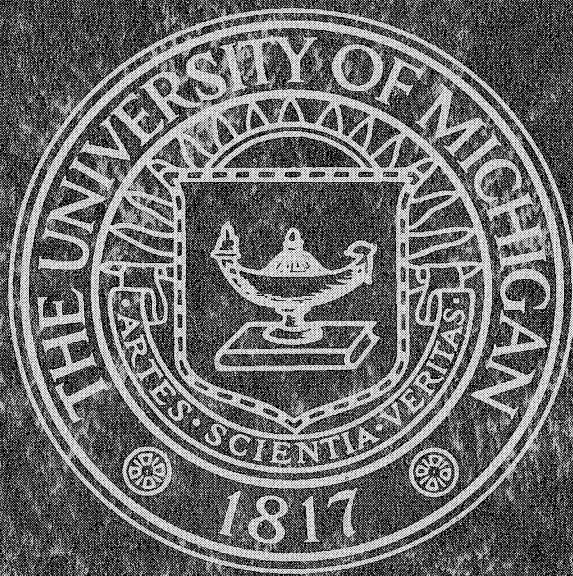


THE UNIVERSITY OF MICHIGAN

Department of Pathology

ANNUAL REPORT



From the library of

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



1 July 1992 - 30 June 1993

THE UNIVERSITY OF MICHIGAN

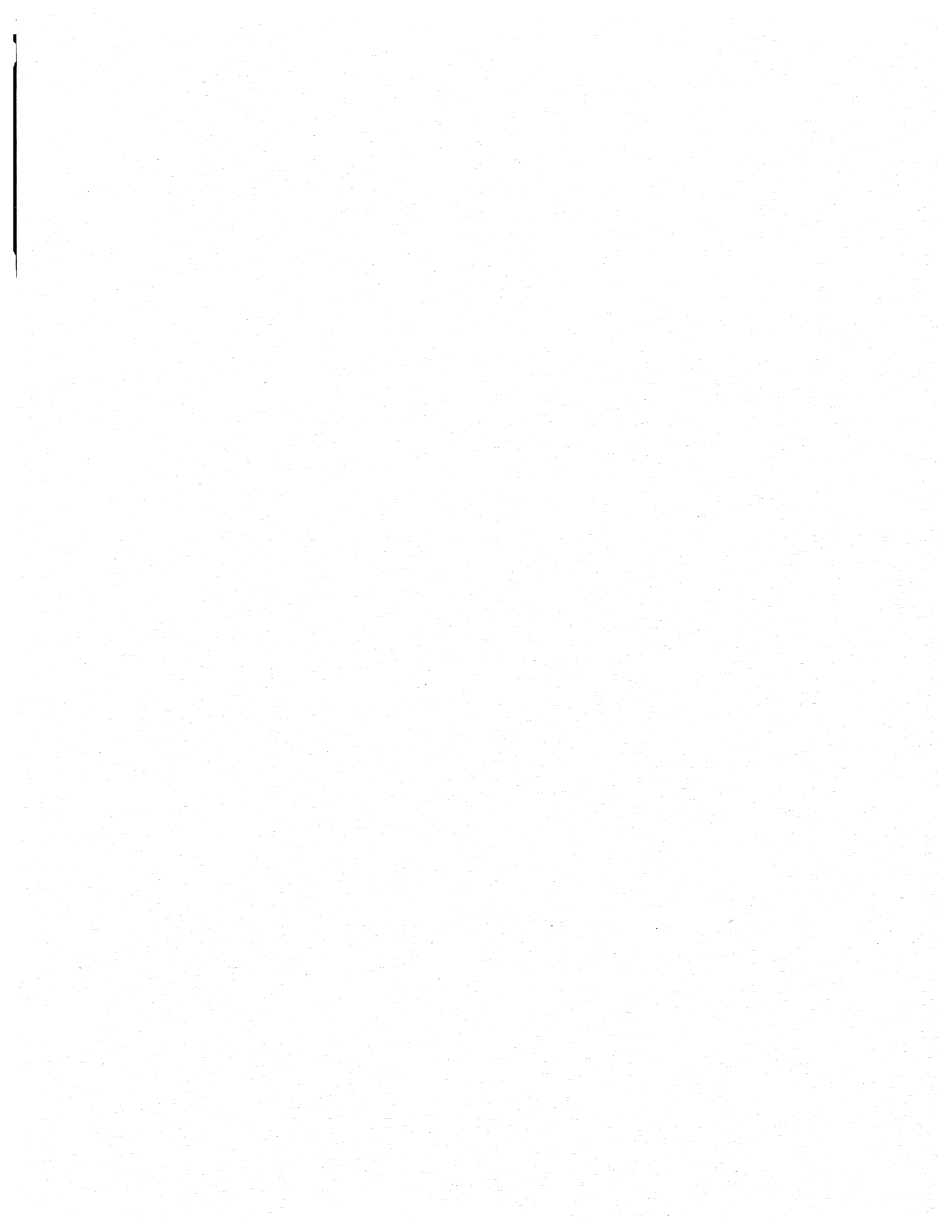
DEPARTMENT OF PATHOLOGY

ANNUAL REPORT



1 JULY 1992 - 30 JUNE 1993

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
Barnes, Barbara A.	Assistant Professor	The University of Michigan
Barr Jr., Mason ⁺	Professor	The University of Michigan
Beals, Theodore F.	Assistant Professor	Veterans Administration Medical Center
Blaivas, Mila I.	Clinical Assistant Professor	The University of Michigan
Bonadio, Jeffrey	Assistant Professor	The University of Michigan
Brawn, Peter	Assistant Professor	Vetrans Administration Medical Center
Capps, Rodney D.	Assistant Professor	The University of Michigan
Chensue, Stephen W.	Assistant Professor	Veterans Administration Medical Center
Crockett-Torabi, Elahe	Assistant Resident Scientist	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
Del Buono, Elizabeth	Assistant Professor	The University of Michigan
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
Hanks, Carl T.*	Associate Professor	The University of Michigan
Hanson, Curtis A.	Assistant Professor	The University of Michigan
Headington, John T.	Professor	The University of Michigan
Heidelberger, Kathleen P.	Professor	The University of Michigan
Hendrix, Robert C.	Professor Emeritus	The University of Michigan
Hicks, Samuel P.	Professor Emeritus	The University of Michigan
Hinerman, Dorin L.	Professor Emeritus	The University of Michigan
Johnson, Kent J.	Professor	The University of Michigan
Judd, W. John	Professor	The University of Michigan
Killen, Paul D.	Assistant Professor	The University of Michigan
Kunkel, Steven L.	Professor	The University of Michigan
Lindsten, Tullia	Assistant Research Scientist	The University of Michigan
Lloyd, Ricardo V.	Professor	The University of Michigan
Lowe, John B.	Associate Professor	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
Miller, Richard A.	Professor	The University of Michigan
Mitra, Raj S.	Assistant Research Scientist	The University of Michigan

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
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.	Associate Professor	The University of Michigan
Pierson, Carl L.	Assistant Professor	The University of Michigan
Rachmaninoff, Nikolai	Lecturer	The University of Michigan
Rasche, Rodolfo	Lecturer	The University of Michigan
Remick, Daniel G.	Assistant Professor	The University of Michigan
Repola, Kenneth L.	Lecturer	The University of Michigan
Ross, Charles W.	Lecturer	The University of Michigan
Rowe, Nathaniel H.*	Professor	The University of Michigan
Schmidt, Robert W.	Professor 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
Smolen, James E. ⁺	Assistant Resident Scientist	The University of Michigan
Stoolman, Lloyd M.	Associate Professor	The University of Michigan
Sulavik, Denise E.	Lecturer	The University of Michigan
Till, Gerd O.	Professor	The University of Michigan
Varani, James	Professor	The University of Michigan

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
Ward, Peter A.	Professor and Chairman	The University of Michigan
Warren, Jeffrey S.	Assistant Professor	The University of Michigan
Weatherbee, Lee	Associate Professor	Veterans Administration Medical Center
Weiss, Bernard	Professor	The University of Michigan
Weiss, Sharon W.	Professor and Director, Anatomic Pathology	The University of Michigan
Wolter, J. Reimer ⁺⁺	Professor Emeritus	The University of Michigan
Yabkowitz, Rachel	Assistant Resident Scientist	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

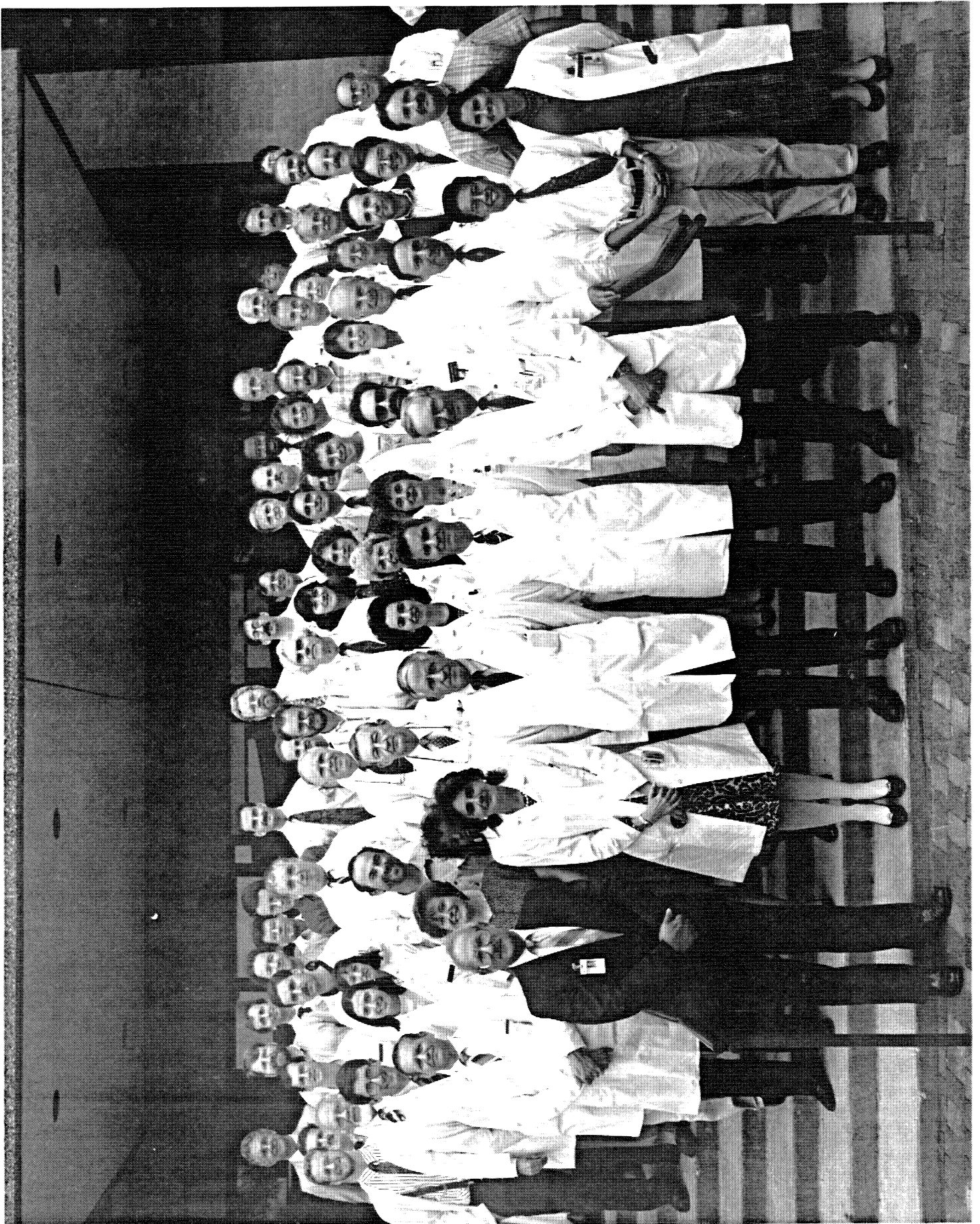


TABLE OF CONTENTS

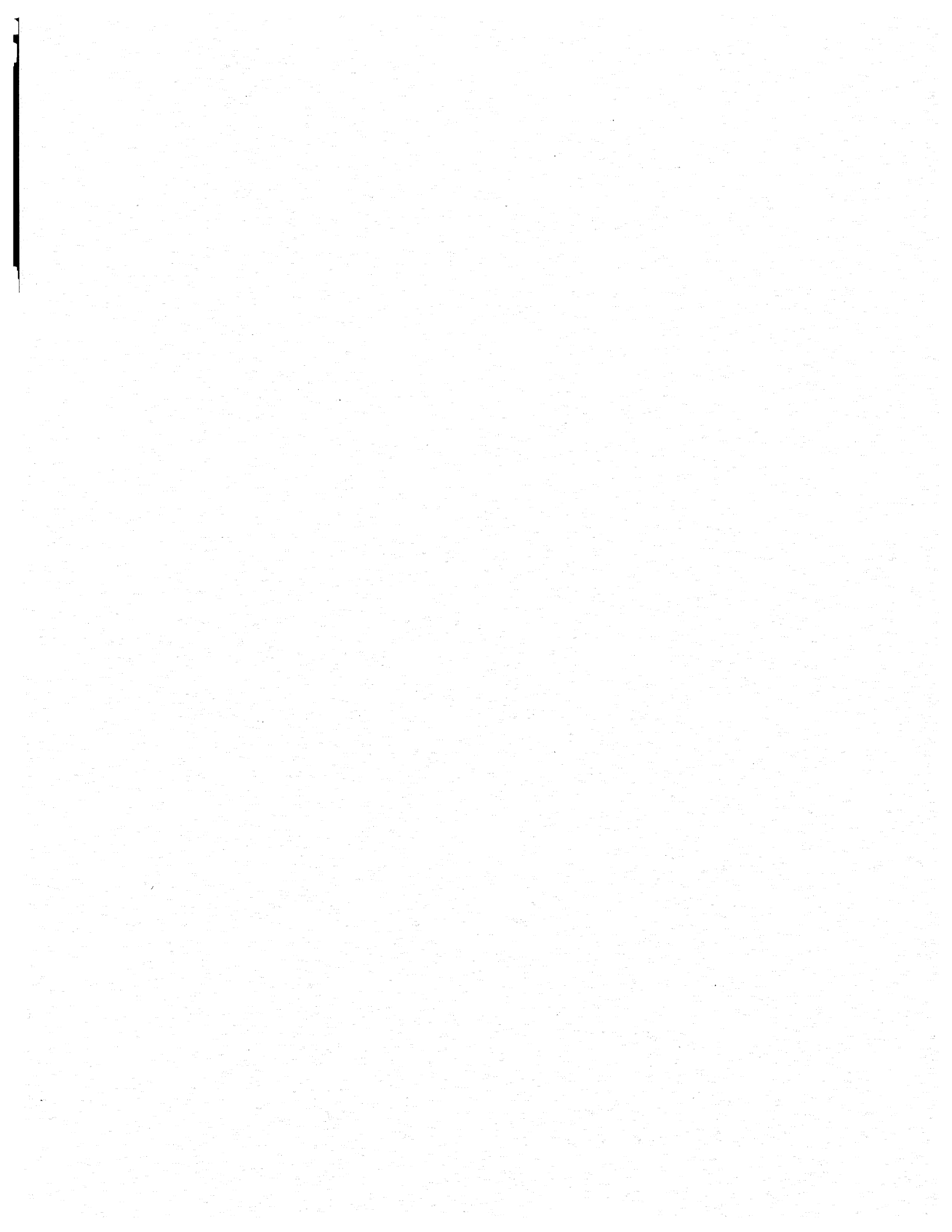
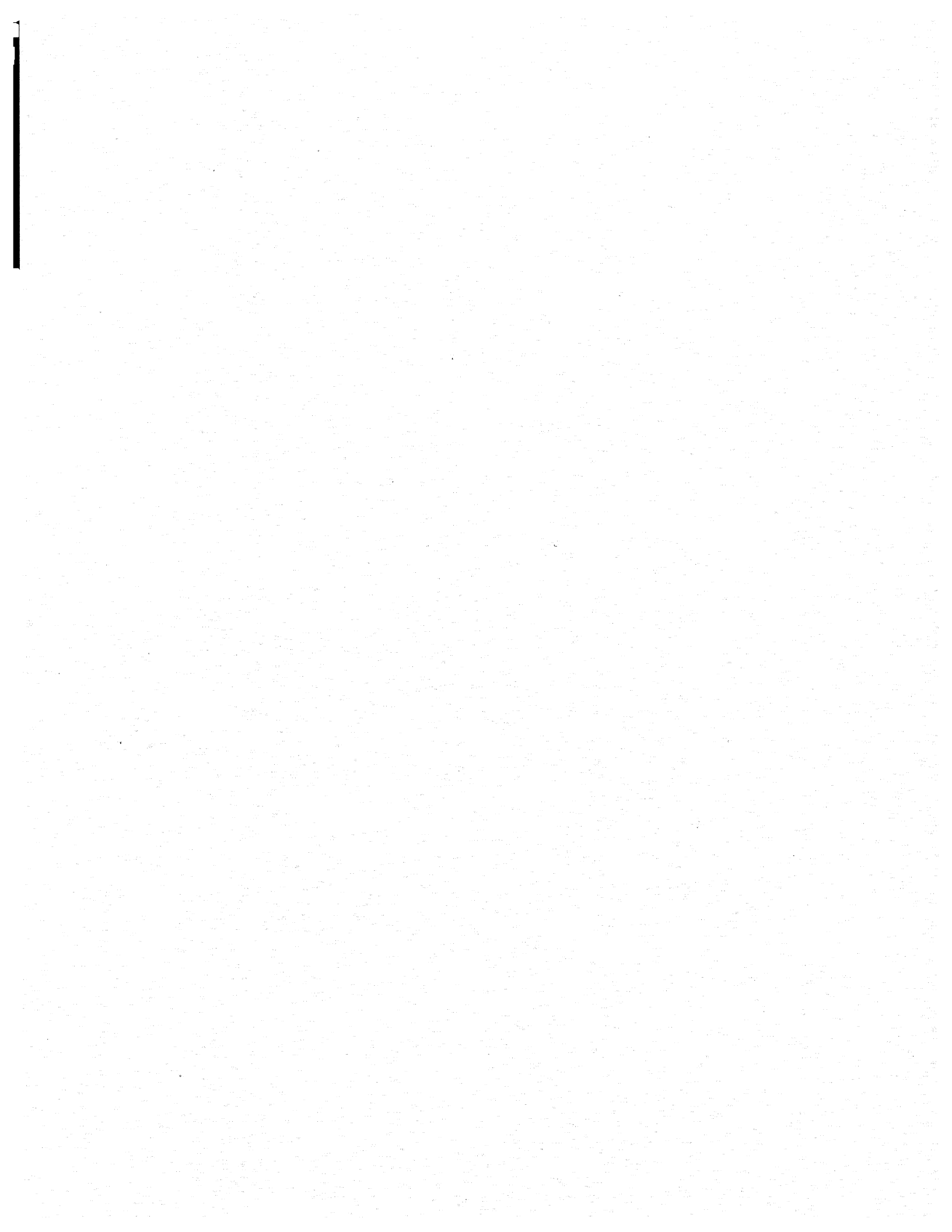


TABLE OF CONTENTS

	<u>Pages</u>
I. <u>OVERVIEW</u>	17- 18
II. <u>INDIVIDUAL FACULTY REPORTS</u>	21-280
III. <u>PROGRAMS AND SECTION REPORTS</u>	281-334
A. <u>Division of Anatomic Pathology</u> (Sharon W. Weiss, M.D.)	281-282
1. Autopsy Service (Daniel G. Remick, M.D.)	283-284
2. Cytopathology Laboratory (Drs. Naylor and Selvaggi)	285-286
3. Dermatopathology Service (Drs. Headington and Nickoloff)	287-288
4. Electron Microscopy Service (Kent J. Johnson, M.D.)	289-290
5. Molecular Diagnostics Service (Tom S. Frank, M.D.)	291-292
6. Neuropathology Service (Paul E. McKeever, M.D., Ph.D.)	293-294
7. Pediatric Pathology Service (Kathleen P. Heidelberger, M.D.)	295-296
B. <u>Surgical Pathology Service</u> (Sharon W. Weiss, M.D.)	297-298
C. <u>Clinical Pathology Laboratories</u> (Jeffrey S. Warren, M.D.)	299-300
1. University Hospitals Blood Bank (Harold A. Oberman, M.D.)	301-304
2. Clinical Cytogenetics Laboratory (Drs. Glover and Sheldon)	305-306
3. Clinical Flow Cytometry Laboratory (Drs. Ross and Stoolman)	307-308
4. Clinical Molecular Diagnostics (Gabriel Nunez, M.D.)	309-310

5.	Clinical Hematology Laboratory (Drs. Schnitzer and Hanson)	311-312
6.	Clinical Immunopathology Laboratory (Jeffrey S. Warren, M.D.)	313-314
7.	Drug Analysis and Toxicology Laboratory (Thomas Annesley, Ph.D.)	315-316
8.	Histocompatibility and Immunogenetics Laboratory (James R. Baker, Jr., M.D.)	317-318
9.	Pathology Data Systems (Bruce A. Friedman, M.D.)	319-320
10.	Phlebotomy Services and Central Distribution (Bruce A. Friedman, M.D.)	321-322
D.	<u>Educational Activities</u> (Joseph C. Fantone, M.D.)	323-328
E.	M-Labs (Eugene M. Silverman, M.D)	329-330
F.	<u>Veterans Administration Medical Center</u> (Lee Weatherbee, M.D.)	331-334

DEPARTMENTAL OVERVIEW



DEPARTMENTAL OVERVIEW 1992/93

The Department of Pathology maintains a steady course in spite of seas of change. With the institution moving toward a "point of service" type of integrated managed care system, there will be profound changes affecting teaching and service activities of all clinical departments. The challenge will be to respond to the needs for change while maintaining integrity of the academic enterprise. The extent to which this institution will adapt to pressures for change in our service activities and the time-frame in which this will occur are current unknowns. There is a degree of urgency for these responses to be accomplished. It is clear that commercial and industrial pressures for change will force adaptations long before the imposition of federal mandates. These events will likely cause clinical departments, as well as the Medical School and Hospital administrations, to forge a new type of relationship in which clinical revenues will not be so directly linked to hospital occupancy and Medical Service Plan activities. This era of change will also cause shifting alliances between Medical Schools and affiliated teaching institutions. In fact, it seems likely that UMMC will develop new associations with professional groups that in the past would not have seemed logical candidates for such associations. There will also be strong pressures for the development of ties with "out-state" groups. These changes will have enormous impacts on the educational missions of UMMC, affecting medical students and house officers. The precise impacts on the Department of Pathology are difficult to predict at present.

The programs in Anatomic and Clinical Pathology seem strong and stable. There is a current focus on further development of molecular diagnostics in both the Anatomic Pathology and Clinical Pathology Divisions. It is also likely that an initiative in the broad area of "gene typing" will be developed, in order to respond to pressing institutional needs. In August of 1993, the Department created a new faculty position in the clinical track in order to respond to the needs of forensic pathology for both service and teaching purposes. This addresses a gap in our coverage of autopsy pathology and should materially enhance the general quality of the Autopsy Service. We are giving careful consideration to the M-Labs program which now has two full-time pathologists associated with it. Important decisions will have to be made regarding the direction and scope of the M-Labs program and the extent to which the M-Labs Program may expand in the future. One likely outcome is that expansion of M-Labs will be largely related to Clinical Pathology linked diagnostic activities.

Educational programs in the Department of Pathology continue to be an important aspect of our academic mission. With the advent of the new curriculum in the Medical School, our Department is playing a key role in providing two faculty who serve as Component Directors for the new first and second year curricula. The new curriculum will feature a basic pathology course in the first year, while the second year will have pathology integrated into the organ system approach. The latter will require careful orchestration in order to maintain the integrity of the pathology component in the face of strong pressures for more clinically relevant material. With respect to graduate teaching, the Department of Pathology currently has six Ph.D. students, two MSTP students and one M.D., Ph.D. student in training. This is in striking contrast to several years ago in which only a handful of graduate students found their way to our laboratories. One area of teaching effort that tends to have little visibility is that involving postdoctoral fellows. At present, there are approximately 40 postdoctoral fellows (M.D., Ph.D., D.V.M) involved in pathology laboratories, positioning the Department second within the Medical School with respect to the size of the postdoctoral training program.

In the broad research area, there continues to be slow, steady growth in the Department's research activities, the overall annual support budget from extramural sources being

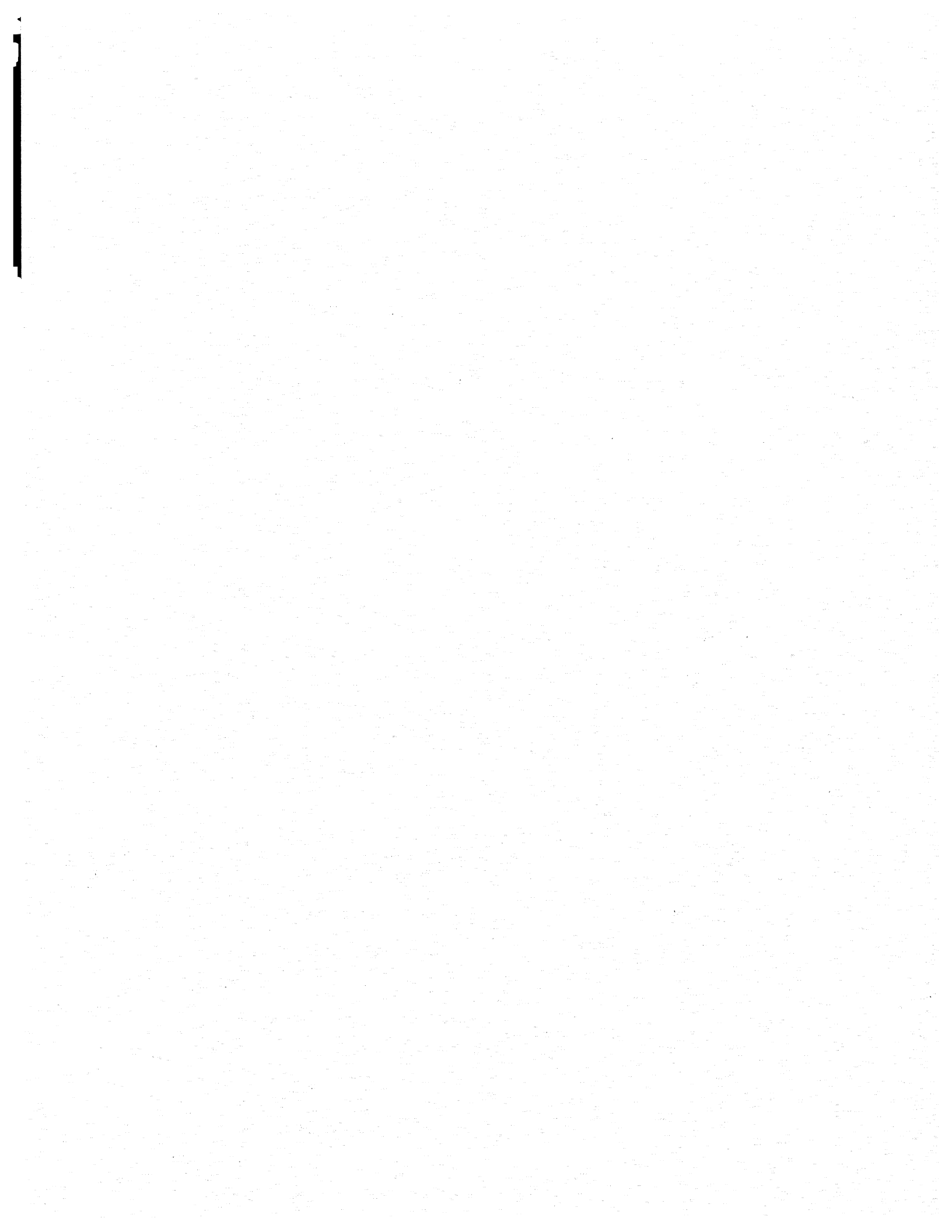
approximately \$7 million per annum. Research topics in the Department range from basic cell biology to applications in immunology and inflammation. There is extensive depth of expertise in these areas, as reflected by the international standing of many faculty, their research funding and publication records, and the key participation of Pathology faculty in a variety of institutional programs and activities (Cancer Center, Gerontology Center, Multipurpose Arthritis Center, Renal Center, Diabetes Research and Training Center, Molecular Medicine Program, etc.).

The challenges we face in the next several years are formidable. However, it should be noted that in 1985, with the passage of TEFRA and initiation of the DRG system, it was predicted that Pathology would vanish as a viable professional entity. Obviously this did not occur. It seems in the coming years we will have to demonstrate once again that Pathology is an essential, adaptable and critical force in the area of Medicine.

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 1992 - 30 JUNE 1993**

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 - eight contact hours.
- B. Sophomore Medical Class:
 - 1. ICS 600, 601 - CPC's - two contact hours.
 - 2. Pathology 600 - six lecture hours.
- C. Hospital Conferences:
 - 1. Cardiovascular Pathology Conference - monthly.
 - 2. Internal Medicine CPC's - occasional.
 - 3. Internal Medicine Necropsy Review - monthly.
 - 4. Pediatric Cardiology Conference - monthly 1/93 to 6/93.
- D. House Officers:
 - 1. Training in Surgical and Necropsy Pathology.
- E. Invited Lectures:
 - 1. Freshman Orientation, August, 1992.
 - 2. Michigan State Medical Society, November, 1992.
 - 3. Midwinter-Cardiovascular Update, February, 1993.
 - 4. Student Biomedical Research Program, June, 1993.

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 in a baboon model, with T. Wakefield.

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, Inteflex Policy Committee and Deans' Advisory Group on the Inteflex Program.
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, Provost's Task Force on Faculty Retirement.
I. Member, Medical Center Educational Space Advisory Committee.

REGIONAL AND NATIONAL:

- A. Editorial Board, "Modern Pathology".
B. Deputy Medical Examiner, Washtenaw County.
C. Manuscript Reviewer for Cancer, Circulation.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Muller, D.W.M., Topol, E.J., Abrams, G., Gallagher, K. and Ellis, S.G.: Intramural methotrexate therapy for prevention of neointimal thickening after balloon angioplasty. *J. Amer. Coll. Cardiol.* 1992;20:460-466.
2. Rosenschein, U., Yakubov, S.J., Gubernich, D., Bach, D.S., Sonda, P.L., Abrams, G.D. and Topol, E.J.: Shock-wave thrombus ablation, a new method for noninvasive mechanical thrombolysis, *Amer. J. Cardiol.* 1992;70:1358-1361.
3. Punch, M.R., Hubbell, G.P., Elkins, T.E. and Abrams, G.D.: Conservative management of bilateral massive edema of the ovary. *J. Reprod. Med.* 1993;38:61-64.
4. Schuger, C.D., McMath, L., Abrams, G., Zhan, H., Spears, J.R., Steinman, R.F. and Lehmann, M.H.: Longterm effects of percutaneous laser balloon ablation from the canine coronary sinus. *Circulation* 1992;86:947-954.
5. Lelli, J.L., Drongowski, R.A., Coran, A.G. and Abrams, G.D.: Hypoxia-induced bacterial translocation in the puppy. *J. Pediat. Surg.* 1992;27:974-981.
6. Schteingart, D.E., Sinsheimer, J.E., Counsell, R.E., Abrams, G.D., McClellan, N., Djanegara, T., Hines, J., Ruangwises, N., Benitez, R. and Wotring, L.L.: Comparison of the adrenalytic activity of mitotane and a methylated homologon normal adrenal cortex and adrenal cortical carcinoma. *Cancer Chemother. Pharmacol.* 1993;31:459-466.
7. Wakefield, T.W., Greenfield, L.J., Rolfe, M.W., DeLucia, A., Strieter, R.M., Abrams, G.D., Kunkel, S.L., Esmon, C.T., Wroblewski, S.K., Kadell, A.M., Burdick, M.D. and Taylor, F.B.: Inflammatory and procoagulant mediator

- interactions in an experimental baboon model of venous thrombosis. *Thromb. Hemostas.* 1993;69:164-172.
8. Williams, D.M., Andrews, J.C., Marx, M.V. and Abrams, G.D.: Creation of reentry tears in aortic dissection by means of percutaneous balloon fenestration: Gross anatomic and histologic considerations. *J. Vasc. Interv. Radiol.* 1993;4:75-83.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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.

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", \$45,00, 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. Standardization of Procedures Committee.
- B. Pharmacokinetics Quality Improvement Team.

REGIONAL AND NATIONAL:

- A. Executive Committee, National Therapeutic Drug Monitoring and Clinical Toxicology Division, American Association for Clinical Chemistry.
- B. National Awards Committee, American Association for Clinical Chemistry.
- C. National Abstracts Committee, American Association for Clinical Chemistry.
- D. Experts Panel Committee, American Association for Clinical Chemistry.
- E. International Abstracts Committee, International Association of Therapeutic Drug Monitoring.
- F. Education Committee, Michigan Section, American Association for Clinical Chemistry.
- G. College of American Pathologists Chemistry Reference Laboratory.
- H. Member, NCAA Drug Testing Team.
- I. Faculty, National Toxicology Review Course, American Association for Clinical Chemistry.
- J. Member, Academy of Clinical Laboratory Physicians and Scientists.
- K. Member, American Association of Pathologists.
- L. Member, American Association for Advancement of Science.
- M. Member, Clinical Ligand Society.
- N. Board of Directors, American Board of Clinical Chemistry.
- O. Secretary, National Therapeutic Drug Monitoring and Clinical Toxicology Division, American Association for Clinical Chemistry.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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

OTHER:

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

INVITED LECTURES/SEMINARS:

1. "Laboratory Needs for Transplantation Support", Chicago, Illinois, May, 1992.
2. "New Immunoassays for Drugs of Abuse Testing", Practical Review of TDM and Toxicology, Detroit, Michigan, November, 1992.
3. "A Solid Phase Detection System for Drugs of Abuse", Practical Review of TDM and Toxicology, Detroit, Michigan, November, 1992.
4. "Cyclosporin G Immunosuppressive Therapy: Monitoring Considerations" Conference on "Clinical Developments in Immunosuppressive Drug Therapy", Chicago, Illinois, January, 1993.
5. "Cyclosporin G Immunosuppressive Therapy: Considerations for Monitoring Therapeutic Levels", University of New Mexico, Albuquerque, New Mexico, May, 1993.
6. "Overdoses and Poisoning: Anticonvulsant Drugs, Cardiac and Antiarrhythmic Drugs", Professional Practice in Toxicology National Review Course, Cincinnati, Ohio, June, 1993.

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

1. Annesley, T.M., Matz, K. and Leichtman, A.B.: High-performance liquid chromatographic analysis of cyclosporin G (Nva-cyclosporine) in human blood. *Ther. Drug. Monitor.* 1992;14:397-401.
2. Burns, M.K., Ellis, C.N., Eisen, D., Duell, E., Griffiths, C., Annesley, T.M., Hamilton, T.A., Birnbaum J.E. and Voorhees, J.J.: Intralesional cyclosporine for psoriasis: relationship of dose, tissue levels, and efficacy. *Arch. Dermatol.* 1992;128:786-790.
3. Turgeon, D.K., Normolle, D.P., Leichtman, A.B., Annesley, T.M., Smith, D.E. and Watkins, P.B.: Erythromycin breath test predicts oral clearance of cyclosporine in kidney transplant patients. *Clin. Pharmacol. Ther.* 1992;52:471-478.
4. Annesley, T.M., Coombs, R. and Orsulak, P.J.: Comparison of cyclosporin G (Nva-cyclosporine) concentrations measured in whole blood by monoclonal fluorescence polarization immunoassay, monoclonal radioimmunoassay, and HPLC. *Clin.Chem.* 1993;39:1050-1053.

BOOKS/CHAPTERS IN BOOKS:

1. Annesley, T.M.: Preanalytical Test Variables, *Clinical Laboratory Medicine*, Williams and Wilkins, New York, New York, In Press.
2. Annesley, T.M.: Anticonvulsant Drugs, Cardiac/Antiarrhythmic Drugs, Nicotine, Atropine, *Professional Practice in Toxicology: A Review*, AACCC Press, Washington, D.C., 1993;123-167.

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

1. Annesley, T.M.: Review of, *Liquid Chromatography in Biomedical Analysis*, *Clin. Chem.* 1992;38:446.

2. Judd, W.J., Annesley, T.M., Kirkegaard, J. and Beck, M.L.: Know your monoclonals: an absolute must for the effective resolution of ABO grouping discrepancies. *Transfusion* 1992;32(S):18.
3. Leichtman, A.B., Turgeon, D.K., Annesley, T.M., Normolle, D.P., Smith, D.E. and Watkins, P.B.: Erythromycin breath test predicts oral clearance of cyclosporin A in renal transplant recipients. *J. Amer. Soc. Nephrol.* 1992;3:866.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. General surgical pathology - two and one-half months.
- B. Gastrointestinal and hepatic pathology consultation services - full time.
- C. Autopsy Service - one week.
- D. Sabbatical, July 1, 1992 - December 31, 1992.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

- A. Medical Students:
 - 1. Pathology 600 - eight full class lectures.
 - 2. Pathology 630 (dental) - three full class lectures.
 - 3. Senior medical student, elective rotation in pathology, supervisor one month.
- B. House Officers:
 - 1. Autopsy service tutoring, one week.
 - 2. Surgical pathology diagnosing room instruction for assigned house officer - two and one-half months.
 - 3. Gastrointestinal and hepatic pathology tutoring - full time.
- C. Interdepartmental:
 - 1. Medical Gastrointestinal Pathology Biopsy Conference - 4th Monday of each month.
 - 2. G-I Tumor Conference - 4th Tuesday of each month.
 - 3. Liver Transplant Conference - Every other Thursday.
 - 4. Liver Biopsy Conference - 1 hour per month

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Hepatic histopathologic changes in methotrexate - treated psoriatics, with A. Flint and members of the Gastroenterology Division.
- B. Appendiceal epithelial neoplasia.
- C. 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. Thymosin Treatment of Chronic Hepatitis B with Milton Mutchnick.
- F. Chronic gastritis in Michigan, with Paul Mazzara.
- G. Morphologic expressions of achalasia, with John Goldblum.
- H. PCNA in gastric and duodenal stromal tumors, with John Goldblum and Ricardo Lloyd.
- I. Crohn's disease of the appendix, with Jane Huang.

- J. Recurrent autoimmune hepatitis in the transplanted liver, with Michael Lucey and Kyle Carr.
- K. 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.
- B. Reviewer, Cancer.
- C. Reviewer, Human Pathology.
- D. Reviewer, Gastroenterology.
- E. Reviewer, American Journal of Gastroenterology.
- F. Chairman, Publications Committee and Member, Executive Committee, Gastrointestinal Pathology Society.
- G. Coordinator for Pathology, Randomized Therapeutic Trail in Cancer of the Esophagus, International Organization for Statistical Studies of Diseases of the Esophagus, Paris, France.
- H. 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.
- I. Member, Education Committee, United States-Canadian Academy of Pathology.
- J. Member, Editorial Board, Human Pathology.

V. OTHER RELEVANT ACTIVITIES:

MISCELLANEOUS

- A. Computer based interactive videoteaching program completed. Large Intestinal Pathology: Colorectal Biopsies, published by Intellipath Pathology Systems, Santa Monica, California, March, 1993.

INVITED LECTURES/SEMINARS:

1. Lecturer, "Histopathology of Chronic Hepatitis B", Chronic Viral Hepatitis Symposium, Wayne State University and Harper Hospital, Mackinac Island, Michigan, September 10-13, 1992.
2. Lecturer, "Histopathology of Chronic Hepatitis C", Chronic Viral Hepatitis Symposium, Wayne State University and Harper Hospital, Mackinac Island, Michigan, September 10-13, 1992.
3. Lecturer, Case Discussions, Chronic Viral Hepatitis Symposium, Wayne State University and Harper Hospital, Mackinac Island, Michigan, September 10-13, 1992.

