonal Antibody CC49. Submitted to *Cancer*.
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. Submitted to *Transplantation*.

BOOK CHAPTERS:

1. Hitchcock, C.L., Greenson, J.K., Sampel, J.W., Houchens, D.P., Saad, A., Isenhardt, C.E., Schneebaum, S. and Cote, R.J.: RIGS pathology and the biologic staging of colorectal carcinomas, in, Martin, E.W., Jr. (ed), *Radioimmunoguided Surgery*, Copyright 1994.

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

1. Gasior, A.E., Tesi, R.J., Kirkpatrick, R. and Greenson, J.K.: Immunophenotypic comparison of hepatitis C virus (HCV) infection and acute rejection (AR) in orthotopic liver transplants (OLT), Platform presentation at the USCAP Meeting, March 14, 1994. *Mod. Pathol.* 7:131A, 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. D.D.S. Level:
 - a. Oral Pathology 694. (Sophomore Core Course).
 - b. Oral Pathology 824. (Senior Dental Students, Advanced Topics in Oral Pathology).
- B. Graduate Dental Level:
 - a. Oral Pathology 694 (Graduate Core Course).
- C. Dental Hygiene Level:
 - a. Dental Hygiene 494 (Clinical Oral Pathology).
 - b. Dental Hygiene 293 (General/Oral Pathology).
- D. Graduate Level Advisement:
 - a. Nahed Mohsen - PhD Program (Engineering) - two years.
 - b. Pin-Pin Lin - PhD Program (School of Public Health) - one year.
 - c. Somjin Ratanasathien, M.S. Program (Dental School; Restorative) - one year.
 - d. Zhilin Sun, M.S. Program (Dental School, Biological Material Science), two years.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Director and Co-Principal Investigator for one of four projects, "Specialized Materials Science Research Center", NIDR, P50-DE09296-4 A I, 30% for this last year (10% of this is cost-shared with the dental school), \$2,657,883 for direct costs, \$500,00/year, total period, 9/29/89-9/28/94.
- B. Participating Investigator, "Restorative Dental Materials", Training Grant, NIDR, T32-DE07057-16, 10% for this last year, \$258,586 for direct costs, \$140,000/year, total period, 7/1/91-6/30/96.
- C. Consultant, "A Study of Gallium Alloys as Dental Restorative Materials", NIDR, R01-DE10178-01AI, \$100,000/yr, 8/1/93-7/31/96.

PENDING:

- A. Co-Principal Investigator and Co-Director, "Specialized Materials Science Research Center (five-year renewal), NIDR, P50-DE09296-06-10, \$500,000/year, 9/29/94-9/28/99.
- B. Principal Investigator, "Resin and BMP Effect on Odontoblast-like Gene Expression", NIDR, \$277,000/year, 12/1/94-11/30/98.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director of Research, School of Dentistry, 1989-1994.
- B. Admissions Committee, School of Dentistry, 1985-1993.
- C. Hazardous Waste Committee, School of Dentistry, 1987-1994, Chairman.
- D. Table Clinics Committee, 1989-1994.
- E. Organizer of Specialized Materials Center Fall Conference, 1990 -1994.
- F. Biomedical Research Council, University of Michigan Medical School, 1990-1994.
- G. Research Advisory Committee, Department of Surgery, University of Michigan Medical School, 1990-1994.
- H. Research Dean's Committee (OVPR, U/M), 1989-1994.
- I. Chair, Search Committee for Biomaterials faculty, 1992-1994.
- J. Research Space Utilization Committee, Dental School, 1991-1994.

REGIONAL AND NATIONAL:

- A. ADA Subcommittee on Biological Evaluation of Dental Materials (Committee Member), 1987-1994.
- B. U.S. Technical Advisory Group for International Standards Organization Tissue Culture Group 194: Biological Evaluation of Medical and Dental Materials and Devices (Nominated Member), 1989-1994.
- C. External Review Board for NIDR Program Project in Materials Science, University of Missouri at Kansas City, 1990-1994.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

- A. Consultant, W. R. Grace Co.
- B. Consultant, Kerr Manufacturing Co.
- C. Consultant, Paladin Medical (Baxter).
- D. Special Study Sections, NIDR, 1988-1994.
- E. International Association for Dental Research.
- F. American Academy of Oral Pathology.
- G. American Association for the Advancement of Science.
- H. Omicron Kappa Upsilon.
- I. Tissue Culture Association (National).
- J. New York Academy of Sciences.
- K. Sigma Xi.
- L. American Association of Dental Schools.

EDITORIAL REVIEW BOARDS:

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

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

1. Hanks, C.T., Fat, J.C., Wataha, J.C. and Corcoran, J.F.: Cytotoxicity and dentin permeability of carbamide peroxide and hydrogen peroxide vital bleaching materials, *in vitro*. J. Dent. Res. 72:931-938, 1993.
2. Wataha, J.C., Hanks, C.T. and Craig, R.G.: The effect of cell monolayer density on the cytotoxicity of metal ions which are released from dental alloys. Dent. Mater. 9:172-176, 1993.
3. Wataha, J.C., Hanks, C.T. and Craig, R.G.: The *in vitro* effects of metal ions on cellular metabolism and the correlation between these effects and the uptake of the ions. J. Biomed. Mater. Res. 28:427-433, 1994.
4. Hanks, C.T., Wataha, J.C., Parsell, R.R., Strawn, S.E. and Fat, J.C.: Permeability of biological and synthetic molecules through dentin. J. Oral Rehabil., In Press, May, 1994.
5. Wataha, J.C., Hanks, C.T., Stawn, S.E. and Fat, J.C.: Cytotoxicity of components of resins and other restorative dental materials. J. Oral Rehabil., In Press, May, 1994.
6. Jontell, M., Hanks, C.T., Bratel, J. and Bergenholtz, G.: Effect of unpolymerized resin components on the function of spleen cells and accessory cells derived from the rat incisor pulp. J. Dent. Res., Submitted, February, 1994.
7. Wataha, J.C., Hanks, C.T. and Sun, Z.L.: Effect of cell line on *in vitro* metal ion cytotoxicity. Dent. Mater., Accepted for publication, May, 1994.

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

1. Hanks, C.T., Takagaki, K., Wataha, J.C. and Takagaki, M.: Complement activation by resin components. J. Dent. Res. 73:IADR Abst. 143, 1994.
2. Wataha, J.C., Hanks, C.T. and Sun, Z.L.: Effect of cell line on *in vitro* metal ion cytotoxicity. J. Dental Res. 73:IADR Abst. 1535, 1994.
3. Nassiri, M.R., Robinson, J.P., Hanks, C.T. and Craig, R.G.: Effect of biomaterial oligomers on differentiation-specific surface HL-60 cells antigen. J. Dental Res. 73:IADR Abst. 1823, 1994.
4. Sun, Z.L., Wataha, J.C. and Hanks, C.T.: Effects of metal ions on ROS 17/2.9 osteoblast-like cell metabolism. J. Dent. Res. 73:IADR Abst. 2389, 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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. Test Committees For Dermatopathology, American Boards of Pathology and Dermatology.
- B. Board of Directors, National Alopecia Areata Foundation.

V. **OTHER RELEVANT ACTIVITIES:**

HONORS:

- A. Pathology Residents Teaching Award 1993-1994
- B. Fellow, Royal College of Medicine

INVITED LECTURES AND SEMINARS:

- 1. Invited Presentation, "A Tutorial in the Diagnosis of Alopecia", American Society of Dermatopathology, Washington, D.C., December, 1993.
- 2. Visiting Professor and Lecturer: Boston University, July, and August, 1993.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. None.

BOOKS/CHAPTERS IN BOOKS

- 1. None.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. Pediatric Surgical and Placental Pathology, daily, twelve months.
- B. Pediatric Necropsies, daily, twelve months.
- C. Pediatric Consultation Cases, daily, twelve months.
- D. Adult Necropsy Service, 0.50 months.
- 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 all pathological material and data necessary for all children registered in national tumor protocols. (Collaborating investigator, NCI #2-U10-CA-02971-33, CCSG, R. Hutchinson, M.D., P.I.).

II. TEACHING ACTIVITIES:

- A. M2: Pathology 600, two hours with class as part of Congenital Heart Sequence of new curriculum.
- B. M4: Pediatric Surgical Pathology, twelve months, while they were on their pathology electives.
- C. House Officers in Pathology, daily reading of pediatric surgicals, twelve months.
- D. House Officers in Pathology, gross and microscopic supervision of most pediatric necropsies, twelve months, and adult cases, 0.50 months plus on-call weekends.
- E. Two Core Curriculum lectures on Pediatric Pathology to Pathology House Officers.
- F. Lecture on Pediatric Necropsy Pathology in Orientation for new House Officers in Pathology.
- G. Gross Necropsy Conference, one hour/week, twelve months.
- H. Supervised Pediatric Hematology Fellows (two) for AP elective period.
- I. 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. Multi-institutional study of molecular variants of congenital alveolar proteinosis caused by inherited surfactant protein B deficiency. (See papers.)
- D. Study of the occurrence of early mucosal colitis as a predictor of future enterocolitis in patients with Hirschsprung's disease with pediatric surgeons. (See abstracts.)
- E. Study of myocardial ventricular fibrosis in various congenital heart defects, with Pediatric Cardiologists.
- F. 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 Hernandez, Ramiero, 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.

REGIONAL AND NATIONAL:

- A. Member, CAP Council on Anatomic Pathology's Autopsy Committee.
- 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. Heidelberg, K.P., Ritchey, M.L., Dauser, R.C., McKeever, P.E. and Beckwith, J.B.: Congenital mesoblastic nephroma metastatic to the brain. *Cancer* 72:2499-2502, 1993.
2. Castle, V.P., Heidelberg, K.P., Bromberg, J., Ou, X., Dole, M. and Nunez, G.: Expression of the apoptosis-suppressing protein Bcl-2, in neuroblastoma is associated with unfavorable histology, and N-myc amplification. *Am. J. of Pathol.* 143:1543-1550, 1993.
3. Freiberg, A.A., Loder, R.T., Heidelberg, K.P. and Hensinger, R.N.: Aneurysmal bone cysts in young children. *J. Pediatr. Orthoped.* 14:86-91, 1994.

4. deMello, D.E., Noguee, L.M., Heyman, S., Krous, H.F., Hussain, M., Merrit, T.A., Hsueh, W., Haas, J.E., Heidelberg, K.P., Schmacher, R and Colten, H.R. Molecular and phenotypic variability in the congenital alveolar proteinosis (CAP) syndrome associated with inherited surfactant protein B (SP-B) deficiency. *J. Pediatr.*, In Press.
5. Hutchins, G.M. and The Autopsy Committee of the College of American Pathologists: (Kathleen P. Heidelberg, Member): Practice Guidelines for autopsy pathology: Autopsy performance. *Arch. Pathol. Lab. Med.* 118:19-25, 1994.
6. Hanzlick, R. and, The Autopsy Committee of the College of American Pathologists, (Kathleen P. Heidelberg, Member): Cause of Death Statements. Guidelines for Pathologists., College of American Pathologists, Northfield, Illinois, In Press.

ABSTRACTS AND INVITED SUBMISSIONS:

1. Elhalaby, E.A., Teitelbaum, D.H., Coran, A.G. and Heidelberg, K.P.: Enterocolitis associated with Hirschsprung's disease: A clinicopathologic correlative study. Presented by Kathleen P. Heidelberg at the Annual Meeting, Society for Pediatric Pathology, San Francisco, March 13-14, 1994. *Mod. Pathol.* 7:3P, 1994, and *Lab. Invest.* 70:1994.
2. Nunez, G., Dole, M.G., Heidelberg, K.P. and Castle, V.P.: The Bcl - 2 oncogene is a novel prognostic marker for neuroblastoma and confers resistance to chemotherapy. Presented by Dr. Nunez at the United States and Canadian Academy of Pathology meeting, San Francisco, March 15, 1994. *Mod. Pathol.* 7:147A, 1994 and *Lab. Invest.* 70, 1994.
3. Heidelberg, K.P.: Case AU-B-09-1993. The College of American Pathologists' Autopsy Pathology Apex Program, Fall, 1993.
4. Heidelberg, K.P. and Silveira, S.: Case #AU-A-05-1994. The College of American Pathologists' Autopsy Pathology Apex Program, Winter, 1994.
5. Heidelberg, K.P. and Henricks, W.: Case #AU-A-01-1995, The College of American Pathologists'. Autopsy Pathology Apex Program, Winter, 1995. (Accepted.)

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993- 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. With C.J. D'Amato prepare microscopic descriptions of most University of Michigan autopsy brains for the Pathology House Officers which after review with the officers are incorporated into the final autopsy report. We also examine many of the brains sent to the Department for diagnosis, and prepare gross and microscopic descriptions. Many of these brains are from patients with clinical dementia.

II. TEACHING ACTIVITIES:

- A. Review microscopics of some of the above brains with house officers in Pathology and other house officers spending time in the department of Pathology.
- B. Neuropathology 858, a laboratory - lecture course for house officers and fellows in Pathology, Neurology, Neurosurgery, Neuroradiology and other areas, graduate students and occasionally faculty and undergraduate students. 18 hours including two lectures.

III RESEARCH ACTIVITIES:

- A. Pathologic studies of the autopsy brains or surgical biopsies of people with various forms of dementia or certain tumors in collaboration with members of the Department of Neurology and Neuroradiology.

IV. PUBLICATIONS:

1. Lloyd, R.V., D'Amato, C.J., Thiny, M.T., Jin, L., Hicks, S.P. and Chandler, W.F.: Corticotroph (basophil) invasion of the pons nervosa in the human pituitary: localization of proopiomelanocortin peptides, galanin and peptidy glycine α -Amidating monooxygenase-like immunoreactivities. *Endocrine Pathology* 4:86-94, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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 for five years.
- B. Principal Investigator, "Oxidants and Glomerular Injury", Project V, Renal Center Grant. National Institutes of Health, \$246,585 for 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. Cyclosporine-induced nephrotoxicity.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

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, New York, Department of Anesthesiology.
2. Invited participate, Symposium on Renal Transplantation, University of Michigan.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Mulligan, M.S., Johnson, K.J., Smith, C.W., Anderson, D.C. and Ward, P.A.: Requirements for leukocyte adhesion molecules in nephrotoxic nephritis. *J. Clin. Invest.* 91:577-587, 1993.
2. Zador, I.Z., Deshmukh, G.O., Kunkel, R., Johnson, K.J., Radin, N.S. and Sheyman, J.A.: A role for glycosphingolipid accumulation in the renal hypertrophy of streptozotocin-induced diabetes mellitus. *J. Clin. Invest.* 91:797-803, 1993.
3. Chan, L.S., Yancey, K.B., Hammerburg, C., Kaz Soong, H., Regezi, J.A., Johnson, K.J. and Cooper, K.D.: Immune-mediated subepithelial blistering diseases of mucous membranes. *Arch. Dermatol.* 129:448-455, 1993.

4. Tait, A.R., Davidson, B.A., Johnson, K.J., Remick, D.G. and Knight, P.R.: Halothane inhibits the intraalveolar recruitment of neutrophils, lymphocytes and macrophages in response to influenza infection in mice. *Anest. Analg.* 76:1106-1113, 1993.
5. Knight, P.R., Rutter, T., Tait, A., Coleman, E. and Johnson, K.J.: Pathogenesis of gastric particulate lung injury: A comparison and intervention with acidic pneumonia. *Anest. Analg.* 77:1-7, 1993.
6. Richardson, B.C., Buckmaster, T., Keren, D.F. and Johnson, K.J.: Evidence that macrophages are programmed to die after activating autologous, cloned antigen specific, CD4+ T cells. *Eur. J. Immunol.* 23:1450-1455, 1993.
7. Johnson, K.J. and Weinberg, J.M.: Post-ischemic renal injury due to oxygen radicals. *Current Opinion in Nephrology and Hypertension* 2:625-635, 1993.
8. Quddus, J., Johnson, K.J., Gavalchin, J., Amento, E., Crisp, C. and Richardson, B.: Treating activated CD4+ T cells with either of two distinct DNA methyltransferase inhibitors, 5-azaeylidine or pro-caenamidine, is sufficient to cause a lupus-like disease in syngeneic mice. *J. Clin. Invest.* 92:38-53, 1993.
9. Hirschl, R.B., Tooley, R., Parent, A., Johnson, K.J. and Bartlett II, R.H.: Partial liquid ventilation improves gas exchange in the setting of respiratory failure during extracorporeal life support (ECLS). *Surg. Forum* 646-649, 1993.
10. Mulligan, M.S., Desrochers, P.E., Chennaiyan, A.M., Gibbs, D.F., Johnson, K.J. and Weiss, S.J.: *In vivo* suppression of immune complex-induced alveolitis by secretory leukoprotease inhibitor and tissue inhibitor of metalloproteinase-2. *Proc. Natl. Acad. Sci. USA* 90:11523-11527, 1993.
11. Shayevitz, J.R., Johnson, K.J. and Knight, P.R.: Halothane-oxidant interactions in the *ex vivo* perfused rabbit lung: edema formation and eicosanoid production. *Anesthes.* 79:129-38, 1993.
12. Colletti, L.M., Johnson, K.J., Kunkel, R.G. and Merion, R.M.: Mechanism of hyperacute rejection in porcine liver transplantation: Antibody mediated endothelial injury. *Transplantation* 57:1357-1363, 1994.
13. Andrews, 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. *J. Vet. Pathol.*, 31:293-300, 1994.
14. Ward, P.A. and Johnson, K.J.: Lung inflammatory mechanisms. *J. Human Pathol.*, In Press.
15. Ward, P.A., Warren, J.S., Remick, D., Varani, J., Gannon, D. and Johnson, K.J.: Cytokines and oxygen radical mediated tissue injury, in Shoemaker, W.C. (ed.), *New Horizons III, Critical Care Medicine*, In Press.
16. Ward, P.A., Johnson, K.J., Till, G.O.: Mechanisms of lung injury. *Prax. Klin. Pneumonol.*, In Press.
17. Varani, J., Ginsburg, I., Johnson, K.J., Gibbs, D.F., Weinberg, J.M., Ward, P.A.: Amino acids and metal ions protect endothelial cells from lethal injury. *FASEB J.*, In Press.
18. Knight, P.R., Druskovich, G., Tait, A.R. and Johnson, K.J.: The role of neutrophils, oxidants and proteases in the pathogenesis of acid pulmonary injury. *Anest.*, In Press.
19. 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.
20. Hirschl, R.B., Parent, A., Tooley, R., McCracken, M., Johnson, K.J., Shaffer, T., Wolfson, M. and Bartlett, R.H.: Liquid ventilation improves pulmonary function and gas exchange in the setting of respiratory failure. *Annals Surg.*, In Press.

21. Colton, D., 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*, In Press.
22. 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.*, In Press.
23. 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.*, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. 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. Submitted for publication.
2. 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.
3. Richardson, B.C., Lalwani, N.D., Johnson, K.J. and Mark, R.M.: FAS ligation triggers apoptosis in macrophages but not endothelial cells. Submitted for publication.
4. Hirschl, R.B., Parent, A., Tooley, R., McCracken, M., Johnson, K.J., Shaffer, T., Wolfson, M. and Bartlett, R.H.: Liquid ventilation improves pulmonary function, gas exchange and lung injury in a model of respiratory failure. Submitted for publication.
5. 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.
6. Hirschl, R.B., Tooley, R., Parent, A., Johnson, K.J. and Bartlett, R.H.: Partial liquid ventilation (PLV) improves gas exchange, pulmonary function, and lung injury in the setting of severe respiratory failure. Submitted for publication.
7. 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. Submitted for publication.
8. 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.
9. Ginsburg I., Schuger L., Gibbs, F., Johnson, K.J., Ryan, U.S., Ward, P.A. and Varani, J.: Endothelial cell killing by polymorphonuclear leukocytes: Independent and synergistic roles for oxygen radicals and proteases. *Am. J. Pathol.* Submitted for publication.
10. 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.
11. Johnson, K.J., Dixit, V.M. and Varani, J.: Role of thrombospondin in the acute inflammatory response. Submitted for publication.
12. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: PAF, cytokines, toxic oxygen products and cell injury. Submitted of publication.

13. Messana, J.M., Johnson, K.J., Leichtman, A.B., Ellis, C.N., Mihatsch, M.J., Hamilton, F.A., Groisser, O.S., Gartside, M.S. and Voorhees, J.J.: A prospective study of the effects of low dose cyclosporine on renal structure and function in psoriasis patients. Submitted for publication.
14. 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.
15. Richardson, B., Buckmaster, T., Keren, D. and Johnson, K.J. Evidence that macrophages are programmed to die after activating cloned, antigen specific CD4+ T cells. 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., Vol. 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, Vol.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., Pergamon 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. Lippinott 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 PUBLICATOINS IN UNREFEREED JOURNALS:**

1. Hirschl, R., Parent, A., Tooley, R., McCracken, M., Johnson, K., Shaffer, Y., Wolfson and Bartlett, R.: Liquid ventilation improves pulmonary function and gas exchange during extracorporeal life support (ECLS). FASEB, 1993.
2. Johnson, K.J., Mulligan, M.S. and Ward, P.A.: Adhesion molecules and cytokines in acute glomerulonephritis. J. Cell Biochem. 17:C523, 1993.
3. Gilardy, A.K., Jones, M.L., Johnson, K.J. and Ward, P.A.: *In vivo* methods of monoclonal antibody production are used extensively. FASEB J. 7:235, 1993.
4. Gibbs, D.F., Varani, J., Johnson, K.J.: The cooperative interactions of oxidants and proteases in endothelial cell injury by rat neutrophils. FASEB J. 7:413, 1993.
5. Hirschl, R., Parent, A., Tooley, R., McCracken, M., Johnson, K., Shaffer, T., Wolfson, M. and Bartlett, R.: Partial liquid ventilation improves gas exchange in the setting of respiratory failure during extracorporeal life support (ECLS). Surgical Forum, 1993.
6. Mulligan, M.S., Ward, P.A. and Johnson, K.J.: Role of serine and metalloproteinases in the dermal vasculitis model. Amer. Assoc. Immunol. B-175, 1993.
7. Gilardy, A.K., Baker, J.R., Ward, P.A. and Johnson, K.J.: An *in vivo* model of pulmonary delayed-phase allergen inflammation. Amer. Assoc. Immunol. 1993:B-222.
8. Young, E.W., Kunkel, R. and Johnson, K.J.: Measurement of renal interstitial fibrosis by digital video microscopy. J. Amer. Soc. Nephrol. 4: 692, 1993.
9. Simpson, K., Grabie, M., Johnson, K.J., Glass, E., Wieder, J. and Lowe, N.J.: Cyclosporine therapy for severe psoriasis: Chronic effects on renal structure and function. J. Invest. Derm. 100:539, 1993.
10. Yung, R., Quddus, J., Chrisp, C., Johnson, K. and Richardson, B.C.: Spectrum of autoimmunity caused by cloned T_H2 cells modified with DNA methyltransferase inhibitors. AFCR/CSCR 1993.
11. Hirschl, R.B., Tooley, R., Parent, A., Johnson, K.J. and Bartlett, R.H.: Pulmonary function and gas exchanges are improved with liquid ventilation during extracorporeal life support. Soc. Crit. Care Med., 1993.
12. Yung, R., Quddus, J., Chrisp, C., Johnson, K.J. and Richardson, B.C.: Spectrum of autoimmunity caused by cloned TH2 cells modified with DNA methyltransferase inhibition. Midwest AFCR, 1993.
13. Young, E.W., Kunkel, R. and Johnson, K.J.: Measurement of renal interstitial fibrosis by digital video microscopy. JASN 4:692, 1993.

14. 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.
15. 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.
16. Lalwani, N.D., Richardson, B. and Johnson, K.J.: Induction of FAS does not mediate apoptosis in human endothelial cells. AFCR, 1994.
17. Colton, D.M., Hirschl, R.B., Johnson, K., 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.
18. Colton, D.M., Hirschl, R.B., Till, G.O., Johnson, K., Wilkins, A., Compton, C. and Bartlett, R.H.: Partial liquid ventilation (PLV) decreases neutrophil infiltration prior to and after the induction of respiratory failure. Surgical Forum, 1994.
19. 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. Transp. Phys. 31:91, 1994.
20. 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.
21. 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. Res. Day, Univ. of Michigan, 1994.
22. Gibbs, D.F., Burmeister, B., Varani, J. and Johnson, K.J.: Characterization of serine and metalloproteinase activities from stimulated rat neutrophils and rat alveolar macrophages. Keystone Symposium, 1994.
23. 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.
24. 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.
25. Johnson, K., Yung, R., Quddus, J., Chrisp and C., Richardson, B.C.: Spectrum of autoimmunity caused by cloned T^{H2} cells modified with DNA methyltransferase inhibitors. FASEB J 8:1535, 1994.
26. Lowe, N.J., Wieder, J., Rosenbach, A., Johnson, K.J., Simpson, K., Glass, E., Gracie, M. and Bainbridge, C.: Cyclosporine therapy for severe psoriasis: chronic effects on renal structure and function. Sixth Intl. Psoriasis Symp. 1994.
27. Leggat, J.E., Johnson, K.J., Kolars, J.C., Schmiedlin-Ren, Watkins, P.B. and Leichtman, A.B.: Immunohistochemical localization of cytochrome P450 3A in normal and neoplastic kidney and urinary bladder epithelium. ASN, 1994.
28. Vogt, B.A., Johnson, K.J., Shanley, T.P., Alam, J. and Nath, K.A.: Acute glomerular inflammation induces heme oxygenase (HO) in renal tubules and confers resistance to tubular oxidant injury. ASN, 1994.

**MICHAEL L. JONES
ASSISTANT RESEARCH SCIENTIST IN PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Direct supervision of molecular research activities of Dr. Peter A. Ward's Postdoctoral Fellows, Medical and Graduate students:
1. Kimberly E. Foreman, Ph.D., Postdoctoral Fellow.
 2. Roscoe L. Warner, Ph.D., Postdoctoral Fellow.
 3. John J. Shannon, M.D., Postdoctoral Fellow.
 4. Thomas P. Shanley, M.D., Postdoctoral Fellow.
 5. Michael J. Eppinger, M.D., Postdoctoral Fellow.
 6. Thomas H Burkey, Ph.D., Postdoctoral Fellow.
 7. Teletha Gipson, Ph.D., Postdoctoral Fellow.
 8. Beatrice Beck-Schimmer, M.D., Postdoctoral Fellow.
 9. Ralph Schimmer, M.D., Postdoctoral Fellow.
 10. Hagen Schmal, M-2 student, Humboldt University, Berlin, Germany.
 11. Jami L. Foreback, MSTP student, University of Michigan Medical School.
- B. Direct supervision of research activities for:
1. Hilliary Cohen (Junior, University of Michigan); 7/1/93-present, sponsored by Undergraduate Research Opportunities Program; Peter A. Ward, M.D., Mentor.
 2. Dorothy Lao (Interflex student); 6/1/94-present, sponsored by Undergraduate Biomedical Research Program; Co-mentor, Gerd O.Till, M.D.
 3. Jai Gilliam (Junior, Eastern Kentucky University), 6/1/94-present, sponsored by the Undergraduate Biomedical Research Program for Minorities, Mentor.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator, "Inflammatory Cells and Lung Injury", NHLBI-HL-31963 (100%), Project I- \$99,927/year (\$1,010,734/five years), 03/01/94-02/28/98.

PENDING:

- A. Co-Investigator, "Pathogenesis of Aspiration Pneumonitis", NIH-HL-48889-01 (25%), \$99,194/year (537,267/five years).
- B. Principal Investigator, "Effects of Microgravity on Leukocyte Differentiation", NRA (25%), \$139,473/year (586,251/four years).
- C. Co-Investigator, "The Use of Low-Shear Microgravity-Simulated Environments to Investigate Human Bone Precursor Cell Development", NRA (15%), \$178,880/year (\$751,891/four years).

PROJECTS UNDER STUDY:

- A. Role of chemokines in inflammatory models of disease.
- B. Cloning and characterization of rat cytokines.
- C. Effects of microgravity on leukocyte function.
- D. Effects of microgravity on leukocyte differentiation.
- E. Role of adhesion molecules in rat models of inflammatory injury.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Interviewer, faculty and postdoctoral candidates for training positions.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Journal of Immunological Methods.
- B. Laboratory Investigation.
- C. Gene.

INVITED LECTURES/SEMINARS:

1. Visiting Scientist and Invited Speaker, "Infectious Disease Risks Associated with Compromised Leukocyte Function", NASA, Microbiology Division, LBJ Space Center, Houston, Texas, July 7, 1993.
2. Invited Speaker, "Strategies for Cloning Rat Genes for *In Vivo* Inflammation Studies", Michigan Workshop on Vascular Injuries, sponsored by the Upjohn Company, University of Michigan, Ann Arbor, Michigan, December 14, 1994.
3. Visiting Scientist and Invited Speaker, "Contrasting Roles for Adhesion Molecules and Chemokines in IgG vs IgA-Induced Immune Complex Alveolitis in the Rat", Parke-Davis Research Division, Immunopathology Section, Ann Arbor, Michigan, March 3, 1994.
4. Invited Speaker, "Leukocyte Migration and Endothelial-Leukocyte Adhesion Quantification by Multi-Well Fluorescence Analysis", Experimental Biology Meetings, Workshop, Anaheim, California, April 25, 1994.
5. Invited Speaker, "ICAM-1 and MCP-1 Regulation *in vivo* and *in vitro* by Interleukin-10", Experimental Biology Meetings, Immunopathology Session, Anaheim, California., April 25, 1994.
6. Visiting Scientist and Invited Speaker, "A Role for MCP-1 in IgA Immune Complex-Induced Alveolitis in the Rat", Syntex Discovery Research, Syntex, Inc., Palo Alto, California, June 1, 1994.
7. Visiting Scientist and Invited Speaker, "Characterization of Inflammatory Mediators in Rat Lung Injury Models", Genzyme Corp., Cambridge, Massachusetts, June 22, 1994.
8. Visiting Scientist and Invited Speaker, "Contrasting Roles for Regulatory Cytokines in IgG vs IgA Immune Complex-Induced Alveolitis in the Rat", Alpha-Beta Technology, Worcester, Massachusetts, June 23, 1994.

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

1. Vaporciyan, A.A., Jones, M.L. and Ward, P.A.: Rapid analysis of leukocyte-endothelial adhesion. *J. Immunol. Methods* 159:93-100, 1993.
2. Mulligan, M.S., Jones, M.L., Bolanowski, M.A., Baganoff, M.P., Deppeler, C.L., Meyers, D.M., Ryan, U.S. and Ward, P.A.: Inhibition of lung inflammatory reactions in rats by an anti-human IL-8 antibody. *J. Immunol.* 150:5585-5595, 1993.
3. Flory, C.M., Jones, M.L. and Warren, J.S.: Pulmonary granuloma formation in the rat is partially dependent on monocyte chemoattractant protein 1. *Lab. Invest.* 69:396-404, 1993.
4. Warren, J.S., Jones, M.L. and Florey, C.F.: Analysis of monocyte chemoattractant protein 1-mediated lung injury using rat lung organ cultures. *Amer. J.Path.* 143:894-906, 1993.
5. Brieland, J.K., Jones, M.L., Flory, C.M., Miller, G.R., Warren, J.S. and Fantone, J.C.: Expression of monocyte chemoattractant protein-1 (MCP-1) by rat alveolar macrophages during chronic lung injury. *Am. J. Resp. Cell Mol. Biol.* 9:300-305, 1993.
6. Mulligan, M.S., Jones, M.L., Vaporciyan, A.A., Howard, M.C. and Ward, P.A.: Protective effects of IL-4 and IL-10 against immune complex-induced lung injury. *J. Immunol.* 151:5666-5674, 1993.
7. Vaporciyan, A.A., DeLisser, H.M., Yan H-C., Mendiguren, I.I., Thom, S.R., Jones, M.L., Ward, P.A. and Albelda, S.M.: Involvement of platelet-endothelial cell adhesion molecule-1 in neutrophil recruitment *in vivo*. *Science* 262:1580-1582, 1993.
8. Mulligan, M.S., Miyasaka, M., Tamatani, T., Jones, M.L. and Ward, P.A.: Requirements for L-selectin in neutrophil-mediated lung injury. *J. Immunol.* 152:832-840, 1994.
9. Kim, J.S., Gautam, S.C., Chopp, M., Zaloga, C, Jones, M.L., Ward, P.A. and Welch, K.M.A.: Expression of monocyte attractant JE/MCP-1 after Ffcal cerebral ischemia in the rat brain. *J. of Neurobiology*, In Press.
10. Foreman, K.E., Vaporciyan, A.A., Jones, M.L., Bonish, B.K., Johnson, K.J., Glovsky, M.M. and Ward, P.A.: C5a-Receptor-Induced Expression of P-selectin in Endothelial Cells. *J. Clin. Invest.*, In Press.

ARTICLES SUBMITTED FOR PUBLICATION

1. Jones, M.L., Vaporciyan, A.A. an Ward, P.A.: A new fluorescent method for quantitative assessment of neutrophil and monocyte chemotaxis. *J. Immunol. Methods*
2. 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 . *J. Exp. Med.*
3. Jones, M.L., Grande, J.P., Swenson, C.L., Killen, P.D. and Warren, J.S.: Lipopolysaccharide induces monocyte chemoattractant protein production by rat mesangial cells. *J. Clin. Lab. Med.*
4. Flory, C.M., Jones, M.L., Miller, B.F. and Warren, J.S.: Regulatory role of tumor necrosis factor-alpha in monocyte chemoattractant protein-1-mediated pulmonary granuloma rormation in the rat. *J. Immunol.*
5. Kim, J.S., Gautam, S.C., Chopp, M., Zaloga, C., Jones, M.L., Ward, P.A. and Welch, K.M.A.: Expression of monocyte attractant JE/MCP-1 after focal cerebral ischemia in the rat brain. *J. Cerebral Blood Flow and Metabolism.*
6. Vaporciyan, A.A., Mulligan, M.S., Jones, M.L. and Ward, P.A.: Autoregulation of acute inflammatory injury in rat lungs following deposition of IgG immune complexes. *J. Clin. Invest.*

7. Shanley, T.P., Jones, M.L., Schmal, H., Friedl, H.P. and Ward, P.A.: Molecular cloning and *in vivo* transcriptional expression of RANTES in a rat model of IgA-induced lung injury. *J. Immunol.*
8. Shanley, T.P., Warner, R.L., Kapur, V., Ward, P.A., Musser, J.M. and Jones, M.L.: Augmentation of IL-1-dependent lung injury in rats by streptococcal extracellular cysteine protease (interleukin-1 β convertase). *J. Clin. Invest.*
9. 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. of Clin. Invest.*
10. Mulligan, M.S., Vaporciyan, A.A., Jones, M.L., Warner, R.L., Foreman, K.E., Miyasaka, M., Todd, R.F. and Ward, P.A.: Compartmentalized roles for leukocytic adhesion molecules in lung inflammatory injury. *J. Clin. Invest.*
11. 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. Clin. Invest.*
12. Schmal, H., Shanley, T.P., Schrier, D.G., Flory, C.M., Friedl, H.P., Ward, P.A. and Jones, M.L.: Transcriptional characterization of IgG immune complex-mediated lung injury by Northern blot and quantitative PCR analysis. *J. Immunol.*

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

1. Zhang, R-L., Chopp, M., Chen, H., Zhang, Z-G., Ward, P.A. and Jones, M.L.: Anti-ICAM-1 reduces Ischemic tissue damage after transient middle cerebral artery occlusion in rat. 19th International Conf. on Stroke & Cerebral Circulation, 1993.
2. Flory, C.M., Barton, P.A., Jones, M.L., Miller, B.F. and Warren, J.S.: Roles of MCP-1, TNF- α , and ICAM-1 in glucan-induced pulmonary vasculitis in the rat. Keystone Symposia. *J. Cell. Biochem.*, 1994
3. Jones, M.L., Vaporciyan, A.A., Bonish, B.K. and Ward, P.A.: *In vivo* and *in vitro* regulation of ICAM-1 and MCP-1 expression by interleukin-10. Keystone Symposia. Molecular Biology of the Endothelial Cell. *J. Cell. Biochem.*, 1994.
4. Kim, J.S., Gautam, S.C., Chopp, M., Zaloga, C., Jones, M.L., Ward, P.A. and Welch, K.M.A.: Expression of monocyte attractant JE/MCP-1 after focal cerebral ischemia in the rat brain. 19th International Joint Conference on Stroke and Cerebral Circulation, 1994.
5. Vaporciyan, A.A., DeLisser, H., Yan, H., Mendiguran, I., Thom, S., Jones, M.L., Ward, P.A. and Albelda, S.M.: Neutrophil recruitment *in vivo* is platelet endothelial cell adhesion molecule-1 (PECAM-1, CD-31)-dependent. Munich Adhesion Molecule Meetings, 1994.
6. Jones, M.L., Bonish, B. K., Vaporciyan, A.A. and Ward, P.A.; *In vivo* and *in vitro* regulation of ICAM-1 and MCP-1 expression by interleukin-10 (IL-10). *FASEB J.*, 1994.
7. Shanley, T.P., Jones, M.L., Schmal, H., Friedl, H.P. and Ward, P.A.: Molecular cloning and *in vivo* transcriptional expression of rat RANTES in lung inflammation. *FASEB J.*, 1994.
8. Eppinger, M.E., Shanley, T.P., Jones, M.L., Deeb, G.M., Bolling, S.F. and Ward, P.A.: Transcriptional upregulation of inflammatory mediator in a rat lung model of ischemia-reperfusion injury. *FASEB J.*, 1994.
9. Bonish, B.K., Jones, M.L. and Ward, P.A.: Expression and nickel affinity purification of a recombinant 1439bp fragment of rat vascular cell adhesion molecule-1 (VCAM-1). *FASEB J.*, 1994.
10. Eppinger, M.J., Jones, M.L., Deeb, G.M., Bolling, S.F. and Ward, P.A.: The bimodal pattern of injury and the role of neutrophils in a rat lung model of ischemia-reperfusion. American Society of Transplant Surgeons Meeting, Chicago, Illinois, 1994.
11. Davidson, B.A., Jones, M.L., Shanley, T.P., Johnson, K.J. and Knight, P.R.: Evidence of PMN chemokine activity in BAL following gastric aspiration. American Society for Anesthesiology Meeting, Charleston, 1994.