4. Lecturer, "Role of the Pathologist in the Diagnosis of the Acutely Presenting Colitides," Memphis Society of Pathologists Winter Meeting, Memphis, Tennessee, December 4, 1992.
5. The Merlin L. Trumbull Lectureship in Pathology, Baptist Hospital, Memphis, Tennessee, Seminar on Gastrointestinal Pathology, December 5, 1992.
6. Lecturer, "Acutely Presenting Colitides: Common Communication Gaps Between Endoscopist and Pathologist", AGSE 10th National Interim Postgraduate Course, La Jolla, California, February 6, 1993.
7. "Acutely Presenting Colitides: The Ultimate Communication Gap", Atlanta Society of Pathologists Meeting, Atlanta, Georgia, February 22, 1993.
8. Visiting Professor, "The Ulcerative Colitis Dysplasia-Carcinoma Sequence and Stromal Tumors of the Gastrointestinal Tract", Department of Pathology and Laboratory Medicine, Emory University School of Medicine, Atlanta, Georgia, February 22-23, 1993.
9. Short course, "Inflammatory Conditions of Esophagus, Stomach and Duodenum", with Donald Antonioli, USCAP, New Orleans, March, 1993.
10. Seminar, "Gastrointestinal Biopsies", 31st Schleifstein Pathology Conference, New York State Association of Public Health Laboratories, Inc., Annual Meeting, Albany, New York, May 21, 1993.
11. Seminar, "Neoplastic Diseases of Intestine", American Society of Clinical Pathologists, Portland, Maine, June 16, 1993.
12. "The Low Tech Approach to Gastrointestinal Lymphomas", Royal College of Physicians and Surgeons of Canada Lectures, Canadian Association of Pathologists, Banff, Canada, June 28-29, 1993. Banff, Canada.
13. "Acutely Presenting Colitides", Royal College of Physicians and Surgeons of Canada Lectures, Canadian Association of Pathologists, Banff, Canada, June 28-29, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Goldblum, J. and Appelman, H.D.: Appendiceal involvement in ulcerative colitis. *Mod. Pathol.* 1992;5:607-610.
2. Lucey, M.R., Graham, D.M., Martin, P., DiBisceglie, A., Rosenthal, S., Waggoner, J.G., Merion, R.M., Campbell, D.A., Nostrant, T.T. and Appelman, H.D.: Recurrence of hepatitis B and delta hepatitis after orthotopic liver transplantation. *GUT* 1992;33:1390-1396.
3. Henley, K.S., Lucey, M.R., Appelman, H.D., et al: Biochemical and histopathological correlation in liver transplant: The first 180 days. *Hepatology* 1992;16:688-693.
4. Appelman, H.D.: The histologic alterations observed in the course of surveillance of Barrett's esophagus. *Acta. Endoscopica* 1992;22:517-530.

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

1. Goldblum, J.R. and Appelman, H.D.: The pathogenesis of achalasia cannot be determined from examination of resected end-stage disease. *Mod. Pathol.* 1993;6:46A.
2. Lindley, P.R. and Appelman, H.D.: Is there a preferred histologic classification scheme for endoscopic gastric polyps? *Mod. Pathol.* 1993;6:48A.

3. Mazzara, P.F. and Appelman, H.D.: Relationship between Helicobacter Pylori infection and intestinal metaplasia. *Mod. Pathol.* 1993;6:49A.
4. Ferraz, M.L.G., Greeve, M., Carr, K., Wright, T.L., Ferrell, L., Appelman, H.D. and Lucey, M.R.: Post-transplant hepatitis in patients with prior autoimmune chronic active hepatitis. All due to hepatitis C? *Gastroenterol.* 1993;104:A900.
5. Masood, S., Lu, L., Rhatigan, R.M., Monteiro, C., Achem, S.R. and Appelman, H.D.: DNA Ploidy study by cell image analysis in Barrett's esophagus. *Gastroenterol.* 1993;104:A425.
6. Wu, G.D., Beer, D.G., Moore, J.H., Orringer, M.B., Appelman, H.D. and Traber, P.G.: Sucrases-isomaltase gene expression in Barrett's esophagus and adenocarcinoma. *Gastroenterol.* 1993;104:A226.

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

**ANNUAL DEPARTMENT REPORT
1 JULY, 1992 - 30 June, 1993**

I. CLINICAL ACTIVITIES:

- A. Director, Histocompatibility and Immunogenetics Laboratory.

II. TEACHING ACTIVITIES:

- A. Director, Basic Immunology Course for Allergy Fellows-In-Training.
B. Instructor, ICS Course 600-601.
C. 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, Amy Gilardy and undergraduate students in research.
G. Supervisor for Dr. Lawrence Hennessey's (Allergy Fellow), Roma Gianchandani's (Endocrinology & Metabolism Fellow), and Richard Shen's (Postdoctoral Fellow) Research Projects.
H. Internal Medicine Grand Rounds.

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, \$70,000/year, May 1, 1992 - April 30, 1993.
B. "John E. Fogarty International Center", National Institutes of Health, 1 R03 TW00192-01, \$20,000/year, January 1, 1993 - December 31, 1994.
C. Core Co-Director, "University of Michigan-MAC: Hybridoma Core", National Institutes of Health, 2 P60 AR20557-15, \$42,853/year, January 1, 1993 - December 31, 1993.
D. Core Co-Director, "MDRTC: Hybridoma Core", National Institutes of Health, 5 P60 DK20572- 16, \$171,413/year, December 1, 1992 - November 30, 1993.
E. Endocrine Fellow Training Grant, Endocrine Society, 5 P32 DK07245 15, \$33,000/year, July 1, 1992 - June 30, 1993.
F. Cystic Fibrosis Foundation: Research Development Program, \$29,456/year, October 1, 1992 - September 30, 1993.
G. The Upjohn Company, \$80,000/year, October 1, 1992 - September 30, 1993.
H. Syntex Corporation, \$93,000/year, October 1, 1992 - September 30, 1993.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Planning Committee, Advances in Internal Medicine, University of Michigan Medical School, 1990-1993.
- B. Executive Board, Michigan Diabetes Research and Training Center.

REGIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

- 1. Editorial Board, Journal of Clinical Endocrinology and Metabolism.
- 2. Reviewer, Annals of Internal Medicine.
- 3. Reviewer, Journal of Clinical Investigation.
- 4. Reviewer, Endocrinology.
- 5. Reviewer, Journal of Leukocyte Biology.
- 6. Reviewer, Autoimmunity.
- 7. Reviewer, Thyroid.
- 8. Reviewer, Journal of Biological Chemistry.
- 9. Reviewer, Journal of New England Journal of Medicine.
- 10. Reviewer, Journal of Endocrinological Investigation.
- 11. Consultant Director, HLA Laboratory, Walter Reed Army Medical Center, Washington, DC.
- 12. Director, Hybridoma Core, University of Michigan Medical School.
- 13. Regional Accreditation Commissioner, American Society for Histocompatibility and Immunogenetics.
- 14. Endocrine Study Section, NIDDK, National Institutes of Health.

INVITED LECTURES/SEMINARS:

- 1. University of Toledo, College of Pharmacy Medical and Biological Chemistry Department Seminar Series, Toledo, Ohio, May, 1992.
- 2. Canadian Health Professional Board, Ottawa, Ontario, September, 1992.
- 3. Endoscopic Sinus Surgery Course, Towsley Center, August, 1992, and April, 1992.
- 4. American Thyroid Association Annual Meeting, Rochester, Minnesota, September, 1992.
- 5. American Academy of Allergy and Immunology Annual Meeting, Chicago, Illinois, March, 1992.
- 6. Symposium on Autoimmune Thyroid Disease, NIDDK/ORWH, Bethesda, Maryland, April, 1993.
- 7. Allergy and Clinical Immunology Division, Medicine Grand Rounds, William Beaumont Hospital, Royal Oak, Michigan, March, 1993.
- 8. Workshop on Autoimmune Thyroid Disease, NIDDK/ORWH, Bethesda, Maryland, April, 1993.
- 9. AAP, ASCI, AFRC Clinical Research Meeting, Washington, DC, April - May, 1993.
- 10. AAI/CIS Joint Meeting, Denver, Colorado, May, 1993.

11. The Endocrine Society 75th Annual Meeting, Las Vegas, Nevada, June, 1993.

VI. PUBLICATIONS

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

1. Wortsman, J., McConnachie, P., Baker, J.R., Jr. and Mallette, L.E.: T-lymphocyte activation in adult-onset idiopathic hypoparathyroidism. *American J. Med.* 1992;92:352-356.
2. Arscott, P., Rosen, E., Koenig, R.J., Kaplan, M.M., Ellis, R., Thompson, N. and Baker, J.R., Jr.: Immunoreactivity to *Yersinia enterocolitica* antigens in patients with autoimmune thyroid disease. *J. Clin. Endo. & Metab.* 1992;75:295-300.
3. Maastricht, J., Koenig, R.J., Kaplan, M.M., Arscott, P., Thompson, N. and Baker, J.R., Jr.: Identification of localized autoantibody epitopes in thyroid peroxidase. *J. Clin. Endo. & Metab.* 1992;75:121-126.
4. Hansen, K.A., Opsahl, M.S., Nieman, L.K., Baker, J.R., Jr. and Klein, T.A.: Natural killer cell activity from pregnant subjects is modulated by RU 486. *Amer. J. Obstet. Gynecol.* 1992;166:87-90.
5. Baker, J.R., Jr.: Review article, The immune response in chronic hepatitis B virus infection: The "core" of the problem? Ehata, T., et al. Variations in codons 84-101 in the core nucleotide sequence correlate with hepatocellular injury in chronic hepatitis B virus infection. (*J. Clin. Invest.* 1992;89:332-338.) *Hematology* 1992;16(2):498-500.
6. Cai, W.-Y., Lukes, Y.G., Burch, H.B., Djuh, Y.-Y., Carr, F., Wartofsky, L., Rhooms, P., D'Avis, J., Baker, J.R., Jr. and Burman, K.D.: Analysis of human TSH receptor gene and RNA transcripts in patients with thyroid disorders. *Autoimmunity* 1992;13:43-50.
7. Baker, J.R., Jr.: Immunologic aspects of endocrine diseases, in deShazo, R.D. (ed.), *Primer of Allergic and Immunologic Diseases.* JAMA, 1992;268:2899-2903.
8. 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.* 1993;305:1-7.
9. Ross, P.V., Koenig, R.J., Arscott, P., Ludgate, M., Waier, M., Nelson, C.C., Kaplan, M. and Baker, J.R., Jr.: Tissue specificity and serologic reactivity of an autoantigen associated with autoimmune thyroid disease. *J. Clin. Endo. Metab.*, In Press.
10. Baker, J.R. Jr.: Dissecting the immune response to the TSH receptor in autoimmune thyroid disease. Editorial: *J. Clin. Endo. Metab.*, In Press.
11. Baker, J.R., Jr. and Fosso, C.K.: Immunologic aspects of cancers arising from thyroid follicular cells. *Endocrine Reviews*, 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 *Yersinia Enterocolitica*. Submitted.
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.
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.
4. McClain, J.B. Col, M.C., Bharati, J., Baker, J.R., Jr. and Cross, A.: Alternative pathway complement activity to *E. Coli* K1 and 25922 contrasted to *Leptospira interrogans* and *Leptospira biflexa*. Submitted.
 5. Bermann, M., Koenig, R.J., Kaplan, M.M., Arscott, P., Maastricht, J., Johnson, J. and Baker, J.R., Jr.: Autoantibody responses to thyroid peroxidase in patients with autoimmune thyroid disease. J. Clin. Endo. Metab., Submitted.

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

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

1. Seifert, M.J., Arscott, P.L. and Baker, J.R., Jr.: The induction of heat shock protein 70 (HSP 70) on human thyroid cells and fisher rat thyroid (FRTL-5) cells. Presented, AAP/ASCI/AFCR Annual Meeting, Baltimore, Maryland, May 1992.
2. Bermann, M., Koenig, R.J., Maastricht, J.L., Kaplan, M., Arscott, P.L. and Baker, J.R. Jr.: The identification of two areas of human auto-antibody binding in thyroid peroxidase. Presented, Endocrine Society Annual Meeting, San Antonio, Texas, June, 1992.
3. Ross, P.V., Koenig, R.J., Ludgate, M., Nelson, C.C., Kaplan, M. and Baker, J.R. Jr.: Tissue specificity and serologic reactivity of an autoantigen associated with autoimmune thyroid disease. Presented, American Thyroid Association Annual Meeting, Rochester, Minnesota, September, 1992.
4. Hennessey, L.R., Pek, S.B. and Baker, J.R. Jr.: Superantigen-like T cell subset alterations in non-obese diabetic (NOD) mice successfully treated with bacillus calmette-guerin (BCG). J. Aller. Clin. Immunol. 1993;91:231.
5. Arscott, P.L., Koenig, R.J., Kaplan, M.M., Glick G.D. and Baker, J.R., Jr.: Identification of a localized autoantibody epitope in thyroid peroxidase (TPO) that is associated with Hashimoto's disease. Presentation scheduled, American Federation of Clinical Research Meeting, Washington, D.C., April, 1993.
6. Arscott, P.L., Koenig, R.J., Kaplan, M.M., Glick G.D. and Baker, J.R. Jr.: Identification of a localized autoantibody epitope in thyroid peroxidase (TPO) that is associated with Hashimoto's disease. Presentation scheduled, NIDDK and ORWH Workshop on Autoimmune Thyroid Disease, Bethesda, Maryland, April, 1993.
7. Baker, J.R. Jr., Arscott, P.L., Shu, S., Thompson, N., Fox, B. and Koenig, R.J.: T cell mediated anti-tumor immunity. Presentation, AAI/CIS Meeting, Denver, Colorado, May, 1993.
8. Gilardy, A.K., Baker, J.R. Jr., Ward, P.A. and Johnson, K.J.: An *in vivo* model of pulmonary delayed-phase allergic inflammation. Poster presented, AAI/CIS Meeting, Denver, Colorado, May, 1993.
9. 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. Presentation, Endocrine Society Annual Meeting, Las Vegas, Nevada, June, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. Medical Director, Myelodysplasia Unit: inpatient and outpatient services for children with spina bifida.
- B. Teratology Unit (see Research Activities).
- C. Attending physician, general pediatric service and newborn nursery.
- D. Genetics/Teratology Consultant, Women's and Holden Hospitals.

II. TEACHING ACTIVITIES:

- A. Teratology-Obstetrics Conference: weekly case review meeting of Obstetrics, Radiology, Teratology, Neonatology for planning management of fetuses with prenatally detected malformations.
- B. Pediatrics-Pathology Conference: organize and present CPC-type conferences to the Department of Pediatrics; four per year.
- C. Neonatology Pathology Conference: quarterly review and discussion of neonatal deaths.
- D. Senior and House Officer electives in teratology (2 per year).
- E. Obstetrics Core Curriculum lectures (2 per year).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

PROJECTS UNDER STUDY:

- A. Detailed postmortem investigations of abortuses, stillborns, and selected neonatal deaths for morphologic, pathologic, and growth characteristics, correlations with family and prenatal histories, and counseling for future reproductive decisions by the parents.
- B. Continuing investigation of normal and abnormal patterns of somatic and visceral growth. Detection of patterns of growth abnormalities associated with specific syndromes, exposures, and obstetrical antecedents.
- C. Quality control investigations for various prenatal diagnostic methodologies.
- D. Teratology Unit Activities: 186 fetal/neonatal examinations (86 from UMMC, 100 referred from 14 outside hospitals)

COLLABORATIVE RESEARCH:

- A. Collection and allocation of fetal tissues for research projects in the Departments of Pediatrics, Pathology, Obstetrics, Anatomy, Genetics, and Howard Hughes Institute. Loan of fetal material for research investigations in the Department of Radiology.
- B. Collaborative research with Central Laboratory for Embryology at the University of Washington (T.H. Shepard, M.D.) and the Department of Pathology at the University of South Alabama (W.R. Blackburn, M.D.) on standards for normal fetal morphometrics.
- C. Research with Wayne State University (M.P. Johnson, M.D.) on fetal growth assessment in aneuploid fetuses.
- D. Investigation of renal tubular dysplasia in human fetuses (with R.A. Martin, University of California - San Diego).

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Departmental - Pathology: none.
- B. Departmental - Pediatrics:
 - 1. Editorial Board, Pediatric Rounds.
 - 2. Resident Advisory Committee.
 - 3. Medical Student Curriculum Committee.
- C. Hospital:
 - 1. Ethics Committee.
 - 2. Standardization and Product Evaluation Committee.
 - 3. Infant and Child Care Ethics Committee (Co-Chair).

REGIONAL AND NATIONAL:

- A. Reviewer for journals: Teratology, Pediatric Pathology, American Journal of Medical Genetics, American Journal of Obstetrics and Gynecology, and American Journal of Public Health.
- B. President, Teratology Society (92-93).

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

- 1. Oakwood Hospital, Dearborn, Michigan.
- 2. Genetic Counselling, Department of Human Genetics, The University of Michigan.
- 3. Dental School, University of Michigan, Ann Arbor, Michigan.
- 4. All-Michigan OB/GYN Review Course, Ypsilanti, Michigan.
- 5. OB/GYN Postgraduate course, Ann Arbor.
- 6. Neurosurgery Grand Rounds, The University of Michigan.

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

1. Martin, R.A., Jones, K.L., Mendoza, A., Barr, M. and Benirschke, K.: The effect of ACE inhibition on the fetal kidney: Decreased renal blood flow. *Teratology*. 1992;46:317-321.
2. Krieborg, S., Barr, M. and Cohen, M.M.: The cervical spine in the Apert syndrome. *Am. J. Med. Genet*. 1992;43:704-708.
3. Pryde, P.G., Sedman, A.B., Nugent, C.E. and Barr, M.: Angiotensin-converting enzyme inhibitor fetopathy. *J. Am. Soc. Nephrol*. 1993;3:1575-1582.
4. Johnson, M.P., Barr, M., Treadwell, M.C., Michaelson J., Isada, N.B., Pryde P.G., Dombrowski, M.P., Cotton, D.B. and Evans, M.I.: Fetal leg and femur:foot length ratio: a marker for trisomy 21. *Am. J. Obstet. Gynecol.*, In Press, 1993.

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

1. Johnson, M.P., Michaelson, J.E., Ayoub, R., Barr, M., Treadwell, M.C., Isada, N.B., Reichler, A., Home, R.F. and Evans, M.I.: Brachycephaly alters biparietal diameter (BPD) in trisomy 21 (T21): Fetal foot length is a better gestational age measurement in sonographic morphologic screening. *Am. Soc. Hum. Genetics.*, 1993.
2. Michaelson, J., Barr, M., Treadwell, M.C., Evans, M.I., Isada, N.B., Pryde, P.G. and Johnson, M.P.: Sonographic screening for trisomy 21: Fetal humerus:foot length ratio, a useful new marker. Presented in San Francisco, California. *Society Perinatal Obstet.*, 1993.
3. Johnson, M.P., Barr, M., Treadwell, M., Isada, M.B. and Evans, M.I.: Femur:foot length ratio as an indicator of fetal aneuploidy. Presented in Evian, France, *International Fetal Medical Surgical Society*, 1992.
4. Barr, M., Blackburn, W.R. and Cooley, N.R.: Fetal morphometric and gravimetric analysis: Normal standards and demonstration of usefulness in the study of syndromes. Presented at D.W. Smith Workshop on Morphogenesis and Malformations, Winston Salem, North Carolina, 1993.
5. Barr, M., Blackburn, W.R. and Codey, N.R.: Fetal growth analysis: New refined standards of normal growth. Presented in Louisville, Kentucky. *Soc. Ped. Pathol.*, 1993.
6. Barr, M.: ACE-inhibitor fetopathy: Introduction and clinical aspects. Presented in Tucson, Arizona, *Teratology Society*. 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. Diagnostic Electron Microscopy, Veterans Affairs Medical Center, Director of Electron Microscopy Center of Excellence.
- B. Cytopathology, Veterans Affairs Medical Center.
- C. Coordinator of Decentralized Hospital Computer Program in Laboratory Service, Veterans Affairs Medical Center.
- D. Fine Needle Aspiration, Veterans Affairs Medical Center.
- E. Surgical/Autopsy Pathology, Veterans Affairs Medical Center.
- F. National Chief of Anatomic Pathology, 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, 10 months.
- B. Diagnostic Electron Microscopy Case Conference, bi-weekly.
- C. Pathology House Officers, fine needle aspiration technique and interpretation.
- D. Pathology 600 Lab Section.
- E. 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. Marijuana-Bronchoscopy Project (Fliigel/Gong/Tashkin), NIH.
- C. A Prospective, Controlled, Randomized and Double-Blind Multi-Center Clinical Evaluation of Monoclonal Antibody 17.13.C1.10 for its Capability to Detect Head and Neck.
- D. Squamous cell carcinoma in Primary Site Malignancies and Lymph Nodes.(Co-Investigators: Baker, Beals, Carey, Krause, McClatchey and Wolf).
- E. Predicting Response to Chemotherapy in Head and Neck Cancer. (Principal Investigator, Bradford).

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. Morphometric analysis of cells and tissue using the scanning light microscope.
- D. Growth of cells on microcarriers (with J. Varani).
- E. Cell damage caused by oxidants (with D. Hinshaw).
- F. DNA content as a predictor of chemotherapeutic response and prognosis in squamous cell carcinoma of the larynx (with C. Gregg and G. Wolf).
- G. Differentiation of isolated renal tubular cells in culture (with D. Humes).
- H. Incidence of Human Papilloma Virus infection in prostate tissues. Comparison of benign hyperplasia and adenocarcinoma. (Doctoral thesis L. Wideroff, SPH).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Electron Microscopy Committee.

MEDICAL SCHOOL/HOSPITAL:

- A. Clinical Executive Committee, elected member, Veterans Affairs Medical Center.
- B. Surgical Case 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 Center.
- F. Medical School Admissions Committee.

REGIONAL AND NATIONAL:

- A. Association of Veterans Affairs Pathologists, Secretary-Treasurer.
- B. Veterans Affairs Central Office Electron Microscopy Review Group.
- C. Veterans Affairs Representative on Scientific Advisory Board, Armed Forces Institute of Pathology.
- D. Consultant, Association of Pathology Chairmen, Veterans Affairs Committee.
- E. American Society of Clinical Pathologists, Quality Assurance Committee.
- F. American Society of Clinical Pathologists, Cytology CheckPath Committee.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Pulmonary Cytopathology: Diagnostic Problems and Ultrastructural Characteristics", Department of Internal Medicine, Pulmonary Conference Series.
2. "Electron Microscopy as an Aid to Diagnostic Cytopathology", Henry Ford Medical Center.
3. Invited Lecturer, "Electron Microscopy in Cytology", Michigan Society of Cytology.

4. Invited Lecturer, "Electron Microscopy of Fine Needle Aspirations", Annual Meeting of Michigan Society of Cytology.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Beals, T.F.: Ultrastructure of in situ hybridization. *Ultrastructural Pathol.* 1992;16:87-93.
2. Beals, T.F.: Scanning electron microscopy of body fluids. *Diagnostic Cytopathol.* 1992;8:266-271.
3. Mierau, G.W., Agostini, R., Beals, T.F., Carlen, B., Dardick, I., Henderson, D.W., Pysker, T.J., Weeks, D.A. and Yowell, R.: The role of electron microscopy in evaluating ciliary dysfunction: Report of a consensus workshop. *Ultrastructural Pathol.* 1992;16:245-254.
4. Truelson, J.M., Fisher, S.G., Beals, T.F., McClatchey, K.D. and Wolf, G.T.: DNA content and histologic growth pattern correlate with prognosis in patients with advanced squamous cell carcinoma of the larynx. *Cancer* 1992;70:56-62.
5. Goldblum, J.R., Beals, T. and Weiss, S.W.: Elastofibromatous change of the rectum: A lesion mimicking amyloidosis. *Am. J. Surg. Pathol.* 1992;16:793-795.
6. 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.*, In Press, 1993.
7. 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.*, In Press, 1993.
8. 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*, In Press, 1993.

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

1. Gregg, C.M., Beals, T.F., Fisher, S.G. and Wolf, G.T.: DNA content and tumor response to induction chemotherapy in patients with advanced laryngeal squamous cell carcinoma. *Third Inter. Conf. Head and Neck Cancer*, 1992.
2. Wideroff, L., Schottenfeld, D., Carey, T., Beals, T., Fu, G., 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.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993

I. CLINICAL ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Histology and histochemistry of orbicularis muscle, normal, aging, diseased.
- B. Pathology of soft palate muscles in cleft palate.
- C. Pathologic changes in rat brain induced by MK-801.
- D. Skeletal muscle and spinal cord in MND mice model.

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

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

1. Simmons, Z., Blaivas, M., Bromber, M.B. and Feldman, E.L.: Polyneuropathy associated with IgA monoclonal gammopathy. *Muscle and Nerve* 1993;16:77-83.
2. Ike, R.W. and Blaivas, M.B.: Corticosteroid responsive puffy hands and occult vasculitic neuropathy: RS3PE plus. *J. Rheumatol.* 1993;20:205-206.
3. Drury, I., Blaivas, M., Abody-Khalil, B.W. and Beydoun, A.: Biopsy results in a kindered with Lafora disease. *Arch. Neurol.* 1993;50:102-105.
4. Meyer, J.R., Gebarski, S.S. and Blaivas, M.: Cerebello-pontine angle invase papillary cystadenoma of endolymphatic sac origin with temporal bone involvement. *AJRN*, In Press.
5. Simmons, Z., Blaivas, M., Aquilera, A., Bromberg, M.D. and Feldman, E.L.: Low diagnostic yield of sural nerve biopsy in patients with peripheal neuropathy and primary amyloidosis. *J. Neurological Sci.*, In Press.
6. O'Rourke, K.S., Blaivas, M. and Ike, R.W.: Utility of needle muscle biopsy in a univeristy rheumatology practice. *Rheumatology*, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Venkayya, R.V., Poole, R.M., Pentz, W.H., Ernst, R.D. and Blaivas, M.: Respiratory failure from Procainamide-induced myopathy. *Annals of Internal Medicine*, Submitted.

BOOKS/CHAPTERS IN BOOKS:

1. McKeever, P.E. and Blaivas, M. and Sima, A.A.F.: Neoplasms of the sellar region (Chapter 13), in, Lloyd, R.V. (ed), *Surgical Pathology of the Pituitary Gland*, MPP Series, Saunders, 1992:141-210.

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

1. Meyer, J.R., Gebarski, S.S., Deveikis, J. and Blaivas, M.: Cerebellopontine angle endolymphatic sac carcinoma with temporal bone involvement. Presented at ASNR meeting in Vancouver, May 13-20, 1993.
2. Cohen, S.R., Corrigan, M., Blaivas, M., Kawamoto, H.K. and Markowitz, B.: Histochemical, morphometric and ultrastructural analysis of human levator

palatini muscle in human cleft palate. Presented at the American Association of Plastic Surgeons Annual Meeting, September 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. Inherited Connective Tissue Diseases Diagnostic Service (Biochemical analysis of skin biopsy material).
- B. Attending Staff, U-M Autopsy Service.

II. TEACHING ACTIVITIES:

- A. Graduate Students, John Germiller (MSTP), Karl Jepsen (Mechanical Engineering, Bioengineering).
- B. Postdoctoral Fellows, Wushan Yin, M.D., Chiara Sanguineti, Ph.D., Yaping Chen, M.D. and Yao-Yao Zhu, M.D., Ph.D.
- C. Medical Student, Lisa Harrell. (Under the auspices of the U-M Summer Medical Student Research Program).
- D. Courses:
 - 1. Pathology 600, Lab instructor.
 - 2. Molecular Cell Biology, Section head.
 - 3. Pathology 581, Invited lecturer.
 - 4. Physiology 519, Invited lecturer.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Transgenic Mouse Model of Osteogenesis Imperfecta Type I", NIAMS, NIH, AR40679 (25% effort), \$162,679/year direct costs, \$462,843/3 years, 1991-1994.

PROJECTS UNDER STUDY:

- A. Structure/function relationships in skeletal connective tissue.

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 -.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

- A. Assistant Investigator, Howard Hughes Medical Institute.
B. Faculty Member, Bioengineering Program, University of Michigan.
C. Ad-hoc Reviewer:
1. The Journal of Clinical Investigation.
2. The Journal of Biological Chemistry.
3. American Journal of Human Genetics.
4. Genomics.
D. Consultant Editor: European Journal of Experimental Musculoskeletal Research 1991-.
E. Study Section, NIH, NCRR (General Clinical Research Center Review), Site Visit Team, 1993.
F. Member:
1. U-M Multipurpose Arthritis Center
2. Michigan Cancer Center
3. U-M Program in Bioengineering

PATENTS PENDING:

1. "Small Intestinal Submucosa as Biomaterial to Promote Gene Transfer." Discovery filed, 2 September, 1992. Co-discoverers: Stephen F. Badylak, Ph.D. and Sherry L. Voytik, Ph.D., Purdue University. Patent application is pending.

INVITED LECTURES/SEMINARS:

1. Invited Presentation, "Biomechanical Assessment of the Extracellular Matrix of Bone: The Contribution of Collagen Type I", XIIIth Meeting of the European Connective Tissue Societies, Davos-Platz, Switzerland, July 12-19, 1992.
2. Invited Presentation, "Neuromuscular Atrophy Alters Pattern Formation, Mechanical Integrity, and Extracellular Matrix Gene Expression in the Chick Embryo Limb", XIIIth Meeting of the European Connective Tissue Societies, Davos-Platz, Switzerland, July 12-19, 1992.
3. Invited Presentation, "Neuromuscular Atrophy Alters Pattern Formation, Mechanical Integrity, and Extracellular Matrix Gene Expression in the Chick Embryo Limb", The Fourth International Conference on Limb Regeneration and Development, Pacific Grove, California, July 19-24, 1992.
4. "Collagen Disorders", Short Course on Molecular Diagnostics, Genetic Counseling, and the Human Genome Project, University of Michigan, August 10, 1992.
5. "Osteogenesis Imperfecta Type I in Mov13 Transgenic Mice", NIH Workshop: "Frontiers in Rehabilitation Medicine: Osteogenesis Imperfecta", Bethesda, Maryland, September 23-25, 1992.
6. Invited Presentation, "An Adaptive Response by Murine Skeletal Tissues that Significantly Increases the Mechanical Properties of Cortical Bone: Implications

- for the Treatment of Human Skeletal Fragility", 6th International Congress of Bone Morphometry (Session Co-Chair, "New Frontiers in Bone Morphometry II"), Lexington, Kentucky, October 4-9, 1992.
7. "A Rationale and Method for Gene Transfer into Skeletal Tissues", Department of Pathology and Laboratory Medicine, Jewish Hospital at Washington University Medical Center, St. Louis, Missouri, October 30, 1992.
 8. "A Rationale and Method for Gene Transfer into Skeletal Tissues", University of California, San Francisco, California, December 16, 1992.
 9. "A Rationale and Method for Gene Transfer into Skeletal Tissues", University of Michigan, Department of Physiology Seminar Series, May 19, 1993.
 10. "Genetic Determinants of Bone Fragility", Endocrinology and Metabolism, Department of Internal Medicine, University of Michigan, June 1, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Niyibizi, C., Byers, P.H., Bonadio, J. and Eyre, D.R.: Incorporation level of a mutant collagen $\alpha 2(I)$ chain into bone matrix in a lethal case of osteogenesis imperfecta. *J. Biol. Chem.*, 1992;267:23108-23112.
2. Pereira, L., D'Alessio, M., Ramirez, F., Lynch, J.R., Sykes, B., Pangilinan, T. and Bonadio, J.: Genomic organization of the sequences coding for fibrillin, the defective gene product in Marfan syndrome. *Hum. Mol. Genetics*, In Press.
3. 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.*, In Press.

BOOKS/CHAPTERS IN BOOKS:

1. Bonadio, J.: Investigation of the pathogenesis of single-gene disorders by molecular methods, in, McClatchey, K.D. (ed), *Clinical Laboratory Methods*, In Press.
2. Bonadio, J. and Goldstein, S.A.: The inherited disorders of the vascular wall, in, Roberts, R. (ed), *Molecular Biology of the Cardiovascular System*, Blackwell Scientific Publications, Cambridge, Massachusetts, 1993:393-414.
3. Wong, M., Germiller, J., Bonadio, J. and Goldstein, S.A.: Neuromuscular atrophy alters collagen gene expression, pattern formation, and mechanical integrity of the chick embryo long bone, in, Fallon, J.F., Goetinck, P.F., Kelley, R.O. and Stocum, D.L., (eds), *Limb Development and Regeneration*, Progress in Clinical and Biological Research, Vol. 383A and B, Wiley-Liss, New York, 1993:587-598.
4. Bonadio, J. and Ramirez, F. Bone collagen: Normal structure-function relationship and pathology. *Ital. J. Mineral Electrolyte Metab.*, In Press.

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

1. Goldstein, S.A., Jepsen, K.J., Kuhn, J.L. and Bonadio, J.: Biomechanical assessment of the extracellular matrix of bone: The contribution of collagen type

- I, XIIIth Meeting of the European Connective Tissue Societies, Davos-Platz, Switzerland, 1992.
2. Wong, M., Germiller, J., Bonadio, J. and Goldstein, S.A.: Neuromuscular atrophy alters pattern formation, mechanical integrity, and extracellular matrix gene expression in the chick embryo limb, XIIIth Meeting of the European Connective Tissue Societies, Davos-Platz, Switzerland, 1992.
3. Germiller, J.A., Wong, S.A., Goldstein, S.A. and Bonadio, J.: Neuromuscular atrophy alters pattern formation, mechanical integrity, and extracellular matrix gene expression in the chick embryo limb, The Fourth International Conference on Limb Regeneration and Development, Pacific Grove, California, July 19-24, 1992.
4. Bonadio, J.: Transgenic mice as models of inherited connective tissue diseases, 6th International Conference of Bone Morphometry (Session Co-Chair), Lexington, Kentucky, 1992.
5. Yin, W., Sanguineti, C., Pangilinan, T., Pereira, L., Ramirez, F.R. and Bonadio, J.: Isolation and characterization of a mouse cDNA clone homologous to human Fib15, Second International Symposium on the Marfan Syndrome, San Francisco, California, November 7-9, 1992.

**PETER BRAUN, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992-30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. AP/CP Pathology, Veterans Administration Hospital.

II. TEACHING ACTIVITIES:

- A. Pathology House Officers, Surgical Pathology/Autopsy, Veterans Administration Hospital.

III. RESEARCH ACTIVITIES:

PENDING:

- A. Co-Investigator, grant submitted to NIH by Dr. Bree, Radiology.

PROJECTS UNDER STUDY

- A. Principal Investigator, "The effect of c-k-ras2 on the histology/behavior of testicular germ cell tumors", submitted for RAG funding.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Research and Development Committee, Veterans Administration Hospital.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

- A. Member, International Society of Urological Pathology.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Mann, N.S., Mann, S.K., Brawn, P.N. and Weaver, B.: Effect of zinc sulfate and acetylcysteine on experimental gastric ulcer. In vitro study. Digestion 1992;53:108-113.
2. Brawn, P.N., Johnson, E.H., Kuhl, D., Riggs, M.W., Speights, V.O., Johnson, C.F., Pandya, P.P., Lind, M.L. and Bell, N.F.: Stage at presentation and survival of white and black patients with prostate carcinoma. Cancer 1993;71:2569-2573.

3. Cohen, M., Spiekerman, M. Brawn, P.N. and Speights, V.O.: PSA levels in stage A prostate carcinoma. Amer. J. Clin. Pathol., August, 1993.
4. Brawn, P.N., Johnson, E.H., Weaver, B., Kuhl, D., Lind, M., Speights, V.O., Bell, N. and Murphy, H.: Prostate carcinoma more than 10 years (10-30 years) after histologically proven benign prostatic hyperplasia. Life Science Advances - Oncology, In Press.

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

1. Several abstracts from published studies reprinted in Urology/Nephrology Digest.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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/yr), 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 (6 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, (one semester, 20 contact hours).
- B. Graduate course, Epidemiology 570, two lecture hours.
- C. Pathology house officers, Surgical Pathology/Autopsy supervision and instruction, four months/year.
- D. Technologists and technicians, ongoing instruction on clinical laboratory topics.
- E. Graduate students, research training toward doctoral degrees.
- F. Physicians, educational lectures regarding aspects of clinical pathology.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Cytokine Cascades in Granuloma Formation", VAMC Merit Review (\$55,000 annual) 1990-1993, Renewed at 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.
- D. Hospital Quality Assurance Investigations, ad hoc committees.
- E. Personnel employment and annual evaluation.
- F. 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. Laboratory Investigation.
- B. Inspector, College of American Pathologists.
- C. Invited consultant for consensus conference, International Conference on Sarcoidosis and Other Granulomatous Diseases, Los Angeles, California.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. Invited Lecturer, Minisymposium on Pathobiology of Pulmonary Inflammation, FASEB, New Orleans, 1993.
- 2. Case presentation at Tumor Board.
- 3. Tissue evaluation for clinical researchers.

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

1. Scales, W.E., Chensue, S.W. and Kunkel, S.W.: Interleukin-6 expression in immunologically elicited murine macrophages. *Pathobiology* 1992;60:289.
2. Olson, A.D., Ayass, M. and Chensue, S.W.: Tumor necrosis factor and IL-1 beta expression in pediatric patients with inflammatory bowel disease. *Pediat. Gastroenterol.* 1993;16:241-246.
3. Kunkel, S.L., Strieter, R.M., Lukacs, N. and Chensue, S.W.: Initiation and maintenance of the granulomatous response. *Chest* 1993;103:135s-137s.
4. Lukacs, N.W., Kunkel, S.L., Strieter, R.M., Warmington, K. and Chensue, S.W.: The role of macrophage inflammatory protein 1a in *Schistosoma mansoni* egg-induced granulomatous inflammation. *J. Exp. Med.* 1993;177:1551-1559.
5. 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 CD8+ cells *in vivo*. *J. Immunol.*, In Press, 1993.
6. Chensue, S.W., Bienkowski, M., Eessalu, T.E., Warmington, K.S., Hershey, 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.*, In Press, 1993.

BOOKS/CHAPTERS IN BOOKS:

1. Kunkel, S.L., Chensue, S.W. and Phillips, S.M.: Mechanisms of immunopathology in parasitic infections, in, Warren, K.S. (ed), *Immunology and Molecular Biology of Parasitic Infections*, Blackwell Scientific Publications, Boston, 1993.
2. Kunkel, S.L., Chensue, S.W., Standiford, T.J. and Strieter, R.M.: Endotoxin-dependent cytokine networks, in, Brigham, K. (ed), *Endotoxin and the Lung*, 1993.
3. Kunkel, S.L., Chensue, S.W., Standiford, T.J. and Strieter, R.M.: Cellular and molecular mechanisms that regulate the production of interleukin-8: The potential role of chemotactic cytokines in acute respiratory distress syndrome and multiple organ failure, in, Faist, Meakins, and Schildberg (eds), *Host Defense Dysfunction in Trauma, Shock and Sepsis*, Springer-Verlag, Berlin, 1993.

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

1. Chensue, S.W., Strieter, R.M., Lukacs, N.W., Warmington, K.S., Burdick, M.D. and Kunkel, S.L.: Monocyte chemotactic protein (MCP-1) expression during schistosome egg granuloma formation. *FASEB J.* 1993.
2. Lukacs, N.W., Kunkel, S.L., Strieter, R.M., Warmington, K.S., Burdick, M.D. and Chensue, S.W.: Participation of macrophage inflammatory protein-1 alpha in pulmonary granuloma formation, ALA/ATS International Conference, San Francisco, California, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992- 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Training and supervision of premedical/medical students in research.
1. Marilyn Kline, medical student, Spring term 1992, project focused on human neutrophil activation and functional responses in addition to development of basic and advanced laboratory skills.
 2. Sharmain Gray, premedical student, Summer term 1992, project focused on monocyte and neutrophil activation in addition to development of basic and advanced laboratory skills.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Mechanisms of Fc Dependent Neutrophil Activation", NIH-1R29 AI/GM 31436, \$350,000 direct costs, 7/1/91-7/1/96.

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

None.

V. OTHER RELEVANT ACTIVITIES:

- A. Designed the T-shirt logo for the joint meeting of the American Association of Immunologists and the Clinical Immunology Society, May 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hughes, B.J., Hollers, J.C., Crockett-Torabi, E. and Smith, C.W.: Recruitment of CD11b/CD18 to the neutrophil surface and adherence-dependent cell locomotion. *J. Clin. Invest.* 1992;90:1687-1696.
2. Crockett-Torabi, E., Smith, C.W., Paterson, R., Kateley, J.R. and Fantone, J.C.: Insoluble immune complex-stimulated neutrophil LTB₄ production is dependent on both FcγRII and FcγRIII and independent of pertussis toxin sensitive signal transduction pathway. *Amer. J. Path.* 1992;140:613-620.

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

1. Crockett-Torabi, E., Tsai, P. and Fantone, J.C.: Insoluble immune complex-induced human neutrophil phospholipase D activation through a pertussis toxin insensitive pathway. *FASEB, AAI Mini-symposium*, 1992:A2747.
2. Crockett-Torabi, E., Wilson, A. and Fantone, J.C.: Activation of phospholipase D in human monocytes. *J. Leukocyte Biol., Suppl.* 1992:A229.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. 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.
- B. 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.

MEDICAL SCHOOL/HOSPITAL:

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

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. Presentation, "Alzheimer's Disease and Other Dementias", Course at Eastern Michigan University, November, 1992.
2. Member, Dementia Subcommittee of the Chronic Disease Advisory Committee (State of Michigan).
3. Member, Executive Committee of the Postmortem Examination Work group of the Dementia Subcommittee (State of Michigan).
- 4.. Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Committee.
5. Presentation, "Alzheimer's Disease and Other Dementias", Alzheimer Association, Catherine McCauley Health Center, June 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Foster, N.L., Gilman, S., Berent, S., Sima, A.A.F., D'Amato, C.J., Koeppe, R.A. and Hicks, S.P.: Progressive subcortical gliosis and progressive supranuclear palsy can have similar clinical and PET abnormalities. *J. Neurol. Neurosurg. Psychiatry* 1992;55:707-713.