12. Jones, M.L., Davidson, B.A., Shanley, T.P., Johnson, K.J., Knight, P.R. . Transcriptional and Molecular Upregulation of Tumor Necrosis Factor-Alpha Following Gastric Aspiration. American Society for Anesthesiology Meeting, Charleston, South Carolina, 1994.
13. 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. Leuk. Biol., 1994.
14. Jones, M.L., Shanley, T.P., Kapur, V., Musser, J.M. and Ward P.A. *In vivo* augmentation of pulmonary injury by *Streptococcal* pyrogenic exotoxin B-conversion of pre-IL-1 β to functionally active IL-1 β . J. Leuk. Biol., 1994.
15. Schmal, H., Shanley, T.P., Friedl, H.P., Ward, P.A. and Jones, M.L.: Cloning and expression of rat macrophage inflammatory protein-2 from a rat model of immune complex-induced lung injury. J. Leuk. Biol., 1994.
16. Pierson, D.L., Gunter, E.G., Stowe, R.P., Mehta, S., Mishra, S.K. and Jones, M.L.: Effect of space flight on neutrophil chemotactic response. J. Leuk. Biol., 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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: Serology and Genetics of ABO, H, Le, Se and P.
- 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. Pediatric Hematology Residents:
 - 1. Provided instruction in immunohematology to Drs. Pipe and Chang (six 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 (60 contact hours).
- G. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
 - 1. Program Director - Planned and coordinated the June, 1994 Current Topics in Blood Banking Symposium and Preconference Workshops.
 - 2. Presented Workshop entitled: Serological Problems: Causes, Prevention, recognition and resolution.

3. Presented talk entitled: Serological Uses and Abuses.
 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., Steiner, E.A., Knafl, P. and Hunter C.: Autoanti-M causing hemolysis under low-ionic strength conditions: a second example. Submitted.
- B. Judd, W.J., Hoschner, J.A., Khan, S., Steiner, E.A., Poole, J., Sausais, L. and Reid, M.E.: Anti-Vw causing hemolytic disease of the newborn with a negative direct antiglobulin test, and comments on the immune response to GP.Vw. In preparation.
- C. Judd, W.J., Beck, M.L., Annesley, T., Kirkegaard, J. and Steiner, E.A.: Observations on monoclonal blood grouping reagents. In preparation.
- D. Butch, S.H., Stoe, M. and Judd, W.J.: Solving the same-day admission identification problem. Accepted for presentation at the 1994 Annual Meeting of the American Association of Blood Banks, San Diego, California, November, 1994.

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 and two full-day workshops for MABB members seeking Certification as a Specialist in Blood Banking.
 2. Member, Annual Meeting Program Committee.
- B. American Association of Blood Banks:
 1. North Central District Representative, AABB Board of Directors.
 2. Member, Awards Committee.
 3. Associate Editor. AABB Technical Manual, edition 11. Bethesda: American Association of Blood Banks, 1993.
- C. Member, Editorial Board, Transfusion.
- D. Reviewer of articles submitted for publication in Transfusion and Immunohematology.
- E. Chair, Productivity Work Group, Ortho Diagnostic Systems, Inc., Raritan, New Jersey.

V. OTHER RELEVANT ACTIVITIES:**HONORS AND AWARDS:**

- A. Recipient of the Founder's Award for Distinguished Service to the Michigan Association of Blood Banks, September, 1993.
- B. Presented the 1994 Ronald L. Scherdt Memorial Lecture, Current Topics in Blood Banking Symposium, Towsley Center for Continuing Medical Education, University of Michigan, Ann Arbor, Michigan.

INVITED LECTURES:

1. "The Electronic Blood Bank: The Computer Crossmatch", Hoxworth Blood Center, University of Cincinnati, Cincinnati, Ohio, July, 1993.
2. "Problems with Monoclonal Antibodies", Research and Progress Session. Annual Meeting of the American Association of Blood Banks, Miami, Florida, October, 1993.
3. "Unnecessary Serological Testing", Ortho Diagnostics Blood Bank Seminar. Flint, Michigan, March, 1994.
4. "The Computer Crossmatch", South-East Association of Blood Banks Annual Meeting, Atlanta, Georgia, April, 1994.
5. The Computer Crossmatch. Ohio Association of Blood Banks Annual Meeting, Columbus, Ohio, April, 1994.
6. "The Computer Crossmatch", National Blood Group Reference Laboratory of the American Red Cross, Rockville, Maryland, April, 1994.
7. "The Computer Crossmatch", New York Society of Blood Banks, New York, New York, April, 1994.
8. "Drug-Induced Immune Hemolysis", Michigan Association of Blood Banks Advanced Lecture Series. American Red Cross Blood Services, Detroit, Michigan, April, 1994.
9. "The Rh Blood Groups", Michigan Association of Blood Banks Advanced Lecture Series. William Beaumont Hospital, Troy, Michigan, June, 1994.
10. "The MN Blood Groups", Michigan Association of Blood Banks Advanced Lecture Series. William Beaumont Hospital, Troy, Michigan, June, 1994.

PANEL DISCUSSIONS/WORKSHOPS

1. Video Conference, "The Right Tools for the Job", American Association of Blood Banks, April, 1994.
2. Slide/Tape Presentation, "Pretransfusion Testing", American Association of Blood Banks, Look, Listen and Learn Series, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER-REVIEWED 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. 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*, Accepted.
3. Judd, W.J.: Prewarmed tests: con. *Transfusion*, Accepted.

BOOKS/CHAPTERS IN BOOKS:

1. Judd, W.J.: *Methods in Immunohematology*, 2nd Edition, Durham, Montgomery Scientific Publications, 1994.
2. Judd, W.J.: Pretransfusion testing, in, McClatchey, K.D. (ed), *Clinical Laboratory Medicine*, Williams and Wilkins, Baltimore, Maryland, pp. 1701-1724, 1994.
3. Judd, W.J.: Blood groups, in, *Encyclopedia of Science and Technology*, McGraw-Hill, New-York, New York, 1994.

ABSTRACTS/LETTERS:

1. Butch, S.H. and Judd, W.J.: Requirements for the computer crossmatch (letter). *Transfusion*. 34:187, 1994.

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

**ANNUAL DEPARTMENTAL REPORT
6 SEPTEMBER 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. Director of Molecular Diagnostics.
- B. Director of Clinical Chemistry Section.
- C. Sign-out of serum 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. Mentor to undergraduate: Mr. Joe Blough.

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.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

HOSPITAL:

- A. Member, Committee on Laboratory Planning for East Medical Campus.

V. REGIONAL AND NATIONAL:

- A. Member, Program and Finance Committee, Academy of Clinical Laboratory Physicians and Scientists.
- B. Member, AACC, ASHG, CAP, ACLPS

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. "Practical Applications of Molecular Diagnostics in Pathology", St. Joseph's Hospital, Ann Arbor, Michigan, March, 1994.
2. "Introduction to DNA" and "Genetic Disorders", M-Labs Second Symposium. Consisted of two lectures to practising pathologists from community hospitals. University of Michigan, April, 1994
3. "DNA, What Is It, and Why Should I Care?", Current Topics in Blood Banking, 21st Annual Symposium, University of Michigan, June, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Killeen, A.A., Ramey, M.L. and Dean, J.J.: High-dose hook effect in an immunoluminometric thyrotropin assay: the open-faced sandwich artifact. *Ann. Clin. Biochemi.* 30:413-414, 1993.
2. Chai, C. and Killeen, A.A.: Carbamazepine measurements in samples from the Emergency Room. *Therapeutic Drug Monitoring*, In Press.
3. 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.
4. Crotty, P.L., Staggs, R.A., Porter, P.T., Killeen, A.A. and McGlennen, R.C.: Quantitative analysis in molecular diagnostics. *Human Pathol.* 25:572-579, 1994.

ABSTRACTS AND PUBLISHED LETTER:

1. Killeen, A.A., Lewis, C.M., Moyer, Y., Staggs, R.A., Litz M C.E., McClure, J.S. and McGlennen, R.C.: Identification and quantitation of BCR-abl transcripts in bone marrow by reverse-transcriptase PCR and high performance liquid chromatography. *Amer. J. Human Genetics* 53:3, 1993.
2. Chibbar, R., Goswitz, J.J., Killeen, A.A., Moyer, Y., Bartow, S.A. and McGlennen, R.C.: Quantitative analysis of estrogen and progesterone receptor expression and detection of variants in breast lesions by RT-PCR and HPLC. *Amer. J. Human Genetics* 53:3, 1993.
3. Reinartz, J.J., Ramey, M.L., Fowler, M.C. and Killeen, A.A.: Plastic vs Glass SST evacuated serum-separator blood drawing tubes for endocrinologic analytes. *Clini. Chem.* 39:2535-2536, 1993.

ARTICLE SUBMITTED:

1. Killeen, A.A.: A visible spectrophotometric assay for submicrogram quantities of DNA, including amplified DNA.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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 pigment 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 expression 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- β 1 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 α 1(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 α 3(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 α 5(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 $\alpha 5(\text{IV})$ 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 $\alpha 3(\text{IV})$ 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/Monocyte Signals 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 tumorigenesis.

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 Responses", 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, Varacruz, 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", Tamaron, 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 New Hampshire, 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 R.M.: 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 R.M.: 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. Karmioli, 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-1 α : 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, pp 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 Health 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 International 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.

BOODS 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, R.M.: The role of MIP-1 alpha in eosinophil 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 T.J.: 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 endotoxemia. *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. Respir. 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, 1994.
21. Burdick, M.D., Polverini, P.J., Kunkel, S.L., Orringer, M.B., Whyte, R.I., Wilke, C.A. and Strieter R.M.: Human bronchiogenic carcinoma angiogenesis 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, R.M.: 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, R.M.: 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 eosinophil 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-1 alpha prevents PLP peptide induced experimental autoimmune encephalomyelitis. *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/reperfusion 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-1 beta: 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 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Supervision of nine postdoctoral fellows: Nozomu Hiraiwa, M.D., Ph.D., Aron Thall, Ph.D., Peter Smith, Ph.D., Yuko Natsuka, Ph.D., Shunji Natsuka, Ph.D., Petr Maly, Ph.D., E. Paul Scheidegger, M.D., Kazuhiro Yago, M.D., and Daniel Legault, M.D.
- B. Lecturer - Postdoctoral Research Training Program.
- C. Lecturer - Biochemistry 576 - Membranes and protein targeting.
- D. Member of Ph.D. five thesis committees: Kevin Gersten, Emma Masteller, Shu-Jen Chen, Peter Lee and Akhilesh Pandey.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. "Analysis of the Roles of Oligosaccharides During Murine Embryogenesis", Howard Hughes Medical Institute.
- B. Principal Investigator, "Molecular Biology of Human α 1,3 Fucosyltransferases", National Institutes of Health, GM47455 (24% effort), \$75,174/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", National Institutes of Health, HL48859 (25% effort), \$69,982/year direct cost (\$276,544/four years direct cost), 8/1/92-6/30/96.
- D. Principal Investigator, Project #4, Program Project, "Oligosaccharides as Anti-Inflammatory Agents", National Institutes of Health, A133189 (15% effort), \$125,665/year direct cost (\$481,355/four years direct cost), 9/1/92-4/30/96.
- E. "Structure-Function Relationships of Fucosyltransferases", Daniel J. Legault Principal Investigator, National Kidney Foundation, 7/1/92-6/30/94.
- F. "Expression Cloning of α (2,8)polysialyltransferase in Carcinoma Cells", Swiss Cancer League, Swiss National Research Foundation, E. Paul Scheidegger, Principal Investigator, Swiss National Foundation Postdoctoral Fellowship, 2/1/93-1/31/95.

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. Research Faculty Search Committee.
- C. Internal Review Committee.

REGIONAL AND NATIONAL:

- A. Member, Editorial Board, Journal of Biological Chemistry.
- B. Member-elect, Pathobiochemistry Study Section, Division of Research Grants, National Institutes of Health.
- C. Member, Rowe Chair External Advisory Committee, University of California Davis Medical School.
- D. Board of Directors, Society for Glycobiology.

V. OTHER RELEVANT ACTIVITIES:

- A. Howard Hughes Medical Institute, Associate Investigator.

VI. INVITED LECTURES AND SEMINARS:

1. "Human Fucosyltransferase Genes and Selectin-Dependent Cell Adhesion in Inflammation", National Institutes of Health, Glycobiology: New Perspectives on Human Disease, Bethesda, Maryland, September, 1993.
- 2.. "Structure and Function of Mammalian Glycosyltransferase Genes", Rinsho-Ken International Conference, Tokyo, Japan, September, 1993.
3. "Structure and Function of Mammalian Glycosyltransferases", 22nd Annual Meeting of the Society for Complex Carbohydrates, San Juan, Puerto, Rico, November, 1993.
4. "Molecular Genetics of Mammalian Glycosyltransferases", Pluto Club Meeting, Breckenridge, Colorado, December, 1993.
5. "Molecular Genetics of Mammalian Glycosyltransferases", 9th Annual Symposium on Biotechnology, The New Biology of Carbohydrates, University College London Medical School, London, England, December, 1993.
6. "Mammalian Genes that Determine Cell Surface Glycosylation Phenotype", University of Alabama, Birmingham, Alabama, January, 1994..
7. "Molecular Genetics of Mammalian Glycosyltransferases", Keystone Symposia on Molecular and Cellular Biology, Frisco, Colorado, March, 1994.
8. "Glycoconjugates: Structure, Metabolism and Molecular Biology", Conference Jacques Monod, La Londe-les-Maures, France, April, 1994.
9. "Mammalian Genes that Determine Cell Surface Glycosylation Phenotype", University of California at San Diego, San Diego, California, April, 1994.
10. "Structure and Expression of Mammalian Fucosyltransferase Genes", Brook Lodge Conference on Adhesion Molecule Biology, Augusta, Michigan, June, 1994.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Yago, K., Zenita, K., Ginya, H., Sawada, M., Ohmori, K., Okuma, M. Kannagi, R. and Lowe, J.B.: Expression of $\alpha(1,3)$ fucosyltransferases which synthesize sialyl Le^x and sialyl Le^a, the

- carbohydrate ligands for E- and P-selectins in human malignant cell lines. *Cancer Res.* 53:5559-5565, 1993.
2. Reguigne, I., James, M.R., Richard, C.W., III, Mollicone, R., Seawright, A., Lowe, J.B., Oriol, R. and Couillin, P.: The gene of the myeloid α -3-fucosyltransferase (FUT4) is located between D11S388 and D11S919 on 11q21. *Cytogenet Cell Genetics* 66:104-106, 1994.
 3. Mollicone, R., Reguigne, I., Fletcher, A., Aziz, A., Rustam, M., Weston, B.W., Kelly, R.J., Lowe, J.B. and Oriol, R.: Molecular basis for plasma α (1,3)fucosyltransferase gene deficiency (FUT6). *J. Biol. Chem.* 269:12662-12671, 1994.
 4. Smith, P.L. and Lowe, J.B.: Molecular cloning of a murine N-acetylgalactosaminetransferase cDNA that determines expression of the T-lymphocyte-specific CT oligosaccharide differentiation antigen. *J. Biol. Chem.* 269:15162-15171, 1994.
 5. Natsuka, S., Gersten, K.M., Zenita, K., Kannagi, R. and Lowe, J.B.: Molecular cloning of a cDNA encoding a novel human leukocyte α (1,3)fucosyltransferase capable of synthesizing the sialyl Lewis x determinant. *J. Biol. Chem.* 269:16789-16794, 1994.
 6. Kelly, R.J., Ernst, L.K., Larsen, R.D., Bryant, J.G., Robinson, J.D. and Lowe, J.B.: Molecular basis for H blood group deficiency in Bombay (Oh) and para-Bombay individuals. *Proc. Natl. Acad. Sci. USA* 91:5843-5847, 1994.
 7. Natsuka, S. and Lowe, J.B.: Glycosyltransferases in oligosaccharide biosynthesis. *Current Opinion in Structural Biology*, In Press.
 8. Mollicone, R., Reguigne, I., Kelly, R.J., Fletcher A., Watt, J., Chatfield, S., Aziz, A. Cameron, H.S., Weston, B.W., Lowe, J.B. and Oriol R.: Molecular basis for Lewis α (1,3/1,4)fucosyltransferase gene deficiency. *J. Biol. Chem.*, In Press.

ARTICLES SUBMITTED OR IN PREPARATION:

1. Kelly, R.J., Rouquier, S., Giorgi, D., Lennon, G.G. and Lowe, J.B.: The human secretor blood group locus represents a novel α (1,2)fucosyltransferase gene that is mutationally inactivated in non-secretor individuals, In Preparation.
2. Rouquier, S., Lowe, J.B., Ferritta, 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, In Preparation.
3. Gersten, K.M., Petryniak, B.L., Kelly, R.J., Natsuka, S., Natsuka, Y., Wong, C-H. and Lowe, J.B.: A murine α (1,3)fucosyltransferase expressed in peripheral lymph node high endothelial venules synthesizes candidate oligosaccharide ligands for L-selectin, In Preparation.
4. Hiraiwa, N., Saunders, T and Lowe, J.B.: Structure and tissue-specific expression of a murine α (1,2)fucosyltransferase gene, In Preparation.
5. Gersten, K.M., Natsuka, S., Hiraiwa, N., Trinchera, M., Jenkins, N. and Lowe, J.B.: Structure and expression of a murine α 1,3 fucosyltransferase gene, and comparison to its orthologous human homologue Fuc-TIV, In Preparation.
6. Hiraiwa, N. and Lowe, J.B.: Dominant pre-implantation lethality in mice directed by aberrant expression of an α (1,2)fucosyltransferase cDNA, In Preparation.
7. Legault, D.J., Kelly, R.J., Natsuka, Y. and Lowe, J.B.: Peptide segments in human α (1,3)fucosyltransferases that determine acceptor substrate recognition, In Preparation.
8. Thall, A., Petryniak, B., Camper, S., Saunders, T. and Lowe, J.B.: Phenotypic consequences of ablation of the murine Fuc-TIV gene, In Preparation.

BOOKS AND CHAPTERS IN BOOKS:

1. Lowe, J.B.: Red cell membrane antigens, in, Stamatoyannopoulos, G., Nienhuis, A.W., Majerus, P.W. and Varmus, H. (eds), *The Molecular Basis of Blood Diseases*, W. B. Saunders, Company, Orlando, Florida, pp. 293-330, 1993.

2. Lowe, J.B.: Carbohydrate-associated blood group antigens: The ABO, H/Se and Lewi loci, in, Garratty, G. (ed), Immunobiology of Transfusion Medicine, Marcel Dekker, Inc., New York, New York, pp. 3-36,1994.
3. Lowe, J.B.: Molecular biology: Basic concepts, in, McClatchey, K.D. (ed), Clinical Laboratory Medicine, Williams & Wilkins, Baltimore, Maryland, pp. 117-152,1994.
4. Lowe, J.B.: Biochemistry and biosynthesis of ABH and Lewis antigens: Characterization of blood group specific glycosyltransferases: Molecular basis of major blood group antigens, in, Cartron, J-P and Rouger, P. (eds), Blood Cell Biochemistry, Volume 6, Plenum Press, London, In Press.
5. Lowe, J.B.: Specificity and expression of carbohydrate ligands, in, Page, C.P. (ed), Handbook of Immunopharmacology - Adhesion Molecules, Academic Press, London, In Press.
6. Lowe, J.B.: Oligosaccharide-dependent mechanisms of leukocyte adhesion, in, Zetter, B.R. (ed), Homing Mechanisms and Cellular Targeting, JAI Press, New York, In Press.
7. 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, In Press.

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

None.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. "Introduction to Immunology", Epidemeology 558, Lecturer.
- B. Supervised undergraduate students: Christy Shaklee, Kolby Keifer and Laurel Goldstein.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Characterization of Cellular Recruitment in a Murine Model of Asthma", Miles Pharmaceuticals, \$25,000, unrestricted.
- B. Principal Investigator, "Role of IL-4 in Eosinophil Airway Inflammation", Phoenix Foundation Grant, University of Michigan, \$6,000, unrestricted.

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.

IV. ADMINISTRATIVE ACTIVITIES:

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. Invited speaker, Northwestern Medical School, Department of Immunology, Chicago, Illinois, December, 1993.
2. Invited speaker, Miles Pharmaceutical, New Haven, Connecticut, January, 1994.
3. Invited speaker, Turino, Italy, 5th International Meeting on Pathophysiology of Pulmonary Cells: Alveolar Macrophage and Pulmonary Fibroblast, February, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lukacs, N.W. and Boros, D.L.: Lymphokine regulation of granuloma formation in murine *schistosomiasis mansoni*. Clin. Immunol. Immunopath. 68:57-63, 1993.
2. Chensue, S.W., Bienkowski, M., Eessalu, T.E., Warmington, K.S., Hersey, S.D., Lukacs, N.W. and Kunkel, S.L.: Endogenous interleukin 1 receptor antagonist protein (IRAP) regulates schistosome egg granuloma formation and the regional lymphoid response. J. Immunol. 151:3654-3662, 1993.
3. 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 adhesion molecules, ICAM-1 and LFA-3. Am. J. Pathology 143:1179-1185, 1993.
4. Lukacs, N.W., Kunkel, S.L., Burdick, M.D., Lincoln, P.L. and Strieter, R.M.: Interleukin 1 receptor antagonist blocks chemokine production in a T lymphocyte-mediated response. Blood 82:3668-3674, 1993.
5. 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, 1993.
6. Lukacs, N.W., Strieter, R.M., Elner, V.M., Evanoff, H.L., Burdick, M.D. and Kunkel, S.L.: Adhesion molecules mediate the expression of monocyte-derived MIP-1alpha during monocyte-endothelial cell interactions. Blood 83:1174-1178, 1994.

7. Lukacs, N.W., Strieter, R.M., Evanoff, H.L., Burdick, M.D. and Kunkel, S.L.: The expression of monocyte-derived VCAM-1 influences lymphocyte proliferation and cytokine production during an allogeneic response. *Cellular Immunol.* 154:88-98, 1994.
8. Zhu, Y., Lukacs, N.W. and Boros, D.L.: Cloning of TH0 and TH2 helper lymphocytes from liver granulomas of *S. mansoni* infected mice. *Infect. Immun.* 62:994-999, 1994.
9. 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.* 152:3559-3569, 1994.
10. Lukacs, N.W., Chensue, S.W., Smith, R.E., Strieter, R.M., Warmington, K., Wilke, C. and Kunkel, S.L.: The production of MCP-1 and MIP-1alpha by inflammatory granuloma fibroblasts. *Am. J. Pathol.* 144:711-718, 1994.
11. Lukacs, N.W., Strieter, R.M., Chensue, S.W. and Kunkel, S.L.: IL-4 dependent pulmonary eosinophil infiltration in a murine model of asthma. *Am. J. Resp. Cell and Mole. Biol.* 10:526-532, 1994.
12. Lukacs, N.W., Chensue, S.W., Strieter, R.M., Warmington, K. and Kunkel, S.L.: Inflammatory granuloma formation is mediated by TNF α inducible ICAM-1. *J. Immunol.* 152:5883-5889, 1994.
13. Lukacs, N.W., Kunkel, S.L., Strieter, R.M. and Chensue, S.W.: The role of chemokines in *S. mansoni* granuloma formation. *Parasitol. Today*, In Press.
14. Boros, D.L. and Lukacs, N.W.: The role of egg antigens, cytokines in granuloma formation in murine *schistosomiasis mansoni*. *Mem. Inst. Oswaldo Cruz, Rio de Janeiro*, In Press.

BOOKS AND CHAPTERS IN BOOKS:

1. Kunkel, S.L., Lukacs, N.W., Chensue, S.W. and Strieter, R.M.: Adhesion molecules and chemokines dictate leukocyte recruitment, in, Faist, E. (ed), 3rd International Congress on the Immune Consequences of Trauma, Shock and Sepsis, Munich, Germany.
2. Kunkel, S.L., Strieter, R.M., Lukacs, N.W. and Chensue, S.W.: Molecular aspects of granulomatous inflammation, in, *EOS Journal of Immunol. Immunopharm.*
3. Kunkel, S.L., Lukacs, N.W. and Strieter, R.M.: The role of interleukin-8 in the infectious process, in, New York Acadademy of Science Press.
4. Kunkel, S.L., Lukacs, N.W. and Strieter, R.M.: Cytokines and inflammatory disease, in, Sirica, Alphonse E. (ed), *Cellular and Molecular Pathogenesis*, Raven Press.

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

1. 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, AFCR Midwest Meeting, November 1993.
2. Allen, R., Kunkel, S.L., Lukacs, N.W., Evanoff, H., Sherman, J., Shaklee, C. and Strieter, R.M.: TH1/TH2 cytokine-induced expression of MIP-1 α /b chemokines from pulmonary vascular smooth muscle cells, *Experimental Biology*, 1994.
3. 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, *Experimental Biology*, 1994.

4. Lukacs, N.W., Strieter, R.M. and Kunkel, S.L.: Increased airway resistance in the late phase of airway inflammation correlates with eosinophil influx and is mediated by IL-4 production in a murine model of asthma, *Experimental Biology*, 1994.
5. Lukacs, N.W., Kunkel, S.L., Burdick, M.D. and Strieter, R.M.: The role of MIP-1 α in eosinophil recruitment into the airway of asthmatic mice, *American Thoracic Society Meeting*, 1994.
6. 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, *National AFCR Meeting*, 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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. Director of Oral Pathology Laboratory, School of Dentistry, 7/1/91-7/1/93.
- G. Professor, Department of Oral Pathology, Oral Medicine, Oral Surgery, School of Dentistry, 1994-present.
- H. Professor, Department of Otorhinolaryngology, 1991-Present.

II. TEACHING ACTIVITIES

MEDICAL SCHOOL/HOSPITAL

- A. Pathology 630/580/631; Course Director, 1983-Present.
- B. Oral Diagnosis 644; lecturer, 1983-1993.
- C. Pathology 600; lecturer, head and neck pathology, 1982-93.
- D. Oral Pathology 695, Lecturer, 1992-93.
- E. 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. Executive Committee; G.T. Wolf, T.F. Beals, A.A. Forastiere, T. Carey, K.D. McClatchey, A. Flint, and J.L. Hudson, "A New Strategy to Preserve the Voice Box in Advanced Laryngeal Cancer", Veterans Administration Co-operative Studies Program, Protocol 582-C, Clinical Research Center, The University of Michigan, 1985-present.
- C. Co-Principal Investigator, "Screening of Papa Smears Using Fluorescently Labeled Markers;" Principal Investigator, Daisy S. McCann, Ph. D., McCann Associates, Wayne, Michigan, 1993-94.

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL

- A. Medical Service Plan Executive Committee, 1979-present.
- B. Director, Clinical Microbiology/Virology Laboratory, 1978-present.

MEDICAL SCHOOL/HOSPITAL

- A. Advisor, Medical and Biological Illustration Program, The University of Michigan Medical School, 1986-present.
- B. Member, Infection Control Committee, The University of Michigan Hospitals, 1978-present.
- C. Chairman, Laboratories Committee of the Medical Staff, The University of Michigan Hospitals, 1987-present.
- D. Chairman, Quality Assurance Committee, The University of Michigan Hospitals, 1989-present.
- E. Medical Liability Review Committee, 1992-present.
- F. Member, Patient Care Advisory Committee, The University of Michigan Hospitals, 1989-present.
- G. Member, Technical Advisory Committee, State of Michigan, Department of Health, Bureau of Laboratory and Epidemiological Services, 1987-present.
- H. Chairman, Standardization and Product Evaluation Committee (SPEC), The University of Michigan Medical Center, 1991-present.
- I. Associate Chief of Clinical Affairs, The University of Michigan Hospitals, 1990-present.
- J. Member, Executive Committee on Clinical Affairs, The University of Michigan Medical Center, 1990-present.
- K. Vice Chairman, Claims Control Committee, The University of Michigan Hospitals, 1990-present.
- L. Clinical Practice Work Group, University of Michigan, 1993-present.
- M. 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. Chairman, Commission on Anatomic Pathology, 1986-93.
 - 3. Council on Scientific Affairs, 1987-93.
 - 4. Chairman, International Committee, 1993-present.
 - 5. Member, Task Force on Laboratory Accreditation, 1992-93.
- 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.
- C. American Society of Clinical Pathologists.
 - 1. ASCP Advisory Council, 1984-94.
- 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.
- F. Member, National Fetal-Infant Mortality Review Program Steering Committee, Grant from the U.S. Department of Health and Human Services, Maternal and Child Health Bureau, 1990-93.

INTERNATIONAL

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

V. OTHER RELEVANT ACTIVITIES**INVITED LECTURES/SEMINARS**

1. Invited speaker, 2-day course, "Integration of Quality and Total Management." Riyadh, Saudi Arabia, September, 1993.
2. Participant, Quality Assurance and Total Quality Management Seminar, International Congress, World Association of Societies of Pathology. October, 1993
3. Participant, International Standardization Seminar, International Congress, World Association of Societies of Pathology, October. 1993.
4. Participant, Integration of Quality Assurance and Total Quality Management in Today's Laboratory--Miles Instruments, Chicago, Illinois, October, 1993.
5. Moderator, Virtual Imaging in Pathology, American Society of Clinical Pathologists and College of American Pathologists, Annual Meeting, October, 1993.
6. Participant, The Clinical Laboratory in the International Environment, National Committee for Clinical Laboratory Standards Annual Meeting, March. 1994.
7. Invited speaker, Clinical Relevance of Prognostic Markers, CAP Conference XXVI, June, 1994.

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. Arch. Otol. - 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. Arch.Otol., June 1994.

ARTICLES SUBMITTED FOR PUBLICATION

1. Ptok, A., Dulon, J., McClatchey, K.D., Szakacs, J.E., Ensminger, W.D., Linder, K.E., Porter S.L., Worsham, M.J., Van Dyke, D.L., McKeever, P.E., Carroll, W.R., Natale, R.B. and Carey, T.E.: UM-VX2-1 and UM-VX2-2, *in vitro* cell lines form the VX2 rabbit carcinoma: attachment and karotype differences correlate with tumor take or rejection. Internatl. J. Cancer, Pending.
2. Carroll, W.R., Bunge, F.R., Wolf, G.T., Carey, T.E., McClatchey, K.D. and Poore, J.: Perilesional interleukin 2 in the VX-2 carcinoma in rabbits. Otolaryngology - Head and Neck Surgery, Pending.
3. Beck, J.E., Carey, T.E. and McClatchey, K.D.: Identification of HPV6 in inverted papilloma arising in a renal transplant recipient. Head and Neck Surg., July, 1994.

BOOKS AND CHAPTERS IN BOOKS

1. McClatchey, K.D., et al.: Clinical Laboratory Medicine, Williams & Wilkins, Baltimore, Maryland, January 1994.
2. McClatchey, K.D.: The Jaws and Oral Cavity, in, Sternberg, Antonioli, Carter, Egglestonn, Oberman and Mills (eds), Diagnostic Surgical Pathology, Raven Press, New York, New York, 1994.

3. McClatchey, K.D. and Peterson, T.: The Laboratory Information System, in, McClatchey, K.D. (ed), Clinical Laboratory Medicine, Williams & Wilkins, Baltimore, Maryland, 1994.
4. Travers, E.M. and McClatchey, K.D.: Laboratory Management in, McClatchey, K.D., Clinical Laboratory Medicine, Williams & Wilkins, Baltimore, Maryland, 1994.

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

1. Pierson, C.L. and McClatchey, K.D.: Clinical application of PCR Technology for the Detection of *Mycobacterium tuberculosis* complex in Pulmonary Specimens, Michigan Infectious Disease Society, East Lansing, Michigan, May, 1994.
2. Blythe, L., Hankerd, R., and McClatchey, K.D.: Comparison of MarDx Western blot and general biometrics immunowell recombinant P39 enzyme-linked immunosorbent assay (ELISA) as confirmatory tests for *Borrelia burgdorferi* ELISA screen positive/borderline sera, American Society for Microbiology, Las Vegas, Nevada, May, 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. Daily surgical neuropathology and electron microscopic neuropathology - six 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 - six months.
- E. Examination of autopsy neuropathologic material - staff rotation and consults to faculty.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Neural and Behavioral Sciences 600, 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, Priscilla Lindley and Barbara Markey: 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.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Antigenic Instabilities and Clonal Heterogeneity in Human Gliomas", National Institutes of Health Grant NIH CA-47558, Changes in malignancy and resistance to treatment of human gliomas, the most common and devastating group of brain tumors, are thought to be related in part to altered gene product expression of these cells. These are followed upon explantation of human glioma cells in vitro and correlated with studies designed to determine the mechanism of these alterations. The extent of changes are studied. Alterations in gene expression are correlated with changes in cellular DNA over time intervals and correlated with changes in clones of cells from the gliomas of individual patients, 1 May 1988 - 30 April 1993.

- B. Co-Investigator, "Antimetabolite Selectivity: Regional Treatment and Modulation", National Institutes of Health Program Project NIH CA-42761-04, 1 August 1993 - 31 July 1996.
- C. 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.
- D. 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. Growth, spread and antigenicity of ENU-induced gliomas in rats with Constance D'Amato and Dr. Terry Hood, submitted to J. Neuro-oncology.
- B. Quantitative analysis of DNA in fresh and cultured cells of brain tumors, with Drs. Karin Muraszko, Donald Ross, William Chandler, and James Varani.
- C. Extracellular matrix products and plasminogen activators of gliomas with Drs. James Varani, Robert Sitrin, Dario Caccamo, and Suzanne Fligel.
- D. Magnetic resonance diffusion and cross relaxation of brain tumors with Drs. James Brunberg, Thomas Chenevert and Brian Ross.
- E. Characterization of Rosai-Dorfman disease in brain with Drs. Michael Boland and Karin Muraszko.
- F. Combined ultrastructural and karyotypic analysis of the VX-2 tumor with Dr. Thomas E. Carey, submitted to Int. J. Cancer.

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 and Neuroradiology.
- E. Quality control of ultrastructural and immunodiagnostic neuropathology. This included scheduled twice monthly meetings and various ad hoc reviews requested by faculty.

REGIONAL AND NATIONAL:

- A. International Editorial Board, Cellular and Molecular Biology.
- B. Primary Review Pathologist, Children's Cancer Study Group CCG 9891 nationwide study of childhood low grade gliomas.
- C. Reviewer, for various pathology, neuroscience and neurooncology journals.
- D. 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-.
 - 1. Pathology Committee, 1989-
- I. Member, Histochemical Society, 1989-.
 - 1. Councilor, 1994-
- J. Member, Constitution Committee, American Association of Neuropathologists, 1990-.

INVITED LECTURES/SEMINARS:

1. Chairperson, Scientific Session on pituitary tumors, American Association of Neuropathologists, & International Society of Neuropathologists, Toronto, Ontario, 1993.
2. Faculty, 32nd Annual AFIP Neuropathology Review, Armed Forces Institutes of Pathology, San Antonio, Texas.

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

1. Ross, D.A., McKeever, P.E., Sandler, H.M., and Muraszko K.M.: Myxopapillary ependymoma. *Cancer* 71:3114-3118, 1993.
2. 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*, In Press.
3. Caccamo, D., Keohane, M.E. and McKeever, P.E.: Plasminogen activators and inhibitors in gliomas: An immunohistochemical study. *Modern Pathology*, In Press.
4. Heidelberger, K.P., Ritchey, M.L., Dauser, R.C., McKeever, P.E., and Beckwith, J.B.: Congenital mesoblastic nephroma metastatic to the brain. *Cancer*, In Press.
5. Meyer, J.R., Quint, D.J., McKeever, P.E., Boland, M., and Ross, D.A.: Giant Rathke's cleft cyst. *Am. J. Neuroradiol*, 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. McLaughlin, P.W., Sdhea, R. McKeever P.E. and Boothman D.A.: Radiobiological effects and changes in gene expression in the central nervous system in response to ionizing radiation, in, Levin, A.J. and Schmidek, H.H. (eds), *Molecular Genetics of Nervous System Tumors*, Wiley-Liss, New York, pp. 163-177, 1993.
3. Blaivas, M. and McKeever, P.E. : The brain, spinal cord, and Meninges, in *Diagnostic Surgical Pathology*, Raven Press, Ltd., New York, New York, pp. 409-492, 1994.