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

1. D'Amato, C., Tworek, J. and Sima, A.A.F.: Primary limbic lobe gliosis mimicking Alzheimer's Disease. *J. Neuropathol. Exper. Neurol.* 1993;52:279.
2. Sima, A.A.F., Douglas, V. and D'Amato, C.: Diffuse Lewy body disease (DLBD): A retrograde degeneration of the mesocortical dopaminergic system? *J. Neuropathol. Exper. Neurol.* 1993;52:282.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Introductory course in Blood Banking/Transfusion Medicine for Pathology House Officers.
- B. Daily teaching rounds for Pathology House Officers assigned to the Blood Bank.
- C. Clinical Pathology Grand Rounds: Other infectious hazards of blood transfusion, May 28, 1992.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Cytokine Roles in Hemolytic Transfusion Reactions", National Institutes of Health, K08-HL02757.
- B. Principal Investigator, "Endothelial Cell Function in Transfusion Reactions", American Heart Association of Michigan, 46G923.

PROJECTS UNDER STUDY:

- A. Cytokine production in hemolytic transfusion reactions.
- B. Leukocyte-associated procoagulant activity induction in whole blood in response to ABO incompatibility.
- C. Endothelial cell expression of adhesion molecules and chemotactic cytokines in transfusion reactions.
- D. Endothelial cell expression of procoagulants and fibrinolytic activity in transfusion reactions.
- E. Safety and efficacy of solvent/detergent treated plasma.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Transfusion Committee.
- B. Quality Improvement Team in Outpatient Care.

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, "Indications for Blood Transfusion", Community Health Center of Branch County, Coldwater, Michigan, July, 1992.
2. Invited speaker, "Role of Cytokines in the Pathogenesis of Hemolytic Transfusion Reactions", American Society of Hematology Transfusion Medicine Subcommittee Symposium, Anaheim, California, December, 1992.
3. Invited Speaker, "Cytokine Roles in Hemolytic Transfusion Reactions", Harvard/Yale Update in Transfusion Medicine, Boston, Massachusetts, April, 1993.
4. Invited speaker, "Cytokine Roles in Hemolytic Ransfusion Reactions", California Blood Bank Society, Newport Beach, California, May, 1993.
5. Invited speaker, "Know Your Hemoflagellates, the Other Transfusion Transmitted Diseases", Chicagoland Blood Bank Society, Chicago, Illinois, May, 1993.
6. Invited speaker, "Transfusion Reactions", Quad State Blood Bank Society, Chicago, Illinois, May, 1993.
7. Invited speaker, "Transfusion Reactions", Heart of America Association of Blood Banks, St. Louis, Missouri, June, 1993.
8. Invited speaker, "Cytokine Production in IgG-mediated Red Cell Incompatibility", Invitational Conference of Investigative Immunohematologists, Minneapolis, Minnesota, June, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Davenport, R.D., Burnie, K.L. and Barr, R.M.: Transfusion management of patients with IgA deficiency and anti-IgA during liver transplantation. *Vox Sang.* 1992;63:247-250.
2. Davenport, R.D., Burdick, M., Moore, S.A. and Kunkel, S.L.: Cytokine production in IgG mediated red cell incompatibility. *Transfusion* 1993;33:19-24.
3. Rolfe, M.W., Paine, R., Davenport, R.D. and Strieter, R.M.: Hard metal pneumoconiosis and the association of tumor necrosis factor-alpha. *Am. Rev. Resp. Dis.* 1992;146:1600-1602.
4. Yamamoto, F., McNeill, P.D., Yamamoto, M., Hakomori, S., Harris, T., Judd, W.J. and Davenport, R.D.: Molecular genetic analysis of the ABO blood group system: 1. Weak subgroups: A3 and B3 alleles. *Vox Sang.* 1993;64:116-119.

5. Kaldjian, E.P., Jin, L., Davenport, R.D. and Lloyd, R.V.: Immunohistochemical analysis of hormone receptors, tumor vascularity and proliferative activity in paraffin-embedded sections of breast carcinoma tissues. *Appl. Immunohistochem.* 1993;1:31-38.

ABSTRACTS:

1. Davenport, R.D., Burdick, M., Strieter, R.M. and Kunkel, S.L.: Interleukin-1 receptor antagonist (IL-1ra) production in IgG mediated hemolysis. *Transfusion* 1992;34:45S.
2. Davenport, R.D. and Kunkel, S.L.: Leukocyte procoagulant activity induced by ABO incompatibility. *Transfusion* 1992;34:53S.
3. Davenport, R.D., Burdick, M. and Kunkel, S.L.: Endothelial cell activation in hemolytic transfusion reactions. *Transfusion* 1992;34:53S.
4. Moore, S.A., Lukacs, N., Davenport, R., Kasama, T. and Kunkel, S.: Constitutive expression of IRAP in inflammatory cells. *FASEB J.* 1993;7:A161.
5. Hagaman, D.D., Kindt, G.C., Moore, S.A., Davenport, R. and Gadek, J.E.: The effect of Fc receptor cross-linking on monocyte interleukin-8 release. *Am. Rev. Resp. Dis.* 1993;147:A753.

—

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Graduate students:

1. Responsible during the current academic year for teaching activities for the following:
 - a. Instructor and Course Coordinator: "Advanced Topics in Toxicology: Toxicologic Pathology".
 - b. Instructor: "Fundamentals in Electron Microscopy".
 - c. Student Training and Doctoral Committees.
 - d. Joint Student Training in Pharmacology and Toxicology with Florida A&M School of Pharmacy, Toxicology Program.
 - e. 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, including a co-sponsored program with the Medical Research Council of Canada.
- B. Collaborates with K. Johnson in developing morphometric models for the evaluation of pathologic changes.
- C. Consultation with Dr. Ward and colleagues regarding application of morphometric techniques.

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, Steering Committee of External Advisors, Wayne State University Institute of Chemical Toxicology.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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

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. "Delayed-type Hypersensitivity Testing in Cynomolgus Monkeys", Society of Toxicology, New Orleans, Louisiana, March 1993.
4. "Quantitative Peroxisome Changes in Rat Liver with CI-981, an HMGCoA Reductase Inhibitor, Society of Toxicology, New Orleans, Louisiana, March 1993.
5. "Absence of K-ras Mutations in CI-945-Induced Pancreatic Lesions in Male Rats", American Association for Cancer Research, Orlando, Florida, May 1993.
6. "Toxicokinetics Interface in Toxicology Studies", Graduate Toxicology Program, University of North Carolina, Chapel Hill, April 1993.
7. "Histopathologic Findings in Rodents Treated Two Years with the Angiotensin Converting Enzyme Inhibitor, Quinapril Hydrochloride", 12th Symposium, Society of Toxicologic Pathologists, Arlington, Virginia, June 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. de la Iglesia, F.A., Gray, R.H. and McGuire, E.J.: Subcellular organelle biogenesis and dynamics in peroxisome proliferation. J. Am. Coll. Toxicol. 1992;11:343-348.
2. McGuire, E.J., Gray, R.H. and de la Iglesia, F.A.: Chemical structure-activity relationships: peroxisome proliferation and lipid regulation in rats. J. Am. Coll. Toxicol. 1992;11:353-361.
3. Bleavins, M.R., Brott, D.A., Alvey, J.D. and de la Iglesia, F.A.: Flow cytometric characterization of lymphocyte subpopulations in the cynomolgus monkey (*macaca fascicularis*). Vet. Immunol. Immunopath. 1993;37:1-13.

4. Brott, D.A., Alvey, J.D., Bleavins, M.R., de la Iglesia, F.A. and Lalwani, N.D.: Cell cycle dependent distribution of PCNA/Cyclin and cdc2 kinase in mouse lymphoma cell line. *J. Cell. Biochem.* 1993;53:1-11.

BOOKS/CHAPTERS IN BOOKS:

1. de la Iglesia, Felix: Perspective and future directions of toxicokinetics in drug development, in, Welling, P.G. and de la Iglesia, F.A. (eds), *Drug Toxicokinetics*, M. Dekker, New York, pp. 381-402, 1993.
2. Welling, P.G. and de la Iglesia, F.A. (eds), *Drug Toxicokinetics*, M. Dekker, New York, 1993.

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. *Am. J. Path.* Submitted, 1993.
2. Bleavins, M.R., de la Iglesia, F.A., White, K.L., McCay, J.A., Fouant, M.M. Stern, M.L.: B.A. s and A. E. Munson immunotoxicologic studies with the novel benzothioephene cell activation inhibitor CI-959 in rats and mice. *Fund. Appl. Toxicol.* Submitted, 1993.
3. Bleavins, M.R. and de la Iglesia, F.A.: Delayed-type hypersensitivity in cynomolgus monkeys. *Fund. Appl. Toxicol.* Submitted, 1993.

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*, In Press, 1993.
2. Gough, A., Sigler, R., Walker R. and de la Iglesia, F.A.: Pancreatic acinar cell tumors in Wistar rats treated with gabapentin. *Epilepsia*, In Press, 1993.
3. Bleavins, M.R. and de la Iglesia, F.A.: Delayed-type hypersensitivity testing in cynomolgus monkeys. *The Toxicologist* 1993;13:105.
4. Haskins, J., Lucas, J., Robertson, D., McGuire, E.J. and de la Iglesia, F.A.: Quantitative peroxisome changes in rat liver with CI-981, an HMGC_oA reductase inhibitor. *The Toxicologist* 1993;13:20.
5. Fowler, M.L., Sigler, R.E., de la Iglesia, F.A., Reddy, J.K. and Lalwani, N.D.: Absence of k-ras mutations in CI-945-induced pancreatic lesions in male rats. *Proceedings, American Association for Cancer Research* 1993;34:99.
6. 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 Pathology*, In Press, 1993.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Supervised the following graduate students: Muneesh Tewari, Akhilesh Pandey, Haining Shao, Mary Benedict, Beth McLaurine.
- C. Supervised the following post doctoral fellows: Vidya Sarma, Donna Osterhout, Aziz Qabar, Sandra Drake, Zhi Zing.
- D. Graduate School Pathology Course. Co-director with Dr. Kunkel.
- E. Cell and Molecular Biology course to clinical fellows.

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, "Thrombospondin Heparin Binding Domain and Platelet Function", #901217 - American Heart Association - Grant-in-Aid, 10% effort, \$35,000 current year; \$105,000 Total; 07/01/90-06/30/93.
- C. 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.
- D. 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.
- E. Principal Investigator, "Heparin and Aortic Smooth Muscle Cell Proliferation", NIH-1R01 HL4785701A1, 20% effort, Budget \$86,621 current year, \$421,592 Total, 08/01/92 - 07/31/95.
- F. Principal Investigator, "Novel Zinc Finger Protein that Inhibits TNF Cytotoxicity", NIH-9R01-CA61348, 20% effort, Budget \$163,278 current year, \$1,201,474 Total, Period 07/01/93 - 06/31/98.
- G. 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.
- H. 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.

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, Keystone Symposia on Molecular and Cellular Biology, Keystone, Colorado, 1992.
2. Invited Speaker, Emory University School of Medicine, Atlanta, Georgia.
3. Invited Speaker, FASEB, Anaheim, California, 1992.
4. Invited Speaker, 4th International TNF Congress, Veldhoven, The Netherlands, 1992.
5. Invited Speaker, Wyeth-Ayerst Research, Princeton, New Jersey, 1992.
6. Invited Speaker, Gordon Conference, Colby-Sawyer College, New London, New Hampshire, 1992.
7. Invited Speaker, Gordon Conference, Salve Regina, Rhode Island, 1992.
8. Invited Speaker, Duke University Medical Center, Durham, North Carolina, 1992.
9. Invited Speaker, FASEB, New Orleans, Louisiana, 1993.
10. Invited Speaker, Parke Davis, Ann Arbor, Michigan, 1993.
11. Invited Speaker, Scripps Research Institute, La Jolla, California, 1993.
12. Invited Speaker, Northwestern University, Evanston, Illinois, 1993.
13. Invited Speaker, Southwestern Medical Center, University of Texas, San Antonio, Texas, 1993.

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

1. Wolf, F.W., Marks, R.M., Sarma, V., Byers, M.G., Katz, R.W., Shows, T.B. and Dixit, V.M.: Characterization of a novel tumor necrosis factor- α induced endothelial primary response gene. *J. Biol. Chem.* 1992;267:1317-1327.
2. Laherty, C.D., O'Rourke, K., Wolf, F.W., Katz, R., Seldin, M.F. and Dixit, V.M.: Characterization of mouse thrombospondin 2 sequence and expression during cell growth and development. *J. Biol. Chem.* 1992;267:3274-3281.
3. Sarma, V., Wolf, F.W., Marks, R.M., Shows, T.B. and Dixit, V.M.: Cloning of a novel tumor necrosis factor- α inducible primary response gene which is differentially expressed in development and capillary tube-like formation *in vivo*. *J. Immunol.* 1992;144:3302-3312.
4. Opipari, A.W., Hu, H.M., Yabkowitz, R. and Dixit, V.M.: The A20 zinc-finger protein protects cells from TNF cytotoxicity. *J. Biol. Chem.* 1992;267:12424-12428.
5. Krikos, A., Laherty, C.D. and Dixit, V.M.: Transcriptional activation of the tumor necrosis factor- α inducible zinc finger protein, A20, is mediated by κ B. *J. Biol. Chem.* 1992;267:17971-17976.
6. Castle, V.P., Ou, X., O'Shea, S. and Dixit, V.M.: The induction of thrombospondin 1 by retinoic acid is essential for the early expression of the differentiated neuronal phenotype. *J. Clin. Invest.* 1992;90:1852-1858.
7. O'Rourke, K.M., Laherty, C.D. and Dixit, V.M.: Thrombospondin 1 and thrombospondin 2 are expressed as both homo and heterotrimers. *J. Biol. Chem.* 1992;267:24921-24924.
8. Laherty, C.D., Hu, H.M., Opipari, A.W., Wang, F. and Dixit, V.M.: The Epstein-Barr virus LMP1 gene product induces A20 zinc finger protein expression by activating NF- κ B. *J. Biol. Chem.* 1992;267:24157-24160.
9. Castle, V.P., Ou, X., O'Rourke, K. and Dixit, V.M.: Thrombospondin 1 expression confers serum and anchorage independent growth. *J. Biol. Chem.* 1993;268:2899-2903.
10. 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.* 1993;268:5032-5039.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Wolf, F.W., Sarma, V., Seldin, M., Drake, S., Suchard, S.J., Shao, H., O'Shea, K.S. and Dixit, V.M.: The tumor necrosis factor- α inducible primary response gene B94 is expressed in developing hematopoietic tissues and the sperm acrosome. *J. Biol. Chem.*
2. Tewari, M., Wolf, F.W., Seldin, M.F., O'Shea, K.S. and Dixit, V.M.: Murine sequence chromosomal localization and developmental expression of the tumor necrosis factor-inducible zinc finger protein, A20. *J. Biol. Chem.*
3. Qabar, A.N., Lin, Z., 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.*

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

- 1. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Characterization of Ceramic Drug Delivery Devices: The Effect of Various Temperature of Incubation on the Delivery of Biological Biomedical Sciences Instrumentation. (ISA, paper #92-0131). 1992;28:129-134.
- 2. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Controlled release of hydrophilic compounds by resorbable and biodegradable ceramic drug delivery devices. Biomedical Sciences Instrumentation (ISA, Paper #92, 0141). 1992;28:179-182.
- 3. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Regulation of fertility in male rodents by sustained delivery of testosterone from biodegradable ceramic devices. Proceedings of the 11th Southern Biomedical Engineering Conference, October 2-4, 1992, Memphis, Tennessee, John Ray (ed.), pp. 30-31, 1992.
- 4. Benghuzzi, H.A., England, B.G. Possley, R.M. and Bajpai, P.K.: The use of tricalcium phosphate ceramic reservoirs to deliver testosterone in adult castrated rams. Proceedings of the 11th Southern Biomedical Engineering Conference, October 2-4, 1992, Memphis, Tennessee, John Ray (ed.), pp. 28-29, 1992.
- 5. Benghuzzi, H.A., Bajpai, P.K. and England, B.G.: Sustained release of progesterone and estradiol in adult female rats by ALCAP delivery devices. Biomedical Sciences Instrumentation (ISA, 1993, paper #93-007). SPON:IEEE, J.D. Enderle (ed.), pp. 51-58, 1993.
- 6. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: *In vivo* sustained release of dihydrotestosterone and estradiol by ceramic delivery system (O-37803-0967-6/93 IEEE). The 12th Southern Biomedical Engineering Conference, April 2-4, 1993, New Orleans, Louisiana, Kirk J. Bundy (ed.), pp. 273-276, 1993.
- 7. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: TCPL delivery system and the effects of molecular structures of steroids on the release profiles (O-7803-0976-6/93 IEEE). The 12th Southern Biomedical Engineering Conference, April 2-4, 1993, New Orleans, Louisiana, Kirk J. Bundy (ed.), pp. 269-272, 1993.

8. I'Anson, H., Quint, E.H., Wood, R.I., England, B.G. and Foster, D.A.: The role of adrenal axis in inducing hypogonadotropism in the growth-restricted female lamb. *Biology of Reproduction*, In Press.
9. 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. *J. Clinical Materials (CMU-9201)*, In Press.
10. Benghuzzi, H.A., England and Bajpai, P.K.: The effects of density of the ceramic delivery devices on sustained release of androgens in castrated rats. *J. Clinical Materials*, In Press.

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

1. Benghuzzi, H.A., England, B.G., Possley, R.M. and Bajpai, P.K.: Histological evaluation of the fibrous capsule around the TCPL delivery system using adult rams. Presented at the Federation of American Societies of Experimental Biologists, March 28-April 1, 1993, New Orleans, Louisiana, A573 (Abstract #3324).
2. England, B.G., Benghuzzi, H.A. and Brownlee, B.E.: The effect of sex-steroid hormones on the modification of LDL and proliferation of aortic endothelial cells in culture. Presented at the Federation of American Societies of Experimental Biologists, March 28-April 1, 1993, New Orleans, Louisiana, A573 (Abstract #3958).
3. Benghuzzi, H.A., England, B.G. and Bajpai, P. K.: Sustained release of progesterone and estradiol in adult female rats by ALCAP delivery devices. Presented at the 30th Annual meeting of the Rocky Mountain Bioengineering Symposium, April 2-3, 1993, San Antonio, Texas.
4. Benghuzzi, H.A., England, G.B. and Bajpai, P.K.: Regulation of fertility in male rodents by sustained delivery of testosterone from biodegradable ceramic devices. Presented at the 11th Southern Biomedical Engineering Conference, October 2-4, 1992, Memphis, Tennessee, John Ray (ed.), pp. 30-31.
5. Benghuzzi, H.A., England, B.G., Possley, R.M. and Bajpai, P.K.: The use of tricalcium phosphate ceramic reservoirs to deliver testosterone in adult castrated rams. *Proceedings of the 11th Southern Biomedical Engineering Conference*, October 2-4, 1992, Memphis, Tennessee, John Ray (ed.), pp. 28-29.
6. Benghuzzi, H.A., England, B.G., Possley, R.M. and Bajpai, P.K.: One year long-term maintenance of testosterone levels in rams using an implantable ceramic delivery system. Presented at the Federation of American Societies of Experimental Biologists, April 5-9, 1992, Anaheim, California, Abstract #6338.
7. Benghuzzi, H.A., Possley, R.M., Bajpai, P.K. and England, B.G.: Suppression of luteinizing hormone and follicle stimulating hormone levels by sustained delivery of testosterone from TCPL in long-term castrated rams. Presented at the 7th Annual Meeting of RSP, November 6, 1992, Ann Arbor, Michigan.

8. Benghuzzi, H.A., Bajpai, P.K. and England, B.G.: Electron and light microscopy examination of fibrous capsule around the ceramic steroid delivery system. Presented at the 8th Annual Scientific Session of the Academy of Surgical Research, September 19-22, 1992, St. Charles, Illinois.
9. Daves, H.N., Williams, M.T., Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Sustained release of testosterone by ALCAP ceramic implants in rats: Behavior evaluation. Presented at the 8th Annual Scientific Session of the Academy of Surgical Research, September 19-22, St. Charles, Illinois.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. Autopsy Service.

II. TEACHING ACTIVITIES:

- A. Director, Resident Training Program.
- B. Graduate Program Committee (Chairman).
- C. Course Director - Pathology 600.
- D. Director - Component I: Medical Student Curriculum.
- E. Lecturer and Laboratory Instructor - Pathology 600.
- F. Coordinator - M1 Histopathology Sequence.
- G. Sequence Coordinator and Lecturer - ICS-600: Immunopathology.
- H. Associate Director - Sophomore Medical Student ICS Course (600/601).
- I. Coordinator, Department of Pathology Summer Clinical Program for Minority Medical Students.
- J. Pulmonary Pathology Conference (6 per year to Pulmonary Division - Internal Medicine).
- K. Lecturer - Microbiology and Immunology 624.
- L. Lecturer, Host Defense Sequence.
- M. Graduate Student Ph.D. Thesis Committee (3).
- N. Faculty Mentor - Baccalaureate Program for Pre-Medical Minority Students.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Mechanisms of Myocardial Ischemia/Reperfusion Injury", NIH-R01-HL44085.
- B. Principal Investigator, "Myocardial Ischemia and Reperfusion Injury", American Heart Association Grant-in-Aid.
- C. Co-Investigator, "Mechanisms and Genetic Regulation of Pulmonary Fibrosis", (S.H. Phan; Principal Investigator), NIH-5-R01-HL-28737.
- D. Co-Investigator, "Pharmacologic Studies on the Ischemic Heart", (B. Lucchesi, Principal Investigator), NIH-R01-HL-19782.

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. Department Photography Committee.

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

- A. NIH Site Visit, SCOR: Acute Lung Injury, San Francisco, California, 1993.
- B. AHA of Michigan, Grant Review Committee, 1993.
- 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.

INVITED LECTURES AND SEMINARS:

- 1. Chairperson, Symposium on Inflammatory Mediators Ischemic Injury, FASEB Meeting, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Brieland, J., Jones, M., Clarke, S., Warren, J. and Fantone, J.C.: Expression of monocyte chemoattractant protein-1 (MCP-1) by rat pulmonary alveolar macrophages during acute inflammatory lung injury. Am. J. Respir. Cell Mole. Biol. 1992;7:134-139.

2. DeForge L.E., Fantone, J.C., Kenney, J.S. and Remick, D.G.: Oxygen radical scavengers selectively inhibit interleukin-8 production. *J. Clin. Invest.* 1992;90:2123-2129.
3. Werns, S.W., Fantone, J.C., Ventura, A. and Lucchesi, B.R.: Myocardial glutathione depletion impairs recovery of isolated blood-perfused hearts after global ischemia. *J. Mol. Cell. Cardiol.* 1992;24:1215-1220.
4. Mickelson, J.K., Hoff, P.T., Homeister, J.W., Fantone, J.C. and Lucchesi, B.R.: High dose intravenous aspirin not low dose intravenous or oral aspirin, inhibits thrombus formation and stabilizes blood flow in experimental coronary vascular injury. *J. Am. Coll. Cardiol.* 1993;21:502-510.
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. Mol. Biol.*, In Press.

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. Wiggins, R., Fantone, J.C. and Phan, S.H.: Mechanisms of vascular injury, in, Tisher C., and Brenner, B. (eds), *Renal Pathology*. 2nd Edition, J.B. Lippincott Co. Publishers, 1993.
3. Walker, B.A.M. and Fantone, J.C.: Inflammation, in Sigal, L.H. and Ron, Y. (eds), *Basic and Clinical Immunology*, McGraw-Hill Publishers, 1993.

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

1. Crockett-Torabi, E., Wilson, A.M. and Fantone, J.C.: Activation of phospholipase D in human monocytes. *Society for Leukocyte Biology*, Charleston, South Carolina, 1992.
2. 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 macrophages during chronic inflammatory lung injury, *FASEB*, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology Rotations, July (2/4), August (2/4), September (1/4), October (2/4), February (2/4), March (2/4), June (2/4).
- B. Autopsy Rotation, June (1/4).

II. TEACHING ACTIVITIES:

- A. Pathology 600 Lectures:
 - 1. Pulmonary Pathology I - March 1, 1992.
 - 2. Pulmonary Pathology II - March 2, 1992.
 - 3. Pulmonary Pathology III - March 3, 1992.
 - 4. Pulmonary Pathology IV - March 4, 1992.
- B. Pathology 630:
 - 1. Respiratory Disease I - October 28, 1992.
 - 2. Respiratory Disease II - October 30, 1992.
- C. Residency Training:
 - 1. Diseases of the Chest I - November 10, 1992.
 - 2. Diseases of the Chest II - November 17, 1992.
 - 3. Diseases of the Chest III - November 24, 1992.
 - 4. Surgical Pathology Consultant's Conference, December, 1992 and April, 1993.
 - 5. Residents' Seminar (Pizza Seminar), October, 1992.
- D. Other educational activities:
 - 1. M4 student elective mentor, March, 1993.
 - 2. Pulmonary Pathology - Radiology Conference, Department of Radiology, April, 1992.
 - 3. Pulmonary Pathology - Radiology Conference, Department of Radiology, December, 1992.
 - 4. Pulmonary Pathology - Radiology Conference, Department of Radiology, September, 1992.
 - 5. Anatomic Pathology Journal Club Discussion Leader, February, 1993.
 - 6. Center for Research on Learning and Teaching Workshop: Introduction to Computer Graphics, October 29, 1992.
 - 7. Center for Research on Learning and Teaching Workshop: Producing Graphs with the Computer, November 5, 1992..
 - 8. Center for Research on Learning and Teaching Workshop: Developing Presentations with the Computer, November 12, 1992.
 - 9. Member, M-2 Respiratory Sequence Committee, 1992-1993.
 - 10. Course Director, M-4 Student Pathology Clerkships.
 - 11. Pathology Resident Mentor.

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. Co-Investigator, "Prognostic Markers of Urinary Bladder Cancer (RFACA 91-09)", H. Barton Grossman, M.D., Principal Investigator.
- C. Co-Investigator, "Role of Urothelial Cell Activation in Interstitial Cystitis (DK-91-04)", Monica Liebert, Ph.D., Principal Investigator.
- D. Co-Investigator, "Interstitial Lung Diseases - Specialized Center of Research (1 P50 HL - 46487-01)" Galen Toews, M.D., Principal Investigator.
- E. Co-Investigator, "Monoclonal Antibodies to Bladder Tumor Antigens", H. Barton Grossman, M.D., Principal Investigator.

PROJECTS UNDER STUDY:

- A. Measurement of Proliferating Cell Nuclear Antigen of low stage renal cell carcinoma and correlation with ploidy measurement and clinical outcome.
- B. Quantitation of immunochemically-determined estrogen and progesterone receptors of breast carcinomas.
- C. Interstitial lung disease: The influence of biopsy site on diagnosis.
- D. PCNA expression of preoperative esophageal biopsy samples: correlation with response to treatment and prognosis.
- E. Regional expression of Ki-67 activity in colonic polyps.
- F. CD 34 expression of solitary fibrous tumors of the pleura.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Interviewed House Officer Candidates, September, 1992-January, 1993.
- B. Coordinator, Senior Staff Service Rotations.
- C. Director, Surgical Pathology Fellowship Program.
- D. Member Credentials Committee (a Continuing Committee of the Medical Staff).
- E. Member Bylaws committee of the Arthur Purdy Stout Society, 1992 - present.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Reviewer, Annals of Thoracic Surgery.
- B. Reviewer, American Journal of Pathology.
- C. Reviewer, American Review of Respiratory Disease.

INVITED LECTURES/SEMINARS:

1. Guest Pathologist, Tri-State Thoracic Society, New Orleans, Louisiana, January, 1993.
2. Panelist, Pulmonary Pathology Specialty Conference, United States Canadian Division, International Academy of Pathology, New Orleans, Louisiana, March, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Flint A.: Interstitial lung disease. Adv. Pathol. Lab. Medicine, In Press.
2. Flint, A., Grossman, H.B., Liebert, M. and Lloyd, R.V.: DNA and PCNA content of renal cell carcinoma: Correlation with prognostic parameters. Amer. J. Clin. Pathol., In Press.
3. Liebert, M., Wedemeyer, G., Stein, J.A., Washington R., Jr., Faerber, G., Flint A. and Grossman, H.B.: Evidence for urothelial cell activation in interstitial cystitis. J. Urol. 1993;149:470-475.

SUBMITTED PUBLICATIONS:

1. Flint A. and Frank, T.S.: Cytomegalovirus detection in lung transplant biopsy samples by polymerase chain reaction. J Heart Lung Transplan. Submitted.
2. Park, J., Shinohara, N., Liebert, M., Noto, L., Flint A. and Grossman, H.B.: P-glycoprotein expression in bladder cancer. J. Urol., Submitted.

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

1. Liebert, M., Brozovich, M., Wedemeyer, G., Flint, A. and Grossman, H.B.: Differentiation in urothelial cells, abstract, American Urological Association Annual meeting, 1993.
2. King, T.E., Jr., Mortenson, R.L., Lynch, D.A., Waldron, J.A., Chericack, R.F.M., Thurlbeck, W.M., Colby, T.V., Flint, A. and Schwarz, M.I.: Respiratory bronchiolitis-associated interstitial lung disease, abstract, 7th International Colloquium on Pulmonary Fibrosis, Cambridge, England.
3. Silveira, S., Flint, A. and Lloyd, R.V.: Immunohistochemical expression of monoclonal antibody Ki-67 in dysplastic epithelium of the uterine cervix, abstract, ASCP Fall meeting.
4. Grossman, H.B., Liebert, M. and Flint, A.: Monoclonal antibody DD23 defines a new bladder tumor associated antigen. American Urological Association Annual Meeting, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology, including consultations on surgical gynecologic pathology from other hospitals and medical centers - 2062 cases.
- B. Necropsy Service - one week.
- C. Molecular Diagnostics for Anatomic Pathology.
- D. Weekly interdisciplinary Gynecologic Oncology Tumor Board Review.

II. TEACHING ACTIVITIES:

- A. Sequence coordinator for revised M2 curriculum (Oncology).
- B. Pathology 600 Lectures:
 - 1. Neoplasia (four hours), January 1993.
 - 2. Gynecology (three hours), March 1993.
- C. Introduction to Clinical Sciences 601 (one hour), January 1993.
- D. Preceptor for medical student research project under auspices of Biomedical Research Program: Genetic alterations in gynecologic malignancy (Rene Bartos, B.A.).
- E. Lecturer, two Anatomic Pathology Didactic Conferences.
- F. Monthly Pathology-Gynecology teaching conference for house officers in OB-GYN.
- G. Presentation of Grand Rounds to Department of Obstetrics and Gynecology: Pathology of the Endometrium, June 1993.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Consultant, "Linkage and Mapping of Breast Cancer to Chromosome 17", NIH Grant RO1 CA57601-01, 7/1/91-6/30/97.
- B. "Significance of Allelic Loss of p53 Tumor Suppressor Gene in Endometrial Neoplasia", University of Michigan Cancer Center Institutional Grant IRG-40-33, 4/1/92-3/31/93.
- C. "Molecular Analysis of Clonality", Horace H. Rackham Faculty Grant from the University of Michigan, 5/1/91-6/30/93.
- D. "Molecular Analysis of Clonality", Phoenix Memorial Research Grant from the University of Michigan, 4/18/91-6/30/92.

- E. "Genetic Markers in Gynecologic Malignancy", Harris Foundation, 1/1/92-1/1/94.
- F. Investigator, "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.

PROJECTS UNDER STUDY:

- A. Overexpression of p53 and HER2/neu in epithelial malignancies of endometrium (with Carolyn Johnston, M.D., Dept. of Obstetrics and Gynecology).
- B. Retrospective analysis of somatic and tumor-associated alterations of p53 gene in familial breast carcinoma (with Barbara L. Weber, M.D. and Francis S. Collins, M.D., Ph.D, Dept. of Internal Medicine).
- C. Mutations and losses of tumor suppressor genes in endometrial carcinoma (with Rosmarie Caduff, M.D., visiting research fellow).
- D. Identification of mycobacterial DNA in paraffin-embedded tissues using the polymerase chain reaction.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Surgical Pathology representative to the departmental quality assurance/quality control committee and specimen accession committee.

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. Member, American Association for the Advancement of Science.
- D. Member, American Society of Clinical Pathologists.
- E. Member, American Society of Human Genetics.
- F. Member, A. James French Society.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

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

INVITED LECTURES/SEMINARS:

1. Lecture, "Applications of PCR to Surgical Pathology", Bowman Gray School of Medicine, Winston-Salem, North Carolina, April 1993.
2. Workshop, "Molecular Probes in Diagnostic Pathology", Universities Associated for Research and Education in Pathology (UAREP), Inc, Aspen, Colorado, July 1992.

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

1. Carr, K.A., Roberts, J.A. and Frank, T.S.: Progesterone receptors in bilateral ovarian ependymoma presenting in pregnancy. *Human Pathology* 1992;23:962-965.
2. Stanley, J.J., Goldblum, J.S., Frank, T.S., Zelenock, G.B. and D'Alecy, L.G.: Attenuation of renal reperfusion injury in rats by the 21-amino steroid U74006F. *J. Vascular Surg.* 1993;16:685-689.
3. Ethier, S.P., Meahacek, M.L., Gullick, W.J., Frank, T.S. and Weber, B.L.: Differential isolation of normal luminal mammary epithelial cells and breast cancer cells from primary and metastatic sites using selective media. *Cancer Res.* 1993;53:627-635.
4. Frank, R.S., Frank, T.S., Zelenock, G.B. and D'Alecy, L.G.: Intermittent reperfusion reduces functional and morphologic damage following renal ischemia in the rat. *Ann. Vascular Surg.* 1993;7:150-155.
5. Chamberlain, J.S., Boehnke, M., Frank, T.S., Kiouisis, S., Xu, J., Guo, S.-W., Hauser, E.R., Norum, R.A., Helmbold, E.A., Markel, D., Keshavarzi, S., Jackson, G., Calzone, K., Garber, J., Collins, F.S. and Weber, B.L.: Further narrowing of the BRCA1 region on chromosome 17q12-21 by genetic analysis. *Amer. J. Human Genetics* 1993;52:792-798.
6. Helvie, M.A. and Frank, T.S.: Enhancing breast metastases from bronchial neuroendocrine (carcinoid) carcinoma. *Breast Disease, an International Journal*, 1993;6:233-236.
7. Frank, T.S., Reed, J.C. and Brooks, J.J.: Absence of *c-sis* and transforming growth factor- β mRNA expression in malignant fibrous histiocytoma. *Surg. Pathol.* 1993;5:141-150.
8. Cook, S.M., Himebaugh, K.S. and Frank, T.S.: Absence of cytomegalovirus in gestational tissue in recurrent spontaneous abortion. *Diagnostic Molecular Pathology* 1993;2:116-119.
9. 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.*, In Press.
10. Perosio, P.M. and Frank, T.S.: Detection of mycobacteria in paraffin-embedded lung biopsies by the polymerase chain reaction. *Amer. J. Clin. Pathol.*, In Press.

11. 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 Pathol*, In Press.
12. 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. *Inter. J. Gynecol. Cancer*, In Press.
13. 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. *Radiology*, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Cook, S.M., Bartos, R.E., Pierson, C.L. and Frank, T.S.: Detection and characterization of atypical mycobacteria by the polymerase chain reaction.
2. 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.
3. Flint, A. and Frank, T.S.: Polymerase chain reaction detection of cytomegalovirus in lung transplant biopsy samples.
4. Ikeda, D.M., Frank, T.S. and Marn, C.S.: Case report: Lymphoma of the breast.
5. 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.
6. Elson, B.C., Helvie, M.A., Frank, T.S., Wilson, T.E. and Adler, M.D.: Tubular carcinoma of the breast: Mammographic appearance with sonographic and clinical correlation.
7. Pearl, M.L., Johnston, C.J., Frank, T.S. and Roberts, J.A.: Synchronous dual primary ovarian and endometrial carcinomas.

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

1. Cook, S.M. and Frank, T.S.: Detection and characterization of atypical mycobacteria by the polymerase chain reaction. *Modern Pathol.* 1993;6:104A. (Winner, Binford-Dammin Award for infectious disease research and Stowell-Orbison Certificate of Merit).
2. Goldblum, J.R., Carr, K.A. and Frank, T.S.: Overexpression and loss of heterozygosity of p53 tumor suppressor gene in hepatocellular carcinoma. *Modern Pathol.* 1993;6:110A.
3. Elson, B.C., Helvie, M.A., Frank, T.S., Wilson, T.E. and Adler, M.D.: Tubular carcinoma of the breast: Mammographic appearance with sonographic and clinical correlation. *American Roentgen Rays Society*, 1993.

4. Pearl, M.L., Johnston, C.J., Frank, T.S. and Roberts, J.A.: Synchronous dual primary ovarian and endometrial carcinomas. American College of Obstetricians and Gynecologists, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

DEPARTMENTAL:

- A. Co-Director of a laboratory section for Pathology 600.
- B. Teaching and supervision of nine Pathology house officers through two-week Pathology Data Systems rotations.

MEDICAL SCHOOL/HOSPITALS:

- A. Program Director of the Eleventh Annual Clinical Laboratory Computer Symposium at the Towsley and Power Centers, June 9-11, 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. Friedman, B.A., Mitchell, W., Singh, K.: Differentiating between marketing-driven and technology driven vendors of medical information systems. Submitted to Archives of Pathology and Laboratory Medicine.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Quality Assurance Committee.
- B. Editor, Pathology Electronic News (PEN).
- C. Clinical Laboratory Directors Committee.

HOSPITAL:

- A. Applied Clinical Informatics Consortium.
- B. Physicians PCIS Task Force.
- C. PCIS Core Committee.

UNIVERSITY:

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

REGIONAL AND NATIONAL:

- A. Council on Medical Informatics of the American Society of Clinical Pathologists.
- B. Member-elect, CAP Committee on Informatics.
- C. Past-Chairman of the Executive Council, Cerner Users' Group.
- D. Editorial Advisory Board, Clinical Laboratory Management Review.
- E. American Board of Pathology ad hoc committee to consider developing a proposal to examine candidates in Medical Informatics and Laboratory Management.
- F. American Board of Pathology, Informatics Test Committee.
- G. Clinical Laboratory Management Association (CLMA) Task Force on Medical Informatics.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. "The Evolving Role of the Medical Technologists in Information Management", an audioconference sponsored as part of a course on "Computers in Clinical Laboratory Science" by the Department of Biology, Catholic University of America, Washington, D.C., July 23, 1992.
2. Lecture, "The Pathologist as Information Manager", Annual meeting of the American Pathology Foundation entitled "Pathology in Transition: Changing Roles for Changing Times," Vancouver, British Columbia, Canada, August 21, 1992.
3. Lecture, "Information Management in Hospitals: A Departmental Perspective", Symposium entitled "The Information Management Executive", sponsored by HIMMS, CHIM, and the University of Michigan Department of Health Services Management and Policy, the University of Michigan, Ann Arbor, Michigan, October 22, 1992.
4. "Managing the Information Product of Pathology", Pathology Update '92, American Society of Clinical Pathologists, Atlanta, Georgia, November 5, 1992.
5. "Planning for Your Laboratory in the Year 2000: Technology in the Year 2000", a VHA/CLMA Video Satellite Network Presentation, Dallas, Texas, February 3, 1993.
6. Workshop, "Managing the Information Product of Pathology", Presented with J. Robert Beck at the ASCP Spring Meeting, Chicago, Illinois, March 30, 1993.
7. Keynote Speaker, "Managing the Information Product of Pathology: A Technological and Organizational Perspective", St. Joseph's Institute of Laboratory Medicine Symposium, London, Ontario, Canada, April 29, 1993.
8. Lecture, "Information Management in Hospitals: A Departmental Perspective", Symposium entitled "The Information Management Executive", sponsored by HIMMS, CHIM, and the University of Michigan Department of Health Services Management and Policy, the University of Michigan, Ann Arbor, Michigan, May 6, 1993.
9. Lecture and Workshop, "Managing a Laboratory Information System: An Operational and Strategic Approach. Information Management in the Clinical

Laboratory in the Year 2000", Tenth Annual Laboratory Information System Symposium, Ann Arbor, Michigan, June 9, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Friedman, B.A. and Mitchell, W.: Integrating information from decentralized laboratory testing sites: The creation of a value-added network. Amer. J. Clin. Pathol. 1993;99:637-642.

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

1. Friedman, B.A. and Barnes, B.W.: Client-server design provides model for 'coopetition' alliances. Comp. Healthc. 1992;September:38-39.
2. Friedman, B.A. and Napolitan, E.J.: A second look at some clinical laboratory dogma. Med. Lab. Obs. (MLO) 1993;March:53-55.
3. Friedman, B.A.: Flounder factors and the laboratory information system. Vision. 1993;March/April:13-15.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. Director, General Chemistry Laboratory.
- B. Daily sign-out and interpretation of electrophoresis results.
- C. Direct operation of blood gas-electrolyte analyzers in operating rooms of Main and Mott Hospitals.
- D. Direct work group 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 Clinical Pathology 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.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Evaluation of myoglobin as a marker for myocardial infarction.
- B. Evaluation and standardization of an assay for Lipoprotein (a).
- C. Evaluation of new methods for drugs of abuse testing.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

- A. Glucose Monitoring/Bedside Testing Work Group.

REGIONAL AND NATIONAL:

- A. Chairman, Michigan Section, AACC.
- B. Coordinator, College of American Pathologists Clinical Chemistry Standards Assay Laboratory.
- C. Lipids and Lipoproteins Division, AACC.
- D. Education Committee, Michigan Section, AACC.
- E. Member, Clinical Ligand Assay Society.
- F. Member, American Association of Pathologists.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. "Evaluation of the Roche ONLINE Drugs of Abuse Testing Reagents", Practical Review of TDM and Toxicology, Detroit, Michigan, November, 1992.
- 2. "Evaluation of the CK-MB Assay on the Opus Plus", PB Diagnostics, Westwood, Massachusetts, February, 1993.
- 3. "Biochemical Markers for Myocardial Infarction", Department of Chemistry and Biochemistry, University of Windsor, April, 1993.

VI. PUBLICATIONS:

ARTICLES SUBMITTED FOR PUBLICATION:

- 1. Giacherio, D. and Annesley, T.: Evaluation of a new solid phase test system for detecting drugs of abuse in urine. *Therapeutic Drug Monitoring and Toxicology*.
- 2. Spengler, R.N., Chensue, S.C., Giacherio, D.A., Blenk, N. and Kunkel, S.L.: Endogenous norepinephrine regulates tumor necrosis factor alpha production from macrophages *in vitro*.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology - Room I and Room II, nine weeks.
- B. Diagnostic Electron Microscopy - share nephropathology work with Drs. Kent Johnson and Paul Killen.
- C. Consultation service for Uropathology.
- D. Conduct monthly conference in Urologic Pathology with Urology Section.
- E. Participate in weekly Renal Biopsy Conference for Nephrology Section with Drs. Kent Johnson and Paul Killen.
- F. Frozen Section "on call" Rotation, seven weeks.
- G. Consultant, Veterans Administration Hospital.
- H. Autopsy Service, one week

II. TEACHING ACTIVITIES:

- A. Lectures to Sophomore Pathology 600 students:
 - 1. Death certification and forensic pathology.
 - 2. Pathogenesis of highway injuries.
 - 3. Renal neoplasms and renal allograft rejection.
 - 4. Diseases of prostate and external genitalia.
 - 5. Testicular disease.
- B. Lecture on Urologic Pathology to Dental Pathology 630 students.
- C. Pathology Resident Teaching.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Collaborating with urology staff and a pathology resident (Cheryl Utiger) on a study to estimate the size of prostatic adenocarcinoma based on the number of random needle biopsy cores involved.
- B. Correlating histopathology of prostatic intraepithelial neoplasia with ultrasonic imaging with two pathology residents (Patricia Perosio and Walter Henricks).

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

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Francis, I.R. and Gikas, P.W.: Metastatic transitional cell carcinoma simulating primary ovarian malignancy. *Urologic Radiology* 1992;14:214-217.
2. Gikas, P.W., Del Buono, E.A. and Epstein, J.I: Florid hyperplasia of mesonephric remnants involving prostate and periprostatic tissue: Possible confusion with adenocarcinoma. *Amer. J. Surg. Path.* 1993;17:454-460.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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 600 course.

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 Drs. Gary and Elizabeth Nabel, Department of Internal Medicine).
- D. Immunosuppressive modifications of transplant rejection (collaborative research with Drs. Larry Turka and Hua Lin in the Departments 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 cell proliferation and collagen gene expression in fibromuscular dysplasia (collaboration with Dr. James Stanley, Peripheral Vascular Surgery).

SPONSORED SUPPORT:

- A. Principal Investigator, "Proliferation and Growth Factors in Atherosclerosis", National Institutes of Health, HL42119, five years, \$710,820, 1988-1993.
- 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", American Heart Association 93013780, three years, \$120,000, 1993-1996.
- D. Principal Investigator, "The Patterns of Collagen Synthesis During Arterial Restenosis", American Heart Association, 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 Fellowship Review Committee.
- B. American Heart Association of Michigan Grant-in-Aid Review Committee.
- C. NIH NHLBI ad hoc Grant Review Committee: Special Emphasis Panel on Women's Health RFA. May, 1993.
- D. United Network for Organ Sharing (UNOS) Minority Advisory Committee.

INVITED LECTURES/SEMINARS:

1. Invited speaker, University of Virginia Medical School Minority Student Summer Program, July, 1992.
2. Invited speaker, University of Alabama Vascular Biology Retreat, October, 1992.
3. Invited speaker, American Heart Association Meeting, New Orleans, Louisiana, November, 1992.
4. Invited speaker, University of Washington, Conference on Arterial Restenosis, Stephen M. Schwartz, organizer, February 1-2, 1993.
5. Invited speaker, Parke-Davis Seminar Series, April 15, 1993.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Rekhter, M., Nichols, S., Ferguson, M. and Gordon, D.: Cell proliferation in human arteriovenous fistulas used for hemodialysis. *Arteriosclerosis and Thrombosis* 1993;13:609-617.
2. Turka, L.A., Linsley, P.S., Lin, H., Brady, W., Leiden, J.M., Wei, R., Gibson, M.L., Zheng, X., Myrdal, S., Gordon, D., Bailey, T., Bolling, S.F. and Thompson, C.B.: T-cell activation by the CD28 ligand B7 is required for cardiac allograft rejection *in vivo*. *Proc. Natl. Acad. Sci. USA* 1992;89:11102-11105.

3. Allen, M.D., Shoji, Y., Fujimura, Y., Gordon, D., Thomas, R., Brockbank, K.G. and Disteche, C.M.: Growth and cell viability of aortic versus pulmonic homografts in the systemic circulation. *Circulation* 1991;84:III94-99.
4. Allen, M.D., McDonald, T.O., Carlos, T., Himes, V., Fishbein, D., Aziz, S. and Gordon, D.: Endothelial adhesion molecules in heart transplantation. *J. Heart Lung Transplant* 1992;11:S8-13.
5. Nabel, E.G., Gordon, D., Yang, Z., San, H., Plautz, G.E., Gao, H., Huang, L. and Nabel, G.J.: Gene transfer *in vivo* with DNA-liposome complexes: Lack of autoimmunity and gonadal expression. *Human Gene Therapy* 1992;3:649-656.
6. Gordon, D.: Cell proliferation in human arteries. *Cardiovascular Pathology*. 1992;1:259-262.
7. Finta, K.M., Fischer, M.J., Lee, L., Gordon, D., Pitt, B. and Webb, R.C.: Ramipril prevents impaired endothelium-dependent relaxation in arteries from rabbits fed an atherogenic diet. *Atherosclerosis* 1993;100:149-156.
8. Nabel, E.G., Yanz, Z., Liptay, S., San, H., Gordon, D., Haudenschild, C.C. and Nabel, G.J.: Recombinant platelet-derived growth factor B gene expression in porcine arteries induces intimal hyperplasia *in vivo*. *J. Clin. Invest.* 1993;91:1822-1829.
9. O'Brien, E.R., Alpers, C.E., Stewart, D.K., Ferguson, M., Tran, N., Gordon, D., Benditt, E.P., Hinohara, T., Simpson, J.B. and Schwartz, S.M.: Proliferation in primary and restenotic coronary atherectomy tissue: Implications for antiproliferative therapy. *Circ. Res.* 1992;73:223-231.
10. Nabel, E.G., Shum, L., Pompili, J.V., Yang, Z.Y., San, H., Shu, H.B., Liptay, S., Gold, L., Gordon, D., Derynck, R. and Nabel, G.J.: Direct gene transfer of transforming growth factor b1 into arteries stimulates fibrocellular hyperplasia. *Proc. Natl. Acad. Sci. USA*, In Press, 1993.

ABSTRACTS:

1. Rekhter, M.D., Kai, Z., Phan, S.H. and Gordon, D.: Type I collagen gene expression in human atherosclerosis: Localization to specific plaque regions. *FASEB J* 1992;7:A785.

**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 1992 - 30 JUNE 1993**

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).
- B. Graduate Level Advisement:
 - a. John C. Fat - MSD Program (Endodontics) - 3.5 years.
 - b. Craig MacKenzie - MSD Program (Endodontics) - 2 years.
 - c. Nahed Mohsen - PhD Program (Engineering) - 2 years.
 - d. Pin-Pin Lin - PhD Program (School of Public Health) - one year.
 - e. Rod Parsell - Summer Research Program (School of Dentistry) - 5 years.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Director and Principal Investigator for one of four projects, "Specialized Materials Science Research Center", NIDR, 25% for this last year (10% of this is cost-shared with the dental school), \$2,657,883 for direct costs, total period, 9/29/89-9/28/94.
- B. Participating Investigator, "Restorative Dental Materials", Training Grant, NIDR, 10% for this last year, \$258,586 for direct costs, total period, 7/1/91-6/30/95.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director of Research, School of Dentistry, 1989-1993.
- B. Admissions Committee, School of Dentistry, 1985-1993.
- C. Hazardous Waste Committee, School of Dentistry, 1987-1993, Chairman.
- D. Table Clinics Committee, 1989-1993.

- E. Organizer of Specialized Materials Center Fall Conference, 1990 -1993.
- F. Biomedical Research Council, University of Michigan Medical School, 1990-1993.
- G. Research Advisory Committee, Department of Surgery, University of Michigan Medical School, 1990-1993.
- H. Research Dean's Committee (OVPR, U/M), 1989-1993.
- I. Chair, Search Committee for Biomaterials faculty, 1992-1993.
- J. Research Space Utilization Committee, Dental School, 1991-1993.

REGIONAL AND NATIONAL:

- A. ADA Subcommittee on Biological Evaluation of Dental Materials (Committee Member), 1987-1993.
- 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), 1989-1993.
- C. Constitution Committee for American Association for Dental Research, 1991-1993.
- D. External Review Board for NIDR Program Project in Materials Science, University of Missouri at Kansas City.

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, 1988-1991.
- 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., Wataha, J.C., Parsell, R.R. and Strawn, S.E.: Delineation of cytotoxic concentrations of two dentin bonding agents in vitro. J. Endodontics. 1992;18:589-596.

2. Wataha, J.C., Craig, R.G. and Hanks, C.T.: The effects of cleaning on the kinetics of invitro metal release from dental casting alloys. *J. Dent. Res.* 1992;71:1417-1422.
3. Wataha, J.C., Hanks, C.T. and Craig, R.G.: In vitro synergistic, antagonistic, and duration of exposure effects of metal cations on eukaryotic cells. *J. Biomed. Mat. Res.* 1992;26:1297-1309.
4. Wataha, J.C., Hanks, C.T. and Craig, R.G.: Uptake of metal cations by fibroblasts in vitro. *J. Biomed. Mat. Res.* 1993;27:227-32.
5. Wataha, J.C., Craig, R.G. and Hanks, C.T.: Precision of and new methods for testing in vitro alloy cytotoxicity. *Dent. Mat.* 1992;8:65-71.
6. Wilmot, J.J., Chiego, D.J., Carlson, D.S., Hanks, C.T. and Moskwa, J.J.: Autoradiographic study of the effects of pulsed electromagnetic fields on bone and cartilage growth in juvenile rats. *Arch. Oral Biol.* 1993;38:67-74.
7. 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.*, In Press.

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

1. Hanks, C.T. and Ferracane, J.L.: Symposium: Cytotoxicity of materials through dentin. *J. Dent. Res.* 72 (sp.iss.) Abst. #1373 pg. 275, 1993.
2. Hanks, C.T.: Permeability of biological and synthetic molecules through dentin. *J. Dent. Res.* 72 (Sp.iss.) Abst. #1378, pg. 275, 1993.
3. Wataha, J.C., Hanks, C.T. and Craig, R.G.: Effect of cell density on metal ion cytotoxicity in vitro. *J. Dent. Res.* 72(sp.iss.) Abst. #2108, pg. 367, 1993.
4. Dahlgren, J.A., Syed, S.A. and Hanks, C.T.: In vitro adhesion of oral bacteria to three biomaterials. *Amer. Soc. Microbiol. National Meeting, Fall, 1992.*
5. Nassiri, M.R., Hanks, C.T. and Craig, R.G.: Flow cytometric evaluation of cellular RNA in UDMA and bis-GMA-exposed mammalian cells. *J. Dent. Res.* 71 (sp.iss.) Abst. #878, pg. 625, July, 1992.
6. Dahlgren, J.A., Hanks, C.T., Syed, S., Dootz, E. and Koran, A.: In vitro evaluation of soft denture liners and maxillofacial materials. *J. Dent. Res.* 72 (sp.iss.) Abst. #194, pg. 128, 1993.
7. Hanks, C.T. and Jontell, M.: Effects of monomeric resin components on pulpal cell-induced T-lymphocyte proliferation. *J. Dent. Res.* 72 (sp.iss.) Abst. #856, pg. 210, 1993.
8. Parsell, R.R., Hanks, C.T. and Wataha, J.C.: Quantifying the molecular adsorptive capacity of dentin disks. *J. Dent. Res.* 72 (sp.iss.) abst. #180, pg. 126, 1993.
9. Sun, Z.L., Wataha, J.C. and Hanks, C.T. Effects of Ti^{+4} and Co^{+2} on osteoblast-like cell metabolism. *J. Dent. Res.* 72(sp.iss.) Abst. #2296, pg. 383, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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. Unclassified malignant cutaneous neoplasms of neural crest origin.
- B. 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. Founders Award, The American Society of Dermatopathology.

INVITED LECTURES AND SEMINARS:

1. Invited Speaker, Oregon Dermatology Society, Ashland, Oregon, August, 1992.
2. Invited Presentation, Seminar in Dermatopathology, XIX International Congress of the International Academy of Pathology, Madrid, Spain, October, 1992.
3. Invited Speaker, Slide seminar on problematic pigmented lesions, Alabama Association of Pathologists, Birmingham, Alabama, November, 1992.
4. Invited Presentation, "A Tutorial in the Diagnosis of Alopecias", American Society of Dermatopathology, San Francisco, California, December, 1992.
5. Invited Speaker, International Course in Dermatopathology, Barcelona, Spain, February, 1993.
6. Invited Speaker, Johnson and Johnson, Raritan, New Jersey, March, 1993.
7. Visiting Professor and Lecturer, University of California, San Francisco, May, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Regezi, J.A., Nickoloff, B.J. and Headington, J.T.: Oral submucosal dendrocytes: factor XIIIa+ and CD34+ dendritic cell populations in normal tissue and fibrovascular lesions. *J. Cutan. Pathol.* 1992;19:398-406.
2. Bulengo-Ransby, S., Headington, J.T., Gonzalez, C.E., et al: Staphylococcal botryomycosis and hyperimmunoglobulin E (Job) syndrome in an infant. *J. Am. Acad. Dermatol.* 1993;28:109-111.
3. Utiger, C.A. and Headington, J.T.: Psammomatous melanocytic schwannoma: A new cutaneous marker for Carney's complex. *Arch. Dermatol.* 1993;129:202-205.
4. Headington, J.T.: Telogen effluvium: Review and new concepts. *Arch. Dermatol.* 1993;356-363.
5. Goldblum, J.R. and Headington, J.T.: Hypophosphatemic vitamin D-resistant rickets and multiple spindle and epithelioid nevi associated with linear nevus sebaceous. *J. Am. Acad. Dermatol.* 1993;29:109-111.

BOOKS/CHAPTERS IN BOOKS

1. Headington, J.T.: Dermal Dendrocytes in Dermal Immune System. Nickoloff, B. (ed), CRC Press, Boca Raton, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. Pediatric Surgical and Placental Pathology, daily, six months.
- B. Pediatric Necropsies, daily, six months.
- C. Pediatric Consultation Cases, daily, six 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.) (Six months due to sabbatical leave)
- H. Sabbatical leave, six months, January 1 to June 30, 1993.

II. TEACHING ACTIVITIES:

- A. M2: Pathology 600, two whole class lectures on Pediatric Pathology.
- B. M4: Surgical Pathology, six months, while they were on their pathology electives.
- C. House Officers in Pathology, daily reading of pediatric surgicals, six months.
- D. House Officers in Pathology, gross and microscopic supervision of most pediatric necropsies, six months, and adult cases, 0.50 months plus on-call weekends.
- E. Surgical Pathology Conference, one hour/week, six months.
- F. Lecture on Pediatric Necropsy Pathology in Orientation for House Officers in Pathology.
- G. Gross Necropsy Conference, one hour/week, six months.
- H. Supervised Pediatric Hematology Fellows (two) for AP elective period.
- I. Conferences: Faculty, House staff and students:
 - 1. Pediatric Cardiology Death Conference, monthly, six months.
 - 2. Pediatric Tumor Conference, twice monthly, six months.
 - 3. Pediatrics CPC/General Death Conference, twice.
 - 4. Pediatric Liver-GI Conference, twice a month for six months.
 - 5. Pediatric General Surgery Conference monthly for six months.

III. RESEARCH ACTIVITIES:

- A. Continued study of effects of various congenital heart defects on the pulmonary vasculature.
- B. Study with pediatric cardiologists and thoracic surgeons of effects of various stents and therapeutic manipulations on different stenotic vessels. (See papers).

- C. Histopathological component of lung changes associated with various cardiopulmonary therapeutic support mechanisms.

PROJECTS UNDER STUDY:

- A. PCR amplification of A. fipia from formalin fixed tissues of histologic cat scratch disease.
- B. Study of the differential development of renal tubules and glomeruli in twin fetuses and newborns with Mason Barr, M.D.
- C. Review of the predictive value of pre-ECMO lung biopsy in determining survival and recovery of pulmonary function (Group study, pathologists, surgeons, pediatricians).
- D. Correlating clinicopathologic study of histopathology of pediatric aneurysmal bone cysts with clinical recurrence risk, with pediatric orthopedic surgeons. (See abstracts and papers.)
- E. Correlation of histopathologic classification of neuroblastoma cell/tumor maturity with different tissue gene expressions. (See papers.)
- F. Multi-institutional study of molecular variants of congenital alveolar proteinosis caused by inherited surfactant protein B deficiency.
- G. Study of the occurrence of early mucosal colitis as a predictor of future enterocolitis in patients with Hirschsprung's disease-with pediatric surgeons.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

- A. Executive Committee for Mott/Women's/Holden/Psychiatric Hospitals.
- B. 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.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Beekman, R.H., Muller, W.W.M., Reynolds, P.I., Moorehead, D., Heidelberger, K.P. and Lupinetti, F.M.: Balloon expandable stent treatment of experimental coarctation of the aorta: Early hemodynamic and pathological evolution. J. Interven. Cardiol., In Press.
2. 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.
3. Castle, V.P., Heidelberger, 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., In Press.
4. Freiberg, A.A., Loder, R.T., Heidelberg, K.P. and Hensinger, R.N.: Aneurysmal bone cysts in young children. J. of Pediatr. Orthoped., In Press.

ABSTRACTS:

1. Freiberg, A.A., Loder, R.T., Heidelberg, K.P. and Hensinger, R.N.: Aneurysmal bone cysts in young children. Presented at the American Academy of Pediatrics, Orthopedic Surgery Section, San Francisco, California, October, 1992.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1992- 30 JUNE 1993

I. CLINICAL ACTIVITIES:

- A. With C.J. D'Amato prepare microscopic descriptions of most UM 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. Neural and Behavioral Sciences 600 for second year medical students - two hours of lecture on neuropathology.
- C. 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. Foster, N.L., Gilman, S., Berent, S., Sima, A.A.F., D'Amato, C.J., Koeppe, R.A. and Hicks, S.P.: Progressive subcortical gliosis and progressive supranuclear palsy can have similar clinical and PET abnormalities. J. Neurol. Neurosurg, Psychiatry, 1992;55:707-713.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Lecturer Genitourinary Pathology - Second year pathology course.
- B. Lectures on Renal Pathology - Nephrology Fellows.
- C. Lectures on Renal and Skin Immunopathology - Pathology Residents.
- D. Lectures on Genitourinary Pathology - Dental Pathology Course.
- 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. Principal Investigator, "Crescentic Nephritis Program Project", Core B, National Institutes of Health, \$204,490.

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, "DNA Methylation and SLE", with Bruce Richardson, Rheumatology, National Institutes of Health.
- C. 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.
- E. Chairman's Advisory Committee.

REGIONAL AND NATIONAL:

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

V. INVITED LECTURES AND SEMINARS:

1. Visiting Professor, Emory University, Division of Hematology/Oncology.
2. Invited Speaker, Symposium on Oxygen Radicals and Tissue Injury, New York Academy of Sciences.
3. Visiting Professor, University of Basle, Basle, Switzerland.

VI. OTHER RELEVANT ACTIVITIES:

- A. Consultant on Dermatology and Nephrology training grants.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Weinberg, J.M., Varani, J., Johnson, K.J., Rosser, N.F., Dame M.K., Davis, J.A. and Venkatachalam, M.S.: Protection of human umbilical vein endothelial cells of glycine and structurally similar amino acids against calcium and hydrogen peroxide-induced lethal cell injury. *Amer. J. Pathol.* 1992;140:457-471.
2. Huber, A.R., Ellis, S., Johnson, K.J., Dixit, V.M. and Varani, J.: Monocyte diapedesis through an in vitro vessel wall construct: Inhibition with monoclonal antibodies to thrombospondin. *J. Leukl. Biol.* 1992;52:524-528.
3. 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. *Anesthesiology* 1992;77:772-778.

4. Johnson, K.J., Varani, J. and Smolen, J.E.: Neutrophil activation and function in health and disease. *Immun. Ser.* 1992;57:1-46.
5. 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.* 1993;91:577-587.
6. Zador, I.Z., Deshmukh, G.O., Kunkel, R., Johnson, K.J., Radin, N.S. and Shayman, J.A.: A role for glycosphingolipid accumulation in the renal hypertrophy of streptozotocin-induced diabetes mellitus. *J. Clin. Invest.* 1993;91:797-803.
7. 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.* 1992;129:448-455.
8. Tait, A.R., Davidson, B.A., Johnson, K.J., Remick, D.G. and Knight, P.R.: Halothane inhibits the intrapulmonary recruitment of neutrophils, lymphocytes and macrophages in response to influenza infection in mice. *Anest. Analg.* 1993;76:1106-1113.
9. Ward, P.A. and Johnson, K.J.: Lung inflammatory mechanisms. *J. Human Path., In Press.*
10. 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.*
11. Ward, P.A., Johnson, K.J. and Till, G.O.: Mechanisms of lung injury. *Prax. Klin. Pneumonol., In Press.*
12. 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.*
13. Huber, A.R., Ellis, S., Johnson, K.J., Dixit, V.M. and Varani, J.: Monocyte diapedesis through an *in vitro* vessel wall construct: Inhibition with monoclonal antibodies to thrombospondin. *J. Leuk. Biol., In Press.*
14. 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. *Anesthesiology, In Press.*
15. 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.*
16. 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 pneumonitis. *Anest. Analg., In Press.*
17. Quddus, J., Johnson, K.J., Gavalchin, J., Amento, E., Crisp, C. and Richardson, B.: Mature T cells treated with a DNA methylation inhibitor induce a lupus-like disease in syngeneic mice. *J. Clin. Invest., In Press.*
18. Mulligan, M.S., Sulavik, C., Ward, P.A., Kunkel, R.G. and Johnson, K.J.: The delayed phase of anti-GBM nephritis is deferoxamine sensitive but catalase insensitive. *Inflammation, In Press.*
19. Knight, P.R., Rutter, T., Tait, A., Coleman, E. and Johnson, K.J.: Pathogenesis of gastric particulate lung injury: A comparison and interaction with acidic pneumonitis. *Anest. Analg., In Press.*
20. Johnson, K.J. and Weinberg, J.M.: Post-ischemic renal injury due to oxygen radicals. *Current Opinion in Nephrology and Hypertension, In Press.*

ARTICLES SUBMITTED FOR PUBLICATION:

1. Ward, P.A., Till, G.O., Kunkel, R.G. and Johnson, K.J.: Protection against neutrophil-mediated lung injury by platelet depletion. Submitted.

2. Shayevitz, J.R., Johnson and K.J., Knight, P.R.: Halothane-oxidant interactions in the *ex vivo* perfused rabbit lung: edema formation and eicosanoid production. Submitted.
3. 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.
4. 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.
5. Johnson, K.J., Dixit, V.M. and Varani, J.: Role of thrombospondin in the acute inflammatory response. Submitted.
6. Johnson, K.J., Sulavik, C. and Rehan, A.: Role of oxygen radicals in autologous anti-GBM nephritis. Submitted.
7. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: PAF, cytokines, toxic oxygen products and cell injury. Submitted.
8. Huber, A.R., Johnson, K.J. and Varani, J.: Monocyte diapedesis through an *in vitro* vessel wall construct: Inhibition with monoclonal antibodies to thrombospondin. Submitted.
9. 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.
10. 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.
11. 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. Submitted.
12. Gilardy, A., Dysko, R.C., Spilman, S.C., Kunkel, R.G., Brammer, D.W. and Johnson, K.J.: Immune complex vasculitis with secondary ulcerative dermatitis in aged C57BL/6NNia mice. Submitted.
13. Mulligan, M.S., Desrochers, P.E., Chimmayyan, A.M., Gibbs, D.F., Johnson, K.J. and Weiss, S.J.: *In vivo* suppression of immune complex alveolitis by secretory leukoprotease inhibitor and tissue inhibitor of metalloproteinases. Submitted.

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), *Progress in Applied Microcirculation*, 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, United Kingdom, 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", 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., 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.
14. 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.
15. 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.
16. 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., Johnson, K.J., Smith, C.W., Anderson, D.C. and Ward, P.A.: Nephrotoxic nephritis: Role of TNF α and adhesion molecules. *JASN* 1991;2(3):555.
2. Rutter, T., Knight, P., Tait, A., Coleman, E. and Johnson, K.J.: Pathogenesis of gastric particulate lung injury. *FASEB*, 1992.
3. Knight, P., Tait, A. and Johnson, K.J.: The role of neutrophils, oxidants, and proteases in pulmonary acid injury. *FASEB*, 1992.
4. Kunkel, R.G., Mulligan, M.S., Johnson, K.J., Riggs, L.K., Riggs, L.K. and Ward, P.A.: Morphologic studies on inhibition of acute glomerulonephritis by TNF α . *FASEB*, 1992.
5. Mulligan, M.S., Johnson, K.J., Tamatini, T., Miyasaka, M., Anderson, D.C., Smith, C.W. and Ward, P.A.: Requirements for CD18 and ICAM.1 in nephrotoxic nephritis. *FASEB*, 1992.

6. Johnson, K.J., Varani, J., Mulligan, M., Smith, C.W., Anderson, D.C. and Ward, P.A.: The role of adhesion molecules in leukocyte mediated glomerular injury. Keystone Symposium, 1992.
7. Young, E.W., Johnson, K.J., Leichtman, A.B., Mihatsch, M.J., Messana, J.M., Ellis, C.N. and Voorhees, J.J: Progressive renal interstitial fibrosis in psoriasis patients treated with low-dose maintenance cyclosporine. ASN, 1992.
8. 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. JASN. 1992;3(3):607.
9. Shayman, J.A., Deshmukh, G.D., Zador, I., Kunkel, R., Johnson, K.J. and Radin, N.S.: Is diabetic nephropathy an acquired sphingolipidosis? JASN 1992;3(3):766.
10. 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.
11. Quddus, J., Galvalchin, J., Amento, E., Johnson, K., Chrisp, C. and Richardson, B.C.: CD4+ T cells modified by the DNA methyltransferase inhibitors 5-azacytidine and rocinamide are sufficient to induce lupus in otherwise healthy mice. Arthritic Rheum. 1992;35:B259.
12. Varani, J., Yeh, K-Y., Shumaker, D.K., Dame, M.K., Riser, B. and Johnson, K.J.: Mesangial cell killing by leukocytes: Involvement of adhesion factors and the role of leukocyte oxidants and proteolytic enzymes. FASEB J. 1992;6:5627.
13. Johnson, K.J., Mulligan, M.S. and Ward, P.A.: Adhesion molecules and cytokines in acute glomerulonephritis. J. Cell Biochem., 1993;17:C523.
14. 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. 1993;7:235.
15. Gibbs, D.F., Varani, J. and Johnson, K.J.: The cooperative interactions of oxidants and proteases in endothelial cell injury by rat neutrophils. FASEB J. 1993;7:4130.
16. 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.
17. Mulligan, M.S., Ward, P.A. and Johnson, K.J.: Role of serine and metalloproteinases in the dermal vasculitis model. Amer. Assoc. Immunol. 1993:B-175.
18. 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.
19. Young, E.W., Kunkel, R. and Johnson, K.J.: Measurement of renal interstitial fibrosis by digital video microscopy. Amer. Soc. Nephrol. 1993.
20. 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. 1993;100:539.

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

**ANNUAL DEPARTMENT REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Director, Weekly Clinical Pathology Grand Rounds.
- B. Coordinator, Weekly Anatomical Pathology Conferences.
- C. Coordinator, Core-Lecture Series in Blood Banking for 1st-year Pathology House Officers.
- D. Participant, Weekly Clinical Pathology Case Study Conferences.
- E. Made presentation at Clinical Pathology Grand Rounds on Prenatal/perinatal immunohematology.
- F. Trained Pediatric Hematology Fellows (Jasty and Rawwas) in immunohematology.
- G. Provided instruction to Pathology Residents during their Blood Bank rotation.
- H. Director, Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
 - 1. Planned and coordinated the June, 1993, Current Topics in Blood Banking Symposium and Preconference Workshops.
 - 2. Presented Workshop entitled: Serological Testing in the Detection, Diagnosis and Transfusion Management of Immune Hemolysis.
 - 3. Presented Workshop entitled: Serological Problems: Causes, Prevention, Recognition and Resolution.
 - 4. Presented talk entitled: Recent Advances in Serological Testing: CAT, GEL, PEG et al.
 - 5. Moderated morning session on Transfusion Management.
- I. Provided discussion of pretransfusion testing to 1st-year minority medical students.
- J. Residency Training Review Committee:
 - 1. Developed core curriculum in Immunohematology.
 - 2. Planned Blood Bank/Immuno/Coagulation and HLA block rotations for house-officer training in clinical pathology.
- K. Clinical Pathology M-4 Elective:
 - 1. Member, Coordinating Committee.
 - 2. Organized electives in Transfusion Medicine for M-4 medical students.
 - 3. Gave two presentations during M-4 Elective (immune hemolysis and prenatal/perinatal testing).
- L. Coordinator and moderator, A Seminar for Barbara Barnes, University of Michigan, October, 1992.

III. RESEARCH ACTIVITIES:

- A. Reid, M.E., Alexander, F., Yacob, M., Oyen, R., Lee, K. and Judd, W.J., "Alloanti-N in an *Msu/Mshe* Woman" 45th Annual Meeting of the American Association of Blood Banks, San Francisco, 1992. *Transfusion*, 1992;32:23.
- B. Judd, W.J., Eisenbrey, L. and Weaver, M., "State Association Sponsored Program for SBB Candidates", 45th Annual Meeting of the American Association of Blood Banks, San Francisco, 1992. *Transfusion*, 1992;32:91.
- C. Butch, S.H., Judd, W.J., Steiner, E.A., Stoe, M. and Oberman, H.A., "The Computer Crossmatch", 45th Annual Meeting of the American Association of Blood Banks, San Francisco, 1992. *Transfusion*, 1992;32:5.
- D. Judd, W.J., Hoschner, J.A., Kahn, S.R., Steiner, E.A., Poole, J., Sausis L. and Reid, M.E., "Anti-Vw Hemolytic Disease of the Newborn with a Negative Direct Antiglobulin Test", 45th Annual Meeting of the American Association of Blood Banks, San Francisco, 1992. *Transfusion* 1992;32:20.
- E. Judd, W.J., Steiner, E.A., Knafl, P. and Hunter, C., "*In vitro* Hemolytic Autoanti-M: The Second Example." 45th Annual Meeting of the American Association of Blood Banks, San Francisco, 1992. *Transfusion* 1992;32:22.
- F. Judd, W.J., Annesley, T., Kirkegaard, J. and Beck, M.L., "Know Your Monoclonals: An Absolute Must for the Effective Resolution of ABO Grouping Discrepancies", 45th Annual Meeting of the American Association of Blood Banks, San Francisco, 1992. *Transfusion* 1992;32:18.
- G. Beck, M.L., Korth, J., Judd, W.J., "High Incidence of Acquired-B Detectable by Monoclonal Anti-B Reagents", 45th Annual Meeting of the American Association of Blood Banks, San Francisco, 1992. *Transfusion* 1992;32:17.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL/NATIONAL:

- A. Chairman, Michigan Association of Blood Banks, Advanced Lectures in Blood Banking Program:
 - 1. Coordinated a series of 60 lectures for MABB members seeking Certification as a Specialist in Blood Banking.
 - 2. Planned and coordinated a one-day lecture on laboratory management.
 - 3. Gave presentations on prenatal testing, hemolytic anemias, drug-induced immune hemolysis, lectins, polyagglutination and sialic acid deficient cells.
- B. American Association of Blood Banks:
 - 1. North Central District Representative, Board of Directors.

2. Editor, Technical Manual Committee, Special Methods Section for 11th edition, published in June, 1993.
- C. Transfusion Editorial Board, 1992--.
- D. Reviewer of articles submitted for publication in *Transfusion*, *Immunohematology* and *Vox Sanguinis*.
- E. Reviewer of grant applications for MILES, Canada and the Canadian Red Cross Research Council.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES:

1. "The Electronic Crossmatch", Annual Meeting of the North Carolina Association of Blood Banks, Durham, North Carolina, September, 1992.
2. "The Electronic Crossmatch", Annual Meeting of Ontario Society for Medical Technology, October, 1992.
3. "The Electronic Crossmatch", American Red Cross Blood Services, Toledo, Ohio, January, 1993.
4. "Immunohematology Review", Review Seminars for Specialist in Blood Banking Candidates, Bowling Green State University, Bowling Green, Ohio, February, 1993.
5. "Antibodies to Associated High- and Low-Incidence Antigens", AABB Immunohematology Reference Laboratory Conference, Peachtree City, Georgia, March, 1993.
6. "The Electronic Blood Bank", Annual Meeting of the Florida Association of Blood Banks, Orlando, Florida, May, 1993.
7. "Blood Derivatives", Annual Meeting of the Florida Association of Blood Banks, Orlando, Florida, May, 1993.
8. "The Electronic Crossmatch", Annual Meeting of the Canadian Society for Medical Technology, Halifax, Nova Scotia, June, 1993.
9. "New Technologies in Blood Banking", Michigan Association of Blood Banks Spring Workshop, Lansing, Michigan, May, 1993.

PANEL DISCUSSIONS/WORKSHOPS

1. Video Conference, "Prenatal/Perinatal Immunohematology", American Red Cross BioLink Productions, March, 1993.
2. Panel Discussant, "Ask the Experts", Annual Meeting of the Florida Association of Blood Banks, Orlando, Florida, May, 1993.

VI. PUBLICATIONS:

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

1. Judd, W.J., Steiner, E.A., Abruzzo, L.V., Davenport, R.D., Oberman, H.A., Pehta, J.C. and Nance, S.J.: Anti-i causing acute hemolysis following a negative immediate-spin crossmatch. *Transfusion*. 1992;32:572-575.
2. Chenoweth, C.E., Judd, W.J., Steiner, E.A. and Kauffman, C.A.: Cefotetan-induced immune hemolytic anemia. *Clin. Infect. Dis.* 1992;15:863-865.
3. Yamamoto, F., McNeil, P.D., Yamamoto, M., Hakomori, S., Harris, T., Judd, W.J. and Davenport, R.D.: Molecular genetics analysis of the ABO blood group system: I. Weak subgroups: A^3 and B^3 alleles. *Vox. Sang.* 1993;64:116-119.
4. Judd, W.J.: Polyagglutination. (Review). *Immunohematology*. 1992;58-69.

BOOKS/CHAPTERS IN BOOKS:

1. Judd, W.J.: Methods in immunohematology, Montgomery Scientific Publications, 2nd edition, Durham, North Carolina, 1993 (400 pages), In Preparation.
2. Judd, W.J.: Pretransfusion testing, in, McClatchey, K.D. (ed), Clinical Laboratory Medicine, Williams and Wilkins, Co., Baltimore, Maryland, In Press.

ABSTRACTS/LETTERS:

1. Judd, W.J., Steiner, E.A. and Nugent, C.E.: Appropriate serological testing in pregnancy, (letter). Vox. Sang. 1992;63:297-8.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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. Pathology 580 - (three contact hours).
- C. Gross Pathology Conference.
- D. Renal Pathology Conference.
- E. Clinical Pathology Conference (one hour).
- F. Renal Pathology for Nephrology Fellows (nine contact hours).
- G. Graduate Students (two).
- H. Dissertation Committees (eight).
- I. Post Doctoral Fellows (six).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, Project VI "Molecular Biology of Alveolar Wall Injury", NIH-P01-HL31963, (40% Effort) \$87,140/year, 3/1/89 - 2/28/94.
- B. 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.
- C. Principal Investigator, Project VI "TGF-b Induced Collagen IV Gene Transcription" NIH-P50-DK39225, (10% Effort) \$49,822/year, 8/1/92-7/30/97.
- D. Co-Investigator, "Renal Fibrosis", NIH-RO1, (10% Effort) \$198,213/first year, 4/1/93-3/30/98.
- E. Co-Investigator, "Role of EDRF in the Juxtaglomerular Apparatus", NIH-RO1-DK40042, (10% Effort) \$164,666/first year, 12/1/93-11/30/98.
- F. Co-Sponsor, "Aldose Reductase Expression in Diabetes", NIH-Physician Scientist Award, \$60,429/year, 4/1/93-3/30/98.

PENDING SUPPORT:

- A. Principal Investigator, Project IV, "Collagen Gene Expression in Lupus Nephritis", NIH-SCOR, SCOR in Systemic Lupus Erythematosus, (20% Effort), \$100,000/year, 3/1/94-2/28/99.

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.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. Invited Speaker, "Collagen IV Expression in Normal and Pathological States", Leiden, The Netherlands, 1992.
- 2. Invited Speaker, "Collagen Expression in Glomerular Disease", in, Molecular Approaches to Nephrology: Prospects in Diagnosis and Management, Bari, Italy, 1992.
- 3. Symposium Organizer and Invited Speaker, "Interstitial Scarring in the Kidney", 25th Meeting of the American Society of Nephrology, 1992.
- 4. Invited Speaker, Department of Anatomy and Cell Biology, University of Kansas, Kansas City, Kansas, 1993.
- 5. Invited Speaker, Second International Workshop on Alport Syndrome, Yale University School of Medicine, New Haven, Connecticut, February 1993.
- 6. Invited Speaker, Graduate Workshop on Tubulointerstitial Disease of the Kidney, Buffalo, New York, April, 1993.
- 7. Advisory Committee and Invited Speaker, VIth International Symposium on Basement Membranes, Hakone, Japan, May 1993.

8. Invited Speaker, "Regulation of Collagen IV Gene Expression", Shiga University, Otsu, Japan, June 1993.
9. Invited Speaker, XIIth International Congress of Nephrology, Jerusalem, Israel, June 1993.
10. Invited Speaker, "Mechanisms of Glomerulonephritis and Glomerulosclerosis", Leiden, The Netherlands, June 1993.

VI. - PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Schuger, L., Killen, P.D., Skubitz, A.P.N., Fin-Chang, J. and Varani, J.: Expression of laminin A and B chains in the epithelium and mesenchyme during murine lung development. *Dev. Dynamics* 1992;195:43-54.
2. Briggs, J.P., Todd-Turla, K.M., Schnermann, J.B. and Killen, P.D.: Approach to the molecular basis of nephron heterogeneity: Application of RT-PCR to dissected tubule segments. *Sem. Nephrol.* 1993;13:2-12.
3. Wiggins, R., Goyal, M., Merritt, S. and Killen, P.D.: Vascular adventitial cell expression of collagen I in experimental anti-GBM antibody-induced crescentic nephritis in the rabbit. *Lab. Invest.* 1993;68:557-565.
4. Simon, R.H., Scott, M.J., Reza, M.M. and Killen, P.D.: Type IV collagen production by rat pulmonary epithelial cells. *Amer. J. Resp. Cell Mol. Biol.* 1993;8:640-646.
5. Todd-Turla, K., Schnermann, J., Fejes-Toth, G., Naray-Fejes-Toth, A., Smart, A., Killen, P.D. and Briggs, J.P.: Distribution of mineralocorticoid and glucocorticoid receptor mRNA along the nephron. *Amer. J. Physiol.*, In Press, 1993.
6. Henry, D.N., Monte M.D., Green, D.A and Killen, P.D.: Altered aldose reductase gene regulation in cultured human retinal pigmant epithelial cells. *J. Clin. Invest.* In Press, 1993.
7. 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.*, In Press, 1993.
8. 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.*, In Press, 1993.
9. Grande, J.P., Melder, D. and Killen, P.D.: TGF- β 1 induces collagen IV gene transcription in NIH-3T3 cells. *Lab. Invest.*, In Press, 1993.
10. 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.*, In Press, 1993.
11. 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, 1993.

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, 1993.
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, 1993.

3. Mitchell, M., Markovitz, D., Killen, P.D. and Braun, D.: Bilateral renal malacoplakia presenting as fever of unknown origin: A case report and review of the literature. Submitted, 1993.
4. 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. Submitted, 1993.
5. Kroll, T.G., Killen, P.D. and Ruddon, R.W.: Stage-specific expression and deposition of laminin isoforms during myogenic differentiation in cultured cells. Submitted, 1993.
6. Funabiki, K., Togawa, M., Chapo, J.A. and Killen, P.D.: The complete primary structure of the murine $\alpha 3(\text{IV})$ collagen chain. Submitted, 1993.
7. 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, 1993.