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

1. Roberson, P.L., Ten Haken, R.K., McKeever, P.E. and Ensminger W.D.: Tumor and normal liver dosimetry for hepatic activated microsphere therapy, Society of Nuclear Medicine 40th Annual Meeting, Toronto, Ontario, Canada.
2. Meyer, J.R., Quint, D.J., McKeever, P.E., Boland, M. and Ross, D.A.: Giant Rathke's cleft cyst. American Society for Neuroradiology, Vancouver, Canada.
3. Liebert, M., Washington, R., Wedemeyer, G., Carey, T.E., McKeever, P.E., Giudice, G. and Grossman, H.B.: Expression of a6b4 integrin on normal non-epithelial tissues.
4. Brunberg, J.A., Chenevert, T.L., Ross, D.A., Junck, L.R. McKeever, P.E. and Betley, A.T.: *In vivo* MR determination of water diffusion coefficients and diffusion anisotropy: Correlation with structural alteration in astrocytoma of the cerebral hemispheres, American Society of Neuroradiology, Vancouver, Canada, 1993.
5. McKeever, P.E., Zhang, K., Nelson, J.S. and Phan, S.H.: Type IV collagen messenger RNA localizes within cells of abnormal vascular proliferations of glioblastoma and sarcomatous regions of gliosarcoma. *J. Histochem. Cytochem.* 41:1124, 1993.
6. Junck, L., Ross, D.A., Brunberg, J.A., McKeever, P.E., Grube, S., Betley, A.T. and Greenburg, H.S.: Glucose metabolism in untreated gliomas. *Brain* 93.
7. Junck, L., McKeever, P.E., Ross, D.A., Brunberg, J.A., Greenburg, 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.
8. McKeever, P.E., Junck, L., Ross, D.A., Brunberg, J.A., Bromberg, J., Wang, M., Onda, K., Grube, S.V. and Greenburg, H.S.: Comparison of MIB-1, BUDR and PCNA labeling index markers of cellular proliferation in grading astrocytic gliomas. The International Society of Neuropathology Meeting, Toronto, Ontario, Canada, 1994.
9. McKeever, P.E. and Wang, M.: Numerical variations in chromosome specific satellite DNA distinguish glioblastoma, lower grade gliomas and brain. The International Society of Neuropathology Meeting, Toronto, Ontario, Canada, 1994.
10. Robertson, P.L., Ten Haken, R.K., McKeever, P.E. and Ensminger, W.D.: Tumor and normal liver dosimetry for hepatic activated microsphere therapy. The Society of Nuclear Medicine 40th Annual Meeting, Toronto, Canada, June 11, 1993.
11. McKeever, P.E., Dennis, T.R., Burgess, A.C., Meltzer, P.S. and Trent, J.M.: Chromosomal breakpoint at 17q11.2 and DNA insertion near the NF-1 and c-erbB-2 gene loci corresponds with expression of glial fibrils in a glioblastoma. *FASEB J.* 8:A392, 1994.
12. McKeever, P.E., Lawrence, T.S., Davis, M.A., Genik, S.J. and Ensminger, W.D.: Quantitative immunohistochemistry (QIHC) reveals topographic differences in iododeoxyuridine (IdUrd) uptake by tumor cells. *J. Histochem. Cytochem.* 42:978; 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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. Lectured to Bioengineering 890, "Use of on-line sensors and immunoassay to study secretory dynamics with a computer-controlled perfusion system and in living animals", September 22, 1993.
 - 2. Served as a primary instructor for a full semester four hours/week laboratory course for dental and health professional students, Pathology 630/631, Fall 1993.
 - 3. Taught portion of Mammalian Reproductive Endocrinology, Physiology 541, Winter, 1994 (six hours lecture; ten contact hours).
 - 4. Taught portion of Cellular Biotechnology Training Program 504, Winter '94 (six hours lecture: Intercellular Communication).
- B. Primary Supervision of Three Graduate Students:
 - 1. Hal Cantor, Bioengineering - received his Ph.D. in 1994. Supported on NCIR grant. Last summer, Mr. Cantor was judged to have presented the best abstract by a young scientist before the Society for the Study of Reproduction and he was awarded the 1993 SSR Young Investigator Award.
 - 2. Karen Heinze, Bioengineering - doctoral student transferred supported on NCIR grant.
 - 3. William Lemon, Bioengineering - supported on Cellular Biotechnology Training Grant.
- C. Supervision of Two Other Students:
 - 1. Mona Prasad, premedical student, June, 1993-present.
 - 2. Jyothi Tirumalasetty, June, 1993-present.
- D. Service on Other Dissertation Committees;

1. Jeaneatte M. 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. Principal Investigator, "Center for the Study of Reproduction", National Institutes of Health, P30 HD18258 (10% effort [5% as Director, Center and Administrative Core; 5% as Director, Standards and Reagents Core]), \$454,537 direct costs year 1, \$2,583,224, five years, 1 April 1994-31 March 1999.
- B. NIH U54 Cooperative Center, "National Center for Infertility Research". \$1,089,187 (overall center, direct costs, year 3), \$5,873,767 (overall center, five years), 30 September 1991-31 August 1996 PI: Nancy Reame (School of Nursing). Role: Associate Director of Center, 3% effort; Director of "Assay Development Core," 5% effort, \$36,202 TDC, year 3, and Principal Investigator of one project, "Gonadotrope response to ovulation-controlling signals." 30% effort, \$185,982 TDC, year 3.
- C. NIH, T32 HD-07048-16, "Training Program in Reproductive Endocrinology", \$155,798, year 4 direct and stipends, \$824,708, all five years, 7/1/90-6/30/95, Mentor, 5% maximum effort.
- D. Ciba Corning Diagnostics, Support for World Health Organization collaborative study of recombinant human FSH.

PROPOSAL WRITING:

- A. NIMH, "Stress and Reproductive Hormones in Depressed Women", \$165,357 year 1 TDC, \$708,446 years 1-4. PI: Elizabeth Young (MHRI & Psychiatry). Role: Co-PI, 10% effort. 12/1/93-11/30/97. Pending with priority score of 128 and 6.8 percentile.
- B. NIH, U01-AG12495-01, PI: "Menopause and Aging in Women: Central Laboratory", requested \$992,689, TDC, 9/1/94 to 8/31/99. Site visited and now being negotiated.
- C. NIMH, "Influence of Gonadal Hormones on the Stress Hormone Axis", Elizabeth Young, PI. Role: Co-Inv. \$654,440 TDC, 2/1/95-1/31/99.
- D. NIH, "Physiologic relevance of FSH heterogeneity", Vasantha Padmanabhan PI. Role: Co-Inv. \$695,019 TDC, 12/1/94-11/30/98.
- E. Assisted Co-PI's Deborah Oakley and Mary Fran Sowers with the development of a proposal to the OVPR for expanded support or the Michigan Initiative for Women's Health.
- F. Assisted individuals in firms (Innovation Associates and Wolpert Polymers) to develop new SBIR grants which, if successful, will involve the University as a subcontractor.
- G. Assisted with pending renewal application for NIH, T32HD-07048, "Training Program in Reproductive Endocrinology", requested \$1,733,416 direct and stipends, 7/1/95-6/30/00, Mentor, 5% maximum effort.

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 perimenopausal 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 term, longitudinal study concerning hormones and behavior in adolescents.
- G. Innovation Associates, Ann Arbor, MI: 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. Michigan State University, Animal Science: James Ireland, Reproductive Biologist: development of a solid state, two site chemiluminescence-based immunoassay for inhibin.
- I. 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 perfusion system.
- J. Wayne State University, Obstetrics and Gynecology: Kamran Moghissi: Co-Associate Director of the NCIR grant and Key Investigator of one of its projects.
- K. 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.
- L. 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.

INTELLECTUAL PROPERTIES ACTIVITY:

- A. None.

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 perfusion 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. July 12-13, 1993, Meeting of Directors of NICHD P30 Centers, Rochester, Minnesota.
2. July 31-Aug. 4, 1993, 26th Annual Meeting of the Society for the Study of Reproduction, Colorado State University, Fort Collins, Colorado.
3. September 8, 1993, Site visit for our P30 Center.
4. September 14, 1993, Presented opening RSP seminar, "25 and Counting: 5, 10, 20, 40...?"
5. October 25-27, 1993, Tri-Annual Meeting of the Steering Committee of the National Collaborative Program for Infertility Research, Boston, Massachusetts.
6. November 5, 1993, RSP Poster Day.
7. November 6-12, 1993, Annual Meeting of the Society for Neuroscience, Washington, D.C.
8. March 1, 1994, NIDDK Endocrine Research Program Advisory Committee, Bethesda, Maryland.
9. March 14, 1994, NIDDK Hormone Distribution Program Committee, Bethesda, Maryland.
10. April 4-6, 1994, Tri-annual Meeting of the Steering Committee of the National Collaborative Program for Infertility Research, Boston, Massachusetts.
11. April 15, 1994, Retreat, National Center for Infertility Research.
12. April 27-28, 1994, Reproductive Toxicology Workshop, University of Michigan.
13. May 12, 1994, Cellular Biotechnology Training Program Poster Day, Waldenwoods Conference Center.
14. June 1-19, 1994, Endocrine Society Meeting, Anaheim, California.

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 radioimmunoassays (and thereby reduction in usage of radioactive isotopies).

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wiesen, J.F. and Midgley, A.R., Jr.: Changes in expression of cx43 gap junction mRNA and protein during ovarian follicular growth. *Endocrinology* 133:741-746, 1993.
2. Wiesen, J.F. and Midgley, A.R., Jr.: Changes in expression of c43 gap junction mRNA and protein during ovarian follicular atresia. *Biol. Reprod.* 50:336-348, 1993.
3. Brand, R.M., Ghazzi, M.N., Rolfes-Curl, A., Cantor, H.C. and Midgley, A.R., Jr.: Use of continuous, on-line hydrogen ion monitoring to examine the flow dynamics of perfusion systems and cellular metabolism. *Am. J. Physiol.* 266:E739-E749, 1994.
4. Brand, R.M., Lyons, R.H. and Midgley, A.R. Jr.: Understanding the dynamics of cellular responsiveness to modifications of metabolic substrates in perfusion. *J. Cellular Physiol.*, In Press.

5. Brand, R.M., Midgley, A.R., Jr. and Williams, W.J.: Convolution: A method or daa analysis inperifusion systems. *Am. J. Physiol.*, In Press.
6. Peeel, H., Randolph, J., Jr., Midgley, A.R., Jr., and Menon, K.M.J.: In situ hybridization of LH/hCG messenger RNA during hormone-induced down regulation and the subsequent recovery in rat corpus luteum. *Endocrinology*, In Press.
7. Halberstadt, C.R., Lee, G.M., Palsson, B.O., and Midgley, A.R., Jr.: Enhanced antibody productivity in a serum-free, low-protein medium from a long-term hybridoma cell culture using the transtubular reactor. *Biotechnology Progress*, In Press.

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. Midgley, A.R., Jr., 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 perfused neuroendocrine tissues to stimuli in real time. Invited Review. In: *Quantitative Neuroendocrinology*, a volume in the series *Methods in Neurosciences*, (eds): Veldhuis and Johnson. Submitted for publication.
4. Halberstadt, C.R., Palsson, B.O., Midgley, A.R., Jr. and Curl, R.L.: Optimization of the transtubular bioreactor for the production of monoclonal antibodies from a hybridoma cell line S3H5/g2bA2. Submitted for publication.
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. Poplawski, M.E., Midgley, A.R., Jr. and Brown, R.B.: Batch fabricated amperometric biosensors. *Biosensors '94*.
2. Padmanabhan, V., Ireland, J.L.H., Good, T.E.M., McConnell, D.S., Midgley, A.R., Jr., Miller, W.L. and Ireland, J.J.: Evidence that molecular variants of bovine inhibin have differential endocrine and paracrine roles in modifying FSH secretion. 76th Annual Meeting, Endocrine Society, June 15-18, 1994.
3. Heinze, K., Padmanabhan, V., Favreau, P.A. and Midgley, A.R., Jr.: Effects of estradiol and changing GnRH frequency/amplitude input on LH secretion from perfused ovine pituitary cells. 76th Annual Meeting, Endocrine Society, June 15-18, 1994.
4. 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 of the Study of Reproduction, July 24-27, 1994.
5. 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.
6. 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.

7. 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.
8. 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 1993 - 30 JUNE 1994**

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."

B. Postdoctoral fellows:

1. Duaine Jackola, Ph.D.
2. Li Shaokang, U.S.
3. Jacek Witkowski, M.D., Ph.D.
4. Jagadananda Ghosh, Ph.D.
5. Michael Angell, Ph.D.
6. Prem Chaudhry, Ph.D.
7. Nathan Bining, Ph.D.
8. William Telford, Ph.D.

III. RESEARCH ACTIVITIES

SPONSORED SUPPORT:

- A. Principal Investigator, "Activation Defects in Aging T Cells", NIH AG-09801 (20%), \$152,738 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%), \$151,583 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, 8/1/91 - 7/31/94.

- D. Principal Investigator, "Genetic Control of Longevity in Mice", NIH AG-11687 (8%), \$189,187 direct costs/year, 9/1/93 - 8/31/98.
- E. Training Supervisor, "Research Training Agreement: Postdoctoral Training in Aging and Growth Control", Boston University (NIH/NIA Prime) (0%), \$20,304 direct costs/year, 10/1/93-9/30/94.
- F. Core Director, "Core Facility for Aged Rodents", NIH AG-08808 (10%), \$66,755 direct costs/year, 9/1/89 - 8/30/94. (Component of Claude Pepper Geriatric Research and Training Center, J. Halter, Program Director).
- G. Core Director, "Research Development Core", NIH AG-08808 (10%), \$41,000 direct costs/year, 9/1/89 - 8/30/94. (Component of Claude Pepper Geriatric Research and Training Center, J. Halter, Program Director).
- H. Program Director, "Research Training in Experimental Immunopathology", NIH AI-07413, \$236,492 direct costs/year, 4/1/93-3/31/98.
- I. Conference Director, "1994 Gordon Research Conference on the Biology of Aging", \$37,130 direct costs, 3/1/94 - 2/28/95.

PENDING

- A. Co-Director, "Breast Cancer in Elderly Women", (M. Wicha, PI), NIH CA-unassigned, \$104,307 direct costs requested/year, 9/30/94 - 9/29/98.
- B. Conference Director, "1994 GSA Meeting: Biology of Aging and Geriatric Disease", NIH AG-12351, \$34,045 direct costs requested, 9/1/94 - 8/31/95.
- C. Principal Investigator, "Participation of P-Glycoprotein and TAP in the Aging of Murine T Cells", Howard Hughes Medical Institute International Program, \$67,500 direct costs/year requested, 1/1/95 - 12/31/99.
- D. Principal Investigator, "Age-Related Changes in Regulatory Interactions of T Lymphocytes", Howard Hughes Medical Institute International Program, \$54,000 direct costs/year requested, 1/1/95 - 12/31/99.
- E. Principal Investigator, "New T Cell Subsets in Aging Mice", Allied Signal Research Award, \$100,000 direct costs/year requested, 1/1/95 - 12/31/96.
- F. Course Director, "Summer Training Courses in Experimental Aging Research", NIH AG-unassigned, \$29,358 direct costs/year requested, 4/1/95 - 3/31/00.
- G. Principal Investigator, "T Cell Subsets Defined by P-Glycoprotein in Aging Mice", Department of Veterans' Affairs, \$98,862 direct costs/year requested, 4/1/95 - 3/31/96.

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL

- A. Committee on Master Planning Analysis.
- B. Graduate Education Committee.
- C. Qualifying Examination Committee.
- D. Research Colloquia, Course Coordinator.
- E. Chair, Steering Committee, 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. Research Retreat Coordinator, Geriatric Research and Training Center.
- F. Member, Dean's Immunology Task Force.

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. Chair, Gordon Research Conference on "Biology of Aging".
- F. Board of Scientific Advisors, American Federation for Aging Research.
- G. Chair-Elect for Biological Sciences, Gerontological Society of America.
- H. Member, Council, Gerontological Society of America.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS

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

INVITED LECTURES/SEMINARS

1. International Congress of Gerontology (Session Chair), Budapest, July, 1993.
2. Rheumatology Training Program, University of Michigan, August, 1993.
3. NIAID Workshop on T and B Cell Memory, Bethesda, Maryland, September, 1993.
4. Laurence Kater Memorial Lecture, Case Western Reserve Hospitals, September, 1993.
5. University of Michigan, Unit for Laboratory Animal Medicine, October, 1994.
6. Symposium on "Nutrition, Aging, and the Immune System", Boston, Massachusetts, November, 1993.
7. Gerontology Society of America Annual Meeting (Session Chair), New Orleans, Louisiana, November, 1993.
8. World Health Organization Conference on Vaccine Development for Immunization of the Elderly (Keynote Speaker), Bethesda, Maryland, January, 1994.
9. NIA Longevity Assurance Gene Consortium Meeting, Santa Barbara, California, January, 1994.
10. Dahlem Conference on Molecular Aspects of Aging, Berlin, Germany, February, 1994.
11. Summer Training Course in Experimental Aging Research, Novato, California, June, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Shi, J. and Miller, R.A.: Differential tyrosine-specific protein phosphorylation in mouse T lymphocyte subsets: Effect of age. *J. Immunol.* 151:730-739, 1993.
2. Ghosh, J. and Miller, R.A.: Suramin, an experimental chemotherapeutic drug, irreversibly blocks T cells CD45-protein tyrosine phosphatase *in vitro*. *Biochem. Biophys. Res. Comm.* 194:36-44, 1993.
3. Li, S.P. and Miller, R.A.: Age-associated decline in IL-4 production by murine T lymphocytes in extended culture. *Cell. Immunol.* 194:36-44, 1993.
4. Miller, R.A.: Nathan Shock Memorial Lecture: Aging and immune function: cellular and biochemical analyses. *Exp. Gerontol.* 29:21-35, 1994.
5. Jackola, D.R. and Miller, R.A.: Age-associated changes in human T cell phenotype and function. *Aging: Clinical and Experimental Research* 6:25-34, 1994.
6. Miller, R.A., Turke, P., Chrisp, C., Ruger, J., Luciano, A., Peterson, J., Chalmers, K., Gorgas, G. and VanCise, S.: Age-sensitive T cell phenotypes covary in genetically heterogeneous mice and predict early death from lymphoma. *J. Gerontol. Biol. Sci.*, In Press.
7. Witkowski, J.M., Li, S.P., Gorgas, G. and Miller, R.A.: Extrusion of the P-glycoprotein substrate rhodamine-123 distinguishes CD4 memory T cell subsets that differ in IL-2 driven IL-4 production. *J. Immunol.* 153:658-665, 1994.

ARTICLES SUBMITTED FOR PUBLICATION

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 stimuli.
2. Li, S.P. and Miller, R.A.: Age-related defects in T cell induction of *in vitro* B cell proliferation and antibody production. Submitted, to
3. Witkowski, J.M., Gorgas, G. and Miller, R.A.: Increased levels of P-glycoprotein accompanied by higher expression of MHC class I antigens and decreased expression of TAP1 and TAP2 in T cells of old mice. Submitted to

BOOKS/CHAPTERS IN BOOKS

1. Miller, R.A., Li, S.P., Patel, H.R., Shi, J. and Witkowski, J.M.: Alterations in T cell heterogeneity and responsiveness in aging mice, in, Powers, D., Morley, J. and Coe, R., (eds), *Aging, Immunity and Infection*, Springer Publishing Company, New York, New York, pp 82 - 94, 1994.
2. Miller, R.A.: The biology of aging and longevity, in, Hazzard W.R. et al (eds), *Principles of Geriatric Medicine and Gerontology*, 3rd Edition, McGraw-Hill, Inc., New York, New York, Chapter 1, pages 3-18, 1994.
3. Miller, R. A.: Aging and the immune system, in, Masoro, E. (ed), *Handbook of the Physiology of Aging*, Academic Press, New York, New York, In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Role of Keratinocytes in Cutaneous Inflammation/Immunity", Johns Hopkins Center for Alternatives to Animal Testing, 2/94-1/97.
- 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. Characterization of epidermal growth factor receptor on normal and psoriatic keratinocytes.
- C. Role of gamma interferon in modulating adherence reactions between resting and activated mononuclear leukocytes and keratinocytes.
- D. Role of urocanic acid and histidine metabolites on tumor necrosis factor alfa induced ICAM-1 expression in cultured keratinocytes.
- E. Safety testing: Skin irritation and contact sensitization.

REVIEWER

- A. NATO Advanced Study Institute.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Responsible for teaching theoretical as well as technical to newcomers to the laboratory.

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Nickoloff, B.J., Mitra, R.S., Green, J., Thompson, C., Turka, L. and Shimizu, Y.: Discordant expression of CD28 ligands-BB-1 and B7 on cultured keratinocytes and psoriatic cells *in vivo*. Amer. J. Pathol. 142:1029-1040, 1993.
2. Nickoloff, B.J., Mitra, R.S., Green, J., Shimizu, Y., Thompson, C. and Turka, L.A.: Accessory cell function of keratinocytes for superantigens: Dependence of LFA-1/ICAM-1 interaction. J. Immunol. 150:2148-2159.
3. Nickoloff, B.J., Mitra, R.S., Green, J., Shimizu, Y., Thompson, C. and Turka, L.: Activated keratinocytes present bacterial-derived superantigens to T lymphocytes: Relevance to psoriasis. J. Dermatol. Sci. 6:127-133, 1993..
4. Mitra, R.S., Shimizu, Y. and Nickoloff, B.J.: Histamine and cis-urocanic acid augment tumor necrosis factor-alpha mediated induction of keratinocyte intercellular adhesion molecule-1 expression. J. Cell Physiol. 156:348-357, 1993.
5. 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.

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. Mitra, R.S., Shimizu, Y. and Nickoloff, B.J.: Cis-urocanic acid and histamine augment TNF-a mediated induction of keratinocyte ICAM-1 expression and suppress IFN-a induction of HLA-DR. J. Invest. Dermatol. 100:490, 1993.
2. Nickoloff, B.J., Mitra, R.S., Shimizu, Y., Thompson, C. and Turka, L.: Role of ICAM-1 and HLA-DR in accessory cell function of gamma interferon treated keratinocyte using lectin,

- superantigen, and immobilized CD3 mAb as T cell mitogens. *J. Invest. Dermatol.* 100:522, 1993.
3. Mitra, R.S. and Nickoloff, B.J.: Substance P augments interferon-gamma but not tumor necrosis factor-alpha mediated induction of keratinocyte ICAM-1 expression. The Second Tricontinental Meeting of the Japanese Society for Investigative Dermatology, the Society for Investigative Dermatology, and the European Society for Dermatological Research, Kyoto, Japan, October, 1993.
 4. Nickoloff, B.J., Mitra, R.S. and Turka, L.A.: Transfection of CD28 ligand B7-1 and anti-IL-10 mAb are important for allogeneic T cell response to IFN- α treated keratinocytes. *J. Invest. Dermatol.* 102:583, 1994.
 5. 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.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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, cytologic technique and aspiration cytology.

PROJECTS UNDER STUDY:

- A. Curschmann's spirals in bronchial aspirates.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

- A. North American Review Board, Acta Cytologica.
- B. Associate Editor, Acta Cytologica.
- C. Editorial Board, The ASC Bulletin.
- D. Editorial Board, Cytopathology.
- E. Membership Committee, International Academy of Cytology.
- F. Budget and Finance Committee, American Society of Cytology.
- G. Chairman, Awards Committee, American Society of Cytology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Lecture, "Differential Diagnostic Problems in Effusion Cytology", Annual Meeting of United States and Canadian Academy of Pathology, San Francisco, California, March, 1994.
2. Lecture, "The Mesothelial Cell and Its Reactions', 35th Annual Postgraduate Institute for Pathologists in Clinical Cytopathology, The Johns Hopkins Hospital, Baltimore, Maryland, April, 1994.

HONORS AND AWARDS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Huang, J.C. and Naylor, B.: Cytomegalovirus infection of the cervix detected by cytology and histology: A report of five cases. *Cytopathology* 4,237-241, 1993.
2. Grant, R., Naylor, B., Greenberg, H.S. and Junck, L.: Clinical outcome in aggressively treated meningeal carcinomatosis. *Arch. Neurol.* 51,457-461, 1994.

BOOKS/CHAPTERS IN BOOKS:

1. Naylor, B.: Pleural, peritoneal, and pericardial fluids, in, Keebler, C.M. and Somrak, T.M. (eds), *The Manual of Cytotechnology*, Seventh edition, Chicago, ASCP Press, pp. 219-237, 1994.

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

1. Laniran, T. and Naylor, B.: Variations on a theme of Papanicolaou. *ASC Bull.* 30, 58-59, 1993.
2. Naylor, B.: In memoriam: Kazumasa Masubichi, M.D. *ASC Bull.* 30, 84, 1993.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1993- 30 JUNE 1994

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.

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. "Role of Adhesion Molecules in Skin Diseases", NIH RCDA (50% effort), \$60,000 Direct Costs, July 1991-June 1994.
- B. "Role of Keratinocyte ICAM-1 in Cutaneous Inflammation," ISIS Pharmaceutical Corp. (5% effort), \$85,800 Direct Costs, April 1993-Jan 1995.
- C. "Immunobiology of Kaposi's Sarcoma Tumor Cells," NIH RO-1 (25% effort), \$194,727 Direct Costs, June 1994-June 1999.
- D. "Role of Scatter Factors in AIDS-Related Kaposi's Sarcoma," NIH RO-1 (5% effort), \$201,011 Direct Costs, June 1994-June 1999.

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. Binding of lymphocytes to epidermis and vessels of frozen sections of psoriatic skin and other dermatoses.
- D. Characterization and biological significance of thrombospondin production by keratinocytes.
- E. Role of endothelial cell adhesion molecules (ICAM-1, ELAM-1, VCAM-1) in cutaneous leukocyte trafficking.

- F. Role of factor XIII a positive dermal dendrocytes in AIDS-related psoriasis.
- G. Dissection of cytokine networks in psoriasis, allergic contact dermatitis to poison ivy, and mycosis fungoides.
- H. Role of Scatter Factor/C-met in Kaposi's Sarcoma.
- I. Role of CD28/BB-1/B7 in Psoriasis.

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

- A. Member, General Medicine A Study Section, National Institutes of Health.
- D. Ad-hoc Reviewer, University of Michigan Multipurpose Arthritis Center.
- E. 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.

INVITED LECTURES/SEMINARS:

1. Invited Speaker, "Molecular Biology of Cutaneous Inflammation", Gordon Conference on Barrier Function of Mammalian Skin, Plymouth, New Hampshire, August 18, 1993
2. "Scatter Factor Induces Transdifferentiation of Endothelial Cells and Growth of Kaposi's Sarcoma Cells", Central Society of Investigative Dermatology, Chicago, Illinois, November 6, 1993.
3. "Hut 78 T cells Express E-Cadherin and Bind to Keratinocytes which also Express Function E-Cadherin Molecules", American Society of Dermatopathology Annual Meeting, Washington, D.C., December 2, 1993.

4. "Dermal Dendrocytes: Important Members of the Dermal Immune System", Invited Speaker: Forum: Antigen Presenting Cells of the Skin, National Meeting - American Academy of Dermatology, Washington, D.C., December 7, 1993.
5. Invited Speaker, "Regulation of Adhesion Molecule Expression in Inflammatory Skin Disease", Adhesion Molecule Symposium, American Academy of Dermatology, Washington, D.C., December 7, 1993.
6. Invited Speaker, "Role of Bacterial-Derived Superantigens in T-cell Mediated Skin Diseases", Departments of Biochemistry and Pathology, Wayne State University School of Medicine, Detroit, Michigan, December 15, 1993.
7. Invited Speaker, "Skin-Related Antigen Presenting Cells", Invited Speaker, Division of Rheumatology-SCOR Program, University of Michigan, Ann Arbor, Michigan, April 14, 1994.
8. Invited Speaker and Visiting Professor, "Newly Recognized Immunocompetent Cells in Skin: Keratinocytes and Dermal Dendritic Cells", Department of Dermatology, Henry Ford Hospital, Detroit, Michigan, April 16, 1994.
9. Invited Speaker, "Barrier Perturbation Initiates Epidermal Cytokine Cascade", Second International Symposium on Irritant Contact Dermatitis, Zurich, Switzerland, April 14, 1994.
10. "Role of Keratinocytes in Irritant and Allergic Contact Dermatitis Reactions", Program Project Update--Center for Alternatives to Animal Testing, Johns Hopkins University, Baltimore, Maryland, April 21, 1994.
11. "Keratinocyte IL-10 Expression in Skin Diseases", Annual Meeting of Society for Investigative Dermatology/American Federation of Clinical Research, Baltimore, Maryland, May 2, 1994.
12. 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.
13. 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.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Mitra, R.S., Shimizu, Y. and Nickoloff, B.J.: Histamine and cis-urocanic acid augment tumor necrosis factor-alpha mediated induction of keratinocyte intercellular adhesion molecule-1 expression. *J. Cell Physiol.* 156:348-357, 1993.
2. Zukerberg, L.R., Nickoloff, B.J. and Weiss, S.W.: Kaposiform hemangioendothelioma of infancy and childhood: An aggressive neoplasm associated with Kasabach-Merritt Syndrome and lymphangiomas. *Am. J. Surg. Pathol.* 17:321-328, 1993.
3. Grant, D.S., Kleinman, H.H., Goldberg, I.D., Bhargava, M.M., Nickoloff, B.J., Kinsella, J.L., Polverini, P. and Rosen EM: Scatter factor induces blood vessel formation *in vivo*. *Proc Nat Acad Sci (USA)* 90:1937-1941, 1993.
4. Altman, D.A., Nickoloff, B.J. and Fivenson, D.P.: Differential expression of factor XIIIa and CD34 in cutaneous mesenchymal tumors. *J. Cut. Pathol.* 20:154-158, 1993.
5. Carr, K.A., Bulengo, S., Weiss, L.M. and Nickoloff BJ: Lymphoepithelioma-like carcinoma of the skin: A case report with immunophenotypic analysis and *in situ* hybridization of Epstein-Barr viral genome. *Am. J. Surg. Pathol.* 16:909-913, 1993.
6. Uyemura, K., Yamamura, M., Fivenson, D.F., Modlin, R.L. and Nickoloff, B.J.: The cytokine network in psoriasis is characterized by a T-helper type 1 cell mediated response. *J. Invest. Dermatol.* 101:701-705, 1993.
7. Nickoloff, B.J., Mitra, R.S., Green, J., Thompson, C., Turka, L. and Shimizu, Y.: Discordant expression of CD-28 ligands BB-1 and B7 on cultured keratinocytes and psoriatic cells *in vivo*. *Am. J. Pathol.* 142:1029-1040, 1993.

8. Nickoloff, B.J.: PECAM-1 (CD31) is expressed on proliferating endothelial cells, stromal spindle-shaped cells and dermal dendrocytes in Kaposi's sarcoma. *Arch. Dermatol.* 129:250-252, 1993.
9. Huang, X., Friedman-Kien, A., Li, J.J. and Nickoloff, B.J.: Kaposi's sarcoma cell lines express factor XIIIa, CD-14 and VCAM-1 but not factor VIII or ELAM-1. *Arch. Dermatol.* 129:1291-1296, 1993.
10. Nickoloff, B.J., Mitra, R.S., Green, J., Shimizu, Y., Thompson, C. and Turka, L.A.: Accessory cell function of keratinocytes for superantigens: Dependence of LFA-1/ICAM-1 interaction. *J. Immunol.* 150:2148-2159, 1993.
11. Weiss, S.W. and Nickoloff, B.J.: CD34 is expressed by a distinctive cell population in peripheral nerve, nerve sheath tumors, and related lesions. *Am. J. Surg. Pathol.* 17:1039-1045, 1993.
12. Nickoloff, B.J. and Turka, L.: Keratinocytes: Key immunocytes of the integument. *Am. J. Pathol.* 143:325-331, 1993.
13. Nickoloff, B.J., Mitra, R.S., Green, J., Shimizu, Y., Thompson, C. and Turka, L.: Activated keratinocytes prevent bacterial-derived superantigens to T lymphocytes: Relevance to psoriasis. *J. Dermatol. Sci.* 6:127-133, 1993.
14. Nestle, F.O., Zheng, X.G., Thompson, C.G., Turka, L.A. and Nickoloff, B.J.: Characterization of dermal dendritic cells obtained from normal human skin reveals phenotypic and functionally destructive subsets. *J. Immunol.* 151:6536-6545, 1993.
15. Nickoloff, B.J. and Naidu, Y.: Perturbation of epidermal barrier function correlates with initiation of cytokine cascade in human skin. *J. Am. Acad. Dermatol.* 30:535-546, 1994.
16. Nestle, F.O., Thompson, C., Shimizu, Y., Turka, L.A. and Nickoloff, B.J.: Co-stimulation of superantigen activated T lymphocytes by autologous dendritic cells is dependent on B7. *Cell Immunol.* 156:220-229, 1994.
17. Koch, A.E., Nickoloff, B.J., Haines, G.K., Burrows, J.C. and Leibovich, S.J.: 4A11: A monoclonal antibody recognizing a novel antigen exposed to aberrant vascular endothelium: Up-regulation in an *in vivo* model of contact dermatitis. *Am. J. Pathol.* 144:244-259, 1994.
18. Regezi, J.A., Daniels, T.E., Saeb, F. and Nickoloff, B.J.: Increased submucosal factor XIIIa positive dendrocytes in oral lichen planus. *J. Oral. Pathol. & Lab. Med.* 23:114-118, 1994.
19. Nickoloff, B.J., Mitra, R.J., 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. Nickoloff, B.J., Nestle, F.O., Zheng, X.G. and Turka, L.A.: T lymphocytes in skin lesion of psoriasis and mycosis fungoides express B7: A ligand for CD28. *Blood* 83:2580-2586, 1994.
21. 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. Natl. Acad. Sci. (USA)* 91:5281-5285, 1994.
22. 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.* 103:129-135, 1994.
23. 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.
24. 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 γ -IFN. *J. Immunol.* 252:5189-5198, 1994.
25. Rosen, E.M., Grant, D.S., Kleinman, H.K., Goldberg, I., Bhargava, M.M., Nickoloff, B.J., Kinsella, J.L. and Polverini, P.: Scatter factor (Hepatocyte growth factor) is a potent angiogenesis factor *in vivo*. In Abercrombie Symposium Proceedings. Society for Experimental Biology, In Press, 1994.
26. Nickoloff, B.J. and Turka, L.A.: Immunologic function of non-professional antigen presenting cells. Insights from keratinocyte: T cell interactions. *Immunol. Today*, In Press, 1994.

27. Nestle, F.O., Mitra, R.S., Bennett, C.D., Chan, M. and Nickoloff, B.J.: Cationic lipid is not required for uptake and selective inhibitory activity of ICAM phosphorothiate antisense oligonucleotides in keratinocytes. *J. Invest. Dermatol.*, In Press, 1994.
28. Nickoloff, B.J., Fivenson, D.P., Kunkel, S.L., Strieter, R.M. and Turka, L.A.: Keratinocyte IL-10 expression is up-regulated in tape stripped skin, poison ivy dermatitis, and Sezary Syndrome, but absent in psoriatic plaques. *Clin. Immunol. and Immunopath.*, In Press, 1994.

BOOKS/CHAPTERS IN BOOKS:

1. Fivenson, D.P. and Nickoloff, B.J.: Cell trafficking networks in cutaneous T cell lymphoma, in, Lambert, W.C. (ed), *NATO meeting-Basic Mechanisms of Physiological and Aberrant Lymphoproliferation in the Skin*, Plenum Publishing, New York, New York, In Press, 1994.
2. Stoof, T., Boorsma, D. and Nickoloff, B.J.: Immunological cytokines of epidermis, in, Leigh, I. (ed), *Keratinocyte Handbook*, Cambridge University Press, In Press, 1994.
3. Nickoloff, B.J.: The immunobiology of dermis, in, Nickoloff, B.J. (ed), *Dermal Immune System*, CRC Press, Inc., Boca Raton, Florida, In Press, 1994.
4. 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, In Press, 1994.
5. Kunkel, S.L., Driscoll, K., Ward, P.A., Nickoloff, B.J. and Strieter, R.M.: Immunopathology of environmental and occupational disease, in, Craighead, J.E. (ed), *Pathology of Environmental and Occupational Diseases*, In Press, 1994
6. 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, In Press, 1994.
7. Nickoloff, B.J.: Role of cytokines in psoriasis and other T-cell mediated dermatoses, in, Aggarwal, G.A. and Pari, R.K. (eds). *Human Cytokines: Their Role in health and Disease*, Blackwell Scientific Publications, Inc., Cambridge, Massachusetts, In Press, 1994.
8. Polverini, P. and Nickoloff, B.J.: Role of scatter factor in AIDS-related Kaposi's sarcoma, in, Klein, G. and Van de Woulde, G.F., *Advances in Cancer Research*, Academic Press, New York, In press, 1994.
9. Karasek M.A. and Nickoloff, B.J.: Guest Editor and Contributor: Festschrift for Dr. Eugene Farber, *International Journal of Dermatology*, In Press, 1994.

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

1. Naidu, Y., Nestle, F., Turka, L., Thompson, C. and Nickoloff, B.J.: T Lymphocytes activated by bacterial superantigens presented by keratinocytes secrete a TH-2 type cytokine profile. *Clin. Res.* 41:256, 1993.
2. Uyemura, K., Nickoloff, B.J., Fivenson, D.P. and Modlin, R.L.: The cytokine network in lesional and lesion-free psoriatic skin is characterized by a T-helper type 1 cell mediated response. *J. Invest. Dermatol.* 100:572, 1993.
3. Nestle, F.O., Mitra, R.S., Bennet, C.F. and Nickoloff, B.J.: Cationic lipid is not required for uptake and inhibiting activity of ICAM-1 antisense oligonucleotides in keratinocytes. *J. Cell Biochem.* 17E, 5312, 1993.
4. Mitra, R.S. and Nickoloff, B.J.: Substance P augments interferon-gamma but not tumor necrosis factor-alpha mediated induction of keratinocyte ICAM-1. *J. Dermatol. Sci.* 6:44, 1993.
5. Nestle, F.O., Trinh, D.T., Naidu, Y. and Nickoloff, B.J.: Kaposi's sarcoma tumor cells differ from endothelial cells and dermal dendrocytes by lack of B7 expression and inability to stimulate T cells. *Clin. Res.* 41:690, 1993.
6. Nickoloff, B.J., Naidu, Y., Nestle, F.O., Zitnick, R., Goldberg, I., Park, M., Polverini, P. and Rosen, E.: Scatter factor induces transdifferentiation of endothelial cells and growth of Kaposi's sarcoma cells. *Clin. Res.* 41:691, 1993.

7. Nickoloff, B.J., Trinh, D.T., Nestle, F.O. and Mitra, R.S.: Hut-78 T cells express E-Cadherin and bind to keratinocytes which also express functional E-Cadherin molecules. *J. Cut. Pathol.* 20:560, 1993.
8. Hsi, E.D. and Nickoloff, B.J.: Dermatofibroma and dermatofibrosarcoma protuberans: an immunohistochemical study reveals distinctive antigenic profiles. *Lab. Invest.* 70:46A, 1994.
9. Fivenson, D., Said, G. and Nickoloff, B.J.: Modulation of IL-10 expression in Hut-78 cells; Insights into the pathobiology and treatment of CTCL. *J. Invest. Dermatol.* 102:585, 1994.
10. Singer, N., Nickoloff, B.J., Richardson, B., Mitra, R.S. and Fox, D.: Keratinocytes do not present nominal antigens to tetanus toxoid specific autologous cloned human T lymphocytes. *Clin. Res.* 42:232, 1994.
11. Nickoloff, B.J., Mitra, R.S. and Turka, L.A.: Transfection CD28 ligand B7-1 and anti-IL-10 mAb are important for allogeneic T cell response to IFN-g treated keratinocytes. *J. Invest. Dermatol.* 102:583, 1994.
12. 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-2 and IFN- γ . *J. Invest. Dermatol.* 102:527, 1994.
13. Naidu, Y., Rosen, E., Park, M., Naujokas, M., Polverini, P. and Nickoloff, B.J.: Scatter factor stimulates Kaposi's sarcoma tumor cells via both autocrine and paracrine pathways. *J. Invest. Dermatol.* 102:544, 1994.
14. Nickoloff, B.J., Fivenson, D.P., Kunkel, S., Strieter, R. 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.* 42:232, 1994.
15. Nestle, F.O., Kunkel, R. and Nickoloff, B.J.: Cultured dermal dendritic cells contain Birbeck granules and are phagocytic. *Clin. Res.* 42:232, 1994.
16. Fivenson, D.P., Faria, D.T., Nickoloff, B.J., Polverini, P. and Strieter, R.M.: Biological wound dressings function as a reservoir for C-X-C chemokines in chronic venous ulcer therapy. *Clin. Res.* 42:232, 1994.
17. Nickoloff, B.J.: Book Review: *Differential Diagnosis of Dermatopathology*, by AB Ackerman. *New Eng. J. Med.* 328:1051-1052, 1994.
18. Goodman, R.E., Naidu, Y., Nestle, F., Green, J.M., Thompson, C., Nickoloff, B.J. and Turka, L.A.: T cell co-stimulation by non-professional antigen-presenting cells: Defective induction of INF-g synthesis due to a lack of IL-12. *Transplant Proc.*, In Press, 1994.
19. Nickoloff, B.J. and Naidu, Y.: Barrier perturbation initiates epidermal cytokine cascade. *Allergologie* 17:79, 1994.
20. Nestle, F.O., Turka, L.A. and Nickoloff, B.J.: Hierarchy of the function significance of B7 expression by antigen-presenting cells: Autologous versus allogeneic reactions. *Arch. Dermatol. Res.* 286:145-231, 1994.
21. Hsi, E.D., Goldblum, J., Nickoloff, B.J. and Frank, T.: Detection of human papilloma virus by polymerase chain reaction in immunocompromised patients with keratocanthomas. *J. Clin. Pathol.*, In Press, 1994.
22. 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.*, In Press, 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

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).
- C. Supervised Donald Zhou (Molecular Diagnostics, three months).
- 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.

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.

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, and Oncogene.
- B. Ad Hoc Reviewer, Research grants, Cell Biology Study Section, American Cancer Society.

INVITED LECTURES AND SEMINARS

- 1. Invited Speaker, Molecular and Cellular Biology Program, University of Michigan, July 19, 1994.
- 2. Invited Speaker, Cell Death in Cancer Development, American Association for Cancer Research, Chatham, Massachusetts, October 17-21, 1993.
- 3. Invited Speaker, Cancer Biology Seminar, University of Michigan Cancer Center, November 10, 1993.
- 4. Invited Speaker, Department of Pathology, University of Geneva, Switzerland, December 17, 1993
- 5. Invited Speaker, Centro de Investigaciones Biologicas, Madrid Spain, December 20, 1993.
- 6. Invited Speaker, Gut Physiology Seminar, University of Michigan, January 11, 1994.
- 7. Invited Speaker, Department of Physiology Seminar, University of Michigan, January 19, 1994.
- 8. Invited Speaker, Hematology/Oncology Seminar, Case Western Reserve University, Cleveland, Ohio, January 21, 1994.
- 9. Invited Speaker, Wayne State University, January 27, 1994.
- 10. Invited Speaker, Parke-Davis, March 7, 1994.
- 11. Invited Speaker, Onyx Corporation, March 16, 1994.
- 12. Invited Speaker, Hematology/Oncology Grand Rounds, University of South Carolina, Charleston.
- 13. Invited Speaker and Co-Chairman, Minisymposium on Apoptosis, Pathology, FASEB, Anaheim, California, April 27, 1994.
- 14. Invited Speaker, Conference on "Apoptosis in Immunology and Hematopoiesis", National Institutes of Health, National Cancer Institute, Bethesda, Maryland, May 10, 1994.
- 15. Invited Speaker, Conference on "Biochemistry of Programmed Cell Death", Juan March Foundation, Madrid, May 23, 1994.
- 16. Invited Speaker, Research Cancer Institute, Barcelona, May 26, 1994.
- 17. Invited Speaker, Molecular Diagnostics Course, M-Labs - one hour.
- 18. Invited Speaker, U-M Cancer Center Retreat, 1994.

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

1. Boise, L., Gonzalez-Garcia, M., Postema, C., Ding, L., Lindsten, T., Turka, L., Mao, X., Nuñez, G. and Thompson, C.: *bcl-x*, a *bcl-2*-related gene that functions as a dominant regulator of apoptotic cell death. *Cell* 74:1-20, 1993.
2. Castle, V., Heidelberger, K.P., Bromberg, J., Ou, X., Dole, M. and Nuñez, G.: Expression of the apoptosis-suppressing protein *Bcl-2* in neuroblastoma is associated with unfavorable histology and *N-myc* amplification. *Am. J. Pathol.* 143:1543-1550, 1993.
3. Merino, R., Ding, L., Veis, D., Korsmeyer, S.J. and Nuñez, G.: Developmental regulation of the *bcl-2* protein and susceptibility to cell death in B lymphocytes. *EMBO J.* 13:683-691, 1994.
4. 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-Ig induced physiological cell death and lack of correlation with *bcl-2* expression. *Int. Immunol.* 6:121-130, 1994.
5. 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.
6. Ryan, J., Gottlieb, C., Merino, R., Nuñez, G. and Clarke, M.: Alteration of the cell cycle regulatory function of p53 by *bcl-2*. *Proc. Natl. Acad. Sci. USA*, In Press.
7. 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 endoplasmic reticulum. *Proc. Natl. Acad. Sci. USA*, In Press.
8. 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*, In Press.
9. González-García, M., Perez Ballesteros, 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*, In Press.
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*, In Press.
11. 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.

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 μ k 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 1993 - 30 JUNE 1994**

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.
- H. Member, Committee on guidelines for blood product utilization.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Lectures on breast pathology and transfusion medicine to sophomore class (five contact hours).
- B. Lecture on breast pathology (Seminars in Medicine) to junior class (two contact hours).
- C. Laboratory Course for sophomore medical students (Pathology 600) January-May, 1993.
- D. Daily case review with pathology house officers assigned to Blood Bank.
- E. Biweekly lecture/discussion with Pathology, Hematology and Pediatric Hematology house officers.
- F. Lectures (two) on Transfusion Medicine to senior student elective course in Laboratory Medicine.
- G. Postgraduate Course, "Current Topics in Blood Banking", Planning Committee.
- H. Lectures on Transfusion Medicine presented to Pathology and Hematology/Oncology House Officers.
- I. Seminars and lectures on Pathology of Breast to Pathology House Officers.
- J. Director, Pathology clerkship for senior medical students, August-September, 1993.
- K. Presentation on Transfusion Medicine to Pharmacology and Therapeutics senior student elective course, February, 1994.
- L. Planning committee for curriculum in hematology for sophomore medical students.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. New Ultrasound Methods for Cancer Diagnosis and Treatment, 3-5 years at 5% effort.
- B. Microvascular and Structural Imaging of Breast Cancer, 3-5 years at 3% effort.
- C. Extranodal Spread of Metastatic Breast Carcinoma in Axillary Lymph Nodes, With L. Pierce and A. Lichter.
- D. Mucinous Carcinoma of the Breast: Correlation of Mammographic Appearance with Histopathology, with M. Helvie and T. Wilson.

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

- A. American Association of Blood Banks:
 - 1. Awards Committee, Chairman.
 - 2. Transfusion Practices Committee.
 - 3. Institutional Dues Structure Committee.
 - 4. 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.
- I. Planning committee, 26th National Conference on Breast Cancer, American College of Radiologists.

DEPARTMENTAL:

- A. Director, Transfusion Medicine Program.
- B. Chairman's Advisory Committee.
- D. Director, Fellowship Program in Blood Banking/Transfusion Medicine.

MEDICAL SCHOOL/HOSPITAL:

- A. Transfusion Committee, Chairman.
- B. Breast Care Center.
- C. Bone Marrow Homotransplantation Task Force.
- D. AIDS Task Force.
- E. Hospital Quality Assurance Committee.
- F. Committee for Development of Guidelines for Use of Blood Products.
- G. Hematology sequence advisory committee, M-2 year.
- H. Medical School Grievance Review Committee.
- I. University of Michigan Senate Assembly.

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.

INVITED LECTURES/SEMINARS:

1. "Noninfectious Complications of Transfusion", presented to the Department of Pediatrics, University of Michigan Medical School, July 27, 1993.
2. "Blood Transfusion: Indications and Complications", Grand Rounds presentation to Department of Obstetrics and Gynecology, University of Michigan Medical School, September 2, 1993.
3. "Diagnostic Problems in Surgical Pathology of the Breast", course presentation with S. Silverberg at the Annual Meeting of the American Society of Clinical Pathologists, Orlando, Florida, October 20, 1993.
4. "Impact of Extracorporeal Membrane Oxygenation(ECMO) on the Blood Banks, presented the Annual Meeting, American Association of Blood Banks, Miami Beach, Florida, October 27, 1993.
5. "Is an Axillary Boost Necessary in Node Positive State II Disease in the Presence of Microscopic Extracapsular Extension?", San Antonio Breast Cancer Symposium, San Antonio, Texas, November 5, 1993.
6. "Problems in the Diagnosis and Management of Breast Cancer", American Society of Clinical Pathologists, three day course organized and presented by Drs. Oberman and P.P. Rosen, Longboat Key, Florida, December 8-10, 1993.
7. "Selected Aspects of Breast Pathology", seminar presented to the Detroit Pathology Society, Detroit, Michigan, February 15, 1994.
8. "Pathology of Noninvasive Breast Cancer", Course: Multimodality Treatment of Breast Cancer, sponsored by the Department of Radiation Oncology, University of Michigan, Pinehurst, North Carolina, March 4, 1994.
9. "Pathology of Invasive Breast Cancer", Course: Multimodality of Treatment of Breast Cancer, sponsored by the Department of Radiation Oncology, University of Michigan, Pinehurst, North Carolina, March 4, 1994.
10. "The Role of the Pathologist in Assessing Prognosis of Breast Cancer", Course: Multimodality of Treatment of Breast Cancer, sponsored by the Department of Radiation Oncology, University of Michigan, Pinehurst, North Carolina, March 4, 1994.
11. "Pathology of Stereotactic Needle Core Biopsies of Breast, 26th National Conference on Breast Cancer, Palm Springs, California, May 9-12, 1994.
12. "The Breast Biopsy", 26th National Conference on Breast Cancer, Palm Springs, California, May 9-12, 1994.
13. "Breast Lesions Confused with Malignancy", 26th National Conference on Breast Cancer, Palm Springs, California, May 9-12, 1994.
14. "Stromal Tumors of the Breast", 26th National Conference on Breast Cancer, Palm Springs, California, May 9-12, 1994.
15. "Selection of Patients for Adjuvant Chemotherapy", 26th National Conference on Breast Cancer, Palm Springs, California, May 9-12, 1994.
16. "Problem Solving in the Blood Bank", workshop, "Current Topics in Blood Banking", 21st annual symposium, University of Michigan, June 1, 1994.
17. "Noninfectious, Non-Hemolytic Transfusion Reactions", workshop, "Current Topics in Blood Banking", 21st Annual Symposium, University of Michigan, June 3, 1994.
18. "Prognostic Assessment of Breast Cancer", University of Michigan Medical School Northern Summer Conference, Bellaire, Michigan, June 23, 1994.

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

1. Oberan, H.A.: Frozen section diagnosis of breast biopsies - A necessary procedure? Arch. Surg. 128:955-956, 1993.

2. Oberman, H.A. and Goldman, E.B.: The patient's decision to be transfused. *Transfusion* 33:540-541, 1993.
3. August, D.A., Carpenter, L.C., Harness, J.K., Delosh, T., Cody, R.L., Adler, D.D., Oberman, H.A., Wilkins, E. and Schottenfeld, D.: Benefits of a multidisciplinary approach to breast care. *J. Surg. Oncol.* 53:161-167, 1993.
4. Oberman, H.A.: Should a febrile transfusion response occasion return of the unit to the blood bank? *Transfusion* 34:353-355, 1994.
5. 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.

BOOKS/CHAPTERS IN BOOKS:

1. Rosen, P.P. and Oberman, H.A.: Tumors of the Breast, Fascicles of Tumor Pathology, Armed Forces Institute of Pathology, Universities Associated for Research and Education in Pathology, Inc., 1993.
2. Oberman, H.A.: Section Editor, Immunohematology, in, McClatchey, K.D. (ed), *Clinical Laboratory Medicine*, Williams and Wilkins Co., Baltimore, Maryland, 1993.
3. Oberman, H.A.: Organization, functions, regulations and legal concerns of blood banks, in, McClatchey, K.D. (ed), *Clinical Laboratory Medicine*, Williams and Wilkins Co., Baltimore, Maryland, 1993.
4. Sternberg, S., Antonioli, D., Carter, D., Mills, S. and Oberman, H.A.: *Diagnostic Surgical Pathology*, Edition 2, Raven Press, New York, New York, December, 1993.

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

1. Butch, S.H., Knafl, P., Oberman, H.A. and Bartlett, R.H.: Impact of extracorporeal membrane oxygenation (ECMO) on the Blood Bank. *Transfusion* 33:58S, 1993.
2. Book Review Editor, *American Journal of Surgical Pathology*.
3. Oberman, H.A.: The hemolytic Anemias. III. The autoimmune hemolytic anemias, Dacie, J., in, *AMA Arch. Pathol. Lab. Med.* 117:1267, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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. Lynda Makowiec, Undergraduate Research, Opportunities Program.
- D. Tiy Smith, Summer Medical Student Research Program.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Mechanisms and Genetic Regulation of Pulmonary Fibrosis", NIH R01-HL28737.
- B. Project Leader, "Macrophage Function in Lung Injury and Fibrosis", Project IV, NIH P01-HL31963.
- C. Co-Investigator, "Hepatic Ischemia-Induced TNF and Multiorgan Injury", RO1-DK42455, 5% effort.
- D. Co-Investigator, "Cytokine Networks Regulating Inflammation of Pulmonary Fibrosis", NIH SCOR in Occupational and Immunologic Lung Diseases, Project 1, P50-HL46487, 5% effort.
- E. Co-Investigator, "Renal Fibrosis", NIH RO1 DK46467, 10% effort.

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. Isolation and characterization of lung fibroblast clones from normal and fibrotic lung to examine extent of and mechanistic basis for heterogeneity.
- D. Regulation of production of fibrogenic mediators and cytokines by pulmonary endothelial cells and 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.

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. Experimental Lung Research.
6. Journal of Clinical Investigation.
7. Journal of Immunology.
8. American Journal of Physiology.
9. American Journal of Respiratory Cell and Molecular Biology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Chair, "Cytokines in Lung Injury," Experimental Biology Annual Meeting, Anaheim, California, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Brieland, J.K., Jones, M.L., Flory, C.M., Miller, G.R., Warren, J.S., Phan, S.H. and Fantone, J.C.: Expression of monocyte chemoattractant protein-1 by rat alveolar macrophages during chronic lung injury. *Am. J. Resp. Cell Molec. Biol.* 9:300-305, 1993.
2. Garner, W.L., Karmioli, S., Rodriguez, J.L., Smith, D.J. Jr. and Phan, S.H.: Phenotypic differences in cytokine responsiveness of hypertrophic scar versus normal dermal fibroblasts. *J. Invest. Dermatol.* 101:875-879, 1993.
3. Rekhter, M.D., Zhang, K., Narayanan, A.S., Phan, S.H., Schork, M.A. and Gordon, D.: Type I collagen gene expression in human atherosclerosis: Localization of specific plaque regions. *Am. J. Pathol.* 143:1643-1648, 1993.
4. Karmioli, S., Remick, D.G. and Phan, S.H.: Regulation of rat pulmonary endothelial cell IL-6 production by bleomycin: Effects of cellular fatty acid composition. *Am. J. Resp. Cell Molec. Biol.* 9:628-636, 1993.
5. Zhang, K., Gharaee-Kermani, M., McGarry, B. and Phan, S.H.: *In situ* hybridization analysis of lung $\alpha_1(I)$ and $\alpha_2(I)$ collagen gene expression in bleomycin-induced pulmonary fibrosis in the rat. *Lab Invest.* 70:192-202, 1994.
6. Zhang, K., Rekhter, M.D., Gordon, D. and Phan, S.H.: Co-Expression of α -smooth muscle actin and type I collagen in fibroblast-like cells of rat lungs with bleomycin-induced pulmonary fibrosis: A combined immunohistochemical and *in situ* hybridization study. *Am. J. Pathol.* 145:114-125, 1994.
7. Smith, R.E., Strieter, R.M., Phan, S.H., Lukacs, N.W., Huffnagle, G., Wilkie, C., Burdick, M., Lincoln, P., Evanoff, H. and Kunkel, S.L.: Production and function of murine macrophage inflammatory protein-1 α in bleomycin-induced lung injury. *J. Immunol.* 1994; In Press.

BOOKS/CHAPTERS IN BOOKS:

1. Wiggins, R.C., Fantone, J.C., Phan, S.H. and Holzman, L.B.: Mechanisms of vascular injury, in, Tisher, C.C. and Brenner, B.M. (eds), Renal Pathology, 2nd edition, J. B. Lippincott Co., Philadelphia, Chapter 33, pp. 1027-1057, 1993.
2. Strieter, R.M., Phan, S.H. and Ward, P.A.: Inflammation, injury, and repair, in, Murray, J. and Nadel, J.A. (eds.), Textbook of Respiratory Medicine, 2nd edition, W. B. Saunders Co., Philadelphia, Chapter 17, pp. 469-497, 1994.

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

1. Phan, S.H. and Zhang, K.: *In situ* hybridization analysis of lung collagen gene expression in pulmonary fibrosis. European Respiratory Society 1993 Annual Congress.
2. Zhang, K. and Phan, S.H.: Monocyte chemoattractant protein-1 gene expression in bleomycin-induced pulmonary fibrosis. Am. J. Resp. Crit. Care Med. 149:A381, 1994.
3. Phan, S.H.: New strategies in therapy of pulmonary fibrosis. Thorax, 1994, In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

I. CLINICAL ACTIVITIES:

- A. Associate Director, Clinical Microbiology/Virology Laboratories.
- B. Coordinator, Infectious Disease laboratory rounds.
- C. Technical Consultant, M-Labs.

II. TEACHING ACTIVITIES:

- A. Coordinator, Pathology House Officer Microbiology rotation.
- B. Lecturer, Clinical Pathology Grand Rounds.
- C. Lecturer, Pathology M-4 Elective Course.
- D. Coordinator, Clinical Microbiology In-service Program.
- E. Lecturer, M-Labs Educational Programs.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. "Candida Vaginosis Study", National Institutes of Health.
- B. "Characterization of Beta-Lactamases Produced by Antimicrobial-Resistant *Escherichia coli* and *Klebsiella* sp", Merck, Sharp & Dohme.
- C. "Comparative Evaluation of the ESP Automated Blood Culture System", Difco Laboratories.
- D. "Changes in the *In Vitro* Susceptibility of the *Bacteroides fragilis* Group", Merck, Sharp & Dohme.
- E. "Survival of Fastidious Bacteria in Swab Transports", StarPlex Scientific.
- F. "Evaluation of Modified 3-Step Gram Stain Product", Difco Labs.
- G. "Clinical Evaluation of Levofloxacin", R.W. Johnson Research Institute.
- H. "Endophthalmitis/Vitreotomy Study (multicenter)", Retina-Vitreous Consultants.
- I. "Effective Selection of Antimicrobics", Small Grants Program.
- J. "Comparative Evaluation of Piperacillin/Tazobactam", Lederle Labs
- K. "Evaluation of Cefipime by E-Test", Institutes for Microbiology Research.

PROJECTS UNDER STUDY:

- A. Development of PCR techniques for the detection of *Herpes simplexvirus* in spinal fluids.

- B. Clinical utility of anaerobic blood cultures.
- C. Antimicrobial usage in ICUs.
- D. Effect of antifungal agents on the detection of yeasts in automated blood culture systems.
- E. Recovery of non-tubercular AFB from cystic fibrosis patients.
- F. Evaluation of the SOLUS system for viral serology.
- G. Comparative evaluation of four mycoplasma antibody detection kits.
- H. Incidence of vancomycin-resistance in clinical isolates of *Enterococcus* spp.
- I. Isolation of anaerobic bacteria in the BacT/Alert automated blood culture system.
- J. Use of pulsed field gel electrophoresis for infectious epidemiology.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Clinical Pathology Laboratory Director's Committee.
- B. Chair, Clinical Microbiology Senior Staff Meeting.

MEDICAL SCHOOL/HOSPITAL:

- A. Hospital Infection Control Committee.
- B. Pharmaceutical & Therapeutics Committee (antimicrobics).

REGIONAL/NATIONAL:

- A. President-elect, 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.
- E. Task force for Test Validation , Clinical Laboratory Improvement Amendments Committee.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

- A. American Society for Microbiology.
- B. Infectious Disease Society of America.
- C. Michigan Infectious Disease Society.
- D. South Central Association for Clinical Microbiology.
- E. Michigan Branch, American Society for Microbiology.
- F. Tri-County Association for Clinical Microbiology.

INVITED LECTURES/SEMINARS:

1. "Comparative Isolation of Anaerobic Bacteria From Blood Cultures", Difco ESP User Group Meeting, Las Vegas, Nevada.
2. "Application of PCR Technology to the Clinical Laboratory", Michigan Infectious Disease Society, Lansing, Michigan.
3. "Recent Changes in *In Vitro* Susceptibility Testing", Michigan Society for Medical Technologists meeting, Romulus, Michigan.
4. "Tunga penetrans", Michigan Branch, American Society for Microbiology, Southfield, Michigan.

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

1. Zwadyk, P., Jr., Pierson, C.L. and Young, C.: Comparison of Difco ESP and Organon Teknika BacT/Alert continuous-monitoring blood culture systems. *J. Clin. Microbiol.* 32:1273-1279, 1994.
2. Aldridge, K.E., Gelfand, M., Reller, L.B., Ayers, L.W., Pierson, C.L., et al. A five-year multicenter study of the susceptibility of the *Bacteroides fragilis* group isolates to cephalosporins, cephamins, penicillins, clindamycin, and metronidazole in the United States. *Diagn. Microbiol. Infect. Dis.* 18:235-241, 1994.
3. Cook, S.M., Bartos, R.E., Pierson, C.L. and Frank, T.S.: Detection and characterization of atypical mycobacteria by the polymerase chain reaction. *Diagn. Molecular Pathol.* 3:53-58, 1994.
4. Dyke, J.W., Brown, W.J., Morris, J.M., Pierson, C.L. and Peters, E.M.: Evaluation of the new DrySlide beta-lactamase test. *Amer. J. Clin. Pathol.* 101:726-728, 1994.
5. MacDonald, L.J., Pierson, C.L. and Chenoweth, C.E.: Penicillin-resistant *Streptococcus pneumoniae* at a tertiary care center. *Clin. Infect. Dis.*, In Press, 1994.

BOOK/CHAPTERS IN BOOKS:

1. Pierson, C.L.: Antimicrobial susceptibility testing, in McClatchey, K.D. (ed), *Clinical Laboratory Medicine*, Williams and Wilkins, Baltimore, Maryland, pgs. 1287-1304, 1994.

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

1. Gilbert, L., Fullarton, L., Young, C. and Pierson, C.L.: Comparative evaluation of a selective Todd-Hewitt broth and latex agglutination for the rapid detection of maternal group B streptococcus colonization. Abstracts, *Amer. Soc. Microbiol.* C-52, pg 499, 1994.
2. Snyder, D. and Pierson, C.L.: Delayed recovery of yeasts from blood cultures containing antifungal agents. Abstracts, *Amer. Soc. Microbiol.* C-478, pg 578, 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

OVERVIEW:

Started full-time at the University of Michigan Department of Pathology July 1, 1993. Sixty-five percent of my activity is to the M-Labs Program, including contacts with existing and potential hospital clients, enhancement of the Spectrum for M-Labs, organizing the M-Labs Symposium, coverage for Clinical and Anatomic Pathology for M-Labs and participation in the expansion plans for the M-Labs Program. In addition to my administrative activities, I am also part of the Cytopathology Laboratory staff and 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 M-Labs Symposium, held three times a year (January, April and September/October). This is a day-long event with lectures and case presentations held on a Saturday, for pathologists from our client hospitals.
- 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. Member, Tissue Transfusion Committee of Albion Community Hospital.
- C. Member, review group for reporting formats with PDS.
- 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 and Central Michigan Community Hospital.
- C. Monthly colposcopy meeting with Gynecology staff at the University of Michigan Health Service.

V. **OTHER RELEVANT ACTIVITIES:**

- A. Enhancement of the M-Labs' version of the Spectrum, which is now sent to client Hospitals and their medical staff. Several review articles covered topics of interest to our clients.
- B. Inspector for College of American Pathologists Inspection and Accreditation Program.
- C. Fellow, College of American Pathologists.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

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 (five weeks).
- E. Forensic Pathology (eight 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. Pathology 850 Course Instructor 26 hours
- F. Laboratory Instructor, Histopathology Laboratory for M1 students.
- G. Mentor - Fourth Year Medical Student Clerkship.
- H. Presentation to Pathology House Officers "Statistics"
- I. Transplant Journal Club, three presentations.
- J. Directed research of Allan Olson, M.D. (Department of Pediatrics), Jorge Rodriguez, M.D. (Department of Surgery); House Officers - Lyndon Su, Devina Prakash (Pediatrics) Eiji Takeuchi, M.D., Visiting Scholar, Postdoctoral fellows, Gordon Wollenberg, D.V.M., Ph.D., Lorelie Villarete, Ph.D.; Graduate students - Jami Foreback, Angela Dyer (Michigan State University).
- K. Postdoctoral Thesis Committee - Carol Conn, Department of Physiology.
- L. Postdoctoral Thesis Committee - Jiang Feng, Department of Physiology.

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, mL-6, hIL-8, MCP, JE.
- F. Mechanisms of organ injury induced by hepatic ischemia/reperfusion.
- G. Mechanisms of nosocomial pneumonia, and association with IL-8.

SPONSORED SUPPORT:

- A. Principal Investigator, "The Role of Cytokines in Sepsis and Trauma", five years, \$906,182, 1990-1995.
- B. Principal Investigator, Long-Term Minority Supplement for Jorge Rodriguez, M.D., \$200,000, 1991-1995.
- C. Principal Investigator, "The Effects of IL-10", one year \$25,000, 1994.
- D. Principal Investigator, "Hepatic Ischemia-Induced TNF and Multi-Organ Injury", National Institutes of Health, four years, \$924,643, 1990-1994.
- E. Principal Investigator, "Measurement of Cytokines in Sepsis Syndrome", Contracts, Cutter Biological, one year, \$183,000, 1992-1993.
- F. Sponsor, Medical Research Council of Canada Training Fellowship, Gordon Wollenberg, D.V.M., Ph.D., recipient.
- G. Principal Investigator, "Correlation of Cytokine Levels with APACHE III Scores" one year, \$3000, 1994

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.

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. Member, Legislative Committee, 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, National Science Foundation grants.
- B. Reviewer, Veterans Administration Merit grants.
- C. Editorial Board: Shock
- D. Reviewer:
 - 1. American Review of Respiratory Diseases.
 - 2. Laboratory Investigation.
 - 3. Journal of Immunology.
 - 4. American Journal of Applied Physiology.
 - 5. Journal Immunopharmacology.
 - 6. Journal Leukocyte Biology.
 - 7. American Journal of Pathology.
 - 8. Oncology Research.
 - 9. Immunology and Infectious Diseases.
 - 10. Circulatory Shock.
 - 11. Journal of Clinical Investigations.
 - 12. Infection and Immunity.
 - 13. Blood.
 - 14. Shock.
 - 15. American Journal of Physiology.
 - 16. Life Sciences.
 - 17. Journal of Immunology.
 - 18. Journal of Gerontology.
- E. Testimony to Judiciary Committee, House of Representatives Michigan State Legislature.

INVITED LECTURES/SEMINARS

- 1. Invited speaker "Cytokines and Extrahepatic Sequelae of Ischemia-Reperfusion Injury to the Liver", New York Academy of Sciences, July, 1993.
- 2. "Oxidant Regulation of Cytokine Gene Expression", Osaka, Japan, October, 1993.
- 3. Invited speaker, Amgen, Thousand Oaks, California, November, 1993
- 4. Invited participant, Immunological Issues Concerning Silicone Breast Implants, Chicago, Illinois January 15, 1994

5. Invited Speaker, "Cytokines", Department of Obstetrics and Gynecology, February 17, 1994.
6. Invited Speaker, Experimental Biology '94, Anaheim, California, April, 1994.
7. Invited participant, Immunological Issues Concerning Silicone Breast Implants, Cincinnati, Ohio, June 8, 1994.
8. Invited participant, Washtenaw County Medical Examiner's Roundtable discussion.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. DeForge, L.E., Preston, A.M., Takeuchi, E., Kenney, J., Boxer, L.A. and Remick, D.G.: Regulation of interleukin 8 gene expression by oxidant stress. *J. Biol. Chem.* 268:12-13, 1993.
2. Karmioli, 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 Mol. Biol.* 9:628-636, 1993.
3. McCurry, K.R., Campbell, Jr., D.A., Warren, J.S., Scales, W.E. and Remick, D.G.: TNF, IL-6 and the acute phase response following hepatic ischemia/reperfusion. *J. Surg. Res.* 54:49-54, 1993.
4. Seekamp, A., Warren, J.S., Remick, D.G., Till, G.O. and Ward, P.A.: Requirements for tumor necrosis factor-alpha and interleukin-1 in limb ischemia/reperfusion injury and associated lung injury. *Am. J. Pathol.* 143:453-463, 1993.
5. Wollenberg, G.K., DeForge, L.E., Bolgos, G. and Remick, D.G.: Differential expression of tumor necrosis factor and interleukin-6 by peritoneal macrophages *in vivo* and *in culture*. *Am. J. Pathol.* 143:1121-1130, 1993.
6. 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.* 144:599-611, 1994.
7. 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).* 86:47-51, 1994.
8. Remick, D.G., Colletti, L.M., Scales, M.A., McCurry, K.R. and Campbell, Jr., D.A.: Cytokines and the extrahepatic sequelae of ischemia/reperfusion injury to the liver. *New York Academy of Sciences* 723:271-283, 1994.
9. 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. *Clin. Infect. Dis.* 1:65-74, 1994.
10. Remick, D.G.: Cytokines and septic shock. *Clin. Infect. Dis.* 1:37-50, 1994.
11. Saravolatz, L.D., Wherry, J.C., Spooner, C., Markowitz, N., Allred, R., Remick, D., Fournel, M. and Pennington, J.E.: Clinical safety, tolerability, and pharmacokinetics of murine monoclonal antibody to human tumor necrosis factor alpha. *J. Infect. Dis.* 169:214-217, 1994.
12. Waage, A., Remick, D., Steinshamn, S., DeForge, L. and Lamvik, J.: Interleukin 8 in serum in granulocytopenic patients with infections. *Brit. J. Haematol.* 86:36-40, 1994.

13. Remick, D.G.: Lung and gut injury induced by tumour necrosis factor. *Res.Immunol.* 144:326-331, 1993.

ABSTRACTS

1. Remick, D.G., Manohar, P., Bolgos, G.L., Rodriguez, J., Moldawer, L. and Wollenberg, G.: Efficacy of anti-TNF therapy is dependent on the sepsis model. 5th international meeting on Tumor Necrosis Factor and Related Cytokines, Monterey California, May, 1994.
2. Bolgos, G.L., Wollenberg, G.K. and Remick, D.G.: Effect of caloric and protein restriction on LPS induced pathophysiology and cytokines. *Experimental Biology '94*, Bethesda, Maryland, 1994.
3. Prakash, D. and Remick, D.G.: Indomethacin fails to augment cytokine production in human whole blood. *Experimental Biology '94*, Bethesda, Maryland, 1994.
4. Preston, A.M., Stern, J.D., Yang, G.Y., Carr, K.A., Betz, A.L. and Remick, D.G.: TNF and IL-6 production after focal cerebral ischemia. *Experimental Biology '94*, Bethesda, Maryland, 1994.
5. Wollenberg, G.K., Bolgos, G., DeForge, L.E. and Remick, D.G.: Murine KC cytokine is potent neutrophil chemo-attractant expressed during acute inflammatory responses. *Experimental Biology '94*, Bethesda, Maryland, 1994.
6. Villarete, L. and Remick, D.G.: Mechanism of IL-8 and TNF mRNA stability. *Experimental Biology '94*, Bethesda, Maryland, 1994.
7. Remick, D., Fantone, J., Boxer, L. and DeForge, L.: Reactive oxygen intermediates (RO1) regulate IL-8 gene expression. Combined Meeting of the 8th International Lymphokine Workshop and The 4th International Workshop on Cytokines, Osaka, Japan, October 17-21, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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:

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.

SPONSORED SUPPORT:

- A. Co-investigator, "The Role of Stromal Dendritic Cells in Cutaneous B Cell Lymphoma", University of Michigan Cancer Center Grant, 3/1/94 through 2/28/95.

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL

- A. Director, Clinical Flow Cytometry Laboratory.
B. Coordinator, CP resident teaching program.
C. M-Labs Committee.

REGIONAL/NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Lecturer, "Principles of Clinical Flow Cytometry", Midwest Clinical Ligand Society, September 9, 1993.
2. Lecturer, "Molecular Approaches to the Diagnosis of Hematologic Malignancies", presented at Henry Ford Hospital course on "Current Concepts in the Management of Hematologic malignancies", October 1, 1993.
3. Lecturer, "Molecular Diagnostics in Hematopathology", Second M-Labs Symposium, University of Michigan, April 23, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kaminski, M.S., Zasadny, K.R., Francis, I.R., Milik, A.W., Ross, C.W., et al: Radioimmunotherapy of B-cell lymphoma with 131-I-anti-B1 (anti-CD20) antibody. *N. Engl. J. Med.* 329:459-465, 1993.
2. Ross, C.W., Schnitzer, B., Sheldon, S., Braun, D.K. and Hanson, C.A.: $\gamma\delta$ T-cell post-transplant lymphoproliferative disorder presenting primarily in spleen. *Am. J. Clin. Pathol.*, In Press.
3. Metzman, M.S., Stevens, S.R., Griffiths, C.E.M., Ross, C.W., Barnett, J.M. and Cooper, K.D.: A clinical and histologic mycosis fungoides simulant occurring as a T cell infiltrate coexisting with B cell leukemia cutis. *J. Am. Acad. Dermatol.*, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. 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.
2. 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.

3. 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.
4. 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.

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 System", AFIP 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-CLL (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 ¹³¹I-anti-B1 (anti-CD20) radioimmunotherapy (RIT) for refractory B-cell lymphoma. *Blood* 82(suppl. 1):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(suppl. 1):577a, 1993.

**NATHANIEL H. ROWE, D.D.S., M.S.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY
PROFESSOR OF DENTISTRY
UNIVERSITY OF MICHIGAN DENTAL SCHOOL**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

INTRADEPARTMENTAL:

- A. Oral Pathology Service Clinic, University Hospitals, Department of Dentistry and Oral Surgery.
- B. Oral Pathology Biopsy Service Rotation, School of Dentistry.
- C. Dental Faculty Associates, School of Dentistry.

INTERDEPARTMENTAL:

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

II. TEACHING ACTIVITIES:

SUMMER TERM, 1993:

- A. Social and Governmental Regulatory Issues, Course 739, to Junior Dental Students.

FALL TERM, 1994:

- A. Oral Pathology, Course 516, to Freshmen Dental Students (course director).
- B. General Pathology, Course 630, to Sophomore Dental Students.
- C. Oral Pathology, Course 824, to Senior Dental Students.
- D. Oral Pathology, Course 694, to Graduate Dental Students.
- E. Dental Hygiene, Course 494, to Senior Dental Hygiene Students.

WINTER TERM, 1994:

- 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.
- E. Community Dent., Course 739, to Junior Dental Students.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Project Director, "Oral Famciclovir in the Treatment of Experimentally Induced Herpes Simplex Labialis", 15% effort, 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:

- 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.

HONORS AND AWARDS:

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:**A. CLINICAL AND PATIENT CARE**

1. Interdepartmental
 - a. Oral Pathology Biopsy Service Rotation, School of Dentistry.
 - b. Clinical Patient Care, Dental Faculty Associates, School of Dentistry.
2. Interdepartmental.
 - a. Oral Pathology, clinical consultations on an as needed basis, the University of Michigan School of Dentistry and Clinics.
 - b. Consultant to Veterans Administration Hospital.

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.