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

1. Funabiki, K., Togawa, M., Chapo, J.A. and Killen, P.D.: Expression of the murine $\alpha 3(\text{IV})$ collagen gene is regulated in a tissue-specific fashion. *J. Amer. Soc. Nephrol.* 1992;3:630.
2. Todd-Turla, K.M., Briggs, J.P., Smart, A.M., Killen, P.D. and Schnermann, J.B.: b-Actin mRNA distribution along the rat nephron. *J. Amer. Soc. Nephrol.* 1992;3:447.
3. Chapo, J.A., Grande, J.P. and Killen, P.D.: Transcriptional regulation of collagen IV gene expression during renal development. *J. Amer. Soc. Nephrol.* 1992;3:631.
4. deMiguel, M., Killen, P., Goyal, M. Merritt, S. and Wiggins. R.: Comparison of $\alpha 1(\text{IV})$ collagen, $\alpha 1(1)$ and $\alpha 2(1)$ procollagen mRNA distribution during evolution of crescentic nephritis in the rabbit using *in situ* hybridization. *J. Amer. Soc. Nephrol.* 1992;3:627.
5. Bergijk, E.C., Bacide, J.J., de Heer, E., Killen, P.D. and Bruijn, J.A. (intr. by Hoedemaeker, Ph. J.): Specific accumulation of exogenous fibronectin plays a major role in the development of experimental glomerulosclerosis. *J. Amer. Soc. Nephrol.* 1992;3:626.
6. Gattone II, V.H., Kraybill, A.L. and Killen, P.D.: Renal extracellular matrix expression in rodent models of inherited polycystic kidney disease. *J. Amer. Soc. Nephrol.* 1992;3:631.
7. Chen, M., Wang, W., Killen, P.D., Briggs, J.P. and Schnermann, J.: Endothelin 1 mRNA in cultured juxtaglomerular cells of the mouse kidney. *J. Amer. Soc. Nephrol.* 1992;3:434.
8. Chen, M., Smart, A.M., Schnermann, J., Killen, P.D. and Briggs, J.P.: Cyclic AMP alters renin mRNA stability in cultured juxtaglomerular cells. *J. Amer. Soc. Nephrol.* 1992;3:518.
9. Togawa, M., Bergijk, E.C., Funabiki, K., Chapo, J.A., Bruijn, J.A. and Killen, P.D.: Developmental expression of the $\alpha 4(\text{IV})$ collagen gene. *J. Amer. Soc. Nephrol.* 1992;3:646.
10. 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.* Submitted.
11. 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.* Submitted.

12. Schieren, G., Park, M.H., Funabiki, K. and Killen, P.D.: Expression of the murine $\alpha 5(\text{IV})$ collagen gene. *Amer. Soc. Nephrol.* Submitted.
13. Park, M.H., Funabiki, K., Togawa, M., Chappo, 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.* Submitted.
14. Funabiki, K., Togawa, M., Chappo, 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.* Submitted.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Inflammation/Immunopathology Series ICS-600.
- B. Pathology 581.
- C. Co-director, "Cellular and Molecular Basis of Disease".
- D. Epidemiology 570.
- E. Member, Pathology graduate program committee.
- F. Member, Molecular Pathogenesis Training Program (Microbiology).
- G. Member, Immunopathology Postdoctoral Training Program (Pathology).
- H. Member, Operating Committee, Systems and Integrative Biology Training Program (Physiology).
- I. Member, Experimental Immunopathology Training Program (Pathology)
- J. Member and Co-Director, Pulmonary Cellular and Molecular Biology Training Program
- K. Supervised the following postdoctoral fellows and graduate students: fellows, Drs. Tsyoshi Kasama, Dan Smith, Glenn VanOtteren, John Orens, Nick Lukacs, Mark Rolfe, graduate student, Rob Smith, Susan Moore.
- L. Undergraduate students: Marc Milia, Gannon Dudlar, Paul Holman, Rick Dwyer, Janet Sherman, Christy Shaklee.
- M. Doctoral Thesis Committee Member/Orals Committee for the following graduate students: Ron Allen, Cindy Hoorn, Rob Smith, Susan Moore, Fran Wolber, Jerry Caldwell, Oswald D'Auvergne, Dominic Justewicz.
- N. Mentor for Dr. Janice Liebler, University of Oregon Health Science Center; Sabbatical leave.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Macrophage/Monocyte Signals in Lung Granuloma Formation", NIH HL-RO1-35276.
- B. Principal Investigator, "Monokine Gene Expression/Regulation in Lung Injury", NIH HL-RO1-31237.
- C. Principal Investigator, "Inflammatory Cells and Lung Injury", NIH HL-31963.
- D. Principal Investigator, "Crescentic Nephritis", NIH P01-DK38149.
- E. Principal Investigator, Tobacco Research Institute.

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. Course co-director Pathology 581.
- E. Divisional Directors Committee.

MEDICAL SCHOOL/HOSPITAL:

- 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, Michigan Cancer Center.
- G. Institute of Gerontology Faculty Search Committee.
- H. Pediatrics Faculty Search Committee.
- I. Pathology Faculty Search Committee.

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. Editorial board, Mediators of Inflammation.
- F. Organizing committee, 1994 International Cytokine Symposium.
- G. Member long range planning committee, American Society of Investigative Pathology.
- H. Member program committee, American Society of Investigative Pathology.
- I. Reviewer for the following journals:
 - 1. American Journal of Pathology.
 - 2. American Review of Respiratory Disease.
 - 3. Circulation.
 - 4. Infection and Immunity.
 - 5. Laboratory Investigation.
 - 6. Science.
 - 7. Journal of Immunology.

- 8. 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. Session chair, Experimental Biology '93/FASEB.
- N. Session chair, Molecular basis of Inflammation, Ares Sero Symposium.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Speaker, Gordon Conference on Vascular Cell Biology, New London, New Hampshire, July, 1992.
2. Invited Speaker, Association of Pathology Chairman, Snowmass, Colorado, July, 1992.
3. Invited Speaker, Third International Conference on Chemotactic Cytokines, Vienna, Austria, September, 1992.
4. Visiting Professor and Lecturer, "Frontiers of Science", St. Louis University, Missouri, October 1992.
5. Invited Speaker, University of Toledo, Toledo, Ohio, October, 1992.
6. Invited Speaker, "Signal Transduction Seminar Series", Parke Davis Research, Ann Arbor, Michigan, October, 1992.
7. Invited Speaker, American Society of Nephrology, Baltimore, Maryland, November, 1992.
8. Invited Speaker, Cytokines and Cytokine Receptors in Health and Disease, Sponsored by the National Heart, Lung and Blood Institute, Bethesda, Maryland, December, 1992.
9. Invited Speaker, Sepsis Experts Panel Meeting, Chicago, Illinois, Dec, 1992.
10. Invited Speaker, Workshop on Vascular Injuries, Ann Arbor, Michigan, December, 1992.
11. Invited Speaker, Inflammation Symposia, McMaster University, Canada, February, 1993.
12. Invited Speaker/Chair, Experimental Biology 93, 'Immunopathology of Cytokines' Symposium, New Orleans, Louisiana, March, 1993.
13. Visiting Professor, Micheal Reese Hospital, Department of Internal Medicine, Chicago, Illinois, April, 1993.
14. Visiting Professor, University of Illinois, Department of Physiology, April, 1993.
15. Invited Speaker, Symposium on "Cells, Signals, and Adhesion Mechanisms in Inflammation", University of Lund, Lund, Sweden, April, 1993.
16. Invited Speaker/Chair, International symposium on "Molecular Basis of Inflammation", Heidelberg, Germany, April, 1993.
17. Invited Speaker, "Expression and Regulation of Inflammatory Cytokines", New York Academy of Science, New York, New York, May 1993.
18. Invited speaker, Athena Neurosciences, San Francisco, California, May, 1993.
19. Visiting Professor, Ohio State University, Columbus, Ohio, May, 1993.
20. Invited speaker, SmithKline and Beechem, Philadelphia, Pennsylvania, June, 1993.
21. Invited Speaker, FASEB Summer Conference, Lymphocytes and Antibodies, Saxtons River, Vermont, June 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Friedland, J.S., Suputtamongkol, Y., Remick, D.G., Chaowagul, W., Strieter, R.M., Kunkel, S.L., White, N.J. and Griffin, G.E.: Prolonged elevation of interleukin-8 and interleukin-6 concentrations in plasma and of leukocyte interleukin-8 mRNA levels during septicemic and localized *pseudomonas pseudomallei* infection. *Infect. Immun.* 1992;6:2402-2408.
2. Bromberg, J.S., Shavin, K.D., and Kunkel, S.L. Anti-tumor necrosis factor antibodies suppress cell mediated immunity in vivo. *J. Immunol.* 1992;148:3412-3417.
3. Phan, S.H., Gharaee-Kermani, M., McGarry, B., Kunkel, S.L., Wolber, F.W.: Regulation of rat pulmonary artery endothelial cell transforming growth factor- β production by IL-1 β and tumor necrosis factor- α . *J. Immunol.* 1992;149:103-106.
4. Standiford, T.J., Strieter, R.M., Allen, R., Burdick, M.D. and Kunkel, S.L.: IL-7 upregulates the expression of IL-8 from resting and stimulated human blood monocytes. *J. Immunol.* 1992;149:2035-2039.
5. Brown, Z., Strieter, R.M., Neild, G.H., Thompson, R.C., Kunkel, S.L., and Westwick, J.: IL-1 receptor antagonist inhibits monocyte chemotactic peptide 1 generation by human mesangial cells. *Kid. International.* 1992;42:95-101.
6. Metinko, A.P., Kunkel, S.L., and Strieter, R.M.: Anoxia-hyperoxia induces monocyte derived interleukin-8. *J. Clin. Invest.* 1992;90:791-798.
7. Strieter, R.M., Kasahara, K., Allen, R.M., Standiford, T.J., Rolfe, M.W., and Kunkel, S.L.: Cytokine-induced neutrophil-derived interleukin-8. *Am. J. Pathol.* 1992;141:397-407.
8. Koch, A.E., Kunkel, S. L., Chensue SW, Haines, G.K. and Strieter, R.M. Constitutive expression of interleukin-1 and interleukin-1 receptor agonist by human rheumatoid synovial tissue macrophages. *Clin Immunol Immunopath* 1992;65:23-29.
9. Scales, W.E., Chensue, S.W. and Kunkel, S.L. Interleukin-6 expression in immunologically elicited murine macrophages. *Pathobiol.* 1992;60:289-296.
10. Strieter, R.M., Kunkel, S.L., Burdick, M.D., Lincoln, D.M. and Walz, A.: The detection of a novel neutrophil-activating peptide (ENA-78) using a sensitive ELISA. *Immunol. Invest.* 1992;21:589-596.
11. Rolfe, M.W., Kunkel, S.L., Standiford, T.J., Orringer, M.B., Phan, S.H., Evanoff, H.L., Burdick, M.D. and Strieter R.M. Expression and regulation of human pulmonary fibroblast-derived monocyte chemotactic peptide (MCP-1): *Am. J. Physiol.: Lung Cell. Molec. Physiol.* 1992;263:536-545.
12. Koch, A.E., Kunkel, S.L., Harlow, L.A., Johnston, B., Evanoff, H.L., Haines, G.K., Burdick, M.D., Pope, R.M., and Strieter, R.M.: Enhanced production of monocyte chemoattractant protein-1 in rheumatoid arthritis. *J. Clin. Invest.* 1992;90:772-779.
13. Strieter, R.M., Kunkel, S.L., Elnor, V.M., Martonyi, C.L., Koch, A.E., Polverini, P.J. and Elnor, S.G.: Interleukin-8: A corneal factor that induces neovascularization. *Am. J. Pathol.* 1992;141:1279-1284.
14. Koch, A.E., Polverini, P.J., Kunkel, S.L., Harlow, L.A., DiPietro, L. A., Elnor, V.M., Elnor, S.G. and Strieter, R.M. Interleukin-8 (IL-8) as a macrophage-derived mediator of angiogenesis. *Science.* 1992;258:1798-1801.
15. Davenport, R.D., Burdick, M., Moore, S.A., and Kunkel, S.L.: Cytokine production in IgG-mediated red cell incompatibility. *Transfusion.* 1993;33:19-24.

16. 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.* 1993;61:57-66.
17. Kunkel, S.L., Strieter, R.M., Lukacs, N., and Chensue, S.W.: Initiation and maintenance of the granulomatous response. *Chest* 1993;103:135S-137S.
18. Donnelly, S.C., Strieter, R.M., Kunkel, S.L., Walz, A., Robertson, D.R., Carter, D.C., Grant, I.S., Pollock, A.J., and Haslett, C.: Interleukin-8 and development of adult respiratory distress syndrome in at-risk patient groups. *Lancet.* 1993;341:643-647.
19. Rolfe, M.W., Kunkel, S.L., DeMeester, S.R., Swiderski, D.L., Lincoln, P.M., Deeb, G.M., and Strieter, R.M.: Expression of interleukin-6 in association with rat lung reimplantation and allograft rejection. *Am. Rev. Respir. Dis.* 1993;147:1010-1016.
20. Wakefield, T.W., Greenfield, L.J., Rolfe, M.W., DeLucia, A, III, Strieter, R.M., Abrams, G.D., Kunkel, S. L., Esmon, C.T., Wroblewski, S.K., Kadell, A.M., Burdick, M.D. and Taylor, F.B.: Inflammatory and procoagulant mediator interactions in an experimental baboon model of venous thrombosis. *Thrombosis and Hemostasis.*1993;69:164-172.
21. DeMeester, S.R., Rolfe, M.W., Kunkel, S.L., Swiderski, D.L., Lincoln, P.M., Deeb, G.M., and Strieter, R.M.: The bimodal expression of tumor necrosis factor-alpha (TNF) in association with rat lung reimplantation and allograft rejection. *J. Immunol.* 1993;150:2494-2505.
22. Koch, A.E., Kunkel, S.L., Pearch, W.H., Shah, M.R., Parikh, D., Evanoff, H.L., Haines, Burdick, M.D., Strieter, R.M.: Enhanced production of the chemotactic cytokines interleukin-8 (IL-8) and monocyte chemoattractant protein-1 (MCP-1) in human abdominal aortic aneurysms. *Am. J. Pathol.* 1993;142:1423-1431.
23. Rolfe, M.W., Kunkel, S.L., Demeester, S.R., Swiderski, D.L., Lincoln, P.M., Deeb, G.M., and Strieter, R.M.: Expresssion of interleukin-6 in association with rat lung reimplantation and allograft rejection. *Am. Rev. Respir. Dis.* 1993;147:1010-1016.
24. Lukacs, N.W., Kunkel, S.L., Strieter, R.M., Warmington, K., and Chensue, S.W.: The role of macrophage inflammatory protein 1 alpha in *Schistosoma mansoni* egg-induced granulomatous inflammation. *J. Exp. Med.* 1993;177:1551-1559.

BOOKS/CHAPTERS IN BOOKS:

1. Kunkel, S.L., Rolfe, M.W., Strieter, R.M.: Expression of tumor necrosis factor during lung allograft revascularization and rejection, in Fiers and Burman, V. (eds.), *Proceedings of The Fourth International TNF Congress*, Springer-Verlag, Heidelberg, Germany, 1992.
2. Strieter, R.M., Colletti, L.M., Metinko, A.P., Rolfe, M.W., DeMeester, S.R., Standiford, T.J., Kunkel, S.L.: The role of cytokine networks mediating inflammation and ischemia-reperfusion injury, in Schlag, G., Redl, H., Traber, D.L. (eds.), *Third Wiggers Bernard Conference Cytokine Network on Shock, Sepsis and Organ Failure*, Springer-Verlag, Heidelberg, Germany, pp. 205-227, 1993.
3. Kunkel, S.L., Standiford, T.J., Rolfe, M.W., Strieter, R.M.: Expression and regulation of chemotactic cytokine genes by non-immune pulmonary cells, in Brody, A., Center, D., Tkachuk, V. (eds.), *Signal Transduction in Lung Cells: Lung Biology in Health and Disease*, Marcel Dekker, Inc., New York, 293-308, 1993.
4. Kunkel, S.L., Chensue, S.W., Standiford, T.J., Strieter, R.M.: Cellular and molecular mechanisms that regulate the production of interleukin-8: The

- potential role of chemotactic cytokines in ARDS and multiple organ failure, in, Faist, Meakins, and Schidberg (eds.), Host Defense Dysfunction in Trauma, Shock and Sepsis, Springer-Verlag, Heidelberg, Germany, 1993.
5. Strieter, R.M. and Kunkel, S.L.: The immunopathology of chemotactic cytokines, in, Kunkel, S.L., Lindley, I., and Warwick, J. (eds.), Chemotactic Cytokines 2, Plenum Publishing Corp., New York, New York, 1993.
 6. Lukacs, N.W., Strieter, R.M., and Kunkel, S.L.: Cytokines in acute inflammation, in, Adamson, J.W.-(ed), Current Opinien in Hematology: Current Science, Philadelphia, Pennsylvania, pp26-31, 1993.
 7. Kunkel, S.L., Standiford, T.J., Kasama, T., Strieter, R.M.: Chemotactic Cytokines: The chemokine family, in, Phan, S.H., Thrall, R.S., (eds.), Pulmonary fibrosis: Lung Biology in Health and Disease, Marcel Dekker, Inc., New York, 1993.
 8. Kunkel, S.L., Chensue, S.W., Standiford, T.J., Strieter, R.M.: Endotoxin-dependent cytokine networks, in, Brigham, K.L. (ed.), Endotoxin and the Lung: Lung Biology in Health and Disease, Marcel Dekker, Inc., New York, 1993.
 9. Kunkel, S.L., Lukacs, N.W., Kasama, T., Strieter, R.M.: Chemotactic cytokines, in, Griffin, G. (ed.), Cytokines in Infection, Bailliere Tindall, London, United Kingdom, 1993.

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

1. Koch, A.E., Kunkel, S.L., Polverini, P.J., Harlow, L.A., DiPietro, L.A., Elner, V.M., Elner, S.G., and Strieter, R.M.: Interleukin-8 is a potent human macrophage-derived mediator of angiogenesis that is blocked by interleukin-8 antibody and antisense oligonucleotide. American College of Rheumatology 56th Annual meeting, October 1992.
2. Koch, A.E., Kunkel, S.L., Harlow, L.A., Johnson, B.A., Evanoff, H.L., Haines, G.K., Burdick, M.D., Pope, R.M., and Strieter, R.M.: The synovium and synovial fluid as a source of monocyte chemoattractant protein-1. American College of Rheumatology 56th Annual meeting, October 1992.
3. Brown, K.A., Strieter, R.M., Kunkel, S.L., Beresford, T.P., and Lucey, N.R.: Effect of ethanol on basal and stimulated cytokine production in humans. American Association For The Study of Liver Diseases Annual meeting, October 1992.
4. Standiford, T.J., Rolfe, M.W., Kunkel, S.L., Lynch, J.P., Becker F.S., Burdick, M.D., Gilbert, A. Orringer M.A., and Strieter, R.M.: Macrophage inflammatory - 1 expression in interstitial lung disease. Clin. Res. 1992;40:722A.
5. Swiderski, D.L., Kunkel, S.L., Rolfe, M.W., DeMeester, S.R., Burdick, M.D., Deeb, G.M., Strieter, R.M.: Neutralizing antibodies to tumor necrosis factor-alpha attenuates lung allograft rejection. Clin. Res. 1992;40:697A.
6. Lukacs, N.W., Kunkel, S.L., Burdick, M.D., Strieter, R.M.: Functional requirement for ICAM-1 and LFA-3 interactions in allogeneic mixed lymphocyte reaction and cytokine production. Clin. Res. 1992;40:742A.
7. Arenberg, D.A., Kunkel, S.L., Standiford, T.J., Brudick, M.D., Strieter, R.M.: Cisplatin inhibits the production of monocyte-derived interleukin-1 receptor antagonist. Clin. Res. 1992;40:737A.
8. Brown, Z., Strieter, R.M., Kunkel, S.L., Neild, G.H., Westwick, J.: Cyclosporin (CS) enhances IL-8 and MCP-1 gene expression and peptide formation by human mesangial cells (MC). Presented to the American Society of Nephrology, Baltimore, Maryland, November, 1992.

9. Schmouder, R.L., Strieter, R.M., Kunkel, S.L.: ENA-78 chemokine production in IL-1b stimulated human renal cortical cells. Presented at the American Society of Transplant Physicians Meeting, Houston, Texas, January 8, 1993.
10. Smith, D.R., Kunkel, S.L., Rolfe, M.W., Standiford, T.J., Orringer, M.B., Whyte, R.I., Burdick, M.D., Gilbert, A.R., Strieter, R.M.: The production of interleukin-1 receptor antagonist by human bronchogenic carcinoma. *Clin. Res.* 1993;41:55A.
11. DeMeester, S.R., Rolfe, M.W., Kunkel, S.L., Swiderski, D., Lincoln, P.M., Deeb, G.M., Strieter, R.M.: The bimodal expression of tumor necrosis factor-alpha (TNF) in association with rat lung reimplantation and allograft rejection. Presented to The Society of University Surgeons Resident's Program, Seattle, Washington, February 13, 1993.
12. Smith, D.R., Kunkel, S.L., Standiford, T.J., Lukacs, N.W., Rolfe, M.W., Orringer, M.B., Whyte, R.I., Burdick, M.D., Danforth, J.M., Gilbert, A.R., Strieter, R.M.: Elaboration of interleukin-1 receptor antagonist by human bronchogenic carcinomas. *FASEB J.* 1993;7:A268.
13. Gilbert, A.R., Kunkel, S.L., Burdick, M.D., Walz, A., Lukacs, N.W., Standiford, T.J., Wilke, C., Strieter, R.M.: Chemokine production by monocytes in response to irradiation. *FASEB J.* 1993;7:A345.
14. Orens, J.B., Lukacs, N.W., Kunkel, S.L., Walz, A., Christensen, P.J., Burdick, M.D., Strieter, R.M.: The production of ENA-78, interleukin-8 (IL-8) and monocyte chemoattractant protein-1 (MCP-1) in the mixed lymphocyte reaction: the role of L-arginine metabolism. *FASEB J.* 1993;7:A268.
15. VanOtteren, G.M., Standiford, T.J., Kunkel, S.L., Danforth, J.M., Burdick, M.D., Strieter, R.M.: Disparate expression of macrophage inflammatory protein 1a by murine alveolar and peritoneal macrophages. *FASEB J.* 1993;7:A712.
16. Smith, R.E., Phan, S.H., Rollins, B., Strieter, R.M., Kunkel, S.L.: Time-dependent expression of JE in association with bleomycin-induced lung injury. *FASEB J.* 1993;7:A506.
17. Colletti, L.M., Kunkel, S.L., Burdick, M.D., Strieter, R.M.: TNF is present locally for prolonged periods of time during acute infection. *FASEB J.* 1993;7:A159.
18. Lukacs, N.W., Strieter, R.M., Burdick, M.D., Kunkel, S.L.: Selective inhibition of allogeneic MLR responses with IL-1 receptor antagonist protein. *FASEB J.* 1993;7:A267.
19. Kasama, T., Strieter, R.M., Standiford, T.J., Burdick, M.D., Kunkel, S.L.: Neutrophil production of macrophages inflammatory protein-1a (MIP-1a): Role of LPS and GM-CSF. *FASEB J.* 1993;7:A364.
20. Standiford, T.J., Kunkel, S.L., VanOtteren, G.M., Danforth, J.M., Kunkel, R.G., Burdick, M.D., Strieter, R.M.: Compartmentalized expression of MIP-1a in vivo endotoxin administration. *FASEB J.* 1993;7:A640.
21. Walz, A., Schnyder, S., Kunkel, S.L., Strieter, R.M.: In human monocytes neutrophil-activating peptide ENA-78 is expressed differently than interleukin-8. *FASEB J.* 1993;7:A427.
22. Metinko, A.P., Kunkel, S.L., Burdick, M.D., Strieter, R.M.: Hyperoxia-induced monocyte-derived interleukin-8 expression is suppressed by the 21-aminosteroids U-83836E and U-74389F. *FASEB J.* 1993;7:A494.
23. Chensue, S.W., Strieter, R.M., Lukacs, N., Warmington, K., Burdick, M., Kunkel, S.L.: Monocyte chemotactic protein (MCP-1) expression schistome egg granuloma formation. *FASEB J.* 1993;7:A160.
24. Koch, A.E., Kunkel, S.L., Harlow, L.A., Mazarakis, D., Haines, G.K., Burdick, M.D., Pope, R.M., Strieter, R.M.: Macrophage inflammatory protein-1a: A chemoattractant for monocytes in arthritis. *Clinical Research* 1993;41:316A.
25. Koch, A.E., Kunkel, S.L., Harlow, L.A., Mazarakis, D., Haines, G.K., Burdick, M.D., Pope, R.M., Walz, A., Strieter, R.M.: Epithelial neutrophil activating

- peptide-78: A chemotactic cytokine for neutrophils in arthritis. *Clinical Research* 1993;41:371A.
26. Arenberg, D.A., Kunkel, S.L., Standiford, T.J., Burdick, M.D., Strieter, R.M.: Regulation of monocyte-derived interleukin-1 receptor antagonist by cisplatin. *Clinical Research* 1993;41:309A.
 27. Lukacs, N.W., Kunkel, S.L., Strieter, R.M., Warmington, K., Burdick, M.D., Chensue, S.W.: Participation of macrophage inflammatory protein-1 alpha in pulmonary granuloma formation. *Am Rev Respir Dis.* 1993;147:A90.
 28. Standiford, T.J., Rolfe, M.W., Kunkel, M.W., Lynch, J.P., III, Burdick, M.D., Gilbert, A.R., Orringer, M.B., Strieter, R.M.: Macrophage inflammatory protein 1 alpha expression in interstitial lung disease. *Am. Rev. Respir. Dis.* 1993;147:A479.
 29. Smith, R., Phan, S.H., Strieter, R.M., Kunkel, S.L.: Time-dependent expression of interleukin-6 in association with bleomycin-induced lung injury. *Am. Rev. Respir. Dis.:* 1993;147:A88.
 30. VanOtteren, G.M., Standiford, T.J., Kunkel, S.L., Danforth, J.M., Burdick, M.D., Strieter, R.M.: Macrophage inflammatory protein 1a expression and regulation by alveolar and peritoneal macrophages. *Am. Rev. Respir. Dis.:* 1993;147:A732.
 31. Smith, D.R., Kunkel, S.L., Rolfe, M.W., Standiford, T.J., Orringer, M.B., Whyte, R.I., Burdick, M.D., Gilbert, A.R., Walz, A., Strieter, R.M.: Chemotactic cytokines associated with human bronchogenic carcinoma. *Am. Rev. Respir. Dis.* 1993;147:A331.
 32. Antony, V.B., Godbey, S.W., Kunkel, S.L., Hott, J.W., Hartman, D.L., Burdick, M.D., Strieter, R.M.: Recruitment of inflammatory cells to the pleural space: IL-8 and MCP-1 in human pleural fluids. *Am. Rev. Respir. Dis.* 1993;147:A794.
 33. Antony, V.B., Godbey, S.W., Kunkel, S.L., Hott, J.W., Hartman, D.L., Burdick, M.D., Strieter, R.M.: Mesothelial cell release of MCP-1: Modulation by inflammatory cytokines. *Am. Rev. Respir. Dis.* 1993;147:A751.
 34. Donnelly, S.C., Strieter, R.M., Kunkel, S.L., Walz, A., Robertson, C.R., Carter, D.C., Grant, I.S., Pollok, A.J., Haslett, C.: Interleukin-8 (IL-8) and the development of the adult respiratory distress syndrome (ARDS) in at-risk patient groups. *Am. Rev. Respir. Dis.* 1993;147:A732.
 35. Donnelly, S.C., Strieter, R.M., Kunkel, S.L., Walz, A., Steedman, D., Grant, I.S., Pollok, A.J., Haslett, C.: Monocyte and neutrophil chemoattractant proteins in bronchoalveolar lavage (BAL) samples from patients with established adult respiratory distress syndrome (ARDS). *Am. Rev. Respir. Dis.* 1993;147:A70.
 36. Elner, V.M., Elner, S.G., Kunkel, S.L., Yue, B.Y.J.T., Strieter, R.M.: IL-8 and MCP-1 gene expression and production by cytokine- and LPS- stimulated human corneal stromal cells. Presented to Association for Research in Vision and Ophthalmology, May, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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 ten postdoctoral fellows: Nozomu Hiraiwa, M.D., Ph.D., Marco Trinchera, M.D., Aron Thall, Ph.D., Peter Smith, Ph.D., Yuko Natsuka, Ph.D., Shunji Natsuka, Ph.D., Petr Maly, Ph.D., Jonathon Homeister, M.D., Ph.D., E. Paul Scheidegger, M.D., and Daniel Legault, M.D. and one M.D., Ph.D. thesis student, Mr. Kevin Gersten.
- B. Lecturer, Pathology 581
Lecturer, Medicinal Chemistry 635, Glycoproteins, Molecular Biology.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. "Analysis of the Roles of Oligosaccharides During Murine Embryogenesis", Howard Hughes Medical Institute.
- B. Principal Investigator, "The Molecular Biology of Intracellular Lipid Transport", NIH DK-38482, (50% effort), \$57,297/year direct cost, \$317,737/five years direct cost, 8/1/86 - 7/31/92.
- C. Principal Investigator, "Molecular Genetics of the Human Lewis and Lewis-Related Blood Group Loci", National Blood Foundation, (5% effort), \$19,500.00/two years direct cost, 7/1/91 - 6/30/93.
- D. Principal Investigator, "Molecular Biology of Human α 1,3 Fucosyltransferases", NIH GM47455 (25% effort), \$67,439/year direct cost, \$286,925/four years direct cost, 5/1/92 - 4/30/96.
- E. Subcontract Principal Investigator, "Controlled Expression of Neoglycans in Animal Cells", NIH GM45914 (5% effort), \$22,205/year direct cost \$43,853/two years direct cost, 8/1/91 - 7/31/93.
- F. Principal Investigator, "Molecular Biology of the Human H and Se Blood Group Genes, NIH HL48859 (25% effort), \$66,757/year direct cost (\$276,544/four years direct cost), 8/1/92 - 6/30/96.
- G. Principal Investigator, Program Project - Project #4, "Oligosaccharides as Antiinflammatory Agents", NIH AI33189 (15% effort), \$104,448/year direct cost, \$481,355/four years direct cost), 9/1/92 - 4/30/96.
- H. Sponsor, "Structure-Function Relationships of Fucosyltransferases", American Society of Nephrology/Marion Merrell-Dow Fellow . Daniel J. Legault, National Kidney Foundation, Inc., 7/1/92 - 7/1/94.

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

1. Resident Selection Committee.

REGIONAL AND NATIONAL:

1. Member, Editorial Board, Journal of Biological Chemistry.
2. Member-elect, Pathobiochemistry Study Section, Division of Research Grants, National Institutes of Health.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

- A. Howard Hughes Medical Institute, Associate Investigator.

INVITED LECTURES AND SEMINARS:

1. Tables Rondes Roussel UCLAF Frontiers in Glycosciences, Versailles, France, July, 1992.
2. "Molecular Genetics of Mammalian Oligosaccharide Biosynthesis", University of Alabama, Birmingham, Alabama, November, 1992.
3. "Structural and Functional Diversity in the Human Fucosyltransferases", 21st Annual Meeting of the Society for Complex Carbohydrates, Nashville, Tennessee, November, 1992.
4. "The Fucosyltransferases", 2nd International Jenner Glycoimmunology Meeting, University of London, London, England, November, 1992.
5. "Structure and Function of Mammalian Genes that Determine Terminal Glycosylation Events. University of Toronto, Toronto, Ontario, Canada, January, 1993.
6. "Mammalian Genes that Determine Terminal Glycosylation Events", La Jolla Cancer Research Foundation, La Jolla, California, February, 1993.
7. "Structure and Function of Mammalian Glycosyltransferase Genes", 1993 Gordon Conference on Glycoproteins and Glycolipids, Ventura, California, February, 1993.
8. "Molecular Genetics of Mammalian Glycosyltransferase Genes", University of Notre Dame, Notre Dame, Indiana, March, 1993.
9. "Oligosaccharide-Dependent Leukocyte Adhesion in Inflammation", Howard and Martha Holley Symposium Research Prize in Rheumatology, American College of Rheumatology Southeast Regional Meeting, Arlington, Virginia, March, 1993.
10. "Mammalian Genes that Determine Glycosylation Phenotype", Case Western Reserve University, Cleveland, Ohio, May, 1993.
11. "Mammalian Glycosyltransferase Genes: Structure, Function, and Utility", Cambridge Healthtech Institute, San Francisco, California, May, 1993.

12. "Mammalian Glycosyltransferase Genes - Molecular Cloning, Structure, Regulation, and Utility", COMETT Summerschool on Glycobiology and Glycochemistry, Lausanne, Switzerland, June, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:-

1. Wong, C.-H., Dumas, D.P., Ichikawa, Y., Koseki, K., Danishefsky, S.J., Weston, B.W. and Lowe, J.B.: Specificity, inhibition and synthetic utility of a recombinant human α 1,3 fucosyltransferase. *J. Am. Chem. Soc.* 1992;114:5449-5451.
2. Weston, B.W., Smith, P.L., Kelly, R.J. and Lowe, J.B.: Molecular cloning of a fourth member of a human α (1,3)fucosyltransferase gene family: Multiple homologous sequences that determine expression of the Lewis^x, sialyl Lewis^x, VIM-2, and difucosyl sialyl Lewis^x epitopes. *J. Biol. Chem.* 1992;267:24575-24584.
3. Mulligan, M.S., Paulson, J.C., De Frees, S., Zheng, Z.-L., Lowe, J.B. and Ward, P.A.: Protective effects of oligosaccharides in P-selectin-dependent lung injury. *Nature* 1993;364:149-151.
4. Sawada, R., Lowe, J.B. and Fukuda, M.: E-selectin-dependent adhesion efficiency of colonic carcinoma cells is increased by genetic manipulation of their cell surface lysosomal membrane glycoprotein-1 expression levels. *J. Biol. Chem.* 1993;268:12675-12681.
5. Mulligan, M.S., Lowe, J.B., Larsen, R.D., Paulson, J.C., Walker, L., Maemura, K., Fukuda, M. and Ward, P.A.: Protective effects of sialylated oligosaccharides in immune complex-induced acute lung injury. *J. Exp. Med.* 1993;178:623-631.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Kelly, R.J., Ernst, L.K., Hiraiwa N., Bryant, J.G., Larsen R.D., Robinson, J.D. and Lowe, J.B.: Structure of the human H blood group α 1,2fucosyltransferase gene in normal and H deficient pedigrees; molecular basis for H blood group deficiency in Bombay and para-Bombay individuals. Submitted.
2. Gersten, K.M., Trinchera, M. and Lowe, J.B.: Structure and expression of a murine α 1,3 fucosyltransferase gene, and comparison to its orthologous human homologue Fuc-TIV. Submitted.

BOOKS/CHAPTERS IN BOOKS:

1. Lowe, J.B.: The blood group-specific human glycosyltransferases: Red cell membrane and red cell antigens, in, Tanner, M.J.A., and Anstee, D.J. (eds.), *Baillières Clinical Haematology International Practice and Research*, Baillière Tindall, W.B. Saunders Company, London, 1993;6(2):465-492.
2. Lowe, J.B.: Molecular biology: Basic concepts, in, McClatchey, K.D. (ed.), *Clinical Laboratory Medicine*, Williams & Wilkins, Baltimore, Maryland, 1993, In Press.
3. Lowe, J.B.: Oligosaccharide-dependent mechanisms of leukocyte adhesion, in, Zetter, B.R. (ed.), *Homing Mechanisms and Cellular Targeting*, Marcel Dekker, New York, 1993, In Press.
4. Lowe, J.B.: Specificity and expression of carbohydrate ligands, in, Page, C.P. (ed.), *Handbook of Immunopharmacology - Adhesion Molecules*, Academic Press, London, 1993, In Press.

5. 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, 1993, In Press.
6. Lowe, J.B.: Carbohydrate recognition in cell-cell interaction, in, Fukuda, M. (ed.), *Molecular Glycobiology - Frontiers in Molecular Biology*, Oxford University Press, Oxford, United Kingdom, 1993, In Press.
7. Lowe, J.B.: Carbohydrate-associated blood group antigens - the ABO, H/Se, and Lewis loci; in, Garratty, G. (ed.), *Immunobiology of Transfusion Medicine*, Marcel Dekker, Inc., New York, New York, 1993, In Press.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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. Associate Professor, Department of Oral Pathology, School of Dentistry, 1984-1991.
- H. Professor, Department of Otorhinolaryngology, 1991-Present.

II. TEACHING ACTIVITIES

MEDICAL SCHOOL/HOSPITALS

- A. Pathology 630/580/631; Course Director, 1983-Present.
- B. Oral Diagnosis 644; lecturer, 1983-Present.
- C. Pathology 600; lecturer, head and neck pathology, 1982-present.
- 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. Consultant, "Impact of Follow-up on Control of High Blood Pressure and Cholesterol"; Principal Investigator, Andrea Foote, Ph.D., Institute of Labor and Industrial Relations, The University of Michigan, 1988-present.
- D. Co-Investigator, "Enzyme Tagging of Malignant Cervical Epithelial Cells"; Principal Investigator, Daisy S. McCann, Ph.D., McCann Associates, Wayne, Michigan, 1991-present.

PENDING SUPPORT

- A. Co-Principal Investigator, "Screening of Pap Smears Using Fluorescently Labelled Markers"; Principal Investigator, Daisy S. McCann, Ph.D., McCann Associates, Wayne, Michigan, 1993-

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL

- A. Medical Service Plan Executive Committee, 1979-present.
- B. Chairman's Advisory Committee, 1988-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. Vice Chairman, Claims Control Committee, The University of Michigan Hospitals, 1990-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, Ex-officio, Executive Committee on Clinical Affairs, The University of Michigan Medical Center, 1990-present.
- K. Member, Utilization Review Work Group, The University of Michigan Medical Center, 1990-present.
- L. Member, Medical Record Work Group, The University of Michigan Medical Center, 1990-present.
- M. Member, Cancer Work Group, The University of Michigan Medical Center, 1990-present.
- N. Medical Liability Review Committee, 1992-present.
- O. Clinical Practice Work Group, University of Michigan, 1993-present.
- P. 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-present.
 - 3. Council on Scientific Affairs, 1987-present.

4. Vice-Chairman, International Committee, Council on Scientific Affairs, 1990-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-present.
- D. Technical Advisory Committee, State of Michigan Department of Health, Bureau of Laboratory and Epidemiological Services, 1987-present.
- E. American Society for Testing Materials (ASTM).
 1. Committee F31 on Health Care Services, member, 1988-present.
- 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-present.

INTERNATIONAL

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

V. OTHER RELEVANT ACTIVITIES

INVITED LECTURES/SEMINARS

1. Invited Participant, "Accuracy and Precision in Clinical Chemistry", Clinical Chemistry Forum, American Association of Clinical Chemists and College of American Pathologists, Washington D.C., November 16, 17, 1992.
2. Invited Speaker, "Integrating Quality Assurance and Continuous Quality Improvement", Advances in Clinical Quality Improvement, Quality Improvement Network of the Healthcare Forum, Albuquerque, New Mexico, October, 1992.
3. Invited Moderator, "Fetal-Infant Mortality Review: A National Response to a National Problem", National Fetal Infant Mortality Review, American College of Obstetrics & Gynecology, California, January 21-24, 1993.
4. "Quality Management in the Clinical Laboratory", Quality Assurance Related to Health Laboratory Technology, World Health Organization, Geneva, Switzerland, April 21-24, 1993.
5. "Laboratory Design and Personnel Issues in Quality Management", Quality Assurance Related to Health Laboratory Technology, World Health Organization, Geneva, Switzerland, April 21-24, 1993.
6. "Integration of Quality Assurance and Quality Improvement in the Clinical Laboratory." EuroLab, Nice, France, April 25-26, 1993.
7. Invited Speaker, "International Performance Standards In Drug Analysis", 3rd International Congress of Therapeutic Drug Monitoring and Clinical Toxicology, Philadelphia, Pennsylvania, May 28, 1993.
8. Guest Speaker, "Head and Neck Pathology/Clinical Laboratory Management Issues", Towsley Conference, Shanty Creek, Michigan, June 21-25, 1993.

VI. PUBLICATIONS

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Zappia, J.J., Bradford, C.R., Winter, P.H. and McClatchey, K.D.: Olfactory neuroblastoma-associated with Kallman's syndrome. *J. Otolaryngol.* 1992;21:1.
2. Truelson, J.M., Fisher, S.G., Wolf, G.T., Beals, T.E. and McClatchey, M.D.: DNA content and histologic growth pattern correlate with prognosis in patients with advanced squamous cell carcinoma of the larynx. *Cancer* 1992;70:56-62.
3. Creps, L.B., Coffey, R.J., Warner, P.A. and McClatchey, K.D.: Improvement of quality through the integration of total quality and quality assessment. *Quality Review Bulletin. Journal of Quality Improvement*, March 1992.
4. Carroll, W.R., Zappia, J.J. and McClatchey, K.D.: Branchiogenic carcinoma. *Laryngoscope* 1993;22(1)26-28.
5. Esclamado, R.M., Disher, M.J., Ditto, J.L., Rontal, E. and McClatchey, K.D.: Laryngeal liposarcoma. *Arch. Otolaryngol. - Head & Neck Surgery*, In Press, 1993.

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*, Submitted March, 1993.
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*, Submitted, June 1993.
3. Sassler, A.M., McClatchey, K.D., Wolf, G.T. and Fisher, S.G.: Eosinophilic infiltration in advanced laryngeal squamous cell carcinoma (LSCC): Correlations with prognosis. *Archives of Otolaryngology*, 1993.
4. McClatchey, K.D. and Shermetaro, C.: Carcinosarcoma of the paranasal sinuses. *J. of Otolaryngology*, 1993.
5. McClatchey, K.D.: Giant cell carcinoma of salivary gland. *J. of Otolaryngology*, 1993.
6. McClatchey, K.D. and Kincer, T.: Keratinizing and calcifying odontogenic cyst (Gorlin's Cyst). *J. of Otolaryngology*, 1993.

BOOKS AND CHAPTERS IN BOOKS

1. McClatchey, K.D. and Peterson, T.: The laboratory information system, in, Kenneth D. McClatchey (ed.), *Clinical Laboratory Medicine*, Williams and Wilkins, Baltimore, Maryland, In Press, 1992.
2. McClatchey, K.D., et al.: *Clinical Laboratory Medicine*, Williams & Wilkins, Baltimore, Maryland, 1989-93, Publication, September, 1993.
3. Travers, E.M. and McClatchey, K.D.: Laboratory management, in, Kenneth D. McClatchey (ed.), *Clinical Laboratory Medicine*, Williams and Wilkins, Baltimore, Maryland, In Press, 1992.
4. Pierson, C.L. and McClatchey, K.D.: Automation, in, *Encyclopedia of Microbiology*, Academic Press, Inc., San Diego, California, 1992.

5. McClatchey, K.D.: The Jaws and Oral Cavity, in, Sternberg, Antonioli, Carter, Eggleston, Oberman and Mills, (eds.), Diagnostic Surgical Pathology, Raven Press, New York, New York, 1993 (revision), In Press.

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

1. Sassler, A.M., McClatchey, K.D., Wolf, G.T. and Fisher, S.G.: Eosinophilic infiltration in advanced laryngeal squamous cell carcinoma (LSCC): Correlations with prognosis. Third International Conference on Head and Neck Cancer. San Francisco, California, July, 1992.
2. Carroll, W.R., Bunge, F.R., Wolf, G.T., Carey, T.E. and McClatchey, K.D.: Intralesional interleukin-2 in the VX-2 carcinoma in rabbits. Third International Conference on Head and Neck Cancer. San Francisco, California, July 1992.
3. Young, C., Hubbard, W. and McClatchey, K.D.: Implementation and impact of new antimicrobial susceptibility order procedure for improved utilization of microbiology resources. 32nd ICAAC, Anaheim, California, October 1992.
4. McClatchey, K.D.: Fine needle aspiration technique; Proposed guidelines, pamphlet, National Committee for Clinical Laboratory Standards, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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 videodisc medical education reference.

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, 5/1/8, 8 - 4/30/93.

- B. Co-Investigator, "Antimetabolite Selectivity: Regional Treatment and Modulation", National Institutes of Health Program Project NIH CA-42761-04, 8/1/93 - 7/31/96.
- 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, 12/1/89-11/30/94.
- D. Co-investigator, "PET, Growth Kinetics and Neuropathology of Brain Tumors", National Institutes of Health Grant NIH CA54104, 5/1/91-4/30/95.

PROJECTS UNDER STUDY:

- A. Growth, spread and antigenicity of ENU-induced gliomas in rats with Constance D'Amato and 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 Fligiel.
- 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. Pathology Committee, Children's Cancer Study Group, Columbus, Ohio.
- D. Member, United States-Canadian Academy of Pathology, 1972-.
- E. Member, Alpha Omega Alpha, Eta Chapter, 1972-.
- F. Member, American Association of Neuropathologists, 1978-.
- G. Member, Society of Neuroscience, 1983-.
- H. Member, American Association of Pathologists, 1984-.
- I. Member, Children's Cancer Study Group, 1985-.
- J. Member, Histochemical Society, 1989-.
- K. Member, Constitution Committee, American Association of Neuropathologists, 1990-.

INVITED LECTURES/SEMINARS:

- 1. Chairperson, Scientific Session on brain tumor proliferation markers, American Association of Neuropathologists, Annual Meeting, Salt Lake City, Utah, June 11, 1993.
- 2. Faculty, 31th Annual AFIP Neuropathology Review, Armed Forces Institutes of Pathology, New Orleans, Louisiana, January 18, 1993.
- 3. Faculty, Neuropathology Specialty Conference on Spinal Tumors, USCAP, New Orleans, Louisiana, March 16, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. McKeever, P.E.: Computerized image analysis of distinct cell marker parameters of glial fibrillary acidic protein: Intensity of immunofluorescence and topography in human glioma cultures. *Cell. Molec. Biol.* 1992;38:175-180.
- 2. Roberson, P.L., Ten Haken, R.K., McShan, D.L., McKeever, P.E. and Ensminger, W.D.: Three-dimensional tumor dosimetry for hepatic Yttrium-90-microsphere therapy. *J. Nuclear Med.* 1992;33:735-738.

3. Lawrence, T.S., Davis, M.A., Maybaum, J., Mukhopadhyay, S.K., Stetson, P.L., Normolle, D.P., McKeever, P.E. and Ensminger, W.D.: The potential superiority of bromodeoxyuridine to iododeoxyuridine as a radiation sensitizer in the treatment of colorectal cancer. *Cancer Res.* 1992;526:3698-3704.
4. Ross, D.A., McKeever, P.E., Sandler, H.M. and Muraszko K.M.: Myxopapillary ependymoma. *Cancer* 1993;71:3114-3118.
5. 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.
6. Caccamo, D., Keohane, M.E. and McKeever, P.E.: Plasminogen activators and inhibitors in gliomas: An immunohistochemical study. *Modern Pathology*, In Press.
7. Heidelberg, 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.
8. 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., Sima, A.A.F. and Blaivas, M.: Neoplasms of the sellar region, in, Lloyd, R.V. (ed.), *Surgical Pathology of the Pituitary Gland, Major Problems in Pathology series, Vol 27*, W.B. Saunders, 1992, pp. 141-210.
2. McKeever, P.E.: Human astrocytic neoplasms, in Murphy, S. (ed.), *Astrocytes: Pharmacology and Function*, Academic Press, New York, 1992, pp. 399-436.
3. McKeever, P.E. and Lloyd, R.V.: Pituitary adenomas and related lesions, in, Garcia, J.H. (ed.), *Diagnostic Neuropathology, Vol. IV*, Field and Wood, New York, In Press.
4. Greenberg, H.S., Chandler, W.F., Ensminger, W.D., Junck, L., Page, M.A., Gebarski, S.S., Hood, T.W., Stetson, P.L., Diaz, R.F., Hegarty, T., Thornton, A., Lichter, A.S., McKeever, P.E. and Tankanow, R.: Radiosensitization with constant intra-arterial infusion of bromodeoxyuridine (BUDR) and focal external beam radiation in the treatment of malignant astrocytoma, *Infusion Systems in Medicine, Neurology Vol 43. Suppl. A. 360*, 1992.

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

1. Sondak, V.K., Stetson, P.L., McKeever, P.E., Change, A.E. and Lawrence, T.S.: IUDR incorporation and washout in normal human tissues after intravenous infusion. *American Association for Cancer Res. San Diego, California, May 20, 1992.*
2. McKeever, P.E. and Gammons, D.T.: Review of book titled, *Textbook of Neuropathology (2nd ed)*, by Richard L. Davis and David M. Roberston. *Amer. J. Surg. Path.* 1992;16:210-211.
3. 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, Toronoto, Ontario, Canada.*
4. 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.*
5. 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.

6. 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.
7. 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.* 1993;41:1124.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

CLINICAL RESEARCH-RELATED ACTIVITIES:

- A. Co-Principal Investigator, preparation of an NIH proposal for studying the effects of clinical depression on the human reproduction. The proposal has a rating of 128, is at the 6.8 percentile and should be funded.
- B. Developed a method for continuous, integrated sampling from human subjects involving collection into a refrigerated fraction collector and continuous monitoring of oxidizable molecules.
- C. Implemented a system for generating protocols and bar-coded labels to facilitate analysis of samples for a large clinical study.

II. TEACHING ACTIVITIES:

- A. Lectures:
 - 1. Primary Instructor, Pathology 630/631, Full semester four hours/week laboratory course for dental and health professional students, Fall, 1992.
 - 2. Taught portion of Mammalian Reproductive Endocrinology, Physiology 541, 6 hrs lecture; 10 contact hours.
- B. Primary supervision of two postdoctoral fellows:
 - 1. Beverly Strassmann - postdoctoral fellow working on F32 fellowship. Appointed as Assistant Professor of Anthropology at the University of Michigan, effective 9/1/93.
 - 2. Daniel McConnell - postdoctoral fellow working on chemiluminescence-based assays (Support received from the Lindbergh Fund; appointed Research Investigator, May, 1993).
- C. Primary supervision of four graduate students:
 - 1. Jane Wiesen, Cellular and Molecular Biology (presented at the Society for the Study of Reproduction) - defense scheduled for August, 1992, supported on RO1 & RSP training grants.
 - 2. Hal Cantor, Bioengineering - defense probably in Spring, 1993, supported on NSF sensor grant.
 - 3. Karen Heinze, Bioengineering - first year doctoral student transferred from Northwestern, supported on NCIR grant.
 - 4. William Lemon, Bioengineering, supported on Cellular Biotechnology Training Grant.
- D. Primary supervision of three pre-medical students:
 - 1. Kristin McFadden, May, 1991-October, 1992.
 - 2. Pamela Russman, June, 1993-.
 - 3. Linh Lam, January - May, 1993.
- E. Service on Other Dissertation Committees.
 - 1. Howard Goldberg, Electrical Engineering Computer Science, successful defense, January, 1993.

2. David Mauger, Biostatistics, member of thesis committee.
- F. Worked with two Visiting Scientists:
 1. Bent G. Boving, Ph.D. Extramural Associate, Dept. of Embryology, Carnegie Institute of Washington.
 2. Robert J. Carrico, Ph.D., President, Software Technologies, Inc., Franklin, Michigan.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Center for the Study of Reproduction", NIH, P30 HD18258, 10% effort (5% as director of Administrative Core; 5% as Director, Standards and Reagents Core), \$326,244 TDC year 3, 3/1/89-2/28/94.
- B. Associate Director of Center, "National Center for Infertility Research", NIH U54, 3% effort, \$1,272,133 (overall center), TDC, year 2, 9/30/91-8/31/96.
- C. Director, "Assay Development Core", NIH U54, 5% effort, \$50,960, TDC, year 2, 9/30/91-8/31/96.
- D. Principal Investigator, "Gonadotrope Response to Ovulation-Controlling Signals", NIH U54, 30% effort, \$176,926, TDC, year 2, 9/30/91-8/31/96.
- E. Mentor, "Training Program in Reproductive Endocrinology", NIH, T32 HD-07048, 5% maximum effort, \$186,439 direct and stipends, 7/1/90-6/30/95.
- F. Co-Investigator, "Site-Directed Bioreagent Immobilization for Development of Microbiosensor Assays", NSF ECS-8915497, 6% effort, cost-shared, \$181,811 3rd year total costs, 9/1/89-8/31/92.
- G. Mentor, "The Reproductive Endocrinology of the Dogon", NIH F32 HD07480, 5% maximum effort, cost shared, Individual postdoctoral fellowship for Beverly I. Strassmann, 02/01/91-01/31/93.
- H. Principal Investigator, "University of Michigan Women's Health Initiative", Office of Vice-President for Research, 2% effort, cost shared, \$5,840, 4/1/92-9/30/92.
- I. Principal Investigator, "Hormones and Behavior: An Interdisciplinary Study of Women and Adolescents", Office of Vice-President for Research, 5% effort, cost shared, \$7,000, 6/15/92-9/30/92.

PROPOSAL WRITING:

- A. Co Investigator, "Stress and Reproductive Hormones in Depressed Women", 10% effort, \$165,357 year 1 TDC, \$708,446 years 1-4. Submitted to NIMH, Pending with priority score of 128 and 6.8 percentile. 12/1/92-11/30/96.
- B. Submitted Competitive renewal to NIH for P30 Center grant. Requesting \$3,230,803 TDC (\$4,887,686 TDC+IDC), 4/1/94-3/31/99.
- C. Assisted Co-Principal Investigators Deborah Oakley and MaryFran Sowers with the development of a proposal to the OVPR for expanded support for the Michigan Initiative for Women's Health.
- D. Assisted individuals in three firms (Innovation Associates, Software Technologies, Inc. and Wolpert Polymers) to develop new SBIR grants which, if successful, will involve the University as a sub-contractor.

SCIENTIFIC COLLABORATIONS:

- A. 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.
- B. Biological Chemistry and Obstetric and Gynecology: K.M.J. Menon: Localization and regulation of mRNA for LH receptor in rat granulosa cells.
- C. Chemistry: Mark Meyerhoff: (with Richard Brown) NSF-funded project aimed at developing multisite, antibody-based solid state microelectrodes.
- D. Electrical Engineering: Richard Brown: (with Mark Meyerhoff) NSF-funded project aimed at developing multisite, antibody-based solid state microelectrodes.
- E. Internal Medicine: David Humes: continuing to study the ability of kidney stem cells to form tubules and perhaps form an artificial kidney using our patented three dimensional bioreactor (we are getting kidney tubules to form from dissociated rabbit kidney cells).
- F. Nursing: Nancy Reame: joint involvement in developing the NIH U54 National Center for Infertility Research.
- G. 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.
- H. Psychology: Jacquelynne Eccles: returning this fall to the University of Michigan. Completing a long term, longitudinal study concerning hormones and behavior in adolescents.
- I. Carnegie Institute of Washington, Embryology and WSU, Anatomy: Bent Boving (retired): Co-investigator in artificial organ development and perfusion programs.
- J. 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 an additional SBIR.
- K. Michigan State University, Animal Science: James Ireland, Reproductive Biologist: development of a solid state, two site chemiluminescence-based immunoassay for inhibin.
- L. Software Technologies, Inc., Franklin, Michigan 48025: Robert J. Carrico, Statistician, Assisted in development of an SBIR proposal re-submitted June 15, 1993 concerning the development of a new computer interface to assist scientists in their access of statistical programs.
- M. Wolpert Polymers, Inc., Southfield, Michigan 48037: Stephen M. Wolpert, Polymer Chemist formerly with Gelman Sciences and KMS Fusion. Helping him develop an SBIR focused on creating a novel affinity matrix-membrane for immunoassays, blotting experiments, etc.
- N. Wayne State University, Obstetrics and Gynecology: Kamran Moghissi: Co-Associate Director of the NCIR grant and Key Investigator of one of its projects.

INTELLECTUAL PROPERTIES ACTIVITY:

- A. Responding to first office action on patent application, Bioreactor System With Alginate Matrix (SN 07/744,109; UM#136c1 RM-6HM).

PROJECTS UNDER STUDY:

- A. Development of a computer-controlled perfusion system for on-line analysis of cellular responses to pulsatile and other controlled signaling.
- B. Analysis of dynamic control of pituitary function by GnRH.
- C. Application of principles of cellular bioengineering to the growth and function of mammalian cells and the development of artificial organs.
- D. Development of novel biosensors and immunoassays.
- E. 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 and Psychiatry.
- F. Member, Local Arrangements Committee for 1994 Annual Meeting of the Society for the Study of Reproduction to be hosted by the University of Michigan.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Twenty-fifth Annual Meeting of the Society for the Study of Reproduction, North Carolina State University, July 27-August 1, 1992.
2. Meeting of Directors of NICHD P30 Centers, Rochester, Minnesota, July 26-27, 1992.
3. Presented opening RSP seminar, "Pulses, Chaos, and Signals", September 14, 1992.
4. Phone review of grant application, Cornell University, September 23, 1992.

5. Annual meeting of the Society for Neuroscience, Anaheim, California, October 24-30, 1992.
6. Bi-annual meeting of the Steering Committee of the National Collaborative Program for Infertility Research, Boston, December 7-9, 1992.
7. NIDDK Endocrine Research Program Advisory committee, Bethesda, Maryland, March 22, 1993.
8. NIDDK Hormone Distribution Program Committee, Bethesda, Maryland, March 22 1993.
9. NIH-NIA Workshop on the Menopause, March 22-24, 1993.
10. Consultant for Personal Bibliographic Software, Ann Arbor, Michigan, May 12, 1993.
11. Endocrine Society meeting, San Antonio, June 9-12, 1993.
12. International Pituitary Congress, Marina del Rey, California, June 13-15, 1993.
13. Hosted bi-annual meeting of the Steering Committee of the National Collaborative Program for Infertility Research, June 28-30, 1993.

MISCELLANEOUS:

1. Developed for the Office of the Vice-President for Research a five year report for the RSP "Review of Progress 1988-1992 and Plans for 1993-1997".
2. Developing an immunoassay analysis system that will assist many investigators.
2. Implementing ELISA and chemiluminescence-based, solid state, two site immunoassays in Standards and Reagents Core as a partial replacement for radioimmunoassays (and thereby reduction in usage of radioactive isotopes).
3. Met with Board of Directors of BioQuant, Inc. on February 5 and June 16, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Halberstadt, C.R., Lee, G.M., Palsson, B.O. and Midgley, A.R.: Enhanced antibody productivity in a serum-free, low protein medium from a long-term hybridoma cell culture using the transtubular bioreactor. *Biotechnology Progress*, In Press.
2. Wiesen, J.F. and Midgley, A.R., Jr.: Changes in expression of cx43 gap junction mRNA and protein during ovarian follicular growth. *Endocrinology*, In Press.
3. Wiesen, J.F. and Midgely, A.R., Jr.: Changes in expression of c43 gap junction mRNA and protein during ovarian follicular atresia. *Biol. Reprod.*, In Press.

ARTICLES SUBMITTED:

1. Brand, R.B., Ghazzi, M.N., Rolfes-Curl, A., Cantor, H.C. and Midgley, A.R.: Use of continuous, on-line hydrogen ion-monitoring to examine the flow dynamics of perfusion systems and cellular metabolism.
2. Brand, R.B., Lyons, R. and Midgley, A.R.: Understanding the dynamics of cellular responsiveness to modifications of metabolic substrates in perfusion.

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

1. Cantor, H.C., Young, E.A., Boving, B.G. and Midgley, A.R.: Monitoring dynamic responses of perfused ovine pituitary corticotropes to hormonal stimuli in real-time. 75th Annual Meeting, Endocrine Society, June 9-12, 1993.

2. Peegel, H., Mazhari, N., Midgley, A.R. and Menon, K.M.J.: *In situ* hybridization of LH/hCG receptor messenger RNA during hormone induced down regulation and the subsequent recovery in rat corpora lutea. 26th Annual Meeting, Society for the Study of Reproduction, August 1-4, 1993.
3. Cantor, H.C., Padmanabhan, V., Boving, B.G. and Midgley, A.R.: Monitoring dynamic responses of perfused ovine pituitary gonadotropes to hormonal stimuli in real-time. 26th Annual Meeting, Society for the Study of Reproduction, August 1-4, 1993.
4. Lemon, W., Padmanabhan, V., Young, E., Favreau, P. and Midgley, R.: The shape of LH pulses in hypophyseal portal blood in ovariectomized Suffolk ewes. Third International Pituitary Congress - A Basic and Clinical Update. Marina del Rey, June 13-15, 1993.
5. McConnell, D.S., Padmanabhan, V., Groome, N., Ireland, J.J. and Midgley, A.R.: Development of a two-site solid phase immuno-chemiluminescent assay for dimeric inhibin. Ares Serono Symposia, II International Symposium on Inhibin and Inhibin-Related Proteins, Siena, Italy, June 17-18, 1993.

**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 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES

None.

II. TEACHING ACTIVITIES

- A. Graduate students:
1. Responsible during the current academic year for teaching activities for the following:
 - a. Two sessions Pathology 581 (Kunkel).
 - b. Thirteen sessions Pathology 850 (Miller).
 - c. Six sessions Cellular and Molecular Biology 850.
 2. Ph.D. Thesis sponsor for Jia Shi (Pathology Department, Boston University).
 3. Laboratory Rotation, Heidi Michaels (Cell and Molecular Biology).
 4. Program Director, "Experimental Immunopathology Training Grant" funded 4/93.
- B. Postdoctoral fellows:
1. Duaine Jackola, Ph.D.
 2. Li Shaokang, U.S.
 3. Jacek Witkowski, Ph.D.
 4. Jagadananda Ghosh, Ph.D.
 5. Paul Turke, Ph.D.
 6. Prem Chaudhry, Ph.D.

III. RESEARCH ACTIVITIES

SPONSORED SUPPORT:

- A. Principal Investigator, "Activation Defects in Aging T Cells", NIH AG-09801 (20%), \$146,896 direct costs/year, 8/1/90-7/31/95. MERIT award.
- B. Principal Investigator, "Immune and Muscle Function Assays as Biomarkers of Aging", NIH AG-11067 (15%), \$145,000 direct costs/year, 4/1/93-3/31/98.
- C. Principal Investigator, "Aging Effects on IL-2 Secreting Helper T Cells", NIH AG-03978 (16%), \$143,647 direct costs/year, 8/1/91 - 7/31/94.
- D. Training Supervisor, "Research Training Agreement: Postdoctoral Training in Aging and Growth Control", Boston University (NIH/NIA Prime) (0%), \$20,304 direct costs/year, 10/1/91-9/30/92.

- E. Core Director, "Core Facility for Aged Rodents", NIH AG-08808 (10%), \$66,755 direct costs/year, 9/1/89 - 8/30/94. (Component of Geriatric Research and Training Center, J. Halter, Program Director).
- F. Core Director, "Research Development Core," NIH AG-08808 (10%), \$41,000 direct costs/year, 9/1/89-8/30/94. (Component of Geriatric Research and Training Center, J. Halter, Program Director).
- G. Program Director, "Research Training in Experimental Immunopathology", NIH AI-07413, \$58,563 direct costs/year, 4/1/93-3/31/98.
- H. Principal Investigator, "Summer Training Course in Aging Research", NIH AG-11332 (2.5%), \$33,651 direct costs, 4/1/93-6/30/93.

PENDING

- A. Principal Investigator, "Genetic Control of Longevity in Mice," NIH AG11687 (10%), \$188,979 direct costs/year requested, 8/1/93-7/31/98.
- B. Principle Investigator, "1994 Gordon Research Conference on the Biology of Aging," \$37,130 direct costs requested, 2/27/94-6/30/94.
- C. Principal Investigator, "T Cell Repopulation After Bone Marrow Transplantation, VA Merit Review Application (15%), \$98,120 direct costs requested, 5/1/94-4/30/99.

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL

- A. Committee on Master Planning Analysis.
- B. Graduate Education Committee.
- C. Qualifying Examination Committee.
- D. Research Colloquia, Course Coordinator.

MEDICAL SCHOOL/HOSPITAL

- A. Geriatrics Center: Research Development Core Director.
- B. Geriatric Center: Director, Core Facility for Aged Rodents.
- C. Member, Geriatric Center Research Operating Committee.
- D. Associate Director for Research, Geriatrics Center.
- E. Research Retreat Co-ordinator, Geriatric Research and Training Center.

REGIONAL AND NATIONAL

- A. Member, National Advisory Council on Aging.
- B. Publications Committee, Gerontological Society of America.
- C. Board of Scientific Advisors, Buck Center for Research on Aging.
- D. Fellow, Gerontological Society of America.
- E. Chair-Elect, Gordon Research Conference on "Biology of Aging".
- F. Board of Scientific Advisors, American Federation for Aging Research.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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

C. Journal of Gerontology: Biological Sciences.

INVITED LECTURES/SEMINARS:

1. Gordon Conference on Biology of Aging (Meeting Vice-Chair), July, 1992.
2. Serling Symposium on Gerontology, Rehovot, Israel, September, 1992.
3. Eleventh Annual Symposium on Gerontology and Geriatrics (St. Louis, VA GRECC), September, 1992.
4. Short Course in Genetics: Introduction to Genetics of Aging.
5. Symposium: Animal Models for Immunological Research in Aging (University of Illinois), October, 1992.
6. Marion Merrill Dow Symposium on "Basic Mechanisms in Aging", Kansas City, October, 1992.
7. Gerontology Society of America Annual Meeting (Session Chair), November, 1992.
8. World Health Organization Program on Research in Aging, Washington, March, 1993.
9. NIA Conference on Endothelial Models for Aging, Bethesda, April, 1993.
10. Department of Pathology, University of Washington, June, 1993.
11. NIA Biomarkers Conference, June, 1993.
12. Summer Training Course in Experimental Aging Research (Course Director), June, 1993.

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

1. Flurkey, K., Miller, R.A. and Harrison, D.E.: Cellular determinants of age-related decrements in the T cell mitogen response of B6CBAF1 mice. *J. Gerontol. Biol. Sci.* 1992;47:B115-B120.
2. Shi, J. and Miller, R.A.: Tyrosine-specific protein phosphorylation in response to anti-CD3 antibody is diminished in old mice. *J. Gerontol. Biol. Sci.* 1992;47:B147-B153.
3. Witkowski, J.M. and Miller, R.A.: Increased function of P-Glycoprotein in T lymphocyte subsets of aging mice. *J. Immunol.* 1993;150:1296-1306.
4. Miller, R.A.: Aging and cancer: Another perspective. *J. Gerontol. Biol. Sci.* 1993;48:B8-B9.
5. Shi, J. and Miller, R.A.: Differential tyrosine-specific protein phosphorylation in mouse T lymphocyte subsets: Effect of age. *J. Immunol.*, In Press.
6. 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.*, In Press.
7. Li, S.P. and Miller, R.A.: Age-associated decline in IL-4 production by murine T lymphocytes in extended culture. *Cell. Immunol.*, In Press.
8. Miller, R.A.: Aging and immune function: Cellular and biochemical analyses. *Exp. Gerontol.*, In Press.

ARTICLES SUBMITTED FOR PUBLICATION

1. Jackola, D.R. and Miller, R.A.: Age-associated changes in human T cell phenotype and function.

BOOKS/CHAPTERS IN BOOKS

1. Miller, R. A.: Accumulation of malfunctioning cells in a complex network: Lessons from immunology for experimental gerontology. Proceedings of the First International Congress on Biomarkers in Gerontology, Bologna, Italy, In Press.
2. Miller, R.A.: Aging and the immune system, in, Masoro, E. (ed.), Handbook of the Physiology of Aging, Academic Press, New York, In Press.
3. 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, In Press
4. Miller, R.A.: The biology of aging and longevity, in, Hazzard, W.R., et al. (eds.), Principals of Geriatric Medicine and Gerontology, McGraw-Hill, Inc., New York, In press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993

I. CLINICAL ACTIVITIES:

- A. None.

II. TEACHING ACTIVITIES:

- A. None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator, "Role of Adhesion Molecules in Psoriasis", National Institute of Health, Grant 1-RO1- \$147,702, direct cost, (B.J. Nickoloff, Principal Investigator), June 1991-July 1993.
- B. Co-Investigator, "Role of Adhesion Molecules in Skin Diseases", National Institutes of Health, (B.J. Nickoloff, Principal Investigator), July 1991-June 1994.
- C. Co-Investigator, "Dermal Dendrocytes and AIDS-Related Psoriasis", \$184,727, direct cost, July 1991-June 1994, (B.J. Nickoloff, Principal Investigator).

PENDING:

- A. Principal Investigator, "Role of Keratinocytes in Cutaneous Inflammation/Immunity", Johns Hopkins Center for Alternative Animal Testing.

PROJECTS UNDER STUDY:

- A. Characterization of gamma interferon receptor on normal and psoriatic keratinocytes.
- B. Characterization of epidermal growth factor receptor on normal and psoriatic keratinocytes.
- C. Role of gamma interteron 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.

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. Mitra, R.S. and Nickoloff, B.J.: Epidermal growth factor and transforming growth factor-alpha decreases gamma interferon receptors and induction of intercellular adhesion molecule (ICAM-1) on cultured keratinocytes. *J. Cell Physiol.* 1992;150:264-268.
2. Stooft, T., Mitra, R.S., Dixit, V.M. and Nickoloff, B.J.: Keratinocyte activation following binding of T lymphocytes. *J. Invest. Dermatol.* 1992;98:92-95.
3. 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.* 1993;142:1029-1040.
4. 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.* 1993;150:2148-2159.
5. 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., In Press, 1993.*
6. 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., In Press, 1993.*

BOOKS/CHAPTERS IN BOOKS:

1. Mitra, R.S. and Nickoloff, B.J.: Culture of epidermal keratinocytes in serum-free growth medium, in, Leigh, I. (ed.), *Keratinocyte Handbook*, Cambridge University Press, In Press, 1993.

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

1. Nickoloff, B.J., Mitra, R.S., Leek, Z., Thompson, C. and Shimizu, Y.: Gamma interferon does not induce expression on keratinocytes of the CD28-ligand B7/BB-1. *Clin. Res.* 1992;40:238.
2. Nickoloff, B.J., Mitra, R.S., Varani, J., Dixit, V.M. and Polverini, P.: Psoriatic keratinocyte induced angiogenesis is inhibited by thrombospondin. *J. Invest. Dermatol.* 1992;98:560.
3. Mitra, R.S., Shimizu, Y. and Nickoloff, B.J.: Histamine synergistically augments tumor necrosis factor alpha mediated induction of keratinocyte ICAM-1 expression. *Arch. Dermatol. Res.* 1992;161:255.
4. Nickoloff, B.J., Mitra, R.S., Green, J., Shimizu, Y. and Thompson, C.L.: Gamma interferon treated keratinocytes present bacterial-derived superantigens to T cells which is blocked by LFA-1/ICAM-1 antibodies. *Clin. Res.* 1992;40:720.
5. Nickoloff, B.J., Mitra, R.S., Green, J., Turka, L., Thompson, C. and Shimizu, Y.: Discordant expression of BB-1 and B7 on cultured keratinocytes *in-vitro* and psoriatic keratinocytes *in vivo*. *J. Cut. Path.* 1992;19:543.

6. Mitra, R.S., Shimizu, Y. and Nickoloff, B.J.: European Congress on Wound Healing and Skin Physiology, Bochum, Germany, November 5-7, 1992.
7. Nickoloff, B.J. and Mitra, R.S.: Intraepidermal psoriatic cytokine network involves gamma interferon, transforming growth factor-alpha and their cell surface receptors: Dysregulation rather than deficiency. *J. Invest. Dermatol.* 1992;99:882.
8. Mitra, R.S., Shimizu, Y. and Nickoloff, B.J.: Cis-urocanic acid and histamine augment TNF- α mediated induction of keratinocyte ICAM-1 expression and suppress IFN- γ induction of HLA-DR. *J. Invest. Dermatol.* 1993;100:490.
9. 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.* 1993;100:522.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Pathology residents - supervision and teaching during cytopathology rotation and when covering necropsies.
- B. Pathology residents - biweekly cytopathology conferences.
- C. Senior medical students during pathology electives.
- D. Sophomore medical students: class lectures, ICS course.
- E. 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. Cross contamination in the cytologic staining circuit.
- B. Prevalence of silicosis in pulmonary specimens.

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. Chairman, Editorial and Publications Committee, International Academy of Cytology.

- F. Membership Committee, International Academy of Cytology.
- G. Budget and Finance Committee, American Society of Cytology.
- H. Chairman, Awards Committee, American Society of Cytology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Lecture and workshop, "Cytology of Serous Effusions: Technical Matters and Diagnostic Problems", Upper New York State Society of Cytology, Buffalo, New York, September, 1992.
2. Teleconference, "Cytology of Serous Effusions: Technical Matters and Diagnostic Problems", American Society of Cytology, January, 1993.
3. Lecture, "Cytology of Serous Effusions: Technical Matters and Diagnostic Problems", Cytology Society of Indiana and Kentuckiana Society of Cytology, French Lick, Indiana, April, 1993.
4. Lecture, "The Origins of Cytology in Michigan and the Michigan Society of Cytology", Michigan Society of Cytology, Grand Rapids, Michigan, May, 1993.
5. Eisenstein Memorial Lecture, "Fine Needle Aspiration Cytology: Historical Development, How it is Done, What It Shows, Pitfalls and Usefulness", Medical Staff, Mercy Hospital, Port Huron, Michigan, June, 1993.

HONORS AND AWARDS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wojcik, E.M. and Naylor, B.: "Collagen balls" in peritoneal washings: Prevalence morphology, origin and significance. Acta Cytol. 1992;36:466-470.
2. Huang, J.C. and Naylor, B.: Cytomegalovirus infection of the cervix detected by cytology and histology: A report of five cases. Cytopathology, In Press.

BOOKS/CHAPTERS IN BOOKS:

1. Naylor, B. and Toivonen, T.: The use of toluidine-blue stained wet films in diagnostic cytology, in, Schmidt, W.A. (ed.), Cytopathology Annual 1993, Williams and Wilkins, Baltimore, pp. 279-287.

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

1. Naylor, B.: Evolution of a society, 1951-1991. American Society of Cytology Lecture, ASC Bulletin. 1993;33:32-34.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993

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 Psoriasis", NIH RO-1 (40% effort), \$147,702 Direct Costs, June 1991-July 1993.
- B. "Role of Adhesion Molecules in Skin Diseases", NIH RCDA (50% effort), \$60,000 Direct Costs, July 1991-June 1994.
- C. "Role of Dermal Dendrocytes in AIDS-Related Psoriasis", NIH RO-1 (10% effort), \$184,727 Direct Costs, July 1991-June 1994).

PROJECTS UNDER STUDY:

- A. Role of gamma interferon in modulating adherence reactions between resting and activated mononuclear leukocytes and keratinocytes.
- B. Characterization of gamma interferon receptor on normal and psoriatic keratinocytes.
- C. Gamma interferon activation of protein kinase C in benign and malignant keratinocytes.
- D. Binding of lymphocytes to epidermis and vessels of frozen sections of psoriatic skin and other dermatoses.
- E. Characterization of type of beta interferon produced by virally infected keratinocytes.

- F. Interrelationship between gamma interferon, and tumor necrosis factor and PGE₂ and IL-1 production by keratinocytes and monocytes.
- G. Characterization and biological significance of thrombospondin production by keratinocytes and melanocytes.
- H. Role of extracellular matrix in adherence reactions involving resting and activated mononuclear leukocytes.
- I. Characterization of epidermal growth factor receptor on normal and psoriatic keratinocytes.
- J. Characterization of effect of cyclosporin A on phorbol ester induced cutaneous inflammation and hyperplasia.
- K. Role of endothelial cell adhesion molecules (ICAM-1, ELAM-1, VCAM-1) in cutaneous leukocyte trafficking.
- L. Role of factor XIII a positive dermal dendrocytes in AIDS-related psoriasis.
- M. Dissection of cytokine networks in psoriasis, allergic contact dermatitis to poison ivy, and mycosis fungoides.

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

- A. 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. Visiting Professor, "Superantigens and Skin Disease: Importance of Streptococcus, Cytokine Activated Keratinocytes, and LFA-1/ICAM-1 Adhesion Molecules", Kaorin University-Dept of Dermatology, October 14, 1992, Tokyo, Japan.
2. Invited Speaker, Special Lecture, "Keratinocytes as Instigators of Cutaneous Inflammation", 17th Annual Meeting of the Japanese Society for Investigative Dermatology, October 16, 1992, Sendai, Japan.
3. "Gamma Interferon Treated Keratinocytes Present Bacterial-Derived Superantigens to T cells Which is Blocked by LFA-1/ICAM-1 Antibodies", Midwest Society for Investigative Dermatology, November 5, 1992, Chicago, Illinois.
4. Invited Speaker, "Keratinocytes as Perpetuators of Immune Reactions in the Skin", Concepts in Cutaneous Immunology Symposium, Annual Meeting of the American Association of Pharmaceutical Scientists, November 19, 1992, San Antonio, Texas.
5. "Immunobiology of Dermal Dendrocytes: Relevance to AIDS-related Kaposi's Sarcoma", New Frontiers in Dermatopathology: Annual Meeting of the American Society of Dermatopathology, December 4, 1992, San Francisco, California.
6. "Discordant Expression of BB-1 and B7 on Keratinocytes", Annual Meeting of the American Society of Dermatopathology, December 4, 1992, San Francisco, California.
7. "Adhesion Molecules in Skin Disease", Faculty-Advanced Immunology Course-102, Annual Meeting of American Academy of Dermatology, December 5, 1992, San Francisco, California.
8. Visiting Professor, "Cytokines, Superantigens and Psoriasis", Department of Dermatology, Yale University School of Medicine, February 11, 1993, New Haven, Connecticut.
9. Invited Speaker, "Cytokines and Skin Diseases", Bone Marrow Transplantation Program, University of Michigan, February 17, 1993, Ann Arbor, Michigan.
10. Invited Speaker, "Keratinocyte-T-Cell Interactions", Royal Society of Medicine Sponsored Symposium on Immunological Aspects of Cutaneous Warts, King's College, London, April 5, 1993, London, England.
11. "Role of ICAM-1 and HLA-DR in Accessory Cell Function in Keratinocytes, Joint SID/FCR Session: New Developments in Immunocompetent Cells in Skin", Annual Meeting of the Society for Investigative Dermatology, April 30, 1993, Washington, D.C.
12. "Perturbation of Epidermal Barrier Function of Skin by Repeated Tape Stripping Correlates with Initiation of Cytokine Cascade", American Federation of Clinical Research Meeting, May 1, 1993, Washington, D.C.
13. Invited Speaker, "Keratinocyte-Key Immunocytes of the Epidermis", Second International Workshop on Adhesion Molecules, May 7, 1993, Vienna, Austria.
14. Invited Speaker, "Inflammatory Mechanisms of Skin Disease", Division of Rheumatology Lectures Series, University of Michigan, Dr. David Fox, June 2, 1993, Ann Arbor, Michigan.
15. Invited Speaker, "Cytokine Network in Psoriasis", Department of Medicinal Chemistry, University of Toledo, June 3, 1993, Toledo, Ohio.
16. Invited Speaker, "Cytokine Networking in Skin Diseases", Detroit Immunological Society, June 9, 1993, Detroit, Michigan.
17. Invited Speaker and Visiting Professor, "CD34 and Kaposi's Sarcoma: Psoriasis, Superantigens, and Cytokines", Collaborative Course on Biology of the Skin, Departments of Dermatology: Boston University, Brown University, Tufts University and Harvard Medical School, June 14, 1993, Boston, Massachusetts.

18. Invited Speaker, "Keratinocyte Participation in Contact Dermatitis", Contact Dermatitis-State-of-the-Art Issues, Penn State University, June 18, 1993, Boston, Massachusetts.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Nickoloff, B.J.: Role of epidermal keratinocytes as key initiators of contact dermatitis due to allergic sensitization and initiation. *Am. J. Contact Dermatitis*. 1992;3:65-69.
2. Mitra, R.S. and Nickoloff, B.J.: Epidermal growth factor and transforming growth factor-alpha decreases gamma interferon receptors and induction of intercellular adhesion molecule (ICAM-1) on cultured keratinocytes. *J. Cell Physiol*. 1992;150:264-268.
3. Stoof, T., Mitra, R.S., Dixit, V.M. and Nickoloff, B.J.: Keratinocyte activation following binding of T lymphocytes. *J. Invest. Dermatol*. 1992;98:92-95.
4. Fivenson, D.P., Becker, R., Dunstan, R.W., Nickoloff, B.J. and Moore, P.F.: Dermal dendrocytes and T cells in mycosis fungoides: Support for an animal model of human cutaneous T cell lymphoma. *J. Cancer Res*. 1992;70:2091-2098.
5. Fivenson, D.P., Douglass, M.C. and Nickoloff, B.J.: Thy-1 positive dermal dendrocytes are increased in mycosis fungoides. *Am. J. Pathol*. 1992;141:1373-1380.
6. Bruynzeel, I., Nickoloff, B.J., Van der Raaij, E.M.H., Boorsma, D.M., Stoof, T.J. and Willemze, R.: Induction of ICAM-1 expression by keratinocytes via a paracrine pathway involving dermal dendritic cells. *Arch. Dermatol. Res*. 1992;284:250-252.
7. Carr, K.A., Bulengo, S., Weiss, L.M. and Nickoloff, B.J.: Lymphoepithelioma-like carcinoma of the skin: A case report with immunophenotypic analysis and in-situ hybridization for Epstein-Barr viral genome. *Am. J. Surg. Pathol*. 1992;16:905-913.
8. Altman, D.A., Nickoloff, B.J. and Fivenson, D.P.: Demonstration of a relationship between factor XIIIa positive and CD34 positive dendrocytes in mesenchymal skin tumors. *J. Cut. Pathol*. 1992;19:1-5.
9. Nickoloff, B.J.: PECAM-1 (CD31) is expressed on proliferating endothelial cells, stromal spindle-shaped and dermal dendrocytes in Kaposi's sarcoma. *Arch. Dermatol*. 1993;129:250-252.
10. 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 lymphangiomatosis. *Am. J. Surg. Pathol*. 1993;17:321-328.
11. Nickoloff, B.J.: Pathophysiology of cutaneous inflammation. *Arch. Dermatol. Res*. 1992;284:10-12.
12. Grant, D.S., Kleinman, H.H., Goldberg, I.D., Bhargava M.M., Nickoloff, B.J., Kinsella, J.L., Polverini, P. and Rosen, E.M.: Scatter factor induces blood vessel formation *in vivo*. *Proc. Nat. Acad. Sci. (USA)* 1993;90:1937-1941.
13. 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*. 1993;142:1029-1040.
14. Nickoloff, B.J., Mitra, R.S., Green, J., Shimizu, Y., Thompson, C. and Turka, L.A.: Accessory cell function of keratinocytes for superantigens: Dependence on LFA-1/ICAM-1 interaction. *J. Immunol*. 1993;150:2148-2159.