INVITED LECTURES/SEMINARS:

1. "Oral Health 2000", Michigan Dental Association, Lansing, Michigan, October 15, 1993.
2. "AIDS", Dexter Kiwanis, Dexter, Michigan, October 19, 1993.
3. "Herpes, Hepatitis and AIDS Revisited", Genesee District Dental Society, Flint, Michigan, February 8, 1994.
4. "Oral Pathology" and "Infection Control", Minnesota Riverland Technical College, Rochester, Minnesota, February 25, 1994.
5. "Infectious Disease: Implications for the Patient and the Dental Personnel", Northland Dental Hygienist Association, Traverse City, Michigan, March 26, 1994.
6. "What Every Member of the Dental Team Needs to Know About Oral Diseases", M.D.A. three-day Traveling Lecture, Lansing, Michigan, May 18, 1994.
7. "What Every Member of the Dental Team Needs to Know About Oral Diseases", M.D.A. three-day Traveling Lecture, Grand Rapids, Michigan, May 19, 1994.
8. "What Every Member of the Dental Team Needs to Know About Oral Diseses", M.D.A. three-day Traveling Lecture, Traverse City, Michigan, May 20, 1994.

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

1. Rowe, N.H. and Chadzynski, L.: A study of the waste management of one regulated infectious medical waste: Sharps disposal. J. Mich. Dent. Assoc. 75:58-61, 1993.
2. Rowe, N.H.: Solving regulatory problems: Are we victims or participants. J. Mich. Dent. Assoc. 75:62, 1993.

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

1. Instructions for Writing an Exposure Control Plan to Conform with OSHA Requirements (OSHA RULES: Written Exposure Control Plans), Special Instructional Material.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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:

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

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.
- B. Southwest Oncology Group, (past President)
 - 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.
- B. Hematologic Pathology . Designated reviewer.
- C. Archives of Patholog and Laboratory Medicine. Designated reviewer

INVITED LECTURES/SEMINARS:

1. "Hodgkin's Disease: Diagnosis and Differential Diagnosis", ASCP Workshop, Orlando, Florida, October, 1993.
2. "A Practical Approach to the Diagnosis and Differential Diagnosis of Extranodal Lymphomas", ASCP Workshop, October, 1993, Orlando, Florida.
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, Santa Barbara, California, November, 1993.
4. "Reactive Lymphadenopathies", Hematopathology Tutorial (Sponsored by the University of Minnesota). San Diego, California, February, 1994.
5. "Hodgkin's Disease: Diagnosis and Differential Diagnosis", ASCP Workshop, April, 1994, Seattle, Washington.

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

1. Hanson, C.A., Abaza, M., Sheldon, S., Ross, C.W., Schnitzer, B. and Stoolman, L.M.: Acute biphenotypic leukemia: Immunophenotypic and cytogenetic analysis. *Brit. J. Haematol.* 83:49-60, 1993.
2. Miller, T.P., Schnitzer, B, et al: Prognostic significance of the ki-67-associated proliferative antigen in aggressive non-Hodgkin's lymphomas: A prospective Southwest Oncology Group Trial. *Blood* 83:1460-1466, 1994.

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

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

1. 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). *Lab. Invest.* 70:111A, 1994; *Mod. Pathol.* 7:111A, 1994.
2. Utiger C.A., Ross, C.W., Schnitzer, B. and Hanson, C.A.: Correlation of CD20 fluorescence intensity (FI) with morphologic parameters in B-cell chronic lymphoproliferative disorders (CLPD). *Lab. Invest.* 70:122A, 1994; *Mod. Pathol.* 7:122A, 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. *Blood (suppl 1)577A*, 1993.
4. Alkan, S., Siddique, J., Ross, C.W., Hanson, C.A. and Schnitzer, B.: Molecular analysis of Whipple's disease presenting in lymph nodes. *Am. J. Clin. Pathol.* 100:342, 1993.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

I. CLINICAL ACTIVITIES:

- A. Cytopathology - 26 weeks.
- 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
 - 2. Reproductive sequence lecture: Gynecologic Pathology, April 6, 1994.
- 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 - two/year.
 - 6. Pizza Conference - Pitfalls in the cytologic diagnosis of squamous lesions of the cervix - one/hour.
- 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. The clinical significance of the development of radiation induced dysplasias (in conjunction with Dr. Hope Haefner, Department of Obstetrics/Gynecology).
- B. Cervical atypia in women with SLE treated with intravenous cyclophosphamide (in conjunction with Dr. J. McCune, Department of Internal Medicine/Rheumatology).
- C. Genital infections as risk factors for low grade squamous intraepithelial lesion progression (in conjunction with Dr. Barbara Reed, Department of Family Practice).

- D. The significance of atypical squamous cells of underdetermined significance on cervical smears (in conjunction with Dr. Hope Haefner, Department of Obstetrics and Gynecology).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Co-Director, Cytopathology Laboratory.
- B. Member, Resident Selection Committee.
- C. Member, Internal Departmental Review Committee

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. Guest Speaker; "The Bethesda Nomenclature System for Cervicovaginal Cytology: Controversial Categories and Management Strategies", Grand rounds, Department of Obstetrics and Gynecology, Bon Secours Hospital, Grosse Pointe, Michigan, July 19, 1993.
2. Guest Speaker, "Fine Needle Aspiration Cytology of Cystic Ovarian Lesions", New South Wales Branch of the Australian Society of Cytology, Sydney, Australia, September 22, 1993.
3. Keynote speaker; Australian Society of Cytology, Topics include the Fine Needle Aspiration Cytology of Cystic Ovarian Lesions, Cytology of Pelvic Fluids and Washings, and Pitfalls in the Cytologic Diagnosis of Squamous Lesions of the Cervix, Perth, Australia, September 25-27, 1993.
4. Guest Speaker; "Squamous and Glandular Cell Atypia of Undetermined Significance", School of Cytotechnology, Henry Ford Hospital and Wayne State University, Detroit, Michigan, October 26, 1993.
5. Cytopathology workshop, "Fine Needle Aspiration Cytology of Cystic Ovarian Lesions in Conjunction with Peritoneal Washing Cytology", Forty-first Annual Scientific Meeting of the American Society of Cytology, Houston, Texas, November 6, 1993.

6. Cytopathology workshop, "Fine Needle Aspiration Cytology of Cystic Ovarian Lesions and Pelvic Washings", The 23rd Annual Mid-Continental Diagnostic Cytopathology Workshop, May 6-7, 1994, Wichita, Kansas.
7. Guest speaker, "Fine Needle Aspiration Cytology of Cystic Ovarian Lesions", Michigan Society of Cytology, Grand Haven, Michigan, June 4, 1994.

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., In Press.
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., In Press.
3. Wojcik, E.M. and Selvaggi, S.M.: Fine needle aspiration cytology of cystic ovarian lesions. Diagn. Cytopathol., In Press.
4. Selvaggi, S.M.: Small cell carcinoma of the ovary in peritoneal fluid. Diagn. Cytopathol., In Press.
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. Cytopathol., In Press.
6. Selvaggi, S.M. and Haefner, H.K.: Reporting of ASCUS on cervical smears: Is it significant? Diagn. Cytopathol., Submitted, 1994.

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

1. 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. (ed.), Cytopathology Annual. ASCP Press, In Press.
2. Selvaggi, S.M.: Quality Improvement Manual in Anatomic Pathology, Contributing Author: Cytopathology Section, College of American Pathologists, Northfield, Illinois, 1993, pp 59-94.
3. Selvaggi, S.M.: Interim Protocol for Cervical Cancer Screening in Women Age 40 and Older, Contributing Author, the Cervical Cancer Advisory Committee, Michigan Department of Public Health, Lansing, Michigan, 1993.
4. Selvaggi, S.M.: Book Review: Fine Needle Aspiration of Palpable Masses, Stanley, M.W. and Lowenhagen, T. (eds.), Butterworth - Heinmann, 1993; Arch. Pathol. Lab. Med., In Press.
5. Lindley, P., Selvaggi, S.M.: Book Review: Benign to Malignant Progression in Cervical Squamous Epithelium, Ehrmann, R.L. (ed.), Igaku-Shoin, 1994, Am. J. Surg. Pathol., In Press.
6. Selvaggi, S.M.: Book Review: Malignant Effusions; A Multimodal Approach to Cytologic Diagnosis, Bedrossian, C.W.M. (ed.), Igaku-Shoin, 1994; Am. J. Surg. Pathol., In Press.
7. Selvaggi, S.M. and Haefner, H.K.: Reporting of ASCUS on Cervical Smears: Is it Significant? Acta. Cytol., Abstract, In Press.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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, thrombosis, and anti-coagulant therapy, 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, "Congenital Coagulation Factor Defects, the 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 Hemostasis plus case presentations and discussions, the University of Michigan.
- G. Weekly conferences on Coagulation, Thrombosis and Component Therapy for Blood Bank Residents, the University of Michigan.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Production of Thrombi on Intact Endothelium", William Beaumont Research Institute (10%) \$57,227, February 1, 1992 - January 1, 1993.
- B. Co-Investigator, "Protamine Filter for Extracorporeal Heparin Removal", The University of Michigan School of Pharmacy, NIH-NHLBI HL-38353 (5%) \$204,000, January 1, 1993 - December 31, 1993.

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. Yang, V.C., Fu, Y-Y., Teng, C-L.C., Ma, S-A. and Shanberge, J.E.: A method for the quantitation of protamine in plasma. *Thromb. Res.* 74:427-434, 1994.
2. Cooper, E.S., Bracey, A.W., Horvath, A.E., Shanberge, J.N., Simon, T.I. and Yawn, D.H.: Practical parameter for the use of fresh-frozen plasma, cryoprecipitate and platelets. *JAMA* 271:777-781, 1994.
3. Shanberge, J.N.: Hemangioma of the uterus associated with hereditary hemorrhagic telangiectasis. *Obstet. Gynecol.*, In Press.
4. Shanberge, J.N., Kajiwara, Y. and Quattrocioni-longe: Effect of aspirin on adhesion of platelets to intact endothelium *in vivo*. *J. Lab. Clin. Med.*, In Press.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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, thrombosis, and anti-coagulant therapy, William Beaumont Hospital, Royal Oak, Michigan.

II. TEACHING ACTIVITIES:

- A. Daily "plasma" rounds, monitoring blood component usage, William Beaumont Hospital.
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SPONSORED SUPPORT:

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- B. Co-Investigator, "Protamine Filter for Extracorporeal Heparin Removal", The University of Michigan School of Pharmacy, NIH-NHLBI HL-38353 (5%) \$204,000, January 1, 1993 - December 31, 1993.

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. Yang, V.C., Fu, Y-Y., Teng, C-L.C., Ma, S-A. and Shanberge, J.E.: A method for the quantitation of protamine in plasma. *Thromb. Res.* 74:427-434, 1994.
- 2. Cooper, E.S., Bracey, A.W., Horvath, A.E., Shanberge, J.N., Simon, T.I. and Yawn, D.H.: Practical parameter for the use of fresh-frozen plasma, cryoprecipitate and platelets. *JAMA* 271:777-781, 1994.
- 3. Shanberge, J.N.: Hemangioma of the uterus associated with hereditary hemorrhagic telangiectasis. *Obstet. Gynecol.*, In Press.
- 4. Shanberge, J.N., Kajiwara, Y. and Quattrocioni-longe: Effect of aspirin on adhesion of platelets to intact endothelium *in vivo*. *J. Lab. Clin. Med.*, In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

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.
- 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 - one lecture.

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. Co-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., Silveira, S., Sheldon, S. and Dabich, L.: Therapy-related AML following immunosuppression with azathioprine. Clin. Lab. Haematol., In. Press.

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

1. Cox, B. and Sheldon, S.: Three cases of ring chromosome 7 in myeloid disorders. ACT Meeting, San Diego, June 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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.
- 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 M-Labs clients.

II. TEACHING ACTIVITIES:

- A. Supervise residents in gross cutting of M-Labs cases and review microscopic material with residents in all interesting cases.
- B. Read out some M-Labs autopsies and some University of Michigan autopsies with residents.
- C. In-service teaching to laboratory staffs at Addison and Albion 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.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, M-Labs:
 - 1. Participate in planning, marketing, and implementation of M-Labs programs.
- B. Director, Laboratory at Albion Community Hospital, Albion, Michigan.
- C. Chairman, Tissue/Transfusion Committee, Albion Community Hospital, Albion, Michigan.
- D. Chairman, Infection Control Committee, Albion Community Hospital, Albion, Michigan.
- E. Director of Laboratories, Addison Community Hospital.

- F. Chair, Tissue Transfusion and Infection Control Committees, Addison Community Hospital, 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:

- 1, Sapala, J.A., Smith, G., Sapala, M.A., Silverman, E.M. and McGee, J.: Post-operative hyperbilirubinemia in the gastric bypass patient; A 10 year clinical experience. Poster presented at the annual meeting of the American Bariatric Society, Minneapolis, Minnesota, May, 1994.

VI. PUBLICATIONS:

None.

**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 - 6 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 Ranvier 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), "Luteotropic 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

VI. 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 Nostrand, 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 functional and structural alterations. *J. of 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 Clinopathological 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 transduction 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-Parkinsonism-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, natural history and therapeutic potentials, in, Vasselli, J.R., Maggio, C.A. and Scriabine, A. (eds), *Drugs In Development, Vol. I, a-Glucosidase 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 renal microangiopathy in the BB/W or rat, in, Vasselli, J.R., Maggio, C.A. and Scriabine, A. (eds), *Drugs In Development, Vol. I, a-Glucosidase Inhibition: Potential Use in Diabetes*, Neva Press, Bradford, 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-Glucosidase 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 power analysis, in, Mogensen, C.E. and Standl, E. (eds), *Diabetes Forum Series V: Research Methodologies in Human Diabetes*, Walter de Gruyter & Co., Berlin, 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 Vieweg 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 experimental 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.: Morphometric 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. Neurodiab. 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.: ¹H 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.: Acetyl-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 mediates 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 regeneration 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 transduction 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-L-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 diabetic rat. Peripheral Nerve Society, St. Paul, Minnesota, June, 1994.

**JAMES E. SMOLEN, PH.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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. Biochimica 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.: Modelling 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 1993 - 30 JUNE 1994

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. Eric Kaldjian, M.D., Pathology Research Fellow (July, 1991 -April,1994) - Dr. Kaldjian's project focuses on the transcriptional regulation of the lymph node homing receptor (L-selectin) in normal and malignant lymphoid cells. Dr. Kaldjian has co-authored two reviews and a manuscript based on his research work is submitted. He is currently serving a Hematopathology/Immunology Fellowship at the NIH under the direction of Drs. Elaine S. Jaffe, M.D. and Steven Shaw, Ph.D..
 2. 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 β 1-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.
 3. Vennay Reddy, undergraduate student (Sept., 1992 - present) - 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.
 4. Randall Knibbs, Ph.D., Research Scientist (January, 1994-present) - Dr Knibbs is a carbohydrate biochemist interested in applying his expertise in the field of selectin biology. Dr. Knibbs is currently studying the regulatory and synthetic pathways involved in the biosynthesis of ligands for the selectins during antigen-driven differentiation of 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 the only instructors in any department with teaching responsibilities 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, Host Defense Section of ICS 600 Course.
 - F. Lecturer, Experimental Pathology (Pathology 580 and 581).
 - G. Member, Graduate Comprehensive Examination Committee - formulate questions, conduct and grade written and oral examinations for Ph.D. candidates in Experimental Pathology Program.
 - H. Daily sign-out of cases in flow cytometry and hematopathology with pathology residents and medical students (three-four months).
 - I. Attending, Autopsy Service (two weeks).
 - J. Preceptor, Senior medical student (M4) elective in Pathology (one month).
 - K. 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. Regulation of selectin-ligand synthesis during T-cell activation: This projects builds on the discovery of T-lymphoblastic cell lines which synthesize functional selectin ligands in response to activation stimuli. Molecular techniques will be used to dissect the pertinent regulatory and synthetic pathways. 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. 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. Our preliminary data suggest that recruitment of infused lymphocytes into metastatic implants will depend on the expression of selected endothelial adhesion molecules in the vascular-bed of the tumor. We plan to first determine which adhesion pathways are used for recruitment in standard immunotherapy protocols. We will then use molecular techniques to determine whether selective induction of these receptors will augment recruitment and enhance the response to treatment.

IV. ADMINISTRATIVE ACTIVITIES:

- A. Co-Director Flow Cytometry Laboratory - managed development and implementation of the new analytic system. This effort involved selection of hardware, design of software and management of a joint effort with the software developers (Verity Software Systems). This system was designed to meet the needs of both the clinical laboratories and research investigators.
- B. Member, Equipment and Space Allocation Committee.
- C. Member, Coordinating Committee for Elective in Laboratory Medicine.
- D. Co-Director, Hematology Sequence in Component II - responsible for design and implementation of laboratory component of this sequence.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Leukocyte-Endothelial Adhesive Interactions in the Pathogenesis of Rheumatoid Arthritis", Experimental Therapeutics Workshop, Annual Meeting of American College of Rheumatology, November, 1993, San Antonio, Texas.
2. "U937 Cells Use Both E-Selectin and $\alpha 4$ -Containing Integrins to Initiate Contact with Cytokine-Treated Endothelium Under Shear-Stress, Leukocyte Adhesion Minisymposium of the North American Vascular Biology Organization at Experimental Biology 94 Annual Meeting, Anaheim, California, April, 1994.
3. Co-chair, Brook Lodge Symposium on "Leukocyte-Endothelial Adhesion", sponsored by Upjohn Pharmaceutical, Company (together with Nancy Hogg, Ph.D., MRC, London), three-day symposium for June, 1994.

MANUSCRIPT REVIEWS:

- A. Journal of Clinical Investigation.
- B. Journal of Laboratory Investigation.
- C. American Journal of Pathology.
- D. Journal of Immunology.
- E. Journal of Experimental Medicine.
- F. Journal of Biological Chemistry.
- G. Nature.

VI. PUBLICATIONS:

ARTICLES SUBMITTED/IN PREPARATION FOR PUBLICATION:

1. Kaldjian, E. and Stoolman, L.M.: Regulation of L-selectin mRNA in Jurkat cells and normal T-lymphocytes: Opposing influences of calcium- and protein kinase C-dependent signaling pathways.
2. Stoolman, L.M., Craig, R., Wolber, F., Smith C.W., McIntire, L. and Abassi, O.: α 4-integrins tether and arrest the forward motion of Jurkat cells under shear-stress without involvement of the selectins.
3. Stoolman, L.M., Craig, R., Smith C.W., McIntire, L. and Abassi, O.: α 4-integrins differ from β 2-integrins in the capacity to initiate selectin-independent attachment under shear-stress.
4. Knibbs, R., Lowe, J.B. and Stoolman, L.M.: Regulatory and synthetic pathways involved in the *de novo* synthesis of selectin-ligands on the T-lymphoblastic cell line Jurkat.
5. Knibbs, R., Lowe, J.B. and Stoolman, L.M.: Regulatory and synthetic pathways involved in the *de novo* synthesis of selectin-ligands following T-cell activation.
6. 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.
7. Ley, K., Zakrzewicz, A., Hanski, C., Kansas, G.S. and Stoolman, L.M.: Sialylated mucins and L-selectin on neutrophils sequentially mediate rolling *in vivo*.
8. 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.

BOOKS/CHAPTERS IN BOOKS:

1. Kaldjian, E. and Stoolman, L.M.: Lymphocyte recirculation and recruitment, in, Shimizu, Y., Landis, R.G. (eds), Lymphocyte Adhesion Molecules, October, 1993.

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

1. Stoolman L.M., Abassi, O. and Craig, R.: U937 cells use both E-selectin and α 4-containing integrins to initiate contact with cytokine-treated endothelium under shear-stress. FASEB Journal, March, 1994.
2. Kaldjian, E.P. and Stoolman, L.M.: Down-regulation of L-selectin transcription in Jurkat cells by a calcium signaling pathway sensitive to cyclosporin. FASEB Journal, March, 1994.

**DENISE SULAVIK, M.D.
LECTURER
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993-30 JUNE 1994**

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:

None.

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 1993 - 30 JUNE 1994**

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. Joseph Lee - Medical Student - Research.
- D. Hagen Schmal - Medical Student - Research.
- E. Dorothy Pao - Undergraduate Student - Research.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. "Lung Injury Produced by Oxygen Metabolites", (NIH GM-29507), Co-Principal Investigator with Dr. P.A. Ward.
- B. "The Effect of Bradykinin Antagonists on CVF-Induced Lung Injury", Scios Nova Inc., Palo Alto, California, Principal Investigator.

PENDING SUPPORT:

- A. "Cytokines and Adhesion Molecules in Thermal Injury", (NIH GM48477-01), Principal Investigator.

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. 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.
- D. Member Dissertation Committee, You-Yin Fu, School of Pharmacy.
- E. Member Dissertation Committee, K.S. Kilgore, Department of Pharmacology

REGIONAL AND NATIONAL:

- A. Reviewer for the following scientific journals:
 - 1. American Journal of Pathology.
 - 2. Blood.
 - 3. Journal of Biological Chemistry.
 - 4. Journal of Leukocyte Biology.
 - 5. Laboratory Investigation.
 - 6. Shock.
- B. Member Scientific Committee of the American Shock Society.
- C. Member Honors and Awards Committee of the American Shock Society.

V. OTHER RELEVANT ACTIVITIES:

- A. Member Editorial Advisory Board Immunobiology.

INVITED LECTURES/SEMINARS:

- 1. Invited speaker and session chairman at a symposium on "Ischemia/Reperfusion Injury", Borgess Medical Center, Kalamazoo, Michigan, September 10, 1993.
- 2. Invited speaker at the First Annual Meeting of the Oxygen Society; Charleston, South Carolina, November 12-17, 1993.
- 3. Invited seminar speaker at the Department of Biological Sciences, College of Arts and Sciences, Western Michigan University, Kalamazoo, Michigan, December 8, 1993.
- 4. Invited seminar speaker at the Department of Pathology, Johns Hopkins Medical Institutions, Baltimore, Maryland, January 20, 1994.
- 5. Invited speaker at the Tenth Spring Meeting of the German Society for Immunology, Heidelberg, Germany, March 9-12, 1994.
- 6. Organizer and moderator of a symposium on "Neutrophil-Endothelial Interactions in Shock and Trauma", at the Seventh Annual Conference on Shock. Big Sky, Montana, June 5-8, 1994.

7. Invited speaker and session chairman at the Seventh European Congress on Intensive Care Medicine, Innsbruck, Austria, June 14-17, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Seekamp, A., Mulligan, M.S., Till, G.O., Smith, C.W., Miyasaka, M., Tamatani, T., Todd, R.F., III and Ward, P.A.: Role of beta 2 integrins and ICAM-1 in lung injury following ischemia-reperfusion of rat hind limbs. *Am. J. Pathol.* 143:464-472, 1993.
2. Wilkins, E. G., Rees, R. S., Smith, D., Cashmer, B., Punch, J., Till, G.O. and Smith, D.J., Jr.: Identification of xanthine oxidase activity following reperfusion in human tissue. *Ann. Plast. Surg.* 31:60-65, 1993.
3. Seekamp, A., Warren J.S., Remick, D.G., Till, G.O. and Ward, P.A.: Requirements for tumor necrosis factor-alpha and interleukin-1 in limb ischemia/reperfusion injury and associated lung injury. *Am. J. Pathol.* 143:453-463, 1993.
4. Rodriguez, J.L., Miller, C.G., Garner, W.L., Till, G.O., Guerrero, P., Moore, N.P., Corridore, M., Normolle, D.P., Smith, D.J. and Remick, D.G.: Correlation of the local and systemic cytokine response with clinical outcome following thermal injury. *J. Trauma* 34:684-694, 1993.
5. Mulligan, M.S., Till, G.O., Smith, C.W., Anderson, D.C., Miyasaka, M., Tamatani, T., Todd, R.F., III, 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.
6. Seekamp, A., Till, G.O., Mulligan, M.S., Paulson, J.C., Anderson, D.C., Miyasaka, M. and Ward, P.A.: Role of selectins in local and remote tissue injury following ischemia and reperfusion. *Am. J. Pathol.* 144:592-598, 1994.
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. Murphy, H.S., Maroughi, M., Till, G.O. and Ward, P.A.: Phorbol ester-stimulated influx of extracellular calcium in endothelial cells. *J. Biol. Chem.*, In Press.
9. 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. *J. Trauma*, In Press.
10. 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.
11. 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 Radic. Biol. Med.*, In Press.
12. Colton, D.M., Hirschl, R.B., Johnson, K., Till, G.O., Dean, S. and Bartlett, R.H.: Neutrophil infiltration is reduced during partial perfluorocarbon liquid ventilation in the setting of lung injury. *Surg. Forum*, In Press.

BOOKS AND CHAPTERS IN BOOKS:

1. Till, G.O.: Chemotaxis., in, Rother, K.O., Till, G.O. and Haensch, G. (eds), *The Complement System*; Springer-Verlag Berlin, Heidelberg, In Press.

2. Till, G.O.: Role of complement in trauma, shock and thermal injury, in, Rother, K.O., Till, G.O. and Haensch, G.M. (eds), *The Complement System*; Springer-Verlag, Berlin Heidelberg, In Press.
3. Rother, K.O., Till, G.O. and Haensch, G.M.: *The Complement System*, Springer-Verlag Berlin Heidelberg, In Press.
4. Till, G.O., Friedl, H.P. and Ward, P.A.: Histamine-dependent modulation of oxygen radical production, in, Farr, C.H. (ed), *Proceedings of the Second International Conference of Bio-Oxidative Medicine*, In Press.
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. Till, G.O., Seekamp, A., Hultquist, D.E., Xu, F. and Ward, P.A.: Riboflavin (vitamin B2) protects from oxidant-mediated acute lung injury. *Free Radic. Biol. Med.* 15:551, 1993.
2. Marak, G.E., Lee, S., Ward, P.A. and Till, G.O.: Xanthine oxidase in experimental phacoanaphylactic endophthalmitis. *Invest. Ophthalmol. Vis. Sci.* 34:1476, 1993.
3. Seekamp, A., Till, G.O., Paulson, J.C., Anderson, D.C., Miyasaka, M. and Ward, P.A.: Role of selectins in local and remote injury following ischemia and reperfusion. 7th Annual Conference on Shock. *Shock (Suppl. 1):55 A*, 1994.
4. Seekamp, A., Till, G.O., Warren, J. S., Remick, D.G., Miyasaka, M. and Ward, P.A.: Role of selectins in local and remote tissue injury following ischemia and reperfusion. Third International Congress on the Immune Consequences of Trauma, Shock and Sepsis - Mechanisms and Therapeutic Approaches, Munich, 2-5 March 1994. *Intensive Care Med.* 20(Suppl. 1):S23, 1994.
5. Marak, G.E., Till, G.O., Schmal, H. and Friedl, H.P.: Antiphlogistic mechanism of xanthine oxidase inhibitors in acute ocular inflammation. 5th International Symposium on the Immunopathology of the Eye, Washington, D.C., In Press.
6. Colton, D.M., Hirschl, R.B., Till, G.O., Johnson, K., Wilkins, A., Compton, C. and Bartlett R.H.: Partial liquid ventilation (PLV) decreases neutrophil infiltration prior to and after the induction of respiratory failure. ACCP 60th Annual International Scientific Assembly, New Orleans, Louisiana, In Press.
7. Rodriguez, J.L., Garner, W.L., Till, G.O., Remick, D.G. and Smith, D.J.: Interleukin-8: Neutrophil dysfunction and nosocomial pneumonia. AAST, In Press.
8. Seekamp, A., Mulligan, M., Till, G.O. and Ward, P.A.: Neutrophil adhesion antagonists and antioxidants provide comparable protection against acute lung injury caused by hind limb ischemia-reperfusion. *Orthopaedic Trauma Assoc.*, In Press.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Training and supervision of premedical/medical student research:

1. Susan Tshi, undergraduate student (Summer, 1994) - Project focused on human neutrophil activation and functional responses in addition to development of basic and advanced laboratory skills.

III. RESEARCH ACTIVITIES:

- A. Signal transduction pathways of neutrophil activation through Mac-1 and L-selectin molecules.
- B. Mechanisms of immune complex-induced human neutrophil activation.
- C. Role of soluble mediators of inflammation on neutrophil activation using endotoxin-stimulated human whole blood.

SPONSORED SUPPORT:

- A. Principal Investigator, "Mechanisms of Fc Dependent Neutrophil Activation", NIH-1R29 AI/GM 31436, \$556,500/total costs, July 1, 1991 - June 30, 1996.
- B. Principal Investigator, "Mechanisms of L-Selectin Dependent Human Neutrophil Activation", American Heart Association of Michigan Grant-in-Aid, 89GB945, \$28,000 total direct costs/year, July 1, 1994 - June 30, 1995.

IV. ADMINISTRATIVE ACTIVITIES:

None.

V. OTHER RELEVANT ACTIVITIES:

- A. Designed the T-shirts logo for the Experimental Biology 94 meeting (April, 1994) of the Federation of American Societies for Experimental Biology.

INVITED LECTURES AND SEMINARS:

1. Minisymposium, "Biochemistry of Leukocyte Activation", Experimental Biology 94 meeting, Anaheim, California, April, 1994.
2. Minisymposium, "Granulocyte Activation and Function: Activation of Human Neutrophils Through L-selectin", the Australian Society for Immunology and the Society of Leukocyte Biology, Sydney, Australia, 1993.

V. PUBLICATIONS:

ARTICLES SUBMITTED FOR PUBLICATION:

1. Crockett-Torabi, E., Smith, C.W. and Fantone, J.C.: Activation of human neutrophils through L-selectin and Mac-1 molecules. Submitted to the J. Immunol.
2. Crockett-Torabi, E. and Fantone, J.C.: Selective regulation of FcγR and Mac-1 CD11b/CD18 molecules in lipopolysaccharide (LPS)-stimulated neutrophils in whole blood: The role of TNF, IL-6, IL-8 and complement derived products. Submitted to J. Leukocyte Biol.

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. and Fantone, J.C.: Cross-linking of L-selectin molecules induced changes in intracellular calcium in human neutrophils, Experimental Biology 94 meetings, Anaheim, California, A60327.
2. Fantone, J.C. and Crockett-Torabi, E.: Mac-1 adhesion molecules induce human neutrophil activation through Ca²⁺-dependent and Ca²⁺-independent pathways, Experimental Biology 94 meetings, Anaheim, California, A40320.
3. Crockett-Torabi, E., Smith, C.W., Simon, S.I. and Fantone, J.C.: Activation of human neutrophils through L-selectin, J. Leukocyte Biology, A627, 1993.

**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.
E. Role of terminal α -galactosyl residues in cancer metastasis.
F. 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, Montana, 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 secretory 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 integrins 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. *Neutrition 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 Fligel, 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 1993 - 30 JUNE 1994**

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. Thomas H. Burkey, Ph.D., Postdoctoral Fellow.
 - c. Michael J. Eppinger, M.D., Postdoctoral Fellow.
 - d. Jami Foreback, Pathology Graduate Program Student (MSTP student) (mentor).
 - e. Kimberly Foreman, M.D., Postdoctoral Fellow.
 - e. Teletha Gipson, Ph.D., Postdoctoral Fellow.
 - f. Ralph C. Schimmer, M.D., Postdoctoral Fellow.
 - g. Thomas Shanley, M.D., Postdoctoral Fellow.
 - h. Roscoe Warner, Ph.D., Postdoctoral Fellow.
 - i.. UROP Undergraduate Students:
 - i.- Hiliary Cohen, Freshman, four hours per week.
 - j. Undergraduate Honors Students:
 - k. Samir Navayan, five hours per week.
 - 2. Indirect supervision of four Research Scientists.
 - 3. Gross Autopsy Conference, 25 hours.
 - B. Undergraduate students:
 - a. Lecture, College Honors Seminar 250, "Lessons from Polio", March 9, 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, 1992 -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 - \$93,321, Section V-\$58,941/year (\$1,010,734/five years), 3/1/89-2/28/94.
- D. Co-Investigator, "Mechanisms of Glomerular and Tubular Injury" (R. Wiggins, Principal Investigator), NIADDK-NIH-DK-39255 (5%), \$45,000/year, August 1, 1993 - July 31, 1993.

- E. Principal Investigator, "Oligosaccharides as Inflammatory Agents" NIH-AI33189-01 (10%), \$449,661/year (\$2,192,155/four years), 9/1/92-6/30/96.

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. Internal Medicine Advisory Committee for the University of Michigan George M. O'Brien Renal and Urologic Center, 1991--
- G. Michigan Eye Bank Research Review Committee, 1980--
- H. Presidential Initiatives Fund, The University of Michigan, March, 1987--
- I. Undergraduate Research Opportunity Program, University of Michigan, 1992--

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. Trustee, 1980--.
 - 2. Immunopathology Test Committee, 1980-85, 1988-.
Vice-Chairman.
 - 3. Anatomic Pathology Examination Committee, 1988--.
 - 4. By-Laws Committee, 1988--.
 - 5. Examination Evaluation Committee, 1988--.
 - 6. Professional Qualification/Competence Committee, 1988--.
 - 7. ABP/ABPRF Research Committee, 1989--.
 - 8. Residency Review Committee for Pathology.
 - 9. Building Committee, 1992--.
 - 10. Planning and Development Committee, 1992--.
 - 11. 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 American 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, "Endothelial-Leukocyte Adherence Molecules in the Pathogenesis of Acute Pulmonary Disease", XIVth International Congress on Thrombosis and Haemostasis, New York Hilton Towers, New York, New York, July 6-7, 1993.
2. Invited Lecturer, "Role of Cytokines and Nitric Oxide in Lung Injury", FASEB Summer Research Conference on Cytokines and Lung Function, Vermont Academy, Saxton River, Vermont, July 10-11, 1993.
3. Participant, "Immunological Mediators of Acute Lung Injury", in the Conference, Nature of the Lung Lesion in Hantaviral Infections, Pathophysiology meeting of the Center for Disease Control, Atlanta, Georgia, July 20, 1993.
4. Invited Lecturer, "Evidence for Toxic Products of L-Arginine in Inflammation", American Society for Pharmacology and Experimental Therapeutics Short Course on the Biologic Functions of Nitric Oxide, San Francisco, California, July 29-August 1, 1993.
5. Invited Lecturer, "Organ Differences in Cytokine Occurrence", American Society for Pharmacology and Experimental Therapeutics Meeting in San Francisco, California, July 29-August 1, 1993.
6. Invited Lecturer, "Regulation of Inflammatory Responses by IL-4 and IL-10", at the Schering-Plough Research Institute, Kenilworth, New Jersey, August 4, 1993.
7. Invited Grand Rounds Speaker, Maine Medical Center, Portland, Maine, August 11, 1993.
8. Invited Lecturer, "Soluble Human Complement Receptor and Tumor Necrosis Factor Receptor as Antiinflammatory Agents", McCormick Place Complex, Chicago, Illinois, August 24-25, 1993.
9. Invited Lecturer, "Pathogenesis of Lung Injury and its Relation to Oxygen Radicals and Inflammatory Reaction", sponsored by the West Virginia University Health Sciences Center, Lakeview Resort and Conference Center, Morgantown, West Virginia, August 29-30, 1993.
10. Invited Lecturer, "Mechanisms of Neutrophil-Mediated Injury", The Fifth International ANCA Workshop, St. John's College, Cambridge, United Kingdom, August 31st-September 1st, 1993.
11. Invited Lecturer, Rheumatology Grand Rounds, "Role of Adhesion Molecules in Inflammatory Lung Injury", University of Alabama at Birmingham, Birmingham, Alabama, September 21-22, 1993.
12. Rheumatology Grand Round Lecturer, "Role of Adhesion Molecules in Inflammatory Lung Injury", University of Alabama at Birmingham School of Medicine, September 21-22, 1993.
13. Invited Lecturer, "Neutrophil Mediated Oxidant Injury to Lung", 7th Annual North American Cystic Fibrosis Conference, Loews Anatole Hotel, Dallas, Texas, October 14-15, 1993.
14. Invited SmithKline Beecham Lecturer, "The Role of the Endothelium in Inflammation", Department of Pathology, State University of New York Health Center, Syracuse, New York, October 19, 1993.
15. Invited Lecturer, "Relationship Between Cytokines and Adhesion Molecules in Lung inflammatory Injury", Department of Pathology, State University of New York Health Center, Syracuse, New York, October 20, 1993.
16. Distinguished Visiting Professor, "The Role of Adhesion Molecules in Inflammatory Lung Injury", Department of Pathology, Johns Hopkins University, Baltimore, Maryland, October 27-28, 1993.
17. Plenary Lecturer, "Interventional Approaches to *In Vivo* Blocking of Adhesion Molecules", Fifth International Conference on Human Leukocyte Differentiation Antigens, Sheraton Hotel, Boston, Massachusetts, November 6, 1993.
18. Invited Lecturer, "Complement Mediated Pulmonary Inflammation" and "Selectins in Pulmonary Inflammation", Mead Johnson Perinatal and Developmental Medicine Symposium, Marriott's Marco Beach Resort, Marco Island, Florida, November 18-20, 1993.
19. Invited Lecturer, "In Vivo studies of the Roles of Adhesion Molecules in Cardiopulmonary Inflammation", Frontiers Symposium on Inflammation in Cardiovascular Lung and Blood Diseases, National Institutes of Health, Bethesda, Maryland, November 28-29, 1993.

20. Invited Lecturer, "In Vivo Relationships Between Cytokines and Adhesion Molecules", Keystone Symposia on Molecular and Cellular Biology, Keystone, Colorado, January 19-21, 1994.
21. Invited Lecturer, "Strategies for Defining the Role of Selectins *In Vivo*", Genentech, Inc., South San Francisco, California, January 26-28, 1994.
22. Panel Discussion, "Inhibition of Leukocyte Adhesion", Society of Critical Care Medicine, Orlando, Florida, February 1-2, 1994.
23. Invited Lecturer, "Leukocyte Adhesion Molecules and Inflammatory Injury", Symposium, Leukocyte Adhesion, Scios Nova, Inc., Mountain View, California, February 13-14, 1994.
24. Invited Lecturer, "Cytokines and Adhesion Molecules", Fifth Conference: Molecular Mechanisms and Physiological Activities of Cytokines, Ein Gedi, Israel, February 19-24, 1994.
25. Invited Lecturer, "Cytokines and Adhesion Molecules in Tissue Injury", 3rd International Congress on The Immune Consequences of Trauma, Shock and Sepsis, Munich, Germany, February 28-March 4, 1994.
26. Invited Lecturer, "Relationship Between Cytokines, Neutrophils and Lung Injury", Scientific Advisory Board Meeting, Onyx Pharmaceuticals, Richmond, California, March 21, 1994.
27. Invited Lecturer, "Selectin Blockade in Models of Acute Lung Injury", Keystone Symposium, Complex Carbohydrates in Biology and Medicine, Frisco, Colorado, March 24-25, 1994.
28. Visiting Professor, Department of Pathology and Microbiology, Grand Rounds, "Adhesion Molecules, Cytokines and Inflammatory Lung Injury", University of Nebraska, Omaha, Nebraska, April 20, 1994.
29. Symposia Speaker, "Role of Complement and Selectins in Immune Complex Mediated Tissue Injury" in the Symposium, Interactions Between Complement and the Immune System, sponsored by ASIP, FASEB Meetings, Anaheim, California, April 27, 1994.
30. Co-Chair Symposium and Lecture, "Mechanisms of Endothelial Cell Injury" in the Symposium, Free Radicals in Disease, FASEB Meetings, Anaheim, California, April 28, 1994.
31. 1994 Moon Memorial Lecturer, "Selectins and Lung Inflammatory Injury", Department of Pathology, University of California, San Francisco, San Francisco, California, May 3-4, 1994.
32. Visiting Professor, "Cytokines, Adhesion Molecules and Inflammatory Lung Injury", Children's Memorial Institute for Education and Research, University of Chicago, Chicago, Illinois, May 15-16, 1994.
33. Invited Lecturer, "Adhesion Molecules: Injury and Inflammation", 4th Annual Wound Society Meeting, Mark Hopkins Hotel, San Francisco, California, May 18-19, 1994.
34. Invited Lecturer, "Role of Selectins in Lung Inflammatory Injury", and Co-Chair session The Role of Adhesion Molecules in Lung Injury, 1994 ALA/ATS International Conference, Hynes Convention Center, Boston, Massachusetts, May 21-22, 1994.
35. Guest Presenter, "Cytokines, Adhesion Molecules and Inflammatory Lung Injury", Department of Pathology, University of Cincinnati, Cincinnati, Ohio, May 25-26, 1994.
36. Invited Lecturer, "Molecular Mechanisms of Ischemia-Reperfusion Injury", University of Michigan Plastic Surgery Research Council Meeting, Molecular Biology Symposium, Ann Arbor, Michigan, June 4, 1994.
37. Invited Lecturer, "Strategies for In Vivo Blocking of P- and E-Selectin in Lung Injury Models", and Co-Chairman of Session V, Yachthotel Chiemsee, Lake Chiemsee, Prien, Bavaria, June 7-11, 1994.
38. Invited Lecturer, "Cytokines, Selectins and Lung Injury", Brook Lodge Conference on Adhesion Molecule Biology, Brook Lodge Conference Center, Augusta, Michigan, June 13-14, 1994.
39. Invited Lecturer, "The Clinical Profile of Inflammation", 1994 NATO Advanced Study Institute Conference on Vascular Endothelium: Responses to Injury, Heraklion, Crete Island, Greece, June 18-21, 1994.
40. Invited Lecturer, "Activation of Endothelial Cells by TNF α and C5a", Copper Mountain Conference on Endothelial and Cardiovascular Control, Copper Mountain, Colorado, June 30-July 1, 1994.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Mulligan, M.S., Jones, M.L., Vaporciyan, A.A., Howard, M.C. and Ward, P.A.: Protective effects of IL-4 and IL-10 against immune complex-induced lung injury. *J. Immunol.* 151:5666-5674, 1993.
2. Mulligan, M.S., Lowe, J.B., Larsen, R.D., Paulson, J., Zheng, Z-L, DeFrees, S., Maemura, K., Fukuda, M. and Ward, P.A.: Protective effects of sialylated oligosaccharides in immune complex-induced acute lung injury. *J. Exp. Med.* 178:623-631, 1993.
3. Mulligan, M.S., Watson, S.R., Fennie, C. and Ward, P.A.: Protective effects of selectin chimeras in neutrophil-mediated lung injury. *J. Immunol.* 151:6410-6417, 1993.
4. Seekamp, A. and Ward, P.A.: Ischemia-reperfusion injury. *Agents and Actions Suppl.* 41:137-152, 1993.
5. Vaporciyan, A.A., DeLisser, H.M., Yan, H-C., Mendiguren, I.I., Thom, S.R., Jones, M.L., Ward, P.A. and Albelda, S.M.: Involvement of platelet-endothelial cell adhesion molecule-1 in neutrophil recruitment *in vivo*. *Science* 262:1580-1582, 1993.
6. Vaporciyan, A.A. and Ward, P.A.: Enhanced generation of O₂⁻ by human neutrophils via a complement iC3b/Mac-1 interaction. *Biological Signals* 2:126-135, 1993.
7. Ward, P.A. and Mulligan, M.S.: Strategies for *in vivo* blocking of adhesion molecules. *Agents and Actions Suppl.* 43:173-186, 1993.
8. Ward, P.A., Mulligan, M.S. and Vaporciyan, A.A.: Endothelial and leukocytic adhesion molecules in the pathogenesis of acute pulmonary injury. *Thrombosis and Haemostasis* 70:155-157, 1993.
9. Albelda, S.M., Smith, C.W. and Ward, P.A.: Adhesion molecules and inflammatory injury. *FASEB J.* 8:504-512, 1994.
10. 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.*, September, 1994, In Press.
11. Mulligan, M.S., Miyasaka, M., Tamatani, T., Jones, M.L. and Ward, P.A.: Requirements for L-selectin in neutrophil-mediated lung injury in rats. *J. Immunol.*, 152:832-840, 1994.
12. Mulligan, M.S., Till, G.O., Smith, C.W., Anderson, D.C., Miyasaka, M., Tamatani, T., Todd, R.F., III, Issekutz, J.C. and Ward, P.A.: Role of leukocyte adhesion molecules in lung and dermal vascular injury following thermal trauma of skin. *Amer. J. Pathol.* 144:1008-1015, 1994.
13. Mulligan, M.S., Tsai, T.T., Kneebone, J.M., Ward, P.A. and Lupinetti, F.M.: Effects of preservation techniques on *in vivo* expression of adhesion molecules by aortic valve allografts. *J. Thorac. Cardiovasc. Surg.* 107:717-723, 1994.
14. Seekamp, A., Till, G.O., Mulligan, M.S., Paulson, J.C., Anderson, D.C., Miyasaka, M. and Ward, P.A.: Role of selectins in local and remote tissue injury following ischemia and reperfusion. *Amer. J. Pathol.* 144:592-598, 1994.
15. Varani, J. and Ward, P.A.: Mechanisms of neutrophil-dependent and neutrophil-independent endothelial cell injury. *Biol. Signals* 3:1-14, 1994.
16. Jones, M.L., Vaporciyan, A.A. and Ward, P.A.: A new fluorescent method for quantitative assessment of neutrophil monocyte chemotaxis. *J. Immunol. Methods.*
17. 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 b2 integrins, VLA-4 and ICAM-1 in nephrotoxic nephritis. *J. Clin. Invest.*, In Press.
18. 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.
19. 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.*

20. 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.
21. Mulligan, M.S., Vaporciyan, A.A., Jones, M.L., Warner, R.L., Foreman, K.E., Miyasaka, M., Todd, R.F. and Ward, P.A.: Compartmentalized roles for leukocytic adhesion molecules in lung inflammatory injury. *J. Clin. Invest.*
22. 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.*, In Press.
23. Rao, N.A., Sevanian, A., Faure, J.-P., Kozak, Y., Ward, P.A., Till, G.O. and Marak, G.E.: The participation of reactive oxygen metabolites in the pathogenesis of experimental allergic uveitis. *Invest. Ophthalmol. Vis. Sci.*, In Press.
24. Schmal, H., Shanley, T.P., Schrier, D.G., Flory, C.M., Friedl, H.P., Ward, P.A. and Jones, M.L.: Transcriptional characterization of IgG immune complex-mediated lung injury by Northern blot and quantitative PCR analysis. *J. Immunol.*, In Press.
25. 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.
26. Seekamp, A. and Ward, P.A.: Ischemia - reperfusion injury. *Agents in Actions (Supplement)*, In Press.
27. Shanley, T.P., Jones, M.L., Schmal, H., Friedl, H.P. and Ward, P.A.: Molecular cloning and *in vivo* transcriptional expression of RANTES in a rat model of IgA-induced lung injury. *J. Immunol.*, In Press.
28. Shanley, T.P., Warner, R.L., Kapur, V., Ward, P.A., Musser, J.M. and Jones, M.L.: Augmentation of IL-1-dependent lung injury in rats by streptococcal extracellular cystine protease (interleukin-1 β convertase). *J. Clin. Invest.*, In Press.
29. 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.*, In Press.
30. 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.
31. 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.
32. Till, G.O. and Ward, P.A.: Immunologic and phagocytic cell defects in thermally injured patients. *J. Crit. Care Med.*, In Press.
33. Vaporciyan, A.A. and Ward, P.A.: Induction by C5a of P-selectin dependent endothelial adhesiveness for neutrophils. *J. Immunol.*, In Press.
34. 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.
35. 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*, In Press.
36. Ward, P.A.: The wound environment - Local and systemic perturbations: Inflammation and the burn wound. *J. Burn Care & Rehab.* In Press.
37. 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.
38. Ward, P.A.: Oxidant damage. Submitted to the Task Force on Allergy and Immunology, National Institutes of Health.
39. Ward, P.A. and Johnson, K.J.: Lung inflammatory mechanisms. *J. Human Path.*, In Press.
40. Ward, P.A., Johnson, K.J. and Till, G.O.: Mechanisms of lung injury. *Prax. Klin. Pneumonol.*, In Press.
41. Ward, P.A. and Marks, R.M.: The acute inflammatory reaction. *Current Opinion on Immunol.*
42. Ward, P.A. and Mulligan, M.S.: Blocking of adhesion molecules *in vivo* as anti-inflammatory therapy. *Therapeutic Immunol.* 1994;1, In Press.

43. Zhang, R.L., Chopp, M., Li, Y., Zaloga, C., Jiang, N., Jones, M., Miyasaka, M. and Ward, P.: Anti-ICAM-1 antibody reduces ischemic cell damage after transient middle cerebral artery occlusion in the rat. *Neurology*, In Press.

BOOKS/CHAPTERS IN BOOKS:

1. Friedl, H.P., Trentz, O., Till, G.O. and Ward, P.A.: Role of oxygen radicals in multiple organ failure, in, Faist, E., Meakins, J.L. and Schildberg, F.W. (eds), *Host Defense Dysfunction in Trauma, Shock and Sepsis: Mechanisms and Therapeutic Approaches*, Springer Verlag, Heidelberg, pp. 287-295, 1993.
2. Marak, G.E., Till, G.O. and Ward, P.A.: Endothelial cell regulation of acute uveitis, in, Dernouchamps, J.P., Verougstraet, C., Caspers-Velu, L. and Tassignon, M.J. (eds), *Proceedings of the Third International Symposium on Uveitis, Recent Advances in Uveitis*, Kugler Publication, Amstelveen, Netherlands, pp. 91-94, 1993.
3. Till, G.O. and Ward, P.A.: 3.1 - Shock and ischemia: Oxygen radical-mediated endothelial cell injury, in, Faist, E., Meakins, J.L. and Schildberg, F.W. (eds), *Host Defense Dysfunction in Trauma, Shock and Sepsis: Mechanisms and Therapeutic Approaches*, Springer-Verlag, Berlin Heidelberg, pp. 85-94, 1993.
4. Ward, P.A., Mulligan, M.S. and Warren, J.S.: Neutrophils, cytokines, oxygen radicals and lung injury, in, Faist, E., Meakins, J.L. and Schildberg, F.W. (eds), *The Immune Consequences of Trauma, Shock and Sepsis - Mechanisms and Therapeutic Approaches*, Proceedings of the Symposium, Munich, Germany, Springer-Verlag, Berlin Heidelberg, pp. 177-180, 1993.
5. Ward, P.A. and Mulligan, M.S.: Role of products of L-Arginine in inflammatory lung damage, in, *Nitric Oxide: Brain and Immune System*, Portland Press, London, England, pp. 237-243, 1993.
6. Warren, J.S. and Ward, P.A.: Role of cytokines in pulmonary diseases, in, Oppenheim, J.J., Rossio, J.L. and Gearing, J.H. (eds), *Clinical Applications of Cytokines: Role in Pathogenesis, Diagnosis, and Therapy*, Oxford University Press, Oxford, United Kingdom, pp. 61-65, 1993.
7. Fantone, J.D. and Ward, P.A.: Inflammation, in, Rubin, E. and Farber, J.L. (eds), *Pathology, Second Edition*, J.B. Lippincott Co., Philadelphia, Pennsylvania, pp. 32-66, 1994.
8. Mulligan, M.S. and Ward, P.A.: Lung inflammation and adhesion molecules, in Metcalf, B.W., Dalton, B.J. and Poste, G. (eds), *Cellular Adhesion: Molecular Definition to Therapeutic Potential*, Plenum Press, New York, pp. 173-186, 1994.
9. Johnson, K.J., Chensue, S.W., Kunkel, S.L. and Ward, P.A.: Immunopathology, in, Rubin, E. and Farber, J.L. (eds), *Pathology, Second Edition*, J.B. Lippincott Co., Philadelphia, Pennsylvania, pp. 96-141, 1994.
10. Strieter, R.M., Phan, S.H. and Ward, P.A.: Inflammation, injury and repair (Chapter 17), in, Murray, J.F. and Nadel, J.A. (eds), *Textbook of Respiratory Medicine, Second Edition*, W.B. Saunders, Co., Orlando, Philadelphia, pp. 469-497, 1994.
11. Varani, J., Mulligan, M.S. and Ward, P.A.: The vascular endothelium and acute inflammation, Section 3, in, Klippel, J.H., Dieppe, P.A., Brooks, P., Carette, S., Dequeker, J., Gerber, L.H., Hazleman, B.L., Keat, A.C.S., Kimberly, R.P., Liang, M.H., Maini, R.N., van de Putte, L.B.A., Sturrock, R.D., Urowitz, M.B., Wollheim, F.A., and Zvaifler, N.J. (eds), *Rheumatology, Mosby-Year Book Europe Limited, London, England, pp. (3)11.1-11.12, 1994.*
12. 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, pp. 497-510, 1994.
13. Chensue, S.W. and Ward, P.A.: Inflammation, in, Damjanov, I. and Linder, J. (eds), *Anderson's Pathology, 10th Edition*, Mosby Year Book, Philadelphia, Pennsylvania, In Press.
14. Fantone, J.C. and Ward, P.A.: Mechanisms of inflammation, in, Cohen, A.S. (ed), *Rheumatology and Immunology*, Grune and Stratton, In Press.

15. 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.
16. Kunkel, S.L., Driscoll, K.E., Ward, P.A., Nickoloff, B. and Strieter, R.M.: Immunopathology of environmental and occupational disease, in, Craighead, J.E. (ed), The Pathology of Human Environmental and Occupational Disease, Mosby Yearbook, In Press.
17. Kunkel, S.L. and Ward, P.A.: The complement system, in, Bellanti, J.A. (ed), Immunology, 3rd Edition, In Press.
18. Maderazo, E.G. and Ward, P.A.: Leukocyte chemotaxis, in, Manual of Clinical Laboratory Immunology, 3rd Ed., American Society for Microbiology, Washington, DC, In Press.
19. Maderazo, E.G., Woronick, C.L. and Ward, P.A.: Inhibitors of chemotaxis, in, Methods in Enzymology, Academic Press, Orlando, Florida, In Press.
20. 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.
21. 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.
22. 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.
23. Till, G.O., Friedl, H.P. and Ward, P.A.: Histamine-dependent modulation of oxygen radical production, in, Farr, C.H. (ed), Proceedings of the Second International Conference of Bio-Oxidative Medicine, In Press.
24. Till, G.O., Johnson, K.J. and Ward, P.A.: Oxygen free radicals in inflammation, in, Messmer, K. and Hammerson, R. (eds), Progress in Applied Microcirculation, Volume 9, Karger, Basel, In Press.
25. 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.
26. Till, G.O. and Ward, P.A.: The lung and rheumatic disease: Role of complement. Butterworth's International Medical Reviews, Rheumatology 3, In Press.
27. Till, G.O. and Ward, P.A.: Thermal injury and lung tissue damage, in, Critical Topics in Pulmonary Pharmacology and Toxicology, In Press.
28. Till, G.O. and Ward, P.A.: Complement-induced lung Injury, in, Said, S.I. (ed), The Pulmonary Circulation and Acute Lung Injury, 2nd Edition, Futura Publishing Co., Mount Kisco, New York, In Press.
29. Vaporciyan, A.A. and Ward, P.A.: The inflammatory response, in, Beutler, E., Lichtman, M.A., Collier, B.S. and Kipps, T.J. (eds), Williams Hematology, McGraw-Hill, Inc., New York, In Press.
30. 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.
31. Varani, J. and Ward, P.A.: The immunobiology of tumor cell chemotaxis, Waters, H. (ed), Handbook of Cancer Immunology, Garland STPM Press, In Press.
32. Ward, P.A.: Inflammation, Chapter 12, in, Bellanti, J.A. (ed), Immunology in Medicine, W.B. Saunders Company, Philadelphia, Pennsylvania, In Press.
33. Ward, P.A.: Overview, in, Kinney, J.M. and Tucker, H.N., Oxygen Metabolism and Nutrition: Ideas for Future Critical Care, Raven Press, New York, In Press, 1994.
34. Ward, P.A., Friedl, H.P. and Till, G.O.: Role of oxygen radicals in experimental shock, Coran, A.G. and Harris, B.H. (eds), 3rd National Conference on Pediatric Trauma, In Press.
35. 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.

36. 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.
37. 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.
38. Ward, P.A., Johnson, K.J. and Till, G.O.: Animal models of oxidant lung injury, in, Proceedings of Stressa Symposium in Zambon, Italy, In Press.
39. Ward, P.A. and Mulligan, M.S.: The role of cytokines and adhesion molecules in lung inflammation, Schlag, G. (ed), Third Wiggers Bernard Conference on Shock, Sepsis, and Organ Failure, Hotel Schloff Obermayerhofen, Vienna, Austria, May 16-21, 1992, In Press.
40. Ward, P.A. and Till, G.O.: The autodestructive consequences of thermal injury, Ninnemann, J. (ed), The Immune Consequences of Thermal and Traumatic Injuries, In Press.
41. Ward, P.A., Warren, J.S. and Johnson, K.J.: Oxygen radicals, inflammation and tissue injury, Pryor, W. and Godber, S.L. (eds), Free Radical Biology and Medicine, In Press.
42. 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.
43. Ward, P.A., Warren, Johnson, K.J. and Varani, J.: Inflammation: Oxygen radicals and tissue injury, in, Oxidative Damage and Repair: Clinical, Biological and Medical Aspects, Proceedings of the 5th Biennial Meeting of the International Society for Free Radical Research, Pasadena, California, Pergamon Press, In Press.
44. 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.
45. Ward, P.A., Warren, J.S., Till, G.O., Varani, J. and Johnson, K.J.: Free radicals in lung disease, Rice-Evans, C. (ed), Free Radicals, Diseased States and Anti-Radical Interventions, Proceedings of the Special Colloquium, London, England, In Press.
46. 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.
47. Ward, P.A. and Mulligan, M.S.: Role of adherence molecules in lung inflammation, Granger, D.N. and Schmid-Schonbein, G.W. (eds), Physiology and Pathophysiology of Leukocyte Adhesion, Bermedica Production, Ltd., Columbia, Maryland, In Press
48. 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.
49. Warren, J.S., Johnson, K.J., Till, G.O., and Ward, P.A.: Mechanisms of oxygen radical-mediated acute tissue injury: In vivo studies. Proceedings of Enzyme Meeting, July, 1986, In Press.
50. 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.
51. 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.
52. Warren, J.S., Ward, P.A. and Johnson, K.J.: Immune complex injury, in, Cantor, J.D. (ed), CRC Handbook of Animal Models of Pulmonary Disease, CRC Press, Boca Raton, Florida, 1987, In Press.
53. Warren, J.S., Ward, P.A. and Johnson, K.J.: The inflammatory response, Chapter 8, in, Williams, W.J. (ed), Hematology, 4th edition, 1991.
54. 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.

55. 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. Mulligan, M.S. and Ward, P.A.: Adhesion molecules and cytokines in acute lung injury in rats. *Free Rad. Biol. Med.* 15:549, 1993.
2. Till, G.O., Seekamp, A. and Ward, P.A.: Riboflavin (vitamin B₂) protects from oxidant-mediated lung injury. *Free Rad. Biol. Med.* 15:551, 1993.
3. Vaporciyan, A.A. and Ward, P.A.: Enhanced generation by human neutrophil of O₂⁻ via a complement iC3b/mac-1 interaction. *FASEB J.* 7:A195, 1993.
4. Ward, P.A. and Varani, J.: Mechanisms of neutrophil-mediated injury. *Clin. Exp. Immunol.* 1:2, 1993.
5. Bonish, B.K., Jones, M.L. and Ward, P.A.: Expression and nickel affinity purification of a recombinant 1439BP fragment of rat vascular cell adhesion molecule-1 (VCAM-1). *FASEB J.* 8:A133, 1994.
6. Eppinger, M.J., Shanley, T.P., Jones, M.L., Deeb, G.M., Bolling, S.F. and Ward, P.A.: Transcriptional upregulation of inflammatory mediators in a rat lung model of ischemia-reperfusion injury. *FASEB J.* 8:A125, 1994.
7. Foreman, K.E., Johnson, K.J., Eddy, S.M. and Ward, P.A.: Identification of a receptor binding site for C5a on human umbilical vein endothelial cells. *FASEB J.* 8:A682, 1994.
8. Jones, M.L., Vaporciyan, A.A., Bonish, B.K. and Ward, P.A.: In vivo and in vitro regulation of ICAM-1 and MCP-1 expression by interleukin-10 (IL-10). *FASEB J.* 8:A266, 1994.
9. Lebedovych, L., McMorris, M.S., Ward, P.A., Johnson, K.J. and Ward, P.A.: Variables altering cutaneous and pulmonary infiltrates in an in vivo model of delayed-phase allergic inflammation. *FASEB J.* 8:A680, 1994.
10. Shanley, T.P., Jones, M.L., Schmal, H., Peter-Friedel, H. and Ward, P.A.: Molecular cloning and in vivo transcriptional expression of rat rantes in lung inflammation. *FASEB J.* 8:A809, 1994.
11. Warner, R.L., Marletta, M.A., Richards, M. and Ward, P.A.: In vitro stimulation of inducible nitric oxide synthase in rat alveolar macrophage. *FASEB J.* 8:A470, 1994.
12. Eppinger, M.J., Jones, M.L., Deeb, M., Bolling, S.F. and Ward, P.A.: The bimodal pattern of injury and the role of neutrophils in a rat lung model of ischemia-reperfusion. *American Society of Transplant Surgeons, Chicago, Illinois, May 18-20, 1994.*
13. Eppinger, M.J., Jones, M.L., Deeb, G.M., Bolling, S.F. and Ward, P.A.: The bimodal pattern of injury and the role of neutrophils in a rat lung model of ischemia-reperfusion. *Association of Academic Surgeons, November, 1994.*

**JEFFREY S. WARREN, M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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 (20 contact hours).
- B. Clinical Pathology Grand Rounds:
 - 1. "Cryoglobulinemia" (12/10/93).
 - 2. "Syphilis" (12/17/93).
 - 3. "Administrative issues - panel discussion" (1/7/94).
 - 4. "Establishing a new laboratory test" (1/14/94).
 - 5. "Autoimmune thyroid disease" (2/8/94).
- C. Immunopathology journal club (one hour; biweekly).
- D. Immunopathology signout: Pathology residents, M-4 medical students, EMU medical technology students (3x/week; 35 weeks/year).
- E. M-4 Laboratory Medicine Elective; 4th year medical students, four week block; (nine contact hours).
- F. M-1 Histopathology sequence; 1st year medical students; (nine contact hours).
- G. Supervision of Research activities for:
 - 1. Craig Flory, Ph.D. (postdoctoral fellow); (6/15/90-10/1/93).
 - 2. Kenneth Kilgore, Ph.D. (postdoctoral fellow); (1/1/94-present).
 - 3. Peter A. Barton (M-2 medical student); (5/1/92-4/30/94) (sponsored by Howard Hughes Medical Institute post-sophomore fellowship).
 - 4. Joseph Shen (interflex student); (5/10/93-7/30/93; 5/10/94-8/15/94) (sponsored by American Heart Association of Michigan summer fellowships).
 - 5. Brigitt Casselman (Sophomore, University of Michigan; 5/1/94 - present).
 - 6. William Tissot (Sophomore, University of Michigan; 9/1/93 - 5/1/94; sponsored by UROP).
 - 7. Daniel Cusmono (Sophomore, University of Michigan; 9/1/93 - 12/15/93 sponsored by UROP).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Monocyte-Macrophage Cytokines in Immune Complex Lung Injury", NIH (R29-HL40526), (50% effort), \$350,000; direct costs, 4/1/89-3/31/94.
- B. 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 submitted 6/30/94).
- C. Consultant, "CRP Peptides Activating Anti-Cancer Networks in the Lung", NIH-RO1, Barbara Barna, Ph.D., Principal Investigator, Cleveland Clinic Foundation.

PROJECTS UNDER STUDY:

- A. Role of cytokines (tumor necrosis factor, interleukin 1) in immune complex lung injury.
- B. Pathogenesis of endotoxic shock in mice with homozygous C5 deficiency.
- C. Role of MCP-1 in pulmonary granulomatous vasculitis.
- D. Modulation of proinflammatory endothelial cell functions by the membrane attack complex (MAC).
- E. Monocyte activation by ANCA.
- F. Biological activity of TNF-induced endothelial protein, B61 (collaboration with Visha Dixit, M.D., Department of Pathology, University of Michigan Medical School).
- G. Role of MCP-1 in luteolysis (collaboration with Landis Keyes, Ph.D., Department of Physiology, University of Michigan Medical School).
- H. Role of MCP-1 in PAN-induced interstitial nephritis (collaboration with Allison Eddy, M.D., Department of Internal Medicine, University of Toronto, Canada).
- I. Pathogenesis of extrinsic allergic encephalomyelitis (collaboration with Joan Berman, Ph.D., Department of Neurology, Albert Einstein, New York).
- J. Ischemia-reperfusion injury in perinatal rat brain (collaboration with Faye Silverstein, M.D., Department of Pediatrics, University of Michigan Medical School).
- K. Role of MCP-1 in cutaneous delayed type hypersensitivity (collaboration with Douglas Ringler, V.M.D., LeukoSite, Inc., Cambridge, Massachusetts).

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

- A. Northeast Ann Arbor (East Medical Campus) Facility Planning Committee, 1994-present.
- B. Chairman, East Medical Campus Laboratory Program Planning Committee, 1994-present.
- C. Contract Advisory Committee, University of Michigan Medical Center, 1994-present.
- D. Medical Center Clinicians Group Communications Committee, 1994-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. 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.

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.
- B. Preparation of Immunopathology Subspecialty Board Exam Questions, 1990-present.
- C. Preparations of Clinical Pathology Board Exam Questions, 1991-present.
- D. Ad hoc reviewer, Research Training Review Committee; Clinical Investigator Development Awards (CIDA/KO8s); National Institutes of Health (NHLBI); Bethesda, Maryland; November 16-17, 1993.

V. **INVITED LECTURES/SEMINARS:**

1. "Update in Immunopathology", Intercellular Adhesion Molecules in Inflammation." ASCP Workshops, Orlando, Florida, October 19, 1993.
2. "Antinuclear Antibody Testing and Autoimmune diseases", ASCP Workshops, Orlando, Florida, October 20, 1993.
3. "Immunopathology of Inflammation", Indiana University, Indianapolis, Indiana, December 3, 1993.
4. "Clinical Immunopathology Laboratory Assays", Rheumatology Division, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, December 13, 1993.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Barton, P.A. and Warren, J.S.: Complement components modulate the systemic tumor necrosis factor response in murine endotoxic shock. *Infect. and Immunol.* 61:1474-1481, 1993.
2. Seekamp, A., Warren, J.S., Remick, D.G., Till, G.O. and Ward, P.A.: Requirements for TNF- α and IL-1 in limb ischemia/reperfusion injury and associated lung injury. *Am. J. Pathol.* 143:453-462, 1993.
3. Warren, J.S., Jones, M.L. and Flory, C.M.: Analysis of monocyte chemoattractant protein 1-mediated lung injury using rat lung organ cultures. *Am. J. Pathol.* 143:894-906, 1993.
4. McCurry, K.A., Campbell, D.A., Jr., Scales, W.E., Warren, J.S. and Remick, D.G.: Tumor necrosis factor, interleukin-6 and the acute phase response following hepatic ischemia/reperfusion. *J. Surg. Res.* 55:49-54, 1993.
5. Brieland, J.K., Jones, M.L., Flory, C.M., Miller, G.R., Warren, J.S., Phan, S.H. and Fantone, J.C.: Expression of monocyte chemoattractant protein-1 (MCP-1) by rat alveolar macrophages during chronic lung injury. *Am. J. Respir. Cell Molec. Biol.* 9:300-305, 1993.
6. Flory, C.M., Jones, M.L. and Warren, J.S.: Pulmonary granuloma formation in the rat is partially dependent on monocyte chemoattractant protein-1. *Lab. Invest.* 69:396-404, 1993.

7. Markey, B.M. and Warren, J.S.: Use of antineutrophil cytoplasmic antibody to distinguish between vasculitis disease activity and complications of immunosuppressive therapy. *Am. J. Clin. Pathol.*, In Press.
8. 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.*, In Press.
9. Flory, C.M., Jones, M.L. 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. *J. Immunol.*, In Press.
10. Eddy, A. and Warren, J.S.: Expression and function of monocyte chemoattractant protein-1 in experimental nephrotic syndrome. *Am. J. Pathol.*, In Press.
11. 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. Immunol.*, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. 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.*
2. Su, L., Keren, D.F. and Warren, J.S.: Failure of anti-lambda immunofixation reagent mimics alpha heavy chain disease. Submitted to *Clin. Chem.*
3. Kilgore, K.S., Miller, B.F. and Warren, J.S.: Neutrophil adhesion to endothelial cells is rapidly induced by the membrane attack complex: The roles of P-selectin and platelet-activating factor. Submitted to *J. Immunol.*
4. 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. Submitted to *J. Immunol.*

BOOKS/CHAPTERS IN BOOKS:

1. Ward, P.A., Mulligan, M.S. and Warren, J.S.: Neutrophils, cytokines, oxygen radicals and lung injury, in, *The Immune Consequences of Trauma, Shock and Sepsis - Mechanisms and Therapeutic Approaches*, Proceedings of the Symposium Munich, German, Springer-Verlag, pp. 177-180, 1973.
2. Warren, J.S. and Ward, P.A.: Role of cytokines in pulmonary diseases, in Gearing, A, Rossio J and Oppenheim JJ (eds), *Clinical Applications of Cytokines: Role in Pathogenesis, Diagnosis, and Therapy*, Oxford University Press, Oxford, United Kingdom, 61-66, 1993.
3. Warren, J.S.: Inflammation, in Spilker, B (ed), *Drug News and Perspectives*, Raven Press, New York, New York, pp. 450-459, 1993.
4. Warren, J.S.: Immunodeficiency disease, in McClatchey, K.D. (ed), *Clinical Laboratory Medicine*, Williams and Wilkins, Baltimore, Maryland, pp. 1579-1598, 1994.

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

1. Flory, C.M., Jones, M.L. and Warren, J.S.: Regulatory Role of TNF-alpha in monocyte chemoattractant protein-1-mediated granulomatous pulmonary vasculitis in the rat. cardiovascular Research Forum, American Heart Association of Michigan, East Lansing, Michigan, September 21, 1993 (abstract).
2. Eddy, A.A. and Warren, J.S.: Expression and function of monocyte chemoattractant protein-1 (MCP-1) in puromycin aminonucleoside nephrosis. *Am. soc. Nephrol.* Baltimore, Maryland, November 18, 1993 (abstract).
3. Flory, C.M., Barton, P.A., Jones, M.L., Miller, B.F. and Warren, J.S.: Roles of MCP-1 TNF- α and ICAM-1 in pulmonary granulomatous vasculitis in the rat. Keystone Symposium on

- Inflammation, Growth Regulatory Molecules and Atherosclerosis, Keystone, Colorado, January 16-23, 1994.
4. 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).
 5. 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).
 6. Barton, P.A., Imlay, M.M., Flory, C.M. and Warren, J.S.: Role of intercellular adhesion molecule-1 (ICAM-1) in glucan-induced pulmonary granulomatosis in the rat. FASEB, Anaheim, California, April 24-28, 1994 (abstract).
 7. Imlay, M.M., Shen, J., Alrawi, T., Flory, C.M. and Warren, J.S.: Locally produced monocyte chemoattractant protein-1 (MCP-1) mediates monocyte-endothelial adhesive and killing interactions. FASEB, Anaheim, California, April 24-28, 1994 (abstract).
 8. Ivacko, J., Melinak, C., Flory, C.M., Warren, J.S. and Silverstein, F.S.: Hypoxic-ischemic brain injury induces expression of monocyte chemoattractant protein-1 (MCP) in perinatal rat brain. Society for Pediatric Research, Seattle, Washington, April 18-21, 1994 (abstract).
 9. 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). Colloquium on the Role of Adhesion Molecules in Cardiovascular Pharmacology. Sponsored by the American Society for Pharmacology and Experimental Therapeutics, Ann Arbor, Michigan, June 27-28, 1994.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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. Consultant for referred bone pathology cases at University of Michigan.
- C. Surgical Pathology, Department of Veterans Affairs Medical Center.
- D. Autopsy Pathology, Department of Veterans Affairs Medical Center.
- E. 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 lectures (two) in bone pathology.
- F. Medical student - second year pathology laboratory.
- G. 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 1993 - 30 JUNE 1994**

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 two postdoctoral fellows.
- C. Advisor for one graduate student, Cellular and Molecular Biology Training Program.
- D. Member, Program Committee - Cellular and Molecular Biology Training Program.
- E. Program Committee, Graduate Program in Pathology.
- F. Chairman, Examination Committee, Graduate Program in Pathology.
- G. Member, dissertation committees for two graduate students.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Mutants for DNA Enzymes", American Cancer Society, NP770-T.
- B. Principal Investigator, "Prevention and Repair of DNA Damage in Bacteria", National Science Foundation, DMB-8922562.
- C. 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.

REGIONAL AND NATIONAL:

- A. Ad hoc grant reviewer for the National Science Foundation.
- B. Referee for the following journals:
 - 1. Molecular and General Genetics
 - 2. Biochemistry.
 - 3. Molecular Microbiology.
 - 4. Current Genetics.
 - 5. Proceedings of the National Academy of Sciences.
 - 6. Free Radical Biology and Medicine.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. International Conference on Superoxide and Superoxide Dismutase, Kyoto, Japan.
- 2. Department of Molecular Biology and Genetics, Johns Hopkins University School of Medicine, Baltimore, Maryland.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Wang, L. and Weiss, B.: De novo synthesis of thymidylate via deoxyctidine in *dcd* (dCTP deaminase) mutants of *Escherichia coli*. J. Bacteriol. 176:2194-2199, 1994.

BOOKS/CHAPTERS IN BOOKS:

- 1. Weiss, B. and Wu, J.: A superoxide response regulon on *E. coli*, in, Asada, K. and Yoshikawa, T. (eds), *Frontiers of Reactive Oxygen Species in Biology and Medicine*, Excerpta Medica, New York, New York, 1994.

**SHARON W. WEISS, M.D.
PROFESSOR OF PATHOLOGY
DIRECTOR OF ANATOMIC PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology Service - four months.
- B. Consultant for Bone and Soft Tissue - 12 months.
- C. Secondary Consultant for Breast Pathology - 12 months.
- D. M-Labs Surgical Pathology Service - as needed.

II. TEACHING ACTIVITIES

- A. Sophomore Medical Class:
 - 1. Pathology 600 - lecture - two contact 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. Young-Chae Chu, Korea, July 1993-March 1994; Dr. Robert Dymock, Australia, September, 1993; Dr. Carlos Santonja, Spain, July-August, 1993; Dr. Maria Hillemanns, Germany, January-February, 1994; Dr. Mary Jane Zimarowski, Harvard, April, 1994; Dr. Jean-Michel Coindre, France, March, 1994, Dr. Greg Pizarro, Pittsburgh, May, 1994.
- E. Medical Student Advisor:
 - 1. Responsible for mentoring of Michelle Mantel (M-4), Rachel Wilks (M-4), Christine Martin (M-4).

III. RESEARCH ACTIVITIES

SPONSORED SUPPORT:

- A. Southwest Oncology Group, SWOG study 9055 (\$3,197).

PROJECTS UNDER STUDY:

- A. Correlation of grade and flow cytometric analysis in soft tissue tumors.
- B. Carpal tunnel syndrome.
- C. Epithelioid smooth muscle tumors of soft tissue.
- D. Borderline vascular tumors.
- E. Typical and atypical giant cell tumors.
- F. Dedifferentiated liposarcoma.

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL:

- A. Director, Division of Anatomic Pathology.
- B. Chief, Surgical Pathology.
- C. Member, Chairman's Advisory 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

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.
- C. Association of Directors of Anatomic Pathology
- D. Chairman, Sarcoma Pathology Subcommittee, Southwest Oncology Group.
- 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).