15. 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.*, In Press, 1993.
16. 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*. Abercrombie Symposium Proceedings. Society for Experimental Biology, In Press, 1993.
17. 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.*, In Press, 1993.
18. 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.*, In Press, 1993.
19. 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.*, In Press, 1993.
20. Nickoloff, B.J. and Turka, L.: Keratinocytes: Key immunocytes of the integuments. *Am. J. Pathol.*, In Press, 1993.
21. 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.*, In Press, 1993.

BOOKS/CHAPTERS IN BOOKS:

1. Nickoloff, B.J: Cytokine networks in skin disease, in, Kunkel, S. and Remick, D. (eds.), *Cytokines in Health and Disease: Physiology and Pathophysiology*, New York, New York, pp. 413-432, 1992.
2. Barker, J.N.W.N. and Nickoloff, B.J.: Leukocyte-endothelium interactions in cutaneous inflammatory processes, in, Hausar, C. (ed.), *Springer Seminars in Immunopathology*, Springer International, In Press, 1993.
3. Fivenson, D.P. and Nickoloff, B.J.: Cell trafficking networks in cutaneous T cell lymphoma. NATO meeting-basic mechanisms of physiological and aberrant lymphoproliferation in the skin, in, Lambert, W.C. (ed.), *Plenum Publishing*, New York, In Press, 1993.
4. Stoof, T., Boorsma, D. and Nickoloff, B.J.: Immunological cytokines of epidermis. in, Leigh, I. (ed.), *Keratinocyte Handbook*, Cambridge University Press, In Press, 1993.
5. Nickoloff, B.J.: The immunobiology of dermis, in, Nickoloff, B.J. (ed.), *Dermal Immune System*, CRC Press, Inc., Boca Ratan, Florida, In Press, 1993.
6. 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, 1993.
7. Kunkel, S.L., Driscoll, K., Ward, P.A., Nickoloff, B.J. and Streiter, R.M.: Immunopathology of environmental and occupational disease, in, Craighead, J.E. (ed.), *Pathology of Enviromental and Occupational Diseases*, In Press, 1993.

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

1. Nickoloff, B.J., Huang, Y.Q., Li, J. and Friedman-Kien, A.: Immunohistochemical detection of papilloma virus antigens in Kaposi's sarcoma. *Lancet* 1992;339:548-549.
2. Nickoloff, B.J. and Mitra, R.J.: Intraepidermal psoriatic cytokine network involves gamma interferon, transforming growth factor-alpha and their cell

- surface receptors: Dysregulation rather than deficiency. *J. Invest. Dermatol.*, In Press, 1992.
3. Brunzeel, I., Nickoloff, B.J., Van der Raaj, E., Boorsman, D., Stoof, T. and Willemze, R.: Induction of ICAM-1 expression by epidermal keratinocytes via a procrine pathway involving dermal dendrocyte cells. *Br. J. Dermatol.* 1992;83:159.
 4. Nickoloff, B.J., Mitra, R., Leek, Zell, T., Thompson, C. and Shimizu, Y.: Gamma interferon does not induce expression on keratinocytes of the CD28-ligand B7/BB-1. *Clin. Res.* 1992;40:238.
 5. Fivenson, D.P., Hanson, C.A. and Nickoloff, B.J.: Specific localization of the malignant clone to the epidermal component in cutaneous T-cell lymphoma. *Clin. Res.* 1992;40:238.
 6. Koch, A.E., Hines, C.K. and Nickoloff, B.J.: Monoclonal antibody 4A11 detects a novel antigen expressed on abnormal vascul endothelium: Upregulation in a human *in vivo* model of contact dermatitis. *Clin. Res.* 1992;40:268.
 7. Huang, Y.Q., Li, J.J., Nickoloff, B.J. and Friedman-Kien, A.: Four different cultured Kaposi's sarcoma cell lines express several monocyte/macrophage antigens. *J. Invest. Dermatol.* 1992;98:618.
 8. Nickoloff, B.J., Mitra, R.J., Varani, J., Dixit, V.M. and Polverini, P.: Psoriatic keratinocyte induced angiogenesis is inhibited by thrombospondin. *J. Invest. Dermatol.* 1992;98:560.
 9. Fivenson, D.P. and Nickoloff, B.J.: CD1b and CD1c expression by dermal dendrocytes and epidermal Langerhans cells in mycosis fungoides and psoriasis. *Clin. Res.* 1992;40:449.
 10. Mitra, R.S., Shimizu, Y. and Nickoloff, B.J.: Histamine synergistically augments tumor necrosis factor alpha mediated induction of keratinocyte ICAM-1 expression. *Arch. Dermatol. Res.* 1992;161:255.
 11. Nickoloff, B.J., Mitra, R.S., Green, J., Shimizu, Y. and Thompson, C.L.: Gamma interferon treated keratinocytes present bacterial-derived superantigens to T cells which is blocked by LFA-1/ICAM-1 antibodies. *Clin. Res.* 1992;40:720.
 12. Saed, G., Fivenson, D.P., Naidu, Y. and Nickoloff, B.J.: Mycosis fungoides and psoriasis exhibit a TH-1 type cell mediated response while Sezary syndrome expresses a TH-2 type response. *Clin. Res.* 1992;40:732.
 13. Altman, D.A., Nickoloff, B.J. and Fivenson, D.P.: Differential expression of factor XIIIa and CD34 in cutaneous mesenchymal tumors. *J. Cut. Path.* 1992;19:476.
 14. Nickoloff, B.J., Mitra, R.S., Green, J., Turka, L., Thompson, C. and Shimizu, Y.: Discordant expression of BB-1 and B7 on cultured keratinocytes *in vitro* and psoriatic keratinocytes *in vivo*. *J. Cut. Path.* 1992;19:543.
 15. Nickoloff, B.J.: Keratinocytes as instigators of cutaneous inflammation. *J. Derm. Sci.* 1992;4:130.
 16. Sakimura, L., Yamamura, M., Sicling, P., Nickoloff, B.J., Rae, T. and Modlin, R.: Expression of interleukin-7 mRNA in human skin. *J. Invest. Dermatol.* 1993;100:490.
 17. 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-g induction of HLA-DR. *J. Invest. Dermatol.* 1993;100:490.
 18. 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.* 1993;100:522.
 19. Fivenson, D.P., Saed, G., Naidu, Y. and Nickoloff, B.J.: Cytokine mRNA profiles in CTCL: Mycosis fungoides is TH₁ and Sezary Syndrome is TH₂. *J. Invest. Dermatol.* 1993;100:556.

20. Naidu, Y. and Nickoloff, B.J.: Cultured endothelial cells express dermal dendrocyte marker-factor XIIIa after exposure to Kaposi's sarcoma growth medium. *J. Invest. Dermatol.* 1993;100:494.
21. Nestle, F., Turka, L. and Nickoloff, B.J.: Comparative functional analysis of dendritic cells obtained from human epidermis (Langerhans cells), dermis (dermal dendrocytes) and peripheral blood. *J. Invest. Dermatol.* 1993;100:562.
22. Nestle, F. and Nickoloff, B.J.: Purification and immunological characterization of dermal dendrocytes obtained from normal skin. *Clin. Res.* 1993;41:178.
23. Nickoloff, B.J. and Naidu, Y.: Perturbation of epidermal barrier function of skin by repeated tape stripping correlates with initiation of cytokine cascade. *Clin. Res.* 1993;41:255.
24. Koch, A.E., Leibovich, J., Haines, G. and Nickoloff, B.J.: Monoclonal antibody 4A11 detects a novel antigen expressed on abnormal vascular endothelium: Upregulation in human *in vivo* model of contact dermatitis. *Arthritis Rheum.* 1993;35:5138.
25. 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.* 1993;41:256.
26. 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.* 1993;100:572.
27. 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., In Press*, 1993.
28. Nickoloff, B.J., Book Review: Differential diagnosis in dermatopathology, by Ackerman, A.B. *N. Eng. J. Med., In Press*, 1993.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993

I. CLINICAL ACTIVITIES:

- A. Director, Molecular Diagnostics Laboratory.
- B. Autopsy Service (two weeks and one weekend on-call).

II. TEACHING ACTIVITIES:

- A. Supervised Dr. Maribel Gonzalez-Garcia, Dr. Ramon Merino, and Mukund Dole (Postdoctoral Fellows).
- B. Supervised Kelvin Li and Edward Kwon (undergraduate students).
- C. Supervised Dr. Kathleen Heidelberger (three months).
- D. Supervised Donald Zhou (Molecular Diagnostics).
- E. Coordinator, Molecular Diagnostics Conference (weekly).
- F. Graduate Pathology Program (Course 581): Two Lectures.
- G. Speaker, Molecular Diagnostics, Clinical Microbiology Section.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Regulation and Function of the Bcl-2 Gene during Thymus Development", National Institute 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, "Functional Cloning of Genes that Suppress Programmed Cell Death", Sandoz Foundation, \$13,000, unrestricted, 6/1/93.
- D. Principal Investigator, "Functional Cloning of Genes that Suppress Programmed Cell Death", Horace H. Rackham School of Graduate Studies, \$15,000, unrestricted, 4/1/93.

PENDING:

- A. 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.

PROJECTS UNDER STUDY

- A. Functional characterization of Bcl-2 and Bcl-x genes during lymphoid development.
- B. Molecular cloning of genes involved in programmed cell death of B lymphocytes.

- C. Regulation and role of Bcl-2 in Neuroblastoma.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Molecular Diagnostics Laboratory.
- B. Interviewer, faculty and postdoctoral candidates for research fellowships.

MEDICAL SCHOOL/HOSPITAL:

- A. Director, Genotyping Core for Cystic Fibrosis Mutations.
- B. Member, University of Michigan Cancer Center.
- C. Member, Transgenic Core Facility Committee, Multi/purpose Arthritis Center.
- D. Reviewer, Departmental Grants.
- E. Interviewer, MSTP Candidates.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Speaker, Symposium on Molecular Aspects of Histocompatibility Testing, Detroit, Michigan, February, 1993.
2. Invited Speaker, National Immunology Congress, Santander, Spain, April, 1993.
3. Invited Speaker, University of West Virginia, Morgantown, West Virginia, April, 1993.
4. Invited Speaker, University of Arizona Cancer Center, Tucson, Arizona, June, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Cuende, E., Ding, L., Ales-Martinez, J.E., Gonzalez-Garcia, M., Marinez-A, C. and Nuñez, G.: Programmed cell death by Bcl-2 dependent and independent mechanisms in B-cell lymphoma cells. *EMBO J.* 1993;12:155-1560.
2. Gratiot-Deans, J., Ding, L., Turka, L.A. and Nuñez, G.: Bcl-2 proto-oncogene expression during human T cell development: Evidence for biphasic regulation. *J. Immunol.*, In Press.
3. 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*, In Press.
4. Castle, V., Heidelberger, K.P., Bromberg, J., Ou, X., Dale, 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.*, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. 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.

2. 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 mk transgenic mice.
3. Ryan, J., Gottlieb, C., Ding, L., Nuñez, G. and Clarke, M.: Alteration of the cell cycle regulatory function of p53 by Bcl-2.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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. Laboratory course for sophomore medical students (Pathology 600) January-May, 1993.
- C. Daily case review with pathology house officer assigned to Blood Bank.
- D. Biweekly discussion sessions with Pathology, Hematology and Pediatric hematology house officers.
- E. Postgraduate course, "Current Topics in Blood Banking", Planning Committee.
- F. Lectures on Transfusion Medicine presented to Pathology and Hematology/Oncology House Officers.
- G. Seminars and lectures on Pathology of Breast to Pathology House Officers.
- H. Director, Pathology clerkship for senior medical students, September-October, 1992.
- I. Lecture to Surgical Intensive Care physicians and nurses: "Blood Component Therapy", August 13, 1992.
- J. Presentation of Grand Rounds to Department of Obstetrics and Gynecology: "Intraductal epithelial proliferation of breast and the risk of carcinoma", September 10, 1992.
- K. Fellowship experience: Diagnosis of breast lesions. Presented to Dr. Murray Rebner, December 8-18, 1992.
- L. Presentation on Transfusion Medicine to Pharmacology and Therapeutics senior student elective course, January 7, 1993.
- M. Planning committee for senior student elective course in Laboratory Medicine.
- N. Planning committee for curriculum in hematology for sophomore medical students in revised curriculum.

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. Blood Utilization in Adult Extracorporeal Membrane Oxygenation.

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.
- 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.
- 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. M-Labs Operation Committee.
- C. 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.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Associate Editor, Transfusion.
- B. American Journal of Surgical Pathology.
- C. American Journal of Clinical Pathology.
- D. Archives of Pathology and Laboratory Medicine.
- E. Reviewer, Cancer.
- F. Reviewer, Journal of the American Medical Association.
- G. Reviewer, Journal of Clinical Oncology.

INVITED LECTURES/SEMINARS:

1. Three-day course organized and presented by Drs. Oberman and P. P. Rosen, "Problems in the Diagnosis and Management of Breast Cancer", American Society of Clinical Pathologists, Santa Fe, New Mexico, December 2-4, 1992.
2. Special Symposium, "The Appropriate Use of Frozen Sections for the Diagnosis of Breast Cancer", Arthur Purdy Stout Society of Surgical Pathologists, New Orleans, Louisiana, March 12, 1993.
3. Lecturer, "The Risks and Benefits of Blood Transfusion", Postgraduate Course, Family Practice, 1993, Towsley Center for Continuing Medical Education, University of Michigan, March 18, 1993.
4. Lecturer, "Problem Solving in the Blood Bank", Postgraduate Course, Current Topics in Blood Banking, Towsley Center for Continuing Medical Education, University of Michigan, June 2, 1993.
5. Lecturer, "Legal issues in Blood Banking", Postgraduate Course, Current Topics in Blood Banking, Towsley Center for Continuing Medical Education, University of Michigan, June 3, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Judd, W.J., Steiner, E.A., Abruzzo, L.V., Davenport, R.D., Oberman, H.A., Pehta, J.C. and Nance, S.J.: Anti-i causing acute hemolysis following a negative immediate-spin crossmatch. Transfusion. 1992;32:572-575.
2. Helvie, M.A., Paramagul, C., Oberman, H.A. and Adler, D.D.: Invasive lobular carcinoma: Imaging features and clinical detection. Investigative Radiology. 1993;28:202-207.
3. Oberman, H.A.: The present and future crossmatch. Transfusion. 1992;32:794-796.
4. Oberman, H.A.: Frozen section diagnosis of breast biopsies - A necessary procedure? Arch. Surg., In Press.
5. Oberman, H.A. and Goldman, E.B.: The patient's decision to be transfused. Transfusion, In Press.
6. Oberman, H.A.: Should a febrile transfusion response occasion return of the unit to the blood bank? Transfusion, In Press.

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

1. Butch, S.H., Judd, W.J., Steiner, E.A., Stoe, M. and Oberman, H.A.: The computer crossmatch. Annual Meeting, American Association of Blood Banks. San Francisco, California, November 10, 1992. *Transfusion* 1992;32:5S.
2. Lloyd, R., Jin, L., Kaldjian, E., Davenport, R.D. and Oberman, H.A.: Immunohistochemical detection of P53 suppressor gene, estrogen receptor and Ki-67 proteins in breast carcinomas. Annual Meeting, U.S. Canada Acad. Pathol. New Orleans, Louisiana, March 17, 1993. *Mod Pathol* 1993;6:17A.

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., In Press.
2. Oberman, H.A. (senior editor): Immunohematology, in, McClatchey, K.D. (ed.), Clinical Laboratory Medicine, Williams and Wilkins Co, Baltimore, Maryland, In Press.
3. Oberman, H.A.: Organization, functions, regulation and legal concerns of blood banks, in, McClatchey, K.D. (ed.), Clinical Laboratory Medicine, Williams and Wilkins Co., Baltimore, Maryland, In Press.
4. Oberman, H.A.: Consideraciones acerca de las transfusiones de plasma y sus componentes y derivados, in, Practica Transfusional Actual, Asociacion Argentina de Hemoterapia e Immunohematologia, 1992.
5. Goulet, J.A. and Oberman, H.A.: Blood and blood products in orthopaedic surgery, in, Chapman, M.W., Operative Orthopaedics. J.B. Lippincott, Philadelphia, 1993;181-188.
6. Sternberg, S., Antonioli, D., Carter, D., Mills, S. and Oberman, H.: Diagnostic Surgical Pathology, Edition 2, Raven Press, New York, New York, In Press.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR:

1. Proposals: Modest and Immodest. Letter to the Editor. *Amer. J. Surg. Path.* 1992;16:809-811.
2. Diagnosis of Adenomyoepithelioma of the Breast. Letter to the Editor. *Arch. Pathol. Lab. Med.* 1992;116:813.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. Autopsy Service.

II. TEACHING ACTIVITIES:

- A. Soverin Karmioli, Ph.D. - Postdoctoral Fellow.
- B. Kai Zhang, M.D. - Postdoctoral Fellow.
- C. Terry Lie and Lynda Makowiec, Undergraduate Research, Opportunities Program.
- D. Delores McBride, Summer Undergraduate Research Program.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Mechanisms and Genetic Regulation of Pulmonary Fibrosis", NIH R01-HL28737-09.
- 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", R01-DK42455, 5% effort.
- D. Co-Investigator, "Cytokine Networks Regulating Inflammation of Pulmonary Fibrosis", NIH SCOR in Occupational and Immunologic Lung Diseases, Project 1, 5% effort.
- E. Co-Investigator, "Renal Fibrosis", NIH R01, 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 and signal transduction by fatty acids.

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.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

- 1. Chair, "Interleukins and Modulation of Inflammation II", Experimental Biology Annual Meeting, New Orleans, Louisiana, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Phan, S.H., Gharaee-Kermani, M., McGarry, B., Kunkel, S.L. and Wolber, F.W.: Regulation of endothelial cell transforming growth factor b production by IL-1 β and TNF α . J. Immunol. 1992;149:103-106.
- 2. Garner, W.L., Karmioli, S., Marcelo, C., Rodriguez, J., Smith, D.J. and Phan, S.H.: Altered cytokine response of hypertrophic scar fibroblasts. Surg. Forum 1992;42:688-691.
- 3. Rolfe, M.W., Kunkel, S.L., Standiford, T.J., Orringer, M.B., Phan, S.H., Evanoff, H.L., Burdick, M.D. and Strieter, R.M.: Expression and regulation of human pulmonary fibroblast-derived monocyte chemotactic peptide (MCP-1). Am. J. Physiol. 1992;263 (Lung Cell Mol. Physiol.):L536-545.
- 4. Noh, J.W., Wiggins, R. and Phan, S.H.: Urine transforming growth factor-b activity is related to the degree of scarring in crescentic nephritis in the rabbit. Nephron 1993;63:73-78.
- 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 by rat alveolar macrophages during chronic lung injury. Am. J. Resp. Cell Molec. Biol., In Press, 1993.

6. 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.*, In Press, 1993.
7. 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.*, In Press, 1993.
8. 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.*, In Press, 1993.

BOOKS/CHAPTERS IN BOOKS:

1. Karmioli, S. and Phan, S.H.: Phenotypic changes in lung fibroblast populations in pulmonary fibrosis, in Phipps, P. (ed.), *Fibroblast Heterogeneity in Pulmonary Fibrosis*, CRC Press, Boca Raton, Florida, Chapter 1, pp. 1-26, 1992.
2. Wiggins, R.C., Fantone, J.C., Phan, S.H. and Holzman, L.B.: Mechanisms of vascular injury, in Tisher, C.C., and Brenner, B.N. (eds.), *Renal Pathology*, 2nd edition, J.B. Lippincott C., Philadelphia, Chapter 32, 1993, In Press.
3. Strieter, R.M., Phan, S.H. and Ward, P.A.: Inflammation, injury, and repair, in Murray, J. (ed.), *Textbook of Respiratory Medicine*, 1993, In Press.

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

1. Wolber, F.W., Kunkel, S.L. and Phan, S.H.: Upregulation of lung endothelial cell monocyte chemoattractant protein-1 production by cytokines and bleomycin. *Europ. Resp. J.* 1992;5:348s, (European Respiratory Societies 2nd Annual Meeting, August 29-September 3, 1992, Vienna, Austria).
2. Phan, S.H., Wolber, F.W. and Wiggins, R.: Fibronectin is the major fibroblast chemotactin in rabbit crescentic nephritis. *J. Am. Soc. Nephrol.* 1992;3:438.
3. Standiford, T.J., Rolfe, M.R., Kunkel, S.L., Lynch, J.P., III, Becker, F.S., Orringer, M.B., Phan, S.H. and Strieter, R.M.: Altered production and regulation of monocyte chemoattractant protein-1 from pulmonary fibroblasts isolated from patients with idiopathic pulmonary fibrosis. *Chest* 1993;103:121S.
4. Karmioli, S., Curry, R. and Phan, S.H.: Fatty acid modification of human lung fibroblasts (HLFS) results in differential IL-6 production due to IL-1 β stimulation. *FASEB J.* 1993;7.
5. Smith, R.E., Phan, S.H., Rollins, B., Strieter, R.M. and Kunkel, S.L.: Time-dependent expression of *JE* in association with bleomycin-induced lung injury. *FASEB J.* 1993;7:A506.
6. 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 inflammatory injury. *FASEB J.* 1993;7:A641.
7. Rekhter, M.D., Kai, Z., Phan, S.H. and Gordon, D.: Type I collagen gene expression in human atherosclerosis: localization to specific plaque regions. *FASEB J.* 1993;7:A785.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993

I. CLINICAL ACTIVITIES:

- A. Associate Director, Clinical Microbiology Laboratory.
- 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 Ground Rounds.
- C. Lecturer, Pathology M-4 Elective Course.
- D. Coordinator, Clinical Microbiology In-service Program.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. "Candida Vaginosis Study", National Institute of Health.
- B. "Characterization of Beta-Lactamases Produced by Antimicrobial Resistant *E coli* and *Klebsiella*", Merck, Sharp, and Dohme.
- C. "Development of Resistance to Topical Mupirocin", Smith Kline Beecham.
- D. "EVS Endophthalmitis Vitrectomy Multi-Center Study", Retina-Vitreous Consultants, Pittsburg, Pennsylvania.
- E. "Yellow Mercuric Oxide Ophthalmic Multi-Center Study", Del Pharmaceuticals.
- F. "Comparative Evaluation of the Difco ESP Automated Blood Culture System", Difco Laboratories.
- G. "Changes in the *In Vitro* Susceptibility of the *Bacteroides fragilis* group", Merck, Sharp and Dohme.
- H. "Alterations in Gastric Acidity and the Influence of Acidulin on Gastric Acidity and Gastric Microbial Colonization in Patients with AIDS", Clinical Research Unit.
- I. "*In Vitro* Susceptibility of *Haemophilis influenzae* to Cefaclor and related antimicrobics", Eli Lilly.
- J. "Determination of Survival Rates for Various Micro-organisms in StarPlex Transport Devices", StarPlex Scientific.

PROJECTS UNDER STUDY:

- A. Development of PCR Techniques for the Detection of Mycobacteria in Clinical Specimens.
- B. Clinical Utility of Anaerobic Blood Cultures.
- C. Clinical Utility of Treating Infected IV Catheters with Antimicrobics.
- E. Utility of Unit-Specific Susceptibility Profiles.

- F. Effect of Antifungal Agents on the Recovery of Fungi from Blood Cultures.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

- A. Hospital Infection Control Committee.
- B. Task Force on AIDS (alternate).
- C. Pharmacy and Therapeutics Committee (Antibiotics).

REGIONAL/NATIONAL:

- A. Board Member, South Central Association for Clinical Microbiology.
- B. Co-chair, TriCounty Clinical Microbiology Association.
- C. Treasurer, Michigan Branch-American Society for Microbiology.
- D. Co-Chair, Michigan Microbiology Laboratory Director's Association.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

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

INVITED LECTURES/SEMINARS:

1. Invited Speaker, TriCounty Clinical Microbiology Association, Fall, 1992, Meeting, Detroit, Michigan, November, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Pierson, C.L., Khalidi, N. and Christen, C.: Sterility of Fentanyl in combination with Bupivacain compounded epidural solution after storage at room temperature for 72 hours. Amer. J. Hosp. Parm. 1993, In Press.
2. Schmid, J., Rotman, M., Reed, B., Pierson, C.L. and Soll, D.: Genetic similarity of *Candida albicans* strains from vaginitis patients and their partners. J. Clin. Microbiol. 1993;31:39-46.
3. Donabedian, S.M., Chow, J.W., Boyce, J.M., McCabe, R.E., Markowitz, S.M., Coudron, P.E., Kurtza, A., Pierson, C.L. and Zervos, M.J.: Molecular typing of ampicillin-resistant, non-B-lactamase-producing *Enterococcus faecium* isolates from diverse geographic areas. J. Clin. Microbiol. 1992;30:2757-2761.

BOOK/CHAPTERS IN BOOKS:

1. Pierson, C.L.: Antimicrobial susceptibility testing, in, McClatchey, K.D. (ed.), Clinical Laboratory Medicine, Williams and Wilkins, Baltimore, Maryland, 1993, In Press.

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

1. Pierson, C.L.: Lyme Disease serology. The University of Michigan Spectrum, October, 1992.
2. Pierson, C.L.: Testing for *Clostridium difficile* toxins. The University of Michigan Spectrum, September, 1992.
3. Turner, N. and Pierson, C.L.: Virology update: EBV serology. The University of Michigan Spectrum, November, 1992.
4. Ross, C., Siddiqui, J., Pierson, C.L. and Hanson, C.: Detection of *Mycobacterium tuberculosis* in auramine-positive specimens by the polymerase chain reaction. Abstracts: General Meeting, Amer. Soc. for Microbiol. 1993;p.178.
5. Hankered, R., Bus, N. and Pierson, C.L.: Evaluation of the Roche Septi-Chek AFB system for recovery of *Mycobacterium spp* from respiratory specimens. Abstracts: General Meeting, Amer. Soc. for Microbiol. 1993;p.182.
6. Hankerd, R. and Pierson, C.L.: Detection of *Neisseria gonorrhoeae* using DNA probe assay. The University of Michigan Spectrum. January, 1993.
7. Young, C. and Pierson, C.L.: Stool cultures, special requests. The University of Michigan Spectrum. February, 1993.
8. Turner, N., Pierson, C.L.: Virology update: Rotavirus, respiratory viruses. The University of Michigan Spectrum. February, 1993.
9. Shalis, P.J., Pierson, C.L.: STAT AFB smears. The University of Michigan Spectrum, June, 1993.

**RODOLFO F.H. RASCHE, M.D.
LECTURER IN PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

OVERVIEW:

A. 1 July 1992 - 31 December 1992:

Part-time employment at the University of Michigan Department of Pathology while Medical Director of Laboratories and Pathologist at Mount Pleasant's Central Michigan Community Hospital (CMCH). During this period I attended meetings at the Department of Pathology as part of the M-Labs program. Assisted M-labs program at Lapeer Regional Hospital and became Director of Laboratory at Addison Community Hospital.

B. 1 January 1993 - 30 June 1993:

Full-time with the M-Labs program and Department of Pathology as Lecturer, covering on a full-time basis at Central Michigan Community Hospital (CMCH). At CMCH continued as Pathologist and Medical Director of Laboratories, Chairman of the Infection Control Committee. Planning of CMCH's change of reference lab from LCM to M-Labs.

C. 1 July 1993

Moved to Ann Arbor, full-time at The University of Michigan Department of Pathology, as Associate Director, M-Labs.

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology coverage for Central Michigan Community Hospital, (4,400 cases a year).
- B. Cytopathology coverage for Central Michigan Community Hospital, (12,000 cases of Gynecologic and non-Gynecologic a year).
- C. Autopsy coverage for Central Michigan Community Hospital, (30 cases a year).

II. TEACHING ACTIVITIES:

- A. Present CPCs, review conferences and lab in-services at Central Michigan Community Hospital.
- B. Teach Pathology to a senior medical student from The University of Michigan who took an elective in pathology for one month at Central Michigan Community Hospital.

III. RESEARCH ACTIVITIES:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director of Laboratories at Central Michigan Community Hospital.
- B. Director of Laboratories at Addison Community Hospital.
- C. Chairman, Infection Control committee at Central Michigan Community Hospital.
- D. Chairman, Transfusion Review at Central Michigan Community Hospital.

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

- 1. Rasche, R.F.H.: Central Michigan Community Hospital Staff Update, Central Michigan Community Hospital Staff Newsletter.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. Director of Autopsy Service.
- B. Supervision of Autopsies (2.5 months).
- C. Coordinator of Senior Staff Autopsy Call Schedule.
- D. Forensic Pathology - 6 weeks.

II. TEACHING ACTIVITIES:

- A. Coordinator, Biweekly Pathology Gross Conference.
- B. Lectures to Pathology House Officers in Anatomic and Clinical Pathology.
- C. Lecturer, Pathology 600 Course.
- D. Pathology 600, Provided written critiques of student autopsy write-ups (200).
- E. Laboratory Instructor, Histopathology Laboratory for M1 students.
- F. Mentor - Fourth Year Medical Student Clerkship - two, one-month rotations.
- G. Directed research of three postdoctoral fellows, one Visiting Scholar, two house officers (one in Pathology, one in Anesthesiology), one veterinary student, two undergraduate students, one high school minority student.
- H. Transplant Journal Club, three presentations.
- I. Directed research of Allan Olson, M.D. (Department of Pediatrics), Jorge Rodriguez, M.D. (Department of Surgery); House officers - Eric Hsi, M.D., and Anna Penna, M.D. (Anesthesiology), Eiji Takeuchi, M.D., Visiting Scholar, Postdoctoral fellows - Laura DeForge, Ph.D., Gordon Wollenberg, D.V.M., Ph.D.; Graduate students - Angela Dyer (Michigan State University); Undergraduate students - Tony Cardello, Connie Ngiu.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Regulation of gene expression of soluble mediators of inflammation using the following models:
 - 1. Endotoxin-stimulated human whole blood.
 - 2. Endotoxin injection in mice.
 - 3. Cecal ligation and puncture.
- B. Toxic effects of immunomodulators.
- C. Pathophysiology of septic shock.
- D. Quantitation of mediators in septic shock.
- E. Cloning, sequencing, and expressing cytokines including mTNF, hTNF, mIL-6, hIL-8, MCP, JE.
- F. Mechanisms of organ injury induced by hepatic ischemia/reperfusion.
- G. Mechanisms of nosocomial pneumonia, and association with IL-8.

- H. Awards: Laura E. DeForge, Ph.D., American Society of Investigative Pathologists Young Investigators Award, Merit Award, Mark E. Eskandari, Sheard Sanford Award, Honorable Mention, American Society of Clinical Pathologists, 1992; Medical Student Research Award, 1993.

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, "Cytokine Measurement in Whole Blood", Pfizer Co., one year, \$52,000, 1992-1993.
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. Co-Investigator, "Monokine Gene Expression/Regulation in Lung Injury", National Institutes of Health, five years, 1990-1995.
G. Co-Investigator on Core II of Program Project, "Inflammatory Cells and Lung Injury", National Institutes of Health - five years, \$48,595, 1984-1994.
H. Co-Investigator, "Mechanisms of Pulmonary Fibrosis", National Institutes of Health, five years, \$215,000.
I. Sponsor, Medical Research Council of Canada Training Fellowship, Gordon Wollenberg, D.V.M., Ph.D., recipient.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director - Autopsy Service.
B. 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.
E. Coordinator - University of Michigan Hospital Medical Examiner On-Call.

REGIONAL AND NATIONAL:

- A. Co-Chair, Michigan Department of Public Health Postmortem Examination Workgroup.
B. Member, Executive Committee, Dementia Subcommittee.
C. Member, Dementia Subcommittee, Chronic Disease Advisory Committee to the Michigan Department of Public Health.
D. Deputy Medical Examiner for Washtenaw County
E. Member, Legislative Committee, Michigan Association of Medical Examiners.

- F. 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.
- G. Reviewer, NIH Teleconferences (two), 1991-1992.
- H. Reviewer, National Science Foundation grants.
- I. Reviewer, Veterans Administration Merit grants.
- J. 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. British Journal of Pharmacology.
 - 9. Biochemica.
 - 10. Biophysica Acta.
 - 11. Journal of Clinical Investigations.
 - 12. Infection and Immunity.
 - 13. Blood.

INVITED LECTURES/SEMINARS:

- 1. Invited Speaker, St. Paul's Hospital, Vancouver, British Columbia, Canada, July, 1992.
- 2. Invited Speaker, Vancouver General Hospital, Vancouver, British Columbia, Canada, July, 1992.
- 3. Invited Speaker, "Hyperalimantation: A Practical Approach", Harvard Medical School, Boston, Massachusetts, September, 1992.
- 4. Invited Participant, "Anti-TNF Therapy in Sepsis Syndrome", Cutter Biological, San Francisco, California, September, 1992.
- 5. Invited Participant, "Quantitation of Human Anti-Mouse Antibodies", Miles, Inc., New Haven, Connecticut, November, 1992.
- 6. Reviewer, NIH Review Section, "Expression of Tuberculosis in the Lung", Bethesda, Maryland, June, 1992.
- 7. NIH Telephone Site Visit, 1992, Supplement to Dr. John Spitzer's Program Project, LSU medical center.
- 8. Invited Speaker, "Oxidant Regulation of Cytokines", Department of Surgery Research Conference, The University of Michigan, Ann Arbor, Michigan, January, 1993.
- 9. Participant, NIH Reverse Site Visit, Case Western Reserve SCOR grant, February, 1993.
- 10. Chair, Anti-Oxidant Defense Session, FASEB, New Orleans, Louisiana, April, 1993.
- 11. Invited Speaker, "Oxidant Regulation of Cytokines", St. Louis University School of Medicine, St. Louis Missouri, April 30 to May 1, 1993.
- 12. Invited Speaker, "Malnutrition in the Hospitalized Patient", Harvard Medical School, Boston, Massachusetts, May, 1993.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Coran, A.G., Drongowski, R.A., Paik, J.J. and Remick, D.G.: Ibuprofen intervention in canine septic shock: reduction of pathophysiology without decreased cytokines. *J. Surg. Res.* 1992;53:272-279.
2. DeForge, L.E., Fantone, J.C., Kenney, J.S. and Remick, D.G.: Oxygen radical scavengers selectively inhibit interleukin 8 production in human whole blood. *J. Clin. Invest.* 1992;90:2123-2129.
3. Rodriguez, J.L., Miller, C.G., DeForge, L.E., Kelty, L., Shanley, C.J., Bartlett, R.H. and Remick, D.G.: Local production of interleukin-8 is associated with nosocomial pneumonia. *J. Trauma* 1992;33:74-81.
4. Friedland, J.S., Shattock, R.J., Johnson, J.D., Remick, D.G., Holliman, R.E. and Griffin, G.E.: Differential cytokine gene expression and secretion after phagocytosis by a human monocytic cell line of *Toxoplasma gondii* compared with *Mycobacterium tuberculosis*. *Clin. Exp. Immunol.* 1993;91:282-286.
5. Friedland, J.S., Shattock, R., Remick, D.G. and Griffin, G.E.: Mycobacterial 65-kD heat shock protein induces release of proinflammatory cytokines from human monocytic cells. *Clin. Exp. Immunol.* 1993;91:58-62.
6. Friedland, J.S., Ho, M., Remick, D.G., Bunnag, D., White, N.J. and Griffin, G.E.: Interleukin-8 and *Plasmodium falciparum* malaria in Thailand. *Trans. R. Soc. Trop. Med. Hyg.* 1993;87:54-55.
7. Lelli, J.L., Drongowski, R.A., Gastman, B., Remick, D.G. and Coran, A.G.: Effects of coenzyme Q10 on the mediator cascade of sepsis. *Circ. Shock* 1993;39:178-187.
8. Remick, D.G. and Kunkel, S.L.: Pathophysiologic alterations induced by tumor necrosis factor. *Int. Rev. Exp. Pathol.* 1993;34 Pt B:7-25.
9. 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* 1993;34:684-94; discussion 694-5.
10. 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 virus infection in mice. *Anesth. Analg.* 1993;76:1106-1113.
11. Ulich, T.R., Yin, S., Remick, D.G., Russell, D., Eisenberg, S.P. and Kohno, T.: Intratracheal administration of endotoxin and cytokines. IV. The soluble tumor necrosis factor receptor type I inhibits acute inflammation. *Am. J. Pathol.* 1993;142:1335-1338.
12. Hsi, E.D. and Remick, D.G.: Rapid determination of cell-associated tumor necrosis factor by flow cytometry. *Lab. Invest.* 1993;69:740-45.

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

1. Bolgos, G.L., Wollenberg, G.K., Preston, A.M. and Remick, D.G.: The effects of caloric restriction on cytokines and LPS-induced pathophysiologic changes. FASEB, New Orleans, Louisiana, 1993.
2. Campbell, D.A., Jr., Scales, W.E., Howatt, M.E. and Remick, D.G.: Hepatic ischemia/reperfusion injury: The importance of oxidant/TNF interaction. FASEB, New Orleans, Louisiana, 1993.

3. Remick, D.G., Cardello, T. and DeForge, L.E.: Prolonged, escalating interleukin 8 gene expression following lipopolysaccharide stimulation. FASEB, New Orleans, Louisiana, 1993.
4. Malak, T.A., DeForge, L.E., Preston, A.M., Takeuchi, E. and Remick, D.G.: LPS stimulation of human whole blood fails to induce soluble TNF receptors. FASEB, New Orleans, Louisiana, 1993.
5. DeForge, L.E., Boxer, L.A. and Remick, D.G.: Oxidant regulation of interleukin expression. FASEB, New Orleans, Louisiana, 1993.
6. Wollenberg, G.K., Bolgos, G., DeForge, L.E. and Remick, D.G.: Tumor necrosis factor and interleukin 6 synthesis by peritoneal macrophages *in vivo* and in culture. FASEB, New Orleans, Louisiana, 1993.
7. Preston, A.M., DeForge, L.E., Malak, T.A. and Remick, D.G.: Stimulants and anti-oxidant modulation of cytokines in human whole blood. FASEB, New Orleans, Louisiana, 1993.
8. Takeuchi, E., DeForge, L.E. and Remick, D.G.: Complete Freund's adjuvant priming decreases cytokine production and organ injury. FASEB, New Orleans, Louisiana, 1993.
9. Remick, D.G. and DeForge, L.E.: Role of reactive oxygen intermediates in modulating interleukin 8 gene expression. USCAP, New Orleans, Louisiana, 1993.
10. Hsi, E. and Remick, D.G.: Monocytes are the major producer of interleukin-1 beta in an *ex vivo* model of local cytokine production. USCAP, New Orleans, Louisiana, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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. Laboratory Instructor (two sessions), Hematopathology - Pathology 600 course.
 - 2. M4 Clerkship in General Pathology, Hematology portion of Clinical Pathology Rotation.
 - 3. Dental School, Lecture on Anemias, Pathology 630.
 - 4. Histopathology Laboratory Instructor, Histology course for 1st year medical students.
 - 5. Instructor, M4 Clerkship in Clinical Pathology.
- B. House Officers:
 - 1. Sign-out of bone marrow biopsies, aspirates, blood smears, and body fluids in Hematology Laboratory.
 - 2. Sign-out of lymph node biopsies and review of hematopathology consultation material.
 - 3. Flow Cytometry sign-out.
 - 4. Molecular Diagnostics sign-out.
- C. Hematopathology teaching:
 - 1. Hematopathology case conferences/biweekly.
 - 2. Leukemia conference/biweekly.
 - 3. Lymphoma conference/weekly.
 - 4. Molecular Diagnostics section conference/weekly.
 - 5. Cutaneous Lymphoma Conference, monthly.
- D. Clinical Pathology Grand Rounds (one lecture).
- E. Clinical Pathology Case Conference/weekly.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Immunophenotyping in acute and chronic leukemias.
- B. Detection of immunoglobulin gene rearrangements by the polymerase chain reaction.
- C. Detection of Epstein-Barr virus in lymphoid lesions by polymerase chain reaction.

- D. Detection of *Mycobacterium tuberculosis* in sputum specimens by polymerase chain reaction.

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL

- A. Director, Clinical Flow Cytometry Laboratory.
- B. Residency Teaching Committee.
- C. M-Labs Committee.