INVITED LECTURES:

- 1. Faculty, "Soft Tissue Sarcomas: An Overview," US-CAP Diagnostic Pathology 1993, Massachusetts Institute of Technology, Boston, Massachusetts, August, 1993.
- 2. Faculty, International Skeletal Society Closed Meeting, "Langerhans cell granulomatosis simulating a sarcoma," International Skeletal Society Annual Meeting, Toronto, Canada, August, 1993.
- 3. Moderator of Group Session, "Ways to Cope with a 30% Budget Reduction," Association of Directors of Anatomic Pathology Annual Meeting, Chicago, Illinois, October, 1993.
- 4. Faculty, Slide Seminar, Oregon Society of Pathologists, Portland, Oregon, November, 1993.
- 5. Faculty, "Critical Errors in the Diagnosis of Soft Tissue Tumors," University of Texas at San Antonio, December, 1993.
- 6. Speaker, 50th Annual Seminar, San Antonio Society of Pathologists, "Tumors and Tumor-like Lesions of Soft Tissue," San Antonio, Texas, December, 1993.
- 7. Moderator, Bone and Soft Tissue Scientific Session, Annual US-CAP meeting, San Francisco, CA, March, 1994.

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

- 1. Weiss, S.W. and Nickoloff, B.J.: CD-34 is expressed by a distinctive cell population in peripheral nerve sheath tumors and related lesions. *Am. J. Surg. Pathol.* 17:1039, 1993.
- 2. Weiss, S.W.: Tumoral amyloidosis of soft tissue ("amyloidoma"): new approaches to an old problem. *Am. J. Clin. Pathol.* 100:91, 1993.
- 3. Goldblum, J.R., Beals, T. and Weiss, S.W.: Neuroblastoma-like neurilemoma. *Am. J. Surg. Pathol.* 18:266, 1994.
- 4. Fisher, C.R., Chappel, M.E. and Weiss, S.W.: Neuroblastoma-like epithelioid schwannoma. *Histopathol*, In Press.
- 5. 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.*, In Press.
- 6. Robertson, J., Lawrence, T., Weiss, S.W., Sondak, V.K. and Chang, A.E.: IUDR and radiotherapy for retroperitoneal sarcomas. *J Rad Oncol Biol Phys*, In Press.

SUBMITTED FOR PUBLICATION:

1. Goldblum, J.R., Frank, T.S., Poy, E. and Weiss, S.W.: p53 mutations and histologic progression in well-differentiated liposarcoma and dermatofibrosarcoma protuberans. Submitted to Am. J. Surg. Pathol.
2. Gross, A.S., Louis, D.S., Carr, K.A. and Weiss, S.W.: Carpal tunnel syndrome: a clinicopathologic study. Submitted to J Occup Health.
3. Flint, A. and Weiss, S.W.: CD-34 and cytokeratin distinguishes solitary fibrous tumor from desmoplastic malignant mesothelioma. Submitted to Hum. Pathol.

BOOKS AND CHAPTERS IN BOOKS:

1. Weiss, S.W. and Sobin, L.H.: WHO Histologic Classification of Soft Tissue Tumours, Springer Verlag, Berlin, 1994.
2. Montgomery, L.A., Kraybill, W.G. and Weiss, S.W.: Soft Tissue Tumors, in Pathology for the Surgeon, W.B. Saunders, New York, In Press.
3. Miettinen, M. and Weiss, S.W.: Soft Tissue Tumors, in, Anderson's Pathology, 10th ed., C.V. Mosby, St. Louis, In Press.
4. Weiss, S.W.: General Consideration, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
5. Weiss, S.W.: Benign Fibrohistiocytic Tumors, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
6. Weiss, S.W.: Fibrohistiocytic Tumors of Intermediate Malignancy, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
7. Weiss, S.W.: Malignant Fibrohistiocytic Tumors, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
8. Weiss, S.W.: An Approach to the Diagnosis of Soft Tissue Tumors, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
9. Weiss, S.W.: Immunohistochemistry of Soft Tissue Tumors, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, in press.
10. Weiss, S.W.: Benign Smooth Muscle Tumors, in Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
11. Weiss, S.W.: Leiomyosarcoma, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
12. Weiss, S.W.: Epithelioid Smooth Muscle Tumors, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
13. Weiss, S.W.: Benign Vascular Tumors, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
14. Weiss, S.W.: Hemangioendothelioma: Vascular Tumors of Intermediate Malignancy, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
15. Weiss, S.W.: Malignant Vascular Tumors, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
16. Weiss, S.W.: Benign Neural Tumors, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
17. Weiss, S.W.: Malignant Neural Tumors, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
18. Weiss, S.W.: Primitive Neuroectodermal Tumors and Related Lesions, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
19. Weiss, S.W.: Paraganglioma, in Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
20. Weiss, S.W.: Perivascular Tumors, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.

21. Weiss, S.W.: Lymphatic Tumors, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.
22. Weiss, S.W.: Synovial Tumors, in, Soft Tissue Tumors, C.V. Mosby, St. Louis, In Press.

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

1. Smith, M. and Weiss, S.W.: Low grade angiectatic sarcoma with pleomorphic features: a low grade lesion resembling neurilemoma. Mod. Pathol. 7:10A, 1994.
2. Pearson, J., Weiss, S.W. and Headington, J.T.: Malignant tumors arising in neurocristic hamartomas. Mod. Pathol. 7:48A, 1994.
3. Goldblum, J.R., Frank, T.S. and Weiss, S.W.: p53 mutations in soft tissue sarcomas: a potential marker of tumor progression. Mod. Pathol. 7:7a, 1994.
4. Perkins, P. and Weiss, S.W.: Spindle cell hemangioendothelioma: a clinicopathologic analysis of 78 cases. Mod. Pathol. 7:9a, 1994.

SECTION REPORTS

DIVISION OF ANATOMIC PATHOLOGY**DEPARTMENT OF PATHOLOGY****ANNUAL REPORT****1 JULY 1993 - 30 JUNE 1994**

During the past year a number of significant changes in our faculty occurred. Dr. Paul Gikas, one of our distinguished senior surgical pathologists, officially retired from our ranks. His benchmark work, which detailed the pattern of traumatic injuries in fatal automobile crashes, was largely instrumental in the passage of legislature mandating seat belt usage. Strongly involved with athletic programs at the University of Michigan, he was also recognized for his deep commitment to the issue of drug testing in athletes. Yet of all his honors he was most proud of the teaching award bestowed upon him by our pathology residents, a sentiment which underscored his belief in the importance of higher education and the strong bond he felt for his professional friends and colleagues. Dr. Robert Hendrix, Professor Emeritus and mainstay of our forensic pathology program, resigned from his role on the autopsy service this past year. The Department gratefully acknowledges his years of contributions. Through his efforts and those of Dr. Remick, the Department has initiated a Forensic Pathology program. Dr. Michael Caplan, recruited from the New York City Medical Examiner's Office, will assume a leadership role in this initiative. Finally, the Division has recruited three new promising pathologists to fill our existing needs: Dr. Kenneth Devaney, joining us from Brown University, will serve on both the Surgical Pathology and Cytopathology Services and provide expertise in the areas of orthopedic and otolaryngic pathology. Dr. Thomas Giordano, recruited from Memorial Sloan Kettering Cancer Center will become our endocrine pathologist and augment our expertise in the area of molecular diagnostics. Dr. Kirk Wojno, who completed his training at the Johns Hopkins Hospitals, joins us as our genitourinary pathologist.

Our clinical services remain active and demanding. Providing support to the Hospital on all diagnostic specimens, we have expanded our services to include routine image analysis evaluations on breast cancers and PCR-based tests for microorganisms. Our faculty participates regularly in the multidisciplinary clinics dealing with breast cancer, melanoma, and soft tissue sarcomas. We maintain strong ties with the Cancer Center not only through scientific collaboration, but also through the Tissue Procurement Core administered through our Division. This facility is responsible for the collection and distribution of all human tissues throughout the Medical Center for investigational uses. Independently funded, it is currently directed by Dr. Thomas Frank who will expand its services to include Preserved Tissue Analysis (DNA Retrieval) Core for Cancer Center researchers.

Our Division is strongly committed to the educational missions of our Department: We maintain high visibility in medical student teaching programs with one of our faculty, Dr. Gerald Abrams, serving as Component II Director. Our faculty actively mentored nine residents who presented papers at the recent US-CAP meeting. Six anatomic pathology fellows completed advanced training. These included: Drs. Suzanne Cook, Kenneth Lidonnici (State University of New York), Philip Perkins and Kyle Carr in surgical pathology and Drs. Priscilla Lindley and Patricia Perosio in cytopathology. Fellowships in neuropathology and nephropathology have been approved for coming years. During the year, we hosted two Visiting Professors. Dr. Tanya Tavassoli, formerly Assistant Chair of the Department of

Gynecologic Pathology, Armed Forces Institute of Pathology, presented a lecture on "Breast Neoplasms" and Dr. Peter Burger, Professor of Pathology, Johns Hopkins Hospital, lectured on "Gliosis vs. Glioma". Our Division has served as host to numerous visiting scientists and trainees, both from this country and abroad, who elected to train in our Division for varying periods of time. They included: Dr. Young-Chae Chu (Korea), Dr. Carlos Santonja (Spain), Dr. Robert Dymock (Australia), Dr. Marija Hillemanns (Germany), Dr. Mary Jane Zimarowski (Harvard), Dr. Jean-Michel Coindre (France), Dr. Greg Pizarro (Pittsburgh, PA), Dr. Rose-Marie Caduff (Switzerland).

As a Division, we are working toward a goal of providing excellent clinical care in a more cost-efficient manner. We recently underwent a detailed external review of our Anatomic Pathology laboratories to determine areas for modification. We foresee the implementation of several broad initiatives which will improve our laboratory efficiency and reduce our costs. These include: 1) computerization of all test ordering and fee coding, 2) full automation of all tissue processing and staining including immunohistochemistry, 3) voice-activated transcription, 4) consolidation of laboratories with cross-training of technical staff, 5) standardization and monitoring of utilization patterns of ancillary tests. We also look upon our ability to forge and maintain strong ties with our regional pathologists as important to the integrity of our M-Labs referral program. Toward this end, the Division will explore the need for an annual Continuing Medical Education course.

Sharon W. Weiss, M.D.
Director

AUTOPSY SERVICE
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

The autopsy service of the University of Michigan continues to provide autopsies to University patients, perform forensic autopsies for the Washtenaw County Medical Examiner's Office, and harvest brains for the Michigan Postmortem Examination Network.

I. Medical Examiner's Cases:

The recruitment of Michael Caplan, M.D. to perform the forensic autopsies at the University of Michigan has resulted in substantial improvements in several areas of the autopsy service. The autopsy report for medical examiner's cases has been redesigned to allow more efficient reporting of results to police investigating agencies. Increased documentation of injuries has been achieved by more detailed photographs of the injuries. The service has been helped in this regard by Mark Deming's attendance of a forensic photography workshop. Active involvement of the medical photographers has enhanced the extent and quality of the photodocumentation of the medical examiner cases, as well as the routine Hospital cases.

The Department of Pathology has assumed all responsibility for medical examiner cases within the University of Michigan Hospitals, and a Deputy Medical Examiner is available 24 hours a day. Within the department, house officers and staff provide coverage at night, and Dr. Caplan serves as the DME during the day. This has resulted in a significant improvement in the availability of DMEs with better documentation of cases.

II. Movement of the Office of Vital Statistics:

Effective September 1, 1994, Cheryl Smith from the Office of Vital Statistics will be relocated to the Department of Pathology. At this time, the Department of Pathology will assume all responsibility for death certificates and release of bodies. This relocation has come about as a result of an extensive study by the Hospital on several matters related to handling of deceased patients at the University. The autopsy service devised a comprehensive plan to effectively solve several of the problems, including removal of medical waste, timely notification of funeral directors, and better tracking of location of patients. This relocation will consolidate most of the activities related to deceased patients within the Department of Pathology.

III. Morgue security system:

The new security system has been installed in the morgue. Card keys are now used to obtain entry, and all other persons requiring access need to contact security who permits them access through remote control.

IV. Autopsy Neuropathology:

Major initiatives have been undertaken to restructure autopsy neuropathology. These have been done in order to increase the training of the house officers in neuropathology, so that they will have confidence to perform both gross and microscopic examination of autopsy brains. Pathology House Officers now have complete control of normal brains, including removal, cutting and taking of sections. Brain cutting sessions have been shortened to permit more rapid processing of material, and allow the house officers more active participation in the selection of the specimens needed to diagnose diseases. A second brain cutting sessions geared to the house officers has been added on Monday.

V. 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 last evaluation of turn-around time showed that the average time to completion of a case was 114 days, with 51% of cases requiring more than 90 days to completion and 27 cases still not signed out after 8 months (21% of the total volume). To determine exactly where the problem lies, the performance of each staff person was evaluated, and they were provided with a written report indicating how long it required them to complete a case. This interesting analysis revealed that some staff required up to 2 months to sign a completed, final report. Staff have been urged to pay close attention to completing their cases.

VI. Surgery Death and Complications Conference:

The House Officers in Pathology have begun presenting their autopsies at the weekly death and complications conference in the Department of Surgery. These presentations are made by the house officer who performed the autopsy, with the staff person always in attendance. These presentations have been well received by the Department of Surgery, and we have received positive feedback from both staff and house officers from the department of Surgery.

VII. Statistics:

	1991/92	1992/93	1993/94
Total U of M cases	322	420	488
M-Labs cases	8	5	3
Medical Examiner's Cases	58	101	159
In hospital	24	47	63
Outside cases	34	54	74
Transferred from other hospitals			22
External examination only			24
Autopsy rate (includes tetralogy)	35%	39%	47%

Some of the numbers require comment. The total number of medical examiner cases was 159, but this included 24 cases of external examination only. Previously, these numbers were not assigned an autopsy number and therefore not included in the annual report. The number of full ME autopsies was 135. The increase in the total number of autopsies done at the University is due to a combination of the increase in the medical examiner cases, and the increase in the number of medical examiner cases (34 cases), and hospital cases (also 34 cases). This information is presented below, where the increase in both total autopsies and the autopsy rate are both observed to increase each year for the past 5 years.

The Autopsy Service of The University of Michigan continues to serve its central goals of resident training, performance of autopsies on University of Michigan patients, and performance of forensic autopsies for Washtenaw County.

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

CYTOPATHOLOGY LABORATORY
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

Over the past year the Cytopathology Service has continued to refine and implement its computer program for the reporting of cervicovaginal cytology. In conjunction with Pathology Data Systems, a new quality assurance/quality control software program for cervicovaginal cytology was developed to comply with the new Federal regulations.

To comply with the Department's cost containment program, laboratory efficiency became a major priority. Paid overtime for the screening of slides has decreased through the diligent efforts of the cytotechnologists. Reorganization of the cytotechnologists' daily work schedule has enabled the laboratory to aid M-Labs by providing slide-screening coverage for several small community hospitals.

In the eighth year of our cytopathology fellowship, Dr. Priscilla R. Lindley and Dr. Patricia M. Perosio completed their training with distinction. Dr. Perosio is eligible to take the examination for the Special Qualification in Cytopathology. Both have taken positions in private practice.

The cytotechnologists have been actively involved in the regional cytology society. Over the past year Mr. Gregory Van Amberg was the Educational Program Director for the Michigan Society of Cytology and Ms. Belinda Davis, our Laboratory Supervisor, is the current Vice-President of the Michigan Society of Cytology. Drs. Naylor and Selvaggi participated in a joint lecture series for the Wayne State University and Henry Ford Hospital programs of Cytotechnology.

The number of fine needle aspirations continues to rise for a total of 1,754 cases. Gynecologic specimens numbered 31,254 and non-gynecologic specimens 6,267, for a total of all cytologic specimens of 37,521.

Bernard Naylor, M.D.
Director, Cytopathology Laboratory

Suzanne M. Selvaggi, M.D.
Co-Director, Cytopathology Laboratory

**DERMATOPATHOLOGY SERVICE
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
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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
HE	731	981	694
ID	5651	4255	4791
MD	--	1347	1663
TD	--	550	709
Misc.	--	--	71
Informal	300	225	254

All sources of cases increased in 1993-1994 except for a decline in HE cases which was due to a shift in clients from HE to MD accounting. Total cases exceeded 8000 for the first time.

The greatest impact on the workload for the Dermatopathology Service has been the continued growth of cutaneous oncology services within the UMMC for both melanoma and non-melanoma skin cancer. This has resulted in the receipt of numerous large and complex specimens in addition to routine biopsy material. There will be continued growth in this area with a substantial increase anticipated with the opening of the new Cancer and Geriatric facility in 1996.

Scheduled dermatopathology teaching in the Department of Dermatology was 1.5 contact hours weekly.

Correlative activities included participation in the Pigmented Lesion Clinics (bi-weekly), Cutaneous Lymphoma Conference (monthly) and Dermatology Grand Rounds (weekly).

Formal lectures were presented to medical and dental students.

John T. Headington, M.D.,
Director, Dermatopathology Service

ELECTRON MICROSCOPY SERVICE

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1993 - 30 JUNE 1994

The electron microscopy service continues to provide important diagnostic services to the University of Michigan. The facility provides high quality diagnostic work for the nephrologists, neuropathologists, hematopathologists, and the general pathologists.

This past year there has been a major effort to decrease the turnaround time required to complete specimens. Several approaches have been used to achieve this goal. The first was the purchase of an automated tissue processor, which permits overnight processing of specimens. A review of procedures at peer institutions disclosed that all used this type of equipment. Use of this equipment permits the EM technicians to focus on other aspects of the work, without constant interruptions. A new, dual headed microscope was also installed in the EM facility to allow staff pathologists to review slides in the EM suite. The following is an analysis of the number of days to complete cases.

	Kidney	Muscle	Nerve	Other
Average number of days to thick sections	2	4	2	3
Average number of days to prints	5	10	5	7

This past summer the present Zeiss microscope was out of service for a three week period. This caused a significant backlog of cases, and only the generosity of Dr. Beals at the VA hospital prevented a complete crisis from occurring. To prevent this from recurring in the future, both of the EM technicians will train on the Philips electron microscope, and will each use this microscope once a month on a case. Dr. Johnson has graciously permitted us access to this equipment. In the event that the Zeiss scope is again out-of-service, the technicians will be already familiar with the other scope. The long range plan is to consider a replacement for the present Zeiss, which is over 14 years old and well beyond the usual life expectancy of 5 to 10 years. We have already contacted the major manufacturers of electron microscopes and are preparing a proposal to the hospital.

This following table is the analysis of the work volume in the EM laboratory for the 1993/1994 year. During the previous year, there were 503 biopsies processed, including 240 renal biopsies. Thus, we have had a decrease of 31 total biopsies, and 22 renal biopsies.

	All Cases	Renal	Nerve & muscle	Other
Total	472	218	188	66
Inside/outside	307/165	120/98	138/50	49/17

Daniel G. Remick, M.D.
Director, Electron Microscopy Service

NEUROPATHOLOGY SERVICE
DEPARTMENT OF PATHOLOGY
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1 JULY 1993 - 30 JUNE 1994

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 Blaiwas, 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 805 neurosurgical cases including CNS, pituitary, muscle and nerve examined this year. 75 of these cases were from outside hospitals in consultation. A portion of these were part of an interdepartmental study of PET/BU DR and neuropathology funded by NIH. Approximately 300 surgical specimens required special neurohistologic procedures.
2. There were 347 brains histologically processed out of 489 autopsies. (Of the 347 brain cases, 20 ADRC cases were processed in the Neuropathology Core Laboratory of the MADRC beginning in January, 1994.) An additional 35 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 170 muscle biopsies, nearly all with histochemistry, 44 with electron microscopy. There were 42 (24 internal, 18 external) peripheral nerve biopsies. There were 17 teased fiber preparations, 25 thick plastic sections and 23 had electron microscopy performed. There were 210 nerve biopsies done for MADRC. The combination of nerve teasing, muscle histochemistry, electron microscopy and morphometry make the service regionally competitive for diagnostic consultation.
4. Faculty interpreted 188 cases in semithin or thin section from electron microscopy (115 processed through immuno and 38 through neuropathology). The majority of these cases were nerve, pediatric muscle, and neurosurgical biopsy cases.
5. The ceroid service, buffy coat division, reported 16 cases. There were six skin biopsies done for storage disease, and there were four rectal biopsies.
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 120 difficult neuro-oncology cases.
7. Eighteen brains were examined for research purposes.
8. Autopsy neuropathology and surgical neuropathology each have monthly quality assurance meetings. 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 in a laboratory setting with a one hour introductory lecture just prior to the laboratories.
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 provided neurological and neurosurgical house staff on clinico-pathological correlations.

3. Electives: Two pathology residents, three neurosurgery residents, and three neurology residents chose elective rotations on the Neuropathology Service.
4. Two Neuromuscular fellows were instructed at conferences held weekly.

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, as of June, 1994.
2. Dr. Blaivas and associates investigate: 1) ocular muscle (aging and botulinum effect), 2) musculature related to cleft palates in children and mice, 3) muscles and spinal cord in mnd mice, 4) histology of animal model of rheumatoid arthritis, 5) 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 measuring DNA content, specific chromosomal markers by *in situ* hybridization, and Ki-67, PCNA and BUdR labeling indices in 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.
Director, Neuropathology Service

PEDIATRIC PATHOLOGY SERVICE

**DEPARTMENT OF PATHOLOGY
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The activities of this service were carried out as in the past, primarily by Kathleen P. Heidelberger, M.D. and Mason Barr, Jr., M.D.

Necropsy figures are as follows:

M/W/H Unit Deaths (22 weeks gestation or any live born, to 18 years)	=209
Necropsies on Above	=122
Necropsy Percentage	=58%

Of the 122 posts, 20 patients' bodies, as defined above, were released to Anatomy for study and disposal. These gross posts were performed by Mason Barr, Jr., M.D., with necessary histology by Dr. Heidelberger. One hundred two were posted by the residents and senior staff in Pathology, primarily Dr. Heidelberger. Necropsies categorized in the adult general hospital statistics as "Medical Legal" posts included 19 posts on pediatric patients including SIDS cases, child abuse cases and trauma cases, most of which were also classified as inpatient deaths, because of treatment here.

The autopsy service of the department lists 488 posts for the fiscal year. This includes 166 Medical Examiner cases (entire Washtenaw County and in-house cases) as well as brain only cases for ADRC. Thus, of the approximately 300 in hospital death cases, 122 are pediatric cases.

It should be noted that as a regional center, with a wide range of subspecialties, the total number of cases examined in the Teratology Unit was 170 - including both all referred fetuses and infants and inborn newborn fetal losses at less than 22 weeks gestational age.

The total number of pediatric surgical specimens (including placentas) examined is approximately 2,400. This number represents those cases sent directly to the subspecialty areas of renal, muscle and skin pathology, as well as to those in the general service. This represents a slight, steady increase over the prior three years.

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

**PRESERVED TISSUE ANALYSIS LABORATORY
(MOLECULAR DIAGNOSTICS FOR ANATOMICAL PATHOLOGY)**

**DEPARTMENT OF PATHOLOGY
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After six months of training and preparation, the Preserved Tissue Analysis (PTA) laboratory began formally offering ancillary diagnostic testing for paraffin-embedded tissues in January of 1994. The tests initially offered, which were developed and adapted to paraffin-embedded tissue within the PTA lab, included the detection of DNA viruses by PCR (including CMV, EBV, hepatitis B, and HPV) as well as the detection and species determination of mycobacteria. In addition to these the lab introduced a commercially available test for the identification of mislabeled specimens using HLA-DQ(alpha) determination. Analysis for hepatitis C in paraffin tissue using a novel strategy is in the final stages of testing and will be offered by October, 1994.

Because so many of the diagnostic tests performed by the PTA lab have been developed within the laboratory, clinical service has been closely interrelated with research and development. Diagnostic tests developed by the PTA lab were featured in publications in *Diagnostic Molecular Pathology*, the *American Journal of Surgical Pathology*, the *American Journal of Clinical Pathology*, and the *Journal of Heart and Lung Transplantation*. Citations to methods developed in the lab have appeared in other journals as well. This increased visibility has led to growing numbers of specimens submitted from other institutions for diagnostic evaluation.

The PTA lab has provided resources for a variety of resident and faculty projects, including evaluation of *M. paratuberculosis* in Crohn's disease, HPV in keratoacanthomas, hepatitis C in transplanted liver biopsies, and mutations and microsatellite instability in endometrial carcinoma. In the near future, resident training will be enhanced by the recent designation of a separate area dedicated for that purpose. The PTA lab has also provided several investigators throughout the institution with DNA extracted from paraffin sections for their research, and plans to offer this formally as a service in October, 1994. In addition, DNA extraction from paraffin slides will be offered as a service to investigators in other departments, scheduled to begin in October 1994.

Tom Frank, M.D.
Director

SURGICAL PATHOLOGY SERVICE

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The surgical pathology service remains one of the most active university services in the country despite the reduced rate of growth experienced over the last two years. Current accessions average 28,000/year with an additional 5,000 personal consultations, many of which require ancillary immunohistochemistry, image analysis, or molecular diagnostic tests. Over 4,000 intraoperative (frozen section) consultations are provided yearly with an accuracy rate of over 98%. Interpretation of several hundred STAT biopsies requiring 4-24 hour turn-around, largely from our transplant services, are provided by our laboratory and professional staff on a virtually 24-hour basis. The surgical pathology service administers, under the direction of Dr. Thomas Frank, the Tissue Procurement Core which annually collects and distributes specimens for researchers throughout the Medical Center.

The Surgical Pathology Fellowship Program remains a vital part of the activity of this service both from the vantage point of service but also education. Four fellows completed advanced training this year (Drs. Phil Perkins, Kyle Carr, Suzanne Cook, and Kenneth Lidonici) and will be followed in the coming year by Drs. Jeffrey Pearson, Eric Hsi, Kathleen Lane (Duke), and David Renado (University of Vermont). This program affords them the opportunity to supervise the frozen section activity, review a broad base of diagnostic material, interact first-hand with clinicians, and engage in clinical and/or basic research with faculty. We continue to attract an exceptional cadre of external candidates in addition to our own house officers for these four positions.

Our challenge in this and future years will be to meet the demands of clinical service in a more cost-efficient fashion. Toward this end, the Anatomic Pathology laboratories and, in particular, Surgical Pathology, underwent a detailed external review to determine areas for improvement. As a result of this review and in conjunction with the faculty consensus developed for our Five-Year Strategic Plan, we foresee certain changes necessary for academic survival in the managed health care milieu. This would include a de-emphasis on dedicated subspecialty sign-outs with an emphasis on broadly trained pathologists with subspecialty expertise. Improved laboratory efficiency will require aggressive computerization of all aspects of surgical pathology case handling and full automation of all areas. Finally, appropriate utilization of tests and resources will be addressed not only as a laboratory but also as an educational initiative with our house officers.

surgical.doc

Sharon W. Weiss, M.D.
Director, Surgical Pathology Service

DIVISION OF CLINICAL PATHOLOGY

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1993 - 30 JUNE 1994

Despite a net loss of laboratory personnel and hospital-imposed budget reductions during the past two years the Clinical Laboratories continued to provide excellent, full-spectrum service. The nearly flat cost per unit of activity provided by the Clinical Labs, in the face of rapidly rising 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 1993-94 the Clinical Labs performed 3.15 million analyses. The Clinical Laboratories successfully completed the biannual College of American Pathologists (CAP) interim self-inspection in May, 1994. Members of the CP Division contributed substantially to a number of Departmental and Institutional initiatives including: expansion of point-of-care testing capabilities, the resident phlebotomy service, laboratory and informatics planning for the East Medical Campus site, and expansion of clinical laboratory molecular diagnostics capabilities. 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.

1993-94 was marked by several new program initiatives and two faculty recruitments. A Clinical Molecular Diagnostics Laboratory was formally established under the direction of Anthony A. Killeen, M.D., Ph.D. Dr. Killeen, who arrived on site in September, 1993 from the University of Minnesota Medical School, is the Director of the Clinical Chemistry Section (Chemistry, Ligand Assay, Drug Analysis, Immunopathology, and Clinical Molecular Diagnostics Laboratories). Dr. Killeen brings expertise in the areas of clinical chemistry, clinical DNA diagnostic testing, and the molecular biology of congenital adrenal hyperplasia. This spring the Division embarked on a clinical interface initiative in which faculty and laboratory staff will endeavor to work aggressively with clinical service chiefs, nursing service representatives, and the Office of Clinical Affairs to prospectively improve the efficiency of laboratory utilization in patient care at the UMMC. Examples of this initiative include consolidation of numerous point-of-care testing venues into a cohesive program, coordination of genetics laboratory testing with the Divisions of Human Genetics in both Internal Medicine and Pediatrics, and the institution of a comprehensive, integrated specimen procurement/resident phlebotomist program. The Clinical Laboratories have supported an aggressively expanding M-Labs (outreach laboratory) program. Finally, Timothy Singleton, M.D. will join the faculty on July 1, 1994. Dr. Singleton completed Hematopathology subspecialty training at Stanford University and the University of Minnesota. He will direct the Hematology Laboratory and serve as Associate Director of the Immunoperoxidase Laboratory. Dr. Singleton brings expertise in the areas of bone marrow pathology and immunohistochemistry, particularly as it applies to hematopathology.

Faculty and laboratory staff participated in a wide variety of intramural and extramural educational programs during 1993-94. For instance, the 25th 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 second M4 Laboratory Medicine course were highly laudatory. A revised clinical pathology residency training format that organizes pathology residents into teams that rotate through three blocks of clinical laboratories which are grouped according to relatedness of discipline was instituted in July, 1993 and met with critical success. The continued high quality of trainees in the Hematopathology Fellowship program has enhanced both the service and academic missions of the Hematopathology group and 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 meetings, 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. Doctors Bertram Schnitzer (Hematopathology) and Harold Oberman (Blood Bank/Breast Pathology) were recognized by their peers for their excellence in the 1994-95 edition of the Best Doctors in America. Numerous faculty members received extramural funding that supported a variety of scholarly activities.

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 CEP, 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
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PATIENT CARE:

Further efforts to control blood utilization in University Hospital were successful, as neither the number of units of Red Blood Cells transfused nor the number of crossmatches performed increased. The number of units of platelets increased, relating to increased demand because of such enlarging clinical programs as Extracorporeal Membrane Oxygenation (ECMO) and Bone Marrow Transplantation. In addition, the volume of plasma components transfused increased primarily related to patients receiving liver homotransplantations or being evaluated for that procedure. An additional factor bearing on blood utilization in University Hospital was the establishment of the Level 1 Trauma Center in the Hospital.

In addition, the number of specially processed units of blood components increased. Although this is not reflected in the annual volume of procedures, processing such units is time-consuming. Leukocyte-reduced Red Blood Cells and platelet concentrates were increasingly utilized for patients who had repeated nonhemolytic febrile transfusion reactions and also to reduce the possibility of CMV transmission. Irradiated blood components were provided to reduce the possibility of posttransfusion Graft v. Host Disease in susceptible patients. Concern regarding the level of potassium in stored Red Blood Cells led to increased attention to the freshness of blood provided for neonatal patients, especially for those patients undergoing cardiac surgical procedures.

The Reference Laboratory of the Blood Bank, an American Association of Blood Banks-recognized reference laboratory, continued to manifest a high level of activity and excellence, enhancing support of patient care. This laboratory expedites patient care, as otherwise it would be necessary to submit specimens to an external laboratory for time-consuming and costly assessment of antibody problems.

The Transfusion and Apheresis area continued to provide outpatient transfusion of blood components and intravenous immune serum globulin and also manifested a modest increase in collection of autologous blood for subsequent transfusion in University Hospital. In addition, the therapeutic plasmapheresis program supported care for patients with neurologic conditions such as myasthenia gravis, Guillain-Barre and chronic inflammatory demyelinating polyneuropathy, as well as for patients with thrombotic thrombocytopenic purpura. Collection of peripheral blood stem cells for patients scheduled for bone marrow transplantation increased, and it is likely this activity will further increase in the coming year.

EDUCATIONAL ACTIVITIES:

The medical, technical and nursing staffs of the Blood Bank and Transfusion Service lectured at a variety of educational programs at departmental, institutional, regional and national levels. A new Blood Bank orientation course was provided for first-year clinical pathology House Officers. Whereas in the past this was a two-week program given only in July, modification of the Clinical Pathology House Officer schedule required that the program be provided both in July and January. Daily "morning report" rounds were conducted by the medical staff of the Blood Bank, and were attended by House Officers and senior technologists. In addition, medical and senior technological staff of the Blood Bank presented Grand Rounds for the clinical pathology training program and also served as program director of both the Clinical Pathology grand rounds and of Anatomical Pathology conferences. The nursing staff of the Transfusion and Apheresis Service presented educational conferences for the nursing staff of University Hospitals on a variety of transfusion-related topics.

The 21st annual postgraduate course, "Current Topics in Blood Banking", was held on June 1, 2 and 3, 1994. As in the past, physicians and technologists from throughout the United States attended. The course, under the direction of Mr. Judd, attracted over 200 attendees. It not only is one of the largest programs hosted by the Postgraduate Department of the University of Michigan Medical Center in 1993-94, but also is the largest hospital-sponsored postgraduate program in the country devoted to blood bank topics.

Members of the Blood Bank and Transfusion Service faculty and staff participated in the Annual Meeting of the American Association of Blood Banks and in the annual programs of the Michigan Association of Blood Banks. In addition, members of the laboratory, including Mr. Judd, Ms. Butch, and Ms. Steiner, as well as the medical directors, presented invited lectures to a variety of regional and national blood banking organizations and state societies.

PROFESSIONAL ACTIVITIES:

As in the past, the Blood Bank and Transfusion Service staff was active at the regional and national levels. Dr. Oberman served as Associate Editor of TRANSFUSION, the major journal in the field. Mr. Judd served on the Editorial Board of TRANSFUSION, was the Associate Editor of the American Association of Blood Banks (AABB) Technical Manual and was a member of the Board of Directors of the AABB. In addition, he received the Founders' Award of the Michigan Association of Blood Banks. Ms. Butch served on the Standards Committee of the AABB and also on the Information Systems Committee and the Administrative Section Coordinating Committee of the AABB. She continued to chair the PathNet Users Group related to the Blood Bank donor module for Cerner, an activity that was beneficial to University Hospital's Laboratory Information Service. She also co-chaired the Department of Pathology's Quality Assurance Program.

Ms. Steiner chaired the Committee on Reference Laboratories and Rare Donor File of the AABB. This Committee coordinated reference laboratory activities throughout the country. She also served as a member of the Executive Board of the Michigan Association of Blood Banks and coordinated the activity of the University Hospital Blood Bank with that of the Department of Obstetrics and Gynecology in management of patients susceptible to hemolytic disease of the newborn. Ms. Stoe

chaired the Department of Pathology's Safety Committee. Ms. Butch, Ms. Steiner and Ms. Stoe served as inspectors for the AABB Inspection and Accreditation program. Ms. Hoffman coordinated the Blood Bank component of the Bone Marrow Transplantation Program, and in this regard presented a new workshop at the annual course, "Current Topics in Blood Banking."

RESEARCH ACTIVITIES:

The individual reports of Drs. Oberman and Davenport, and of Mr. Judd, record their publications and investigative efforts related to Blood Banking and Transfusion Medicine. Ms. Butch presented the experience of the laboratory in managing adult patients undergoing ECMO at the annual meeting of the American Association of Blood Banks. In cooperation with medical staff of the Blood Bank, she will publish this information in the coming year.

Harold A. Oberman, M.D.
Director, Blood Bank and Transfusion Service

CHEMICAL PATHOLOGY LABORATORY**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

The Chemical Pathology Laboratory has had an incredibly hectic and challenging, but overall very successful year. After countless hours of planning meetings with architects and lab staff, the consolidation of the Chemistry, Ligand Assay, and Immunology Labs into one large operational unit finally occurred. The lab maintained full service functions through a three month long renovation project to prepare for the physical move of the Ligand Assay Laboratory into the joint chemistry and Immunology lab space. In February of 1994, the anxiously awaited consolidation took place. After a rocky period of adjustment, all three labs have settled back into smooth running order. Cross training of technologists from Chemistry and Immunology has begun. This will ultimately allow the labs to function more efficiently.

CLINICAL ACTIVITIES

The laboratory experienced a slight drop in overall workload for the fiscal year. The lab performed slightly over three million tests this past year, down 1-2% from 1992-93. This decrease resulted from a slow first quarter of 1994.

The laboratory has made a major commitment to expand its role in point of care testing. In collaboration with PDS, we are evaluating and modifying 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. In addition, a small portable blood gas analyzer and a meter to measure prothrombin time (PT) have been placed at the Briarwood Medical Group lab. The Chemistry lab has instituted a program to review quality control and certify the training of the operators of these instruments. Plans to expand PT testing to other health care centers and to the operating rooms are now being finalized. Finally, two U of M health care clinics labs supervised by Chemistry personnel have been inspected and accredited by COLA.

The lab now maintains quality control and proficiency testing records on 75 whole blood glucose meters stationed throughout the institution. In conjunction with nursing and PDS, we are actively pursuing options for the computerized collection and analysis of quality control data from these meters.

The laboratory evaluated and implemented testing for myoglobin this past year. This test, which was set up to support the activity of the Chest Pain Evaluation Unit in the Emergency Department, is now available STAT 24 hours a day. In additional moves to provide better service to the Emergency Department, pregnancy tests are performed in the ER lab and quantitative beta-HCG is now available STAT 24 hours a day. Chemistry personnel also provide on-call coverage for the ER blood gas/electrolyte analyzer during those hours that the ER lab is not staffed.

In a move designed to provide better service to Ob-Gyn physicians attempting to assess fetal lung maturity, the lab now offers the Foam Stability Index (FSI) or "shake test." This rapid turnaround time procedure is available 24 hours a day, and eliminates the need for off-hours L/S ratio testing.

RESEARCH AND DEVELOPMENT

The laboratory has participated in a pre-market release evaluation of an assay for troponin T on the BMD ES-300 analyzer. Troponin T is a sensitive marker for myocardial injury, and may be useful in stratifying angina patients as to risk for myocardial infarction. The laboratory continues its active role in evaluating new markers for predicting risk of coronary disease. We are involved in a project with Roche Diagnostics to develop a turbidimetric immunoassay for lipoprotein (a). The lab is collaborating with both the pediatric and adult nephrology divisions to develop an HPLC assay for iohexol, a contrast agent which can be administered in low doses and used to assess glomerular filtration rate in patients with compromised renal function. A faster, more automated assay for angiotensin converting enzyme (ACE) activity was developed on the Cobas FARA analyzer and introduced this year. Immunology lab personnel were trained on the analyzer as part of the efforts to cross-train technologists through the consolidated labs. Finally, the laboratory has agreed to be a beta site evaluator for a new Kodak Ektachem 950 analyzer which will have both routine chemistries and therapeutic drug assays on its test menu.

TEACHING/PROFESSIONAL

The lab director, chief technologist, supervisors, and medical technologists all participated in the instruction of Pathology residents as they rotated through the lab. The new block scheduling of residents enhanced opportunities for interaction and was perceived as an improvement by all involved. Medical technology students from Eastern Michigan University completed their training by doing one month rotations through the laboratory. Two clinical pathology grand rounds lectures on Point of Care testing were presented by Dr. Giacherio. Dr. Giacherio completed his term as the Chair of the Michigan section of the American Association for Clinical Chemistry, and also received a Clinical Chemist Recognition Award from the AACC.

CLINICAL FLOW CYTOMETRY LABORATORY**DEPARTMENT OF PATHOLOGY
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1 JULY 1993-30 JUNE 1994**

Over the past year, the Clinical Flow Cytometry Laboratory processed approximately 2700 immunophenotyping specimens. This included approximately 600 specimens submitted for leukemia/lymphoma immunophenotyping, nearly 900 specimens for monitoring of acquired and inherited immunodeficiencies, and over 500 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 2700 specimens of peripheral blood for flow cytometric reticulocyte analysis.

The laboratory has continued to increase its volume of work through the MLabs Program. The comprehensive hematopathology consultation service provided by the laboratory has helped to attract this enlarging referral base. For the past year, MLabs referrals comprised 38% of all acute leukemia immunophenotyping panels, 44% of all chronic leukemia/lymphoma profiles, and 21% of all non-transplant immunodeficiency monitoring.

The implementation of three-color phenotypic analysis for leukemia and lymphoma has been completed, as has a three-color approach for monitoring acquired immunodeficiencies. The cell antigen profile for acquired immunodeficiency monitoring has also been simplified; in conjunction with three-color analysis, this has afforded a significant reduction in the cost of this high-volume test. Other tests implemented in the past year include a two-color assay for nuclear TdT and an immunocytochemical staining procedure that may be used as a supplement to flow analysis for selected markers. Institution of direct transfer of patient report data from the cytometry computers to Pathnet has dramatically reduced manual data entry and enhanced report accuracy.

Projects under development include a method for assessing cellular viability by flow, and improved means of enumerating stem cells in bone marrow/peripheral stem cell harvest specimens. The laboratory has also provided collaborative support to several investigators in other departments; ongoing projects include phenotyping of lymphocytes in lymphoma patients receiving experimental anti-CD20 therapy (Division of Hematology/Oncology) and immunophenotyping studies in patients with cutaneous lymphoma (Department of Dermatology).

The laboratory staff continued efforts to improve our quality assurance program. The hematopathologists staffing the laboratory must triage all requests for leukemia/lymphoma phenotyping; inappropriate requests (approximately 230 specimens last year) are cancelled. 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, Clinical Flow Cytometry Laboratory

Lloyd M. Stoolman, M.D.
Co-director

CLINICAL CYTOGENETICS LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1993 - 30 JUNE 1994

The Clinical Cytogenetics Laboratory has reached a plateau in volume in some areas, while others have continued to expand. In the area of prenatal diagnosis, 930 amniotic fluid specimens, 50 tissues and 84 chorionic villus biopsy specimens were analyzed: this is a slight increase from last year. Chorionic villus sampling as a means of prenatal diagnosis decreased both locally and nationally following negative publicity in the popular press; at this point, despite a negative report from the CDC in the popular press, the volume is again increasing. The number of bone marrow specimens increased again by 20% to 480; 352 routine blood specimens, 37 high resolution studies and 58 fragile X analyses were done as well. The laboratory had decreased the number of neonatal emergent marrows for diagnosis of genetic disease by instituting new culture procedures which reliably decreased the turnaround time for blood specimens in newborns to 50-55 hours (from 4-5 days) in the last year; we are now instituting procedures to obtain results in less than 36 hours.

After almost four years with the laboratory in two locations (Med Sci I and Med Sci II), Clinical Cytogenetics was consolidated on a temporary basis into Med Sci I in April, 1993. The hope was to increase efficiency and to provide supervision for the Prenatal Cytogenetics area. The Photography Laboratory and Clinical Flow Cytometry have been very generous in sharing their space. It has been very disappointing to learn that this space may be more permanent than anticipated, particularly after spending substantial amounts of time planning for two separate moves, to two separate locations, both of which have been canceled.

Cytogenetic analysis of solid tumors continues to expand; this is in routine use by the Pediatric Services primarily for sarcomas but also as a back-up in cases which may present diagnostic difficulties.

Molecular cytogenetic analysis is being offered by the clinical laboratory. Fluorescent probes specific for the centromeres of all chromosomes as well as the so-called "painting probes" for many chromosomes are available. These are being used for identification of marker chromosomes in both amniotic fluid specimens as well as in peripheral blood samples. Studies are underway to assess the utility of these probes in evaluation of bone marrow specimens for minimal residual disease once an abnormal karyotype has been ascertained. This is becoming a necessity as our volume continues to grow with the expansion of the bone marrow transplant program. In addition, these probes may be useful in diagnostic surgical pathology for confirmation of whether a lesion represents a new primary or metastatic disease following cytogenetic analysis of the lesion and in situ hybridization of the original tumor with an appropriate probe. We have also begun using probes that are closely linked to loci associated with Prader Willi and Angelmans syndrome on chromosome 15 and with DiGeorge syndrome on chromosome 22.

Susan Sheldon, Ph.D.
Co-Director, Clinical Cytogenetics

CLINICAL HEMATOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1993 - 30 JUNE 1994

LABORATORY ACTIVITIES:

- A. Implemented autoverification for 1) partial results of CBC's; 2) initial results from specimens of patients not previously tested; and 3) normal differential counts, thus decreasing turn-around time and decreasing number of incoming telephone queries.
- B. As a result of comparison studies between "flagged" automated WBC, platelet counts and normal values, we have discontinued the majority of manual WBC's and platelet counts. These studies resulted in a decrease in TAT and in savings of \$25,000 per year for commodities.
- C. Minor alteration and construction in the automated instrument area of the Main Hematology Laboratory resulted in better work flow and increased efficiency.
- D. The Rapimat urine analyzer was upgraded to a new automated CUA instrument.
- E. A Coulter MAX M was placed into service in the Taubman Hematology Laboratory.
- 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.
- I. A quality assurance program has continued in the area of bone marrow cytochemical stains for leukemia and other labor intensive "specialty" tests within the laboratory, leading to a substantial decrease in the number of special tests and cytochemical stains performed, and resulting in improved utilization of resources.
- J. Quality assurance indicators comparing positive fluids in Hematology with Cytology results and monitoring turn-around times for PHO patient results in the Taubman Hematology Laboratory.

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) 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. Review of SWOG cases.
 - 8. Weekly Interdepartmental Lymphoma Conference.

- 9. Biweekly Interdepartmental Leukemia Conference.
- 10. 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 1994/1995 GOALS:

- A. Continuation of cost-containment programs.
- B. Continued review and development of laboratory utilization.
- C. Implement limits on repetitive differential requests.
- D. Continue to liberalize automated differential criteria.
- E. Continue studies of limiting WBC requests from intensive care units.
- F. Continue to enhance the overall efficiency of the laboratory operation.
- G. Continue to monitor utilization of special tests (osmotic fragility, Inulin, etc.) and cytochemistries for acute leukemias.
- H. Transfer of hemoglobin electrophoresis from the Chemistry Laboratory to the Hematology Laboratory.

Bertram Schnitzer, M.D.
Director, Clinical Hematology Laboratory

CLINICAL IMMUNOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1993 - 30 JUNE 1994

OVERVIEW

The Immunopathology Laboratory experienced a modest increase in test volume and several new assays/programs were instituted. Anthony A. Killeen, M.D., Ph.D. provided an invaluable service commitment to the laboratory. Kent Johnson, M.D., and Kevin Cooper, M.D. (Dermatology) continued to signout tissue immunofluorescence studies under the auspices of the Anatomical Pathology Division. Paul Killen, M.D., Ph.D. and Dr. Johnson, also under the auspices of Anatomical Pathology, markedly enhanced the renal biopsy service. Dr. Killen provided invaluable technical oversight of tissue immunofluorescence studies and leadership in the area of case-handling and tracking.

CLINICAL SERVICES

As the fiscal year approached its conclusion, the laboratory had experienced a modest increase in total volume (approximately 5%). Particularly gratifying was the continued growth in several relatively new assays; most notably the neutrophil cytoplasmic antibody (ANCA) test. Neutrophil cytoplasmic antibody determinations increased from approximately 70/month. An indirect immunofluorescence assay for anti-glomerular basement membrane antibodies was added. New procedures were also implemented in protein electrophoresis 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 \$10,000 savings. Finally, laboratory personnel began crosstraining 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 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 (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 completed two QA projects. These related to proper specimen procurement for CSF oligoclonal bands and proper screening requests for Bence Jones proteins. Ongoing efforts have also been directed towards controlling the utilization of circulating immune complex assays, utilization of serum protein electrophoresis, assessment of inadvertent IgM/IgG quantitations (instead of acute and convalescent viral titers) and a clinical correlation study of TdT results.

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. Clinical Pathology Grand Rounds included "Monoclonal Gammopathy" by Dr. John Carey (Henry Ford Hospital, Detroit), "Bence Jones Proteinuria" and "Running a Reference Laboratory" by Dr. David Keren (Warde Medical Laboratory, Ann Arbor) and Dr. Warren (see individual faculty report). Dr. Keren was appointed as a Clinical Professor of Pathology and Dr. Warren initiated a new 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**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT****1 JULY 1993 - 30 JUNE 1994****CLINICAL ACTIVITIES**

The Clinical Microbiology section of the Microbiology/Virology laboratory has demonstrated a 3.2% increase in volume in the past year. The virology section has demonstrated a 23.5% increase in overall volume. M-Labs represents 5% of the total laboratory volume. Laboratory testing demonstrating an increase in volume included gram stains, Neisseria testing, chlamydia testing, antimicrobial sensitivity testing, and non-sterile cultures. Significant increases in virology lab testing included: viral antigen testing, Ig and IgG antibody testing, rubella IgG antibody testing, and viral culture. Significant new tests implemented in the Microbiology/Virology laboratory include rubella and rubeolla IGG antibody testing for Employee Health Services, Mycoplasma pneumoniae antibody screening tests, and PCR testing for Mycobacterium tuberculosis.

The laboratory also demonstrated leadership in intralaboratory cost efficiency by establishing transport usage forms for development of monthly statistics on media usage, as well as non-media tracking forms to better track inventory in the laboratory. In addition, the laboratory established cost savings in specific laboratory testing such as mycoplasma antibody screening, anaerobic culture procedures and Herpes simplex antibody testing

The laboratory has continued to be active in the Hospital's Total Quality program. The laboratory quality improvement team, focusing on reduction of unacceptable sputum specimens, has been extremely successful.

Finally, the Microbiology/Virology laboratory has continued to be active in developing laboratory-based information services to improve the quality of laboratory data, especially to our clinical colleagues in Infectious Disease and Infection Control. The data is used, for example, to augment the clinical-pathologic correlates that are used in clinical/laboratory rounds daily in the laboratory.

RESEARCH ACTIVITIES

The laboratory completed a 2-center comparative evaluation of automated blood culture systems that required the cooperation and participation of numerous laboratory, nursing and phlebotomy service personnel. We are currently involved in other studies to determine the effects of delayed bottle entry, new media formulations, anaerobic atmosphere and residual antimicrobics on the recovery of bacteria and yeasts from one of these automated systems. Several investigations involving antimicrobial resistance were conducted. Thorough screening of isolates of Streptococcus pneumoniae revealed that our local incidence of penicillin-resistance is about 35%, a much higher rate than anticipated. We are currently conducting a similar survey to determine the rate of vanomycin resistance in the enterococci. We continue to participate in the multicenter study monitoring antimicrobial resistance in the *Bacteroides fragilis* group.

The laboratory was awarded two grants form the Hospital Small Grants Program to investigate 1) the possible overutilization of blood cultures on a clinical service and 2) to monitor antimicrobial usage in intensive care unit settings with intervention where appropriate in an attempt to affect change in ordering patterns. These investigations are in progress and will be reported to the hospital shortly.

The laboratory also assisted in the planning and execution of several interdepartmental investigations. The NIH-funded Candida Vaginosis Study (Family Practice) and two studies involving the control of eye infections (Ophthalmology) were completed. Two clinical investigations are underway in the Department of Pediatrics: the effects of the colonization of cystic fibrosis patients with non-tubercular mycobacteria, and the effect administration of anti-RSV immunoglobulin to children at risk. Both require significant participation by the Microbiology and Virology Labs. We also provided laboratory support for two other clinical departments, Obstetrics and Gynecology and Internal Medicine, during their investigations to study the clinical efficacy of a new quinolone antimicrobial, levofloxacin, to control infections.

These studies and the other activities in the laboratory resulted in the publication of four papers and four abstracts that were presented at local, regional, and national scientific meetings.

Kenneth D. McClatchey, MD, DDS
Director, Microbiology/Virology Laboratory

Carl L. Pierson, PhD
Associate Director

CLINICAL MOLECULAR DIAGNOSTICS LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1993 - 30 JUNE 1994

PATIENT CARE

The Molecular Diagnostics Laboratory has undergone considerable expansion in the past year consistent with the Department's view of the increasing importance of nucleic acid analysis for diagnostic work in Pathology. The laboratory has four full time technology staff, including a senior clinical technologist. We anticipate that during the 1994 calendar year, we will perform 3,000 nucleic acid analyses for a variety of disorders including TB, Hepatitis C, and Fragile-X Syndrome. We are also performing gene rearrangement studies for genotyping certain leukemias and lymphomas, and detection of the bcr-abl translocation. Tests for certain lipoproteins and other cardiovascular risk factors are about to be introduced. This level of activity represents a 10-fold increase in test volume in the past year. This dramatic expansion was achieved by directing new test implementation into areas of high volume, particularly TB and Hepatitis C. While it is unlikely that such an expansion will be repeated in the next few years, it is difficult to make predictions in this field. The global efforts to clone disease-causing genes may well result in a demand for new services which the laboratory will attempt to meet. The availability of automated DNA analyzers will greatly facilitate the introduction of tests in the future and help us to meet these demands.

Of necessity, the laboratory has developed a range of tests for cancer markers, infectious agents, and genetic disorders. A goal of the laboratory in the next few years is to focus its expertise in a defined range of tests, such as cardiovascular risk markers.

EDUCATION AND TRAINING

The laboratory is at the frontier between developments in the basic sciences such as biochemistry and molecular biology and the implementation of these discoveries to patient care. There are, therefore, educational and research opportunities available to residents and fellows in this laboratory in both basic and applied research. I personally strongly encourage residents to spend time here and avail themselves of these opportunities. During the 1993-94 academic year, residents from pathology and from genetics spent time in the laboratory. We are establishing growing ties with the clinical programs which use our services to foster collaboration and collegiality.

RESEARCH

The laboratory has been involved in several research projects during the year. In conjunction with members of the Department of Internal Medicine we are looking at strain variants in the HCV genome among our patient population to aid in epidemiologic study of this organism. We are also

beginning to measure transcription of specific mRNAs in human leukocytes which may have diagnostic utility in cardiovascular disorders.

Anthony A. Killeen
Director, Clinical Molecular Biology Laboratory

DRUG ANALYSIS AND TOXICOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1993 - 30 JUNE 1994

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.

Several new procedures were implemented during the last year. An assay for the new anticonvulsant Felbamate was introduced and is being used by medical center physicians as well as by M-Labs clients. Several quantitative assays for drugs of abuse in urine were developed. These include selected benzodiazepines and barbiturates. At the present time, the laboratory is working with the Transplant Program and the Chemical Pathology laboratory to initiate testing for the new immunosuppressant Tacrolimus.

The laboratory finished its first year of expanded 24-hour service. The expansion of hours necessitated adjustments in scheduling for a majority of the staff, many of whom have contributed to the success of this change.

The laboratory continues to be certified by the College of American Pathologists for the forensic drug testing program. The laboratory successfully passed the 1994 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 also underwent the regularly scheduled interim 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.

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 of the NCAA and IOC, having participated in the Olympic Festival held in San Antonio. Dr. Annesley is 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. The laboratory has also been involved as a reference facility for several external commercial research projects.

Thomas Annesley, Ph.D.
Director, Drug Analysis and Toxicology Laboratory

HISTOCOMPATIBILITY & IMMUNOGENETICS LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JUNE 1993 - 30 JUNE 1994

The HLA laboratory has had a very successful year. The laboratory has made a number of changes that have increased both the efficiency and the function of the facility. It has also moved into larger space to better accommodate the increased activity. This resulted in increased revenues for the Department.

CLINICAL ACTIVITIES

Clinical activities in the Histocompatibility Laboratory showed a consistent increase from last year with an increase in the number of tests performed. A new laboratory test, the lymphocyte proliferation assay, has progressively increased its activity to approximately 3 to 4 per week.

Technical improvement in the laboratory included the full implementation of Class II HLA typing by magnetic beads, which has resulted in a tremendous improvement in the ability to identify Class II antigens on samples. In addition, DNA analysis of Class II antigens was also initiated and is currently being quality controlled before its introduction into clinical use.

The automation of the laboratory was finished and this also increased efficiency. Jeff Hayward, the former Data Supervisor of the Laboratory, in conjunction with Thomas Peterson and James Dignan of Pathology data services were key in achieving these gains.

TEACHING ACTIVITIES

Every member of the laboratory was involved in the teaching activities of the laboratory and they were effective in their work. The laboratory was involved in the instruction of Pathology Residents, Allergy Fellows, Renal Fellows and Postdoctoral Candidates from the Department of Hematology. Dr. Baker, the Laboratory Director, took an active role and also served as the Regional Councilor for ASHL. Ms. Cynthia Schall, the Laboratory Supervisor, was involved in teaching review courses at Henry Ford Hospital and the University of Michigan. She also oversaw the activities for Residents in the Laboratory and several "Woman in Science" Interns.

NEW GOALS

The goals of the laboratory in the coming year include implementing HLA Class II typing by DNA analysis as a standardized test and attempting to increase the overall efficiency of the laboratory to better meet the needs of both the solid organ and bone marrow transplant programs. In addition, the laboratory is a key to the development of a basic-science research program in Transplantation

Immunology. This program will center its investigations on clarifying the role of cell surface antigen recognition in allograft transplantation and the immune response to allografts.

James R. Baker, Jr., M.D.
Director, Histocompatibility & Immunogenetics Laboratory

LIGAND ASSAY LABORATORY
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

CLINICAL ACTIVITIES

The long anticipated move of the Ligand Assay Laboratory into the main hospital was completed this year. The Chemistry, Immunology and Ligand laboratories occupy common space in the space formerly occupied by Chemistry and Immunology with some operational changes designed to increase laboratory efficiency. The change has been accepted by all personnel and we are operating smoothly with minimal problems.

Several changes in technology are ongoing with the eventual goal of converting the majority of immunoassays requiring the use of radioisotopes to non-isotopic procedures, including chemiluminescent, fluorescent and colorimetric methods. Part of this change has included the development of a super sensitive assay for thyroid stimulating hormone capable of distinguishing hyperthyroid patients from those who are thyrotoxic. The increased sensitivity of the new procedure (.01 uU/ml) will also provide for increased efficiency in diagnosis of thyroid disease with a minimal number of laboratory analyses. The development of an algorithm for the diagnosis of thyroid disease using free thyroxine and the super sensitive TSH assay is almost complete and shows considerable promise for improving differential diagnostic capability. We have thyroid peroxidase, growth hormone, intact parathormone, and ACTH. Each of these new procedures represents an increase in assay sensitivity and improves diagnostic capabilities of the laboratory.

Volumes of current laboratory analyses continues to increase, as does the number of different analyses. A total of 16,089 specimens was processed during the 93-94 fiscal year.

Barry G. England, Ph.D.
Director, Ligand Assay Laboratory

PATHOLOGY DATA SYSTEMS
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994

A number of major projects were initiated in Pathology Data Systems during the past year, including the following:

- Planning for the installation of two new clustered VAX 6630 CPUs that will enhance PathNet performance
- Serving as the alpha-site for the deployment of version 306 of Cerner PathNet software
- Extension of autoverification from Hematology, where it has been successfully running, to selected Chemistry tests performed on outpatients; this approach now permits total automation of routine testing from the time that a specimen is loaded into an analytical instrument until the test result is reported electronically to the physician
- Pilot program for computerized speech recognition in Central Distribution to allow hands-off test ordering into PathNet of most laboratory tests
- Continuing enhancements of wireless communication between phlebotomists located in patient care units and PathNet, an important first step in large-scale development of point-of-care testing
- Strategic planning for the PC network and network manager including the upgrade of network servers to more powerful PCs with more disk storage
- Development and maintenance of a computerized and prioritized lists of ongoing projects in PDS
- Refinement of help-desk software in PDS to automatically track requests for service coming into the unit
- Sponsorship of the 12th annual LIS symposium in June, 1994, that attracted 32 vendors and 200 registrants from 30 states and Canada
- Installation of an HL-7 interface between PathNet and the hospital's new Apache system for the assessment of severity of illness of ICU patients
- Early planning for the installation of a hub (interface engine) that will accept laboratory information from PathNet via an innovative HL-7 interface to be written by Cerner; the information passing through the hub can be routed to various hosts, including the TDS system, a planned institutional Oracle database server, and MLabs clients running foreign LISs
- Planning for the installation of the TDS order-entry and result-reporting software to be deployed on the hospital mainframe computer
- Development of an enhanced interface between analytic instruments, both in the central laboratories and distributed throughout the hospital, that will allow easy uploading of data to the laboratory database

- Preliminary planning for conversion of PDS-DB (the departmental relational database server) to an enhanced database server running Oracle.

Bruce A. Friedman, M.D.
Director, Pathology Data Systems

PHLEBOTOMY SERVICES AND CENTRAL DISTRIBUTION

DEPARTMENTAL OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1993 - 30 JUNE1994

A number of major projects were initiated in Phlebotomy Services and Central Distribution during the past year, including the following:

- Hospital-wide analysis of blood drawing services from the perspective of physicians, nurses, and units secretaries under the auspices of a Blood Drawing Quality Improvement Team (QIT); this project resulted in a better understanding of physician needs regarding blood drawing services and input into how to handle timed draws and peak-and-trough analyses.
- Planning and implementation of a “unit phlebotomist” program in high-volume patient care units whereby an individual phlebotomist is assigned to a specific unit and handles all blood drawing tasks in that unit, including timed and stat blood draws.
- Hired and trained an additional 19.5 FTEs transferred from the Messenger Service as part of a transfer of responsibility for transportation of laboratory specimens on a 7/24 basis to Phlebotomy Services.
- Cooperation with M-Labs in a project to redesign the workflow of MLabs specimens within the laboratories.
- Planning and running a conference on management of the phlebotomy team on April 22-23, 1994, at the Towsley Center that attracted 125 registrants.

Bruce A. Friedman, M.D.
Director, Phlebotomy Services and Central Distribution

EDUCATIONAL ACTIVITIES

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT

1 July 1993 - 30 June 1994

- I. The Department of Pathology has active educational programs in The University of Michigan Medical and Dental Schools, a Ph.D. program in the Horace H. Rackham Graduate School, and both Post-Doctoral Fellow and Resident Training Programs. The Education Office continues to serve as a centralized resource center for the administration of the Department's educational programs. Services provided include 1) overall coordination of the multiple educational programs of the Department, 2) functioning as a liaison between students, faculty, course directors and outside units, 3) assisting course directors in the development and coordination of individual Pathology courses, 4) developing student and faculty evaluation programs, 5) revising and maintaining all course materials and evaluations, 6) scheduling classroom facilities and preparing course materials, and 7) answering/directing inquiries regarding Departmental programs/courses. In addition, the Education Office prepares annual course summaries on courses/programs and faculty teaching activities, as well as provides data on the Department's educational programs for intra-University/inter-University surveys/reports.

The Educational Office also provides full range secretarial support for Dr. Joseph Fantone, Coordinator of the Department's educational activities and Director of the Residency Training Program, Dr. Daniel Remick, Director of the Autopsy Service and Electron Microscopy Unit, Dr. David Gordon, and Dr. Gabriel Nunez.

II. Administrative Activities Accomplishments During the Past Fiscal Year

- A. Assisted in, or directed, the preparation, coordination and execution of the following Pathology courses/programs: Pathology 630/631/580, Pathology 850, Pathology 581, Pathology 500, Pathology Sequence for the M1 Histology Course, M4 Clerkships, and Pathology Summer Clinical/Research Program for M1 minority Students.
- B. Assisted Sequence Directors with the set-up, integration and preparation of course materials for the Pathology sequences of Component II curriculum, including laboratory examinations, for both Fall and Winter terms.
- C. Responded to requests for information regarding the Pathology Graduate Program, as appropriate, prepared materials for review of applications by the Pathology Graduate Program Committee, arranged and coordinated applicant interviews, initiated correspondence and completed paper work associated with the acceptance/rejection of applicant admission into the Program.

- D. Assisted in the preparation and submission of grades for students currently enrolled in Pathology Medical School, Dental School and Graduate courses.
- E. Assisted in the preparation and submission of Candidacy applications of three Pathology Graduate Program students and provided assistance to all current students with regards to any questions or concerns they had. Maintained academic files on all current students.
- F. Directed the preparation, distribution, collection, and tabulation of student evaluations related to the Pathology 630/631/580 Course, Pathology M2 laboratories, M4 Clerkship Program, and Residency Training Program, as well as student/resident evaluation of individual faculty teaching, as it relates to each of these courses/programs. In addition, prepared course and faculty teaching summary report for the Chairman's Office. Prepared and submitted data for the for Medical School Administration, as well as for other inter- and intra-University surveys. Assisted in the preparation of write-ups Departmental courses/programs for brochures, posters, etc.
- G. Functioned as a resource for Graduate, Medical, Dental and summer students regarding programs and institutional administrative issues.
- H. Assisted in the interview process of candidates for secretarial positions.
- I. Supervised three full-time secretarial staff and one part-time, temporary employee whose role is to provide assistance in the fulfillment of the Education Office's responsibilities.

III. Data Pertinent to the Educational Programs 1993-1994

- A. **Pathology 630/631/580.** Pathology lecture/laboratory course for Sophomore Dental students, as well as graduate students from the various programs within the School of Public Health and Medical Illustration. The lecture component of the course had an enrollment of 122 students (90 Graduate, 87 Dental) and the laboratory component's enrollment was 91 (4 Graduate and 87 Dental). Pathology 630 consisted of 45 hours of lecture/examination time and Pathology 631 was comprised of 240 hours of laboratory/examination time. Teaching Staff: 1 Course Director, 14 Lecturers, 4 Laboratory Instructors, 8 Residents.
- B. **Component II Pathology Sequences.** Due to the revised Medical School curriculum, Pathology for Sophomore medical students has been integrated into 13 organs systems and was taught over Fall and Winter semesters. Current estimates indicate approximately 50 contact hours of Departmental faculty lecture and 68 contact hours of laboratory instruction in six separate laboratories (68 x 6 = 408 total contact hours). Total involvement includes 12 faculty sequence representatives, 13 faculty laboratory instructors, and 13 resident laboratory instructors.
- C. **Pathology Sequence for M1 Histology Course.** As part of the new Medical School curriculum this sequence involved the instruction of general Pathology to approximately 200 first year medical students. The

sequence consisted of 6 hours of lectures and 10-12 hours of laboratory. Teaching staff: 1 Course Director, 1 Lecturers, 6 Laboratory Instructors.

- D. M4 Clerkship Program.** The program was comprised of 7 rotations. Each rotation was one month long with Senior Medical students rotating through Anatomic Pathology and Clinical Pathology. Each rotation was mentored by one Departmental faculty member with 4-5 students per rotation. For FY 1993-1994, 26 students participated in the AP/CP rotation in Pathology and 1 student participated in a 2-month research elective, resulting in a total of 27 students for the Program. Teaching Staff: 1 Program Director, 7 mentors, staff on service. The focus of the clerkship is in reinforcing the basic principles of laboratory medicine, both from a basic science and clinical perspective. Twelve students participated in this rotation which was very well received by the students. Teaching staff: 1 Course Director, 8 lecturers and small group leaders.

- E. Pathology Summer Clinical/Research Program for Minority Students.** The program provides the opportunity for underrepresented first year minority students at The University of Michigan Medical School to increase their interest and knowledge of Pathology. The goal is that this clinically-oriented experience will reinforce and motivate students in their Basic Science studies with, perhaps, a few of the students eventually pursuing careers in Pathology. Thirteen underrepresented minority students attended a Department-sponsored forum entitled "Career Opportunities in Pathology" and 10 responded to the Department's recruitment effort and participated in the program.
- F. Graduate Program in Pathology.** Thirty-one applications were received for the Fall-1994 admission. Seven applicants were invited to the Department to interview. Four offers for full-time positions were extended: two declined, two accepted. Students beginning the Program in Fall/1994: Ms. Amy Bryant Mr. John Osterholzer. The Program currently has nine students enrolled: Mr. Douglas Gibbs (Candidate), Mr. Haining Shao (Candidate), Mr. Robert McCullumSmith (MSTP - Candidate), Mr. Akhilesh Pandey (Candidate), Ms. Jami Foreback (MSTP - Candidate), Mr. Arul Chinnaiyan (MSTP), Ms. Frances Wolber (Candidate), Mr. Hangjun Duan, Mr. Shimin Hu.
- H. Residency Training Program.** Currently, there are 26 residents in the Department, 23 of whom are receiving training in both anatomic and clinical pathology and three receiving training in anatomic pathology alone. Incoming residents are: Carolyn Pearsall, Brian Hunter, Mathew Putzi, Douglas Fullen, James McConnell, Leslie Bruch, Stephen Ramsburgh. Dr. Fantone continues in his role as Director of the Residency Training Program. Primary secretarial support is provided by Ms. Carla Lorenzen with additional support provided by the Education Office.

IV. Training Program Attended

Robyn Lucas - Academic Secretary II - Workshop of the 90's
Kathleen Atkins - Basic Management I: Roles, Functions, and Competencies,
Basic Management II: Rights and Responsibilities, Basic Management III:
Managing Performance Improvement.

V. Goals and Objectives for FY 1994/95

- A.** Maintain high quality administrative support for the Department's teaching programs, Autopsy Service, and Drs. Fantone, Remick, Nunez and Gordon.
- B.** Continue to upgrade student teaching materials and to assist in the development and distribution of teaching materials for the Pathology Sequence of the Histology Course for first year medical students and new Dental sets.

- C.** Continue to work with the faculty and Component I&II Director in coordinating Pathology sequences and development of sequence materials.

Joseph C. Fantone, M.D.
Coordinator, Educational Activities

M-LABS
DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1993 - 30 JUNE 1994

The M-Labs program has suffered the loss of two client hospitals in the last year. In one case the changes followed a complete turnover in the medical staff of a very small hospital. In the other case the client hospital merged with a larger hospital and the directorship of the laboratory as well as the anatomic pathology service were made the responsibility of that larger hospital's pathology department. For the present, we retain the clinical pathology reference work.

In October 1992, M-Labs added two new client hospitals. One, Addison Community Hospital is a small hospital specializing in obesity surgery. We supply them with anatomic pathology and reference clinical pathology services as well as a director of laboratories. The other hospital is Toledo Hospital, a 900 bed institution. We furnish reference clinical pathology services to them and our residents can take elective training rotations there.

Dr. Rodolfo Rasche has joined the M-Labs staff on a full-time basis. Central Michigan Community Hospital in Mt. Pleasant, Michigan, his former place of employment, will begin sending us their clinical pathology reference work beginning July 22, 1993. Within the next three months we expect to become the major reference laboratory for Mt. Clemens General Hospital, a 300 bed hospital with a successful outreach program. We anticipate that revenues from M-Labs activities with this client will approximate \$400,000 per year, the amount being somewhat dependent upon the success of the client's outreach efforts. Our anticipated success (we have been told we can begin our service to them this fall) is the result of a year-long effort on the part of the M-Labs staff to convince this demanding client that we can give them the best service at a competitive price. Susan Sadler made the initial contact with the laboratory supervisor and diligently developed a working relationship with the client so that even without a contract, current billings to the client exceed \$14,000 per month (net >\$4,000 per month). Very early, we took the position that we would supply them with a courier even for a few specimens. We had the expectation that the number of specimens would grow and this expectation was fulfilled. It has been our position that we would meet any service expectations demanded by the client. This has involved consultations with myself and Drs. Rasche with the client's pathologists, use of cabs for stat tests, and asking that occasional tests be done by our laboratories at unaccustomed times. We have been pleased at the staff's willingness to accommodate our efforts. Major factors in our success with the client have been more competitive pricing than we have offered previous potential clients and support from Path Data Systems.

We also expect to become the major reference laboratory for clinical pathology testing for the University of Michigan Health Service. In these competitive times, it has been unthinkable that our own Health Service should be sending their reference work outside the institution. Largely through the efforts of the Pathology Department's administration's creativity in pricing, we have been able to resolve the financial issues with the decision makers in the Health Service and we expect to capture their clinical pathology reference work this fall. This undertaking will involve a major effort on our parts to conform to their ordering and reporting requirements now that financial matters appear to be resolved.

We have addressed several M-Labs operational issues. M-Labs staff now meet on a regular basis with Central Distribution staff to discuss accessioning issues and problems related to delivery of specimens by our contract couriers. We will also meet with the owners of the courier service. I envision that it will be in our long-term interest to have our own courier service before long.

All complaints and untoward incidents that we hear of are now recorded in a log and reviewed by the M-Labs director.

The review of the M-Labs program by Chi Laboratory Systems, a consulting firm, is underway. Some operational and marketing issues have been raised. Development of a strategic plan and a business plan for M-Labs are now underway. I believe that the consultants will agree with our belief that the main focus of our efforts should be directed towards forming networks with hospital and large group practice clients. We expect our efforts will be most successful in the areas of clinical pathology reference and "niche" laboratory testing. We anticipate less success in our full service anatomic pathology services to small hospitals as these hospitals merge with larger institutions or cease operations.

I believe that one factor that has helped us attract Mt. Clemens General Hospital and Central Michigan Community Hospital is our policy of not competing with our hospital clients for the individual doctor's office reference work. All of the large independent laboratories actively market individual physicians' offices and compete with their client hospitals. Our focus will be on helping client hospitals by giving them first rate reference tests along with support for their pathologists and other medical staff in choosing appropriate tests and interpreting the results. We can use our expertise to help them develop cost effective test menus and profiles, in selecting appropriate equipment and information systems, with quality assurance, and with their outreach marketing efforts. "What's good for our clients is good for us" is the philosophy with which Mayo Medical Laboratories has succeeded. I believe that philosophy will also work for M-Labs.

Although several of our small client hospitals are at risk because of potential mergers or other changes, I am optimistic that the next year, as we deal with some operational barriers to growth and increase our marketing efforts, will show increased growth of activity and revenues from M-Labs activity.

E.M. Silverman, M.D.
Director, M-Labs Program

**DEPARTMENT OF VETERANS AFFAIRS MEDICAL CENTER
PATHOLOGY AND LABORATORY MEDICINE SERVICE**

**DEPARTMENT OF PATHOLOGY - UNIVERSITY OF MICHIGAN
ANNUAL DEPARTMENTAL REPORT
1 JULY 1993 - 30 JUNE 1994**

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 have academic appointments and participate in University departmental activities in a manner similar to other sections within the University. 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 there are no vacancies at this time. Three resident training positions have been maintained at the VAMC of 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. Dr. Beals has been appointed National Director of Surgical and Cytopathology within the Department of Veterans Affairs and is responsible for oversight of the scope and quality improvement in these disciplines.

ANATOMIC PATHOLOGY:

- A. **Surgical Pathology:** 4,410 surgical cases have been accessioned and reported during this period of time. 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 thus obtaining a broad educational experience and 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. Occasionally, as an elective, a more experienced resident will read out cases independently with the first year resident and subsequently review each case with the staff pathologist prior to issuing a report.
- B. **Autopsy Pathology:** 58 autopsies were performed during this year. 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 31 cases presented. Several autopsies performed at the VAMC were also presented at the extended Gross Conference at the University. In cases with brain involvement, the resident presents findings at a biweekly neuropathology conference.

- C. Electron Microscopy:** 371 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 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 Hospitals, and to other hospitals by contract.

CLINICAL PATHOLOGY:

During the last fiscal year (Fiscal Year 1993) 1,301,877 clinical pathology procedures were done in the laboratory. These tests covered a broad range of chemistry, microbiology, hematology and blood bank. This medical center is considered a hospital of large size and complexity within the VA System. 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 the 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 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 periodic surgical pathology conference 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 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 which will be renewed for four years as of 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 has submitted a research proposal for VA funding and has been appointed to the VA Research and Development Committee as of 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 VAMC the pathology staff members serve on all major committees involved with institutional policies and procedures. In his role as National Director of Surgical and Cytopathology, Dr. Beals has been instrumental in developing policies and procedures related to anatomic pathology within the Department of Veterans Affairs.

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 extensive quality improvement program that integrates with that of the hospital as a whole. The laboratory 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