REGIONAL/NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Lecturer, "Immunophenotyping in Hematopathology by Flow Cytometry", Midwest Clinical Ligand Assay Society, 16th Annual Meeting, October 23, 1992.
2. Lecturer, Surgical Pathology of the Spleen course, presented at American Society of Clinical Pathologists National Meeting, March, 1993.
3. Lecturer, "Flow Cytometry in the Diagnosis and Monitoring of Acquired Immunodeficiencies", Michigan Society for Medical Technology, April 14, 1993.
4. Lecturer, "Immunophenotyping in Infant Acute Leukemia", Flow Cytometry Users' Meeting, Wayne State University, May 27, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ross, C.W., Schlegelmilch, J.A., Grogan, T.M., Weiss, L.M., Schnitzer, B. and Hanson, C.A.: Detection of Epstein-Barr virus genome in Ki-1 (CD30)-positive large cell anaplastic lymphomas using the polymerase chain reaction. *Am. J. Pathol.* 1992;141:457-465.
2. Perkins, P.L., Ross, C.W. and Schnitzer, B.: CD30-positive, anaplastic large cell lymphomas that express CD15 but lack CD45: A possible diagnostic pitfall. *Arch. Pathol. Lab. Med.* 1992;116:1192-1196.
3. Ross, C.W., Hanson, C.A. and Schnitzer, B.: CD30 (Ki-1)-positive anaplastic large cell lymphoma mimicking gastrointestinal carcinoma. *Cancer* 1992;70:2517-2523.
4. 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.* 1993;84:49-60.
5. Hansen, E.R., Vejlsgaard, G.L., Cooper, K.D., Heidenheim, M., Larsen, J.K., Ho, V.C., Ross, C.W., Fox, D.A., Thomsen, K. and Baadsgaard, O.: Leukemic T-cells from patients with cutaneous T-cell lymphoma demonstrate enhanced activation through CDw60, CD2, and CD28 relative to activation through the T-cell antigen receptor complex. *J. Invest. Dermatol.* 1993;100:667-673.

6. Kaminski, M.S., Zasadny, K.R., Francis, I.R., Milik, A.W., Ross, C.W., et al.: Radioimmunotherapy of B-cell lymphoma with ¹³¹I-anti-B1 (anti-CD20) antibody. NEJM, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Ross, C.W., Schnitzer B., Sheldon, S., Braun, D.K. and Hanson, C.A.: γ/δ T-cell post-transplant lymphoproliferative disorder presenting primarily in spleen.

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, In Press.

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

1. Kaminski, M.S., Zasadny, K.R., Moon, S., Ross, C.W., et al.: Radioimmunotherapy of refractory B-cell lymphoma with ¹³¹I-anti-B1 (Anti-CD20) antibody: Promising early results using non-marrow ablative radiation doses. Blood 1992;80(suppl 1):43A.
2. Ross, C.W., Abaza, M., Hanson, C.A. and Schnitzer, B.: Red pulp splenic infiltrates in peripheral T-cell lymphomas diagnosed by splenectomy. Am. J. Clin. Pathol. 1992;98:369A.
3. Ross, C.W., Nakagawa, A., Schnitzer, B., Sheldon, S. and Hanson, C.A.: Acute leukemia in infants. Modern Pathol. 1993;6:99A.
4. Alkan, S., Ross, C.W., Siddiqui, J., Sheldon, S. and Hanson, C.A.: Polymerase chain reaction detection of myl/RAR α in acute promyelocytic leukemia using nested primers. Modern Pathol. 1993;6:84A.
5. Ross, C.W., Siddiqui, J., Pierson, C. and Hanson, C.A.: Detection of mycobacterium tuberculosis (MTb) in auramine-positive specimens by the polymerase chain reaction (PCR). American Society for Microbiology, 93rd General Meeting Abstracts, page 178, May 1993.
6. Terhune, M., Oberhelman, L., Ross, C., Neckel, S., Mostow, E., Merkle, S. and Cooper, K.: A logistic regression model to improve and standardize the early diagnosis of mycosis fungoides. J. Invest. Dermatol. 1993;100:538.
7. Ross, C.W.: Book review, "Tumors of the Hematopoietic System", AFIP fascicle 28, by Lukes, R.J. and Collins, R.D. (eds.). Am. J. Surg. Pathol., In Press.
8. Alkan, S., Ross, C.W., Hanson, C.A. and Schnitzer, B.: Transformed follicular lymphoma mimicking splenic maginal cell lymphoma: Morphologic, immunologic, and molecular analysis. Canadian Congress of Laboratory Medicine. Banff, Alberta, June, 1993.
9. Alkan, S., Ross, C.W., Hanson, C.A. and Schnitzer, B.: Lack of bcl-2 protein expression and Epstein-Barr virus EBER-1 RNA expression in nodular lymphocyte predominant Hodgkin's disease. Canadian Congress of Laboratory Medicine. Banff, Alberta, June, 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 1992 - 30 JUNE 1993**

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, 1992:

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

FALL TERM, 1991:

- A. Oral Pathology, Course 516, to Freshmen Dental Students (course director).
- B. Oral Pathology, Course 630, to Sophomore Dental Students.
- C. Oral Pathology, Course 824, to Senior Dental Students.
- D. Dental Hygiene, Course 220, to Dental Hygiene Students.
- E. Oral Pathology, Course 694, to Graduate Dental Students.
- F. Perio Seminar, Course 781, to Graduate Dental Students (course director).

WINTER TERM, 1992:

- A. Oral Pathology, Course 624, to Sophomore Dental Students.
- B. Oral Pathology, Course 818, Senior Dental Students.
- C. Dental Hygiene, Course 321, Dental Hygiene Students.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Project Director, "Determination of the Feasibility and Economy of Central Coordination of the Collection and Disposal of Medical Waste",

10% effort, a Cooperative effort: Cosponsored by Delta Dental Plan of Michigan/Michigan Department of Public Health/Michigan Dental Association/The University of Michigan, total direct costs \$82,192.00, 6/92-7/92.

- B. Project Director, "Oral Famciclovir in the Treatment of Experimentally Induced Herpes Simplex Labialis, 15% effort, Smith Kline Beecham Pharmaceuticals, total direct costs \$180,000.00, 12/1/92-1/1/95.

UNDER CURRENT NEGOTIATION:

- A. Project Director, Placebo-Controlled Evaluation of Acyclovir/348U87 Cream for the Treatment of Herpes simplex Labialis Infection (Protocol P120-008), Burroughs Wellcome Co.

IV. ADMINISTRATIVE ACTIVITIES:

SCHOOL OF DENTISTRY COMMITTEES:

- A. Human Subjects committee, School of Dentistry.

REGIONAL:

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

NATIONAL:

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

INTERNATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

- A. Attended, MiOSHA Hearing, Michigan Department of Public Health, Lansing, August 15, 1992.
- B. Attended, M.D.A. Annual Session, Grand Rapids, Michigan, April, 1991.

HONORS AND AWARDS:

- A. 1992 Michigan Dental Association's Public Service Award.

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.

MISCELLANEOUS:

- A. Intradepartmental:
 - 1. Oral Pathology Service Clinic, University Hospitals, Department of Dentistry and Oral Surgery.
 - 2. Dental Faculty Associates, School of Dentistry.
 - 3. Oral Pathology Biopsy Service Rotation.
- B. Interdepartmental:
 - 1. Oral Pathology, clinical consultations on an as needed basis, The University of Michigan Medical School of Dentistry Clinics.
 - 2. Consultant, Veterans Administration Hospital, Ann Arbor.

INVITED LECTURES/SEMINARS:

- 1. "OSHA Regulations in the Dental Office", Dr. Picken's Office, Ann Arbor, Michigan, July 1, 1992.
- 2. "Non-Infectious Diseases of the Oral Cavity", Southwest District Dental Society, Coldwater, Michigan, September 17, 1992.
- 3. "Smoking, Smokeless Tobacco and Oral Cancer", West Virginia Institute of Technology, October 17, 1992.
- 4. "OSHA Regulations in the Dental Office", Dr. John Hatch's Office, Ann Arbor, Michigan, December 3, 1992.
- 5. "Infectious Disease in the Dental Office", Southwestern Michigan Orthodontists, Sturgis, Michigan, March 11, 1993.
- 6. Public Hearing, Michigan State Board of Dentistry, March 16, 1993.
- 7. "What Every Patient with Scleroderma Should Know", The Scleroderma Foundation, Hutzel Hospital, Detroit, Michigan, April 3, 1993.
- 8. "Lesions Mimicking Periapical Pathosis and an Update on AIDS", Michigan Association of Endodontists, Southfield, Michigan, May 26, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Rowe, N.H: Readers ask about handpieces, medical waste. J. Mich. Dent. Assoc. 1992;74:14-16.
2. Rowe, N.H. and Chadzynski, L.: Sharps disposal update. A study of one regulated medical waste (Sharps) in the dental office: An interim report. J. Mich. Dent. Assoc. 1992;74:32-37.
3. Rowe, N.H.: Infection control and exposure control: Are these terms interchangeable? J. Mich. Dent. Assoc. 1992;74:14.
4. Rowe, N.H. and Chadzynski, L.: Requirements for extracted teeth disposal. J. Mich. Dent. Assoc. 1993;75:66.

BOOKS AND CHAPTERS IN BOOKS:

2. Rowe, N.H.: Dental caries (revision), Chapter 17, in, Regezi, J.A. and Sciubba, J.J. (eds.), Oral Pathology, 2nd edition, W.B. Saunders Company, Philadelphia, 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).

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. Director, Clinical Hematology Laboratory.
- B. Director, University of Michigan Health Services Laboratories.
- C. Diagnostic Surgical Pathology, Hematopathology.
- D. Diagnostic Hematopathology Consultant, Veterans Administration Hospital.
- E. Diagnostic Hematopathology of M-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. President, Society for Hematopathology.
- B. Society for Hematopathology, Executive Committee.
- C. Southwest Oncology Group:
 - 1. Lymphoma Subcommittee.
 - 2. Leukemia Subcommittee.
- D. Children's Cancer Study Group: Review of in-house cases of lymphoma cases.
- E. Regional Center Review Pathologist, Southwest Oncology Group.
- F. Member, Review Panel for Lymphomas, Southwest Oncology Group.
- G. Member, Hematology Council, American Society of Clinical Pathologists.
- H. Member, Hematology Workshop Review Committee, American Society of Clinical Pathologists.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARD:

- A. Human Pathology. Designated reviewer.
- B. Hematologic Pathology . Designated reviewer.
- C. Archives of Pathology and Laboratory Medicine, Designated reviewer

INVITED LECTURES/SEMINARS:

1. "Hodgkin's Disease: Diagnosis and Differential Diagnosis", ASCP Workshop, Las Vegas, Nevada, October 1992.
2. "A Practical Approach to the Diagnosis and Differential Diagnosis of Extranodal Lymphomas", ASCP Workshop, October, 1992, Las Vegas, Nevada.
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) Immunologic Classification of Acute Lymphoblastic Leukemias, San Antonio, Texas, November, 1992.
4. "Surgical Pathology of the Spleen: Diagnosis and Differential Diagnosis," ASCP Workshop, April, 1993, Chicago, Illinois.
5. "Hodgkin's Disease: Diagnosis and Differential Diagnosis", ASCP Workshop, April, 1993, Chicago, Illinois.
6. "Diagnosis and Classification of Lymphomas", Topics in Contemporary Hematopathology, A Tribute to Douglas A. Nelson, SUNY Health Science Center at Syracuse, Syracuse, New York, June 1993.

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

1. Ross, C.W., Schlegelmilch, J.A., Grogan, T.M., Weiss, L.M., Schnitzer, B. and Hanson, C.A.: Detection of Epstein-Barr virus genome in Ki-1 (CD30)-positive, large cell anaplastic lymphomas using the polymerase chain reaction. *Am. J. Pathol.* 1992;141:457-466.
2. Perkins, P., Ross, C.W. and Schnitzer, B.: CD30-positive, anaplastic large-cell lymphomas that express CD15 but lack CD45. A possible diagnostic pitfall. *Arch. Pathol. Lab. Med.* 1992;116:1192-1196.
3. Ross, C.W., Hanson, C.A. and Schnitzer, B.: CD30 (Ki-1)-positive anaplastic large cell lymphoma mimicking gastrointestinal carcinoma. *Cancer.* 1992;70:2517-2523.
4. 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.* 1993;83:49-60.

BOOKS AND CHAPTERS IN BOOKS:

1. Schnitzer, B.: Benign lymphoproliferative disorders, in Knowles, D.M. (ed.), *Neoplastic Hematopathology*, Williams-Wilkins Company, 1992.
2. 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.

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

1. Ross, C.W., Abaza, M., Hanson, C.A. and Schnitzer, B.: Red pulp splenic infiltrates in peripheral T-cell lymphomas diagnosed by a splenectomy. *Am. J. Clin. Pathol.* 1992;98:369.
2. Schnitzer, B.: Biopsy interpretation of lymph nodes by Steven H. Swerdlow. (Book Review) *Hum. Pathol.* 1992;23:1441.
3. Grogan, T., Brazier, R., Banks, P., Foucar, K., Levy, N., Tubbs, R., Kjeldsberg, C., Schnitzer, B., Spier, C. and Miller, T.: The proliferative rate of aggressive non-Hodgkin's lymphomas identifies a patient group with fatal disease: a prospective Southwest Oncology Group Trial. *Lab. Invest.* 1993;68:91A, *Mod. Med.* 1993;6:91A.
4. Ross, C.W., Nakagawa, A., Schnitzer, B., Sheldon, S. and Hanson, C.A.: Acute leukemia in infants. *Lab. Invest.* 1993;86:99A, *Mod. Med.* 1993;6:99A.
5. Hsi, E., Zuckerberg, L.R., Schnitzer, B. and Harris, N.L.: Development of extrasalivary gland lymphoma in myoepithelial lymphadenitis (benign lymphoepithelial lesion). *Lab. Invest.* 1993;68:92A, *Mod. Med.* 1993;6:92A.
6. Alkan, S., Ross, C.W., Hanson, C.A. and Schnitzer, B.: Transformed follicular lymphoma mimicking splenic marginal cell lymphoma: Morphologic immunologic and molecular analysis. *Canadian Congress of Laboratory Medicine*, Banff, Alberta, June, 1993.
7. Alkan, S., Ross, C.W., Hanson, C.A. and Schnitzer, B.: Lack of bcl-2 protein expression and Epstein-Barr virus (EBV) EBER-1 mRNA expression in nodular

lymphocyte predominant Hodgkin's disease. (NLP-HD). Canadian Congress of Laboratory Medicine, Banff, Alberta, June, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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.
- E. M-Labs Surgical Pathology Service (Gyn) - As needed.

II. TEACHING ACTIVITIES:

- A. Medical Students:
 - 1. Pathology 600 laboratory instructor, January-April.
 - 2. Pathology 600 Lecture: Gynecologic Pathology I, April 7, 1993.
- 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-Ostetric/Gynecologic Pathology- one hour.
 - 5. Instruction in Obstetric/Gynecologic Pathology and Cytopathology (Hope Haefner, M.D., Fellow, Dept. Ob/Gyn)
- C. Other Education Activities:
 - 1. Cytotechnologists-Cytopathology conferences - three/year.
 - 2. Gynecologic Oncology Tumor Board Conference-weekly.
 - 3. Obstetric/Gynecologic Colposcopy/Pathology Conference-bi-monthly.
 - 4. Coordinator, Histotechnologist/Cytotechnologist Conference-monthly.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Computer Applications to Cytology.
- B. Neovagina cytology following total pelvic exenteration for gynecologic malignancies.
- C. The clinical significance of the development of radiation induced dysplasias (in conjunction with Dr. Hope Haefner, fellow, Department of Obstetrics/Gynecology).
- D. Fluid cytology of unusual gynecologic malignancies.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Co-Director, Cytopathology Laboratory.
- B. Member, Resident Selection Committee.

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Quality Assurance/Quality Control Committee.
- B. Member, M II Curriculum Committee-Reproductive Medicine.

REGIONAL AND NATIONAL:

- A. Reviewer, Diagnostic Cytopathology.
- B. Member, Cytopathology Committee, College of American Pathologists.
- C. Member, Cervical Cancer Advisory Committee, Michigan Department of Public Health, Lansing, Michigan.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Keynote Speaker, Cytopathology Workshop, Topics included: "Cytopathology of the Uterine Cervix", "The Bethesda Nomenclature System for Cervicovaginal Cytology", "Fine Needle Aspiration Cytology of the Breast and Fine Needle Aspiration Cytology of Cystic Ovarian Lesions", West Virginia Society of Cytology, Charleston, West Virginia, September 12, 1992.
2. "Neovaginal Cytology Following Total Pelvic Exenteration for Gynecologic Malignancies", Poster, Annual Scientific Meeting of the American Society of Cytology, Quebec, Canada, October, 1992.
3. Guest Speaker, "Fine Needle Aspiration Cytology of Cystic Ovarian Lesions", School of Cytotechnology, Henry Ford Hospital, Detroit, Michigan, November 25, 1992.
4. Guest Speaker, "The PAP smear in the 1990's", Women's Health Care for the Primary Care Provider, Sponsored by The University of Michigan Medical School, Departments of Family Practice and Obstetrics and Gynecology. Ann Arbor, Michigan, December 5, 1992.
5. Guest Speaker, "The Bethesda Nomenclature System for Cervicovaginal Cytology", Controversial Categories, Michigan Society of Pathologists, Novi, Michigan, February 20, 1993.
6. Guest Speaker, "HPV and the Abnormal Pap Smear", Michigan Academy of Family Physicians, Ann Arbor, Michigan, March 17, 1993.
7. Guest speaker, "Squamous and Glandular Cell Atypia of Undetermined Significance", Michigan Society of Cytology, Grand Rapids, Michigan, May 22, 1993.
8. Guest Speaker, "Cytologic Criteria and Significance of ASCUS on Cervical Smears", Cytology Standardization Conference, Sponsored by SmithKline Beecham Clinical Laboratories, St. Louis, Missouri, May 26, 1993.
9. Guest Speaker, "The PAP Smear in the 1990's", Department of Obstetrics and Gynecology, Genesys Regional Medical Center, Flint, Michigan, June 2, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Wojcik, E.M. and Selvaggi, S.M.: Factors influencing fine needle aspiration cytology in the management of recurrent gynecologic malignancies. *Gynecol.Oncol.* 1992;46:281-286.
2. Selvaggi, S.M.: Cytologic features of malignant ovarian monodermal teratoma with ependymal component in pelvic washings. *Int. J. Gynecol. Pathol.* 1992;11:299-303.
3. Wojcik, E.M. and Selvaggi, S.M.: Diagnostic accuracy of fine needle aspiration cytology in persistent or recurrent gynecologic malignancies. *Diagn. Cytopathol.* 1992;8:322-326.
4. Selvaggi, S.M.: Bronchoalveolar lavage in lung transplant patients. *Acta. Cytol.* 1992;36:674-679.
5. Selvaggi, S.M.: Cytologic features of squamous cell carcinoma-in-situ involving endocervical glands in endocervical cytobrush specimens. *Acta Cytol., In Press.*
6. 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.*
7. Wojcik, E.M. and Selvaggi, S.M.: Fine needle aspiration cytology of cystic ovarian lesions. *Diagn. Cytopathol., In Press.*

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

1. Selvaggi, S.M.: Polypoid carcinoma of the esophagus on brush cytology. (Letter to the editor). *Acta Cytol.* 1992;36:650-651.
2. Nunez, C. and Diaz, J.I.: Ovarian follicular cysts: A Potential source of false-positive diagnoses in ovarian cytology. (Editorial). *Diagn. Cytopathol.* 1992;8:536-537.
3. Selvaggi, S.M., Lelle, R.J. and Roberts, J.R.: Neovaginal cytology following total pelvic exenteration for gynecologic malignancies. *Acta. Cytol.* 1992;36:633-634.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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. Six lectures to intensive care unit residents, Blood component therapy, William Beaumont Hospital.
- C. Lecture to emergency room staff, Blood component therapy, William Beaumont Hospital.
- D. Two coagulation conferences for pathology residents, William Beaumont Hospital.
- E. Medical resident's noon conference, Use of blood components, William Beaumont Hospital.
- F. Seven lectures for medical technology students, coagulation and hemostasis, William Beaumont Hospital.
- G. Seven didactic lectures on hemostasis and thrombosis plus case presentations and discussions, Clinical Pathology elective for senior medical students, The University of Michigan.
- H. Ten conferences for blood bank residents, Coagulation and component therapy, The University of Michigan.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Investigation of Platelet Thrombosis on Intact Endothelial Surfaces, *In Vivo*", William Beaumont Research Institute, 10%, \$87,000, 2/1/92-2/28/93.
- B. Co-Investigator, "Protamine Filter for Extracorporeal Heparin Removal", The University of Michigan School of Pharmacy, NIH-NHLBI HL-38353, 5%, \$192,104, 1/1/93-12/31/93.

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.

INVITED LECTURES/SEMINARS:

1. "Blood Component Therapy for Coagulation Disorders", Symposium of Transfusion Medicine and Blood Banking, Ponte Vedra Beach, Florida, September 26, 1992.
2. Poster, "Effect of Low Molecular Weight Heparin and Hirudin on Adhesion of Platelets to Intact Endothelium", VII International Symposium on the Biology of Vascular Cells, San Diego, California, November 13, 1992.
3. "Treatment of Coagulopathies", Michigan Association of Blood Banks, Advances in Transfusion Medicine, Lansing, Michigan, May 6-7, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Shanberge, J.N. and Quattrociocchi Longe, T.: Analysis of fresh frozen plasma administration with suggestions for ways to reduce usage. *Transfusion Medicine* 1992;2:189-194.
2. Shanberge, J.N.: Adaptor for Jamshidi needles to enhance penetration of hard bone. *Blood* 1992;80:2687-2688.

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

1. Shanberge, J.N.: Guidelines for blood component therapy. *J. Florida M.A.* 1993;80:43-45.
2. Shanberge, J.N., Kajiwara, Y. and Quattrociocchi-Longe, T.: Production of platelet thrombi on intact endothelium *in vivo* - effect of low molecular weight heparins, hirudin and aspirin. *Thromb. Haemostas.* 1993;69:1026.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993

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: 8 hour lecture/laboratory.

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 deletions of 12p 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: -

1. "Some Perspectives on the Cytogenetics of Leukemia and Solid Tumors", Genetics and IVF Institute, Fairfax, Virginia, November, 1992.
2. "Chromosomes, Cancer and Counseling", University of Maryland, February, 1993.
3. "Cytogenetics of Some Leukemias and Solid Tumors", Childrens Hospital National Medical Center, April 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hanash, S., Beretta, L., Glover, T., Sheldon, S., Barcroft, C., Ungar, D. and Sonenberg, N.: Mapping of the gene for interferon-inducible dsRNA-dependent protein kinase to chromosome 2p21. *Genes, Chrom. Cancer*, In Press.
2. Ghaziuddin, M., Sheldon, S., Venkataraman, S., Tsai, L. and Alessi, N.: Autism associated with tetrasomy 15: A further report. *Eur, Child and Adolescent Psych.* 1993;2:1.

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

1. Sheldon, S. and Hanson, C.A.: Two histologically and cytogenetically distinct populations of cells in a patient with acute promyelocyte leukemia. *Amer. J. Human Genet.* 1992.
2. Ross, C.W., Nakagawa, A., Schnitzer, B., Sheldon, S. and Hanson, C.A.: Acute leukemia in infants. *Lab. Invest.* 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology Coverage of M-Labs cases including most cases from:
 - 1. Albion Community Hospital, Albion, Michigan.
 - 2. Thorn Hospital, Hudson, Michigan.
 - 3. University of Michigan Health Service, Non-derm cases, Ann Arbor, Michigan.
 - 4. Addison Community Hospital, Addison, Michigan.
 - 5. Other various clients.
- B. Autopsy Coverage for Albion Community Hospital, Albion, Michigan, and Thorn Hospital.
- C. Rotation with other staff pathologists.
 - 1. Seven weeks coverage at the University Hospital of weekend autopsy call.

II. TEACHING ACTIVITIES:

- A. Supervise residents in gross cutting of M-Labs cases and review microscopic material with residents in all interesting cases.
- B. Read out some M-Labs autopsies and some University of Michigan autopsies with residents.
- C. In-Service teaching to laboratory staffs at Addison, Albion, Lapeer, and Thorn 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, Thorn Hospital, Hudson, Michigan, 1/93 - 3/93.
- F. Chairman, Tissue/Transfusion Committee, Thorn Hospital, Hudson, Michigan, 1/93-3/93.

- G. Chairman, Infection Control Committee, Thorn Hospital, Hudson, Michigan, 1/93-3/93.
- H. Director of Laboratories, Lapeer Regional Hospital, Lapeer, Michigan, 1/93-6/93.
- I. Member, Tissue/Transfusion Committee, Infection Control Committee and Ethics Committee, Lapeer Regional Hospital, Lapeer, Michigan, 1/93 - 6/93.
- J. Pathologist, Addison Community Hospital, 9/92-.
- K. Chair, Tissue Transfusion and Infection Control Committees, Addison Community Hospital, 9/92 -.

V. **OTHER RELEVANT ACTIVITIES:**

None.

VI. **PUBLICATIONS:**

None.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. 33% Neuropathology Service.

II. TEACHING ACTIVITIES:

- A. Graduate students:
1. Responsible during the current academic year for teaching activities for the following:
a. Neuropathology 858 - six hours.
b. CME accredited Conferences.
Brain Conference - 40 hours.
Neuromuscular Conference - 12 hours.
Neuropathology Conference for house staff - 16 hours.
- B. Undergraduate students:
1. Neuropathology (NSB 600) - four hours.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Pathology of the Node of Ranvier in Diabetic Neuropathy", RO1-DK 43884-01 (40%), National Institutes of Health, with Tennekoon, G. and Rutkowski, J.L., \$1,472,882/5 years, 4/1/91 - 3/31/96.
- B. Co-Investigator, (5% effort), "Molecular Elements, Neurocircuits and Mental Illness", Watson, S. (PI), National Institute of Mental Health. \$5,166,343/5 years, 12/1/91-11/30/96.
- C. Co-Investigator, (5% effort), "Luteotrophic Actions of Insulin-like Growth Factor I", Keyes, L. (PI), National Institutes of Health, \$404,922, 7/1/92-6/30/95.
- D. Co-Investigator, (10% effort), Greene, D.A. (PI), Michigan Diabetes Research and Training Center, National Institutes of Health, 5P60 DK20572-16, \$1,250,000/annual, 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. 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. Co-Investigator, Greene, D.A. (PI), "Phase I Studies: Effects of Acetyl-L-Carnitine (ALCAR) on Ketogenesis in Rats and on Nerve Structure and Function in Diabetic Rats", Sigma-Tau Pharmaceuticals, \$420,162 direct costs, 9/1/92-8/31/93.

PENDING:

- A. Principal Investigator, (20% effort), Neuropathology Core, Michigan Alzheimer's Disease Research Center, National Institutes of Health, \$225,027/yr, 10/1/94-9/30/99.
- B. Principal Investigator, (10% effort) Diffuse Lewy Body Disease (DLBD), Michigan Alzheimer's Disease Research Center, National Institutes of Health, \$105,600/year, 10/1/94-9/30/99.

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. Ad hoc Reviewer for nine journals (Neuropathology and Diabetes).
- G. Study sections:
 - 1. Medical Research Council of Canada.
 - 2. Juvenile Diabetes Foundation International.
 - 3. American Diabetes Association.

INVITED LECTURES/SEMINARS:

1. International Congress of the International Academy of Pathology, Madrid, Spain, 1992.
2. Wyeth Ayerst Research, Princeton, New Jersey, 1992.
3. Wyeth Ayerst Research, Phoenix, Arizona, 1992.
4. International Symposium on Diabetic Neuropathies, University Erlangen-Nuremberg, Germany, 1993.
5. The Royal College of Physicians, William Harvey Research Conference, London, England, 1993.
6. Fujisawa Meeting, Phoenix, Arizona, 1993.
7. University of Turku, Finland - Visiting Professor, Opponent for Doctoral Thesis, 1993.
8. Canadian Congress of Neurological Sciences, Toronto, Ontario, Canada, 1993.
9. International Neuropathy Meeting, Rome, Italy, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Sima, A.A.F. and Chakrabarti, S.: Long-term suppression of post-prandial hyperglycemia with acarbose retards the development of neuropathies in the BB/W-rat. *Diabetologia* 1992;35:325-330.
2. Chakrabarti, S. and Sima, A.A.F.: The effect of myo-inositol treatment on basement membrane thickening in the BB/W-rat retina. *Diab. Res. Clin. Prac.* 1992;16:13-17.
3. Simmons Z., Ablers, J.W. and Sima, A.A.F.: Case of the Month: Perineuritis presenting as mononeuritis multiplex. *Muscle and Nerve.* 1992;15:630-635.
4. Sima, A.A.F. and Greene, D.A.: Morphologie der peripheren diabetischen neuropathie und ihre korrelation mit funktionstesten. *Diabetes und Stoffwechsel.* 1992;1:45-51.
5. Greene, D.A. and Sima, A.A.F.: Stellenwert der aldoserduktase-hemmer in der therapie der diabetischen neuropathie des menschen. *Diabetes und Stoffwechsel.* 1992;1:45-51.
6. Sima, A.A.F.: Structural-functional interactions in the therapeutic response of diabetic neuropathy. *J. Diabetic Complications* 1992;6:40-44.
7. Sima, A.A.F., Brown, M.B., Prashar, A., Chakrabarti, S., Laudadio, C. and Greene, D.A.: The reproducibility and sensitivity of sural nerve morphometry in the assessment of diabetic peripheral polyneuropathy. *Diabetologia.* 1992;35:560-569.

PENDING:

- A. Principal Investigator, (20% effort), Neuropathology Core, Michigan Alzheimer's Disease Research Center, National Institutes of Health, \$225,027/yr, 10/1/94-9/30/99.
- B. Principal Investigator, (10% effort) Diffuse Lewy Body Disease (DLBD), Michigan Alzheimer's Disease Research Center, National Institutes of Health, \$105,600/year, 10/1/94-9/30/99.

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. Ad hoc Reviewer for nine journals (Neuropathology and Diabetes).
- G. Study sections:
 - 1. Medical Research Council of Canada.
 - 2. Juvenile Diabetes Foundation International.
 - 3. American Diabetes Association.

INVITED LECTURES/SEMINARS:

1. International Congress of the International Academy of Pathology, Madrid, Spain, 1992.
2. Wyeth Ayerst Research, Princeton, New Jersey, 1992.
3. Wyeth Ayerst Research, Phoenix, Arizona, 1992.
4. International Symposium on Diabetic Neuropathies, University Erlangen-Nuremberg, Germany, 1993.
5. The Royal College of Physicians, William Harvey Research Conference, London, England, 1993.
6. Fujisawa Meeting, Phoenix, Arizona, 1993.
7. University of Turku, Finland - Visiting Professor, Opponent for Doctoral Thesis, 1993.
8. Canadian Congress of Neurological Sciences, Toronto, Ontario, Canada, 1993.
9. International Neuropathy Meeting, Rome, Italy, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Sima, A.A.F. and Chakrabarti, S.: Long-term suppression of post-prandial hyperglycemia with acarbose retards the development of neuropathies in the BB/W-rat. *Diabetologia* 1992;35:325-330.
2. Chakrabarti, S. and Sima, A.A.F.: The effect of myo-inositol treatment on basement membrane thickening in the BB/W-rat retina. *Diab. Res. Clin. Prac.* 1992;16:13-17.
3. Simmons Z., Ablers, J.W. and Sima, A.A.F.: Case of the Month: Perineuritis presenting as mononeuritis multiplex. *Muscle and Nerve.* 1992;15:630-635.
4. Sima, A.A.F. and Greene, D.A.: Morphologie der peripheren diabetischen neuropathie und ihre korrelation mit funktionstesten. *Diabetes und Stoffwechsel.* 1992;1:45-51.
5. Greene, D.A. and Sima, A.A.F.: Stellenwert der aldosereduktase-hemmer in der therapie der diabetischen neuropathie des menschen. *Diabetes und Stoffwechsel.* 1992;1:45-51.
6. Sima, A.A.F.: Structural-functional interactions in the therapeutic response of diabetic neuropathy. *J. Diabetic Complications* 1992;6:40-44.
7. Sima, A.A.F., Brown, M.B., Prashar, A., Chakrabarti, S., Laudadio, C. and Greene, D.A.: The reproducibility and sensitivity of sural nerve morphometry in the assessment of diabetic peripheral polyneuropathy. *Diabetologia.* 1992;35:560-569.

8. Sima, A.A.F., Zhang, W-X, Cherian, P.V. and Chakrabarti, S.: Impaired visual evoked potentials and primary axonopathy of the optic nerve in the diabetic BB/W-rat. *Diabetologia*. 1992;35:602-607.
9. Sima, A.A.F.: Pathogenesis, progression and therapeutic intervention of diabetic neuropathy. *J. Ocular Pharmacology*. 1992;8:173-181.
10. Foster, N.L., Gilman, S., Berent, S., Sima, A.A.F., D'Amato, C., Koeppe, R.A. and Hicks, S.P.: Progressive subcortical gliosis and progressive supranuclear palsy can have similar clinical and PET abnormalities. *J. Neurol. Neurosurg. and Psychiatry*. 1992;55:707-713.
11. Greene, D.A., Sima, A.A.F., Stevens, M.B., Feldman, E.L. and Lattimer, S.A.: Complications: Neuropathy, pathogenetic considerations. *Diabetes Care* 1992;15:1902-1925.
12. Multiple Authors: Proceedings of a consensus development conference on standardized measures in diabetic neuropathy. *Neurology* 1991;42:1823-1839; *Diabetes Care* 1992;15:1080-1083; *Muscle and Nerve* 1992;15(10):1167-70.
13. Uccioli, L., Magnani, P., Tilli, P., Cotroneo, P., Manto, A., Greco A.V., Sima A.A.F., Greene, D.A., Menzinger G. and Ghirlanda, G.: Abnormal agonist-stimulated cardiac parasympathetic acetyl-choline release in streptozotocin diabetes. *Diabetes* 1993;42:141-147.
14. Sima, A.A.F., Prashar, A., Nathaniel, V., Bril, V., Werb, M.R. and Greene, D.A.: Overt diabetic neuropathy: Repair of axo-glial dysjunction and axonal atrophy by aldose reductase inhibition and its correlation to improvement in nerve conduction velocity. *Diabetic Medicine*. 1993;10:115-121.
15. Greene, D.A., Sima, A.A.F., Pfeifer M.A., Feldman, E.L. and Stevens M.J.: Diabetic neuropathy: Screening and management. *Contemporary Internal Medicine*. 1993;5:79-91.
16. Goodison, K.L., Parhad, I.M., White, C.L., Sima, A.A.F. and Clark, A.W.: Neuronal and glial gene expression in neocortex of Down's Syndrome and Alzheimer's disease. *J. Neuropath. Exp. Neurol.* 1993;52:192-198.
17. Sima, A.A.F. and Greene, D.A.: Structural-functional interactions in the therapeutic response of diabetic neuropathy. *Diabetic Medicine* 1993;10:33S-34S.
18. Greene, D.A. and Sima, A.A.F: Effects of aldose reductase inhibitors on the progression of nerve damage. *Diabetic Medicine* 1993;10:31S-32S.
19. 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*, In Press.
20. 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 non-immunosuppressed BB diabetic rat following abdominal, intratesticular, islet transplantation. *Transplantation*, In Press.
21. Liang, B.C., Sima, A.A.F. and Albers, J.W.: Case of the month: Paraneoplastic pseudo-obstruction, mononeuritis multiplex, and sensory neuronopathy. *Muscle and Nerve*, In Press.
22. Sima, A.A.F., Greene, D.A., Brown, M.B., Hohman, T.C., Hicks, D., Graepel, G.J., Bochenek, W.J., Beg, M., Gonen, B. and the Tolrestat Study Group: Effect of hyperglycemia and the aldose reductase inhibitor tolrestat on sural nerve biochemistry and morphometry in advanced diabetic peripheral polyneuropathy. *J. Diab. Compl.*, In Press.
23. Sima, A.A.F.: Diabetic neuropathy - the presence and future of a common but silent disorder. Editorial. *Modern Pathology*, In Press.
24. Sima, A.A.F., Caplan M., D'Amato, C.J., Pevzner, M. and Furlong, J.W.: Fulminant multiple system atrophy in a young adult presenting as motor neuron disease. *Neurology*, In Press.

25. Stevens M.J., Lattimer, S.A., Kamijo, M., Van Huysen, C., Sima, A.A.F. and Greene, D.A.: Osmotically induced nerve taurine depletion in experimental diabetes: An hypothetical mediator of painful neuropathy. *Diabetologia*, In Press.
26. 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*, In Press.
27. Greene, D.A., Sima, A.A.F., Stevens, M., Feldman, E., Killen, P., Henry, D., Thomas, T., Dannenberg, J. and Lattimer, S.: Aldose reductase inhibitors: An approach to the treatment of the nerve damage of diabetic neuropathy. *Diabetes/Metabolism Reviews*, In Press.
28. 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*, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Felice K., Feldman, E., Fratkin, J. and Sima, A.A.F.: Sudden death in Dejerine-Sottas Disease: A clinico-pathologic case study. *Pediatric Neurology*, submitted.
2. Lindström, P., Brismar, T. and Sima, A.A.F.: Impaired recovery in diabetic rat following anoxic conduction block. *Muscle and Nerve*, submitted.
3. 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.*, submitted.
4. Paro, M., Prashar, A., Prosdociami, M., Cherian, P.V., Fiori, M.G. and Sima, A.A.F.: Autonomic bladder dysfunction in the BB/W rat: Effect of ganglioside treatment on functional and structural alterations. *J. of Urology*, submitted.
5. Sima, A.A.F., Douglas, V. and D'Amato, C.J.: Diffuse Lewy body disease - A retrograde degeneration of cortical dopaminergic afferent? *Ann. Neurol.*, submitted.
6. 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. *J. Clin. Invest.*, submitted.
7. 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.*, submitted.

BOOKS/CHAPTERS IN BOOKS:

1. McKeever, P.E., Sima, A.A.F. and Blaivas, M.: Neoplasms of the sellar region, in, Lloyd, R.V. (ed.), *Surgical Pathology of the Pituitary Gland*, W.B. Saunders, Philadelphia, pp. 141-210, 1992.
2. Stevens, M.J., Feldman, E.L., Funnell, M.M., Sima, A.A.F. and Greene, D.A.: Optimal methods for detecting early neuropathy and its progression, in, Mogensen, C.E. and Standl, E. (eds.), *Concepts for the Ideal Diabetes Clinic*, Diabetes Forum Series IV, Walter de Gruyter, New York, pp.315-332, 1992.
3. Sima, A.A.F., Stevens, M.J., Feldman, E.L., Cherian, P.V. and Greene, D.A.: Animal models as tools for the testing of preventive and therapeutic measures in

- diabetic neuropathy, in, Lessons from Animal Diabetes IV, Chapter 16, Smith Gordon, pp. 177-191, 1993.
4. Sima, A.A.F.: The natural history of diabetic neuropathy in the BB-rat, in, Sharma, A.K., et al. (eds.), Diabetes Mellitus and Its Complications - An Update, Macmillan India Limited, Delhi, pp. 315-325, 1993.
 5. Sima, A.A.F. and Greene D.A.: Morphological changes in diabetic neuropathy and responses to ARI-treatment, in, Sharma, A.K., et al. (eds.), Diabetes Mellitus and Its Complications - An Update, Macmillan India Limited, Delhi, pp.376-384, 1993.
 6. Chakrabarti, S. and Sima, A.A.F.: Animal models of diabetic retinopathy, in, Sharma, A.K., et al. (eds.), Diabetes Mellitus and Its Complications - An Update, Macmillan India Limited, Delhi, pp. 397-410, 1993.
 7. Sima, A.A.F.,: Diabetic neuropathy: Pathogenesis, natural history and therapeutic potentials, in, Vasselli, J.R., Maggio, C.A., Scriabine, A. (eds.), Drugs in Development, Vol. I, a-Glucosidase Inhibition: Potential Use in Diabetes, Neva Press, Bradford, Connecticut, In Press, June 1993.
 8. Chakrabarti, S. and Sima, A.A.F.: Diabetic retinal microangiopathy in the BB/W rats: The effects of myo-inositol supplementation, in, Vasselli, J.R., Maggio, C.A., Scriabine, A. (eds.), Drugs in Development, Vol. I, a-Glucosidase Inhibition: Potential Use in Diabetes, Neva Press, Bradford, Connecticut, In Press, June 1993.
 9. 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., Scriabine, A. (eds.), Drugs in Development, Vol. I, a-Glucosidase Inhibition: Potential Use in Diabetes, Neva Press, Bradford Connecticut, In Press, June 1993. (Proceedings of the 1991 Acarbose Preclinical Workshop).
 10. 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.
 11. Greene, D.A., Sima, A.A.F. and Brown, M.: Conducting clinical trials in diabetic neural disease, including poser 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.

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

1. Sima, A.A.F., Cherian, P.V., Albers J.W., Greene, D.A. and the Tolrestat Study Group: Nerve fiber loss in diabetic neuropathy correlates with impaired evoked potential amplitudes and nerve conduction velocity. Diabetologia 1992;35:A157.
2. Steiner K., Sima, A.A.F., Hohman, T.C., Greene, D.A. and the Tolrestat Study Group: Use of morphometry in the assessment of biochemistry in sural nerve biopsies from diabetic neuropathic patients. Diabetologia 1992;35:A16.
3. Kamijo, M., Cherian, P.V. and Sima, A.A.F.: Nerve growth factors and regeneration in diabetic neuropathy of the BB/W rat. Neurodiab Meeting, Bratislava, Czechoslovakia, September 13-14, 1992.
4. Sima, A.A.F., Kamijo, M. and Cherian, P.V.: Central sensory neuropathy in the BB/W-rat and its prevention by aldose reductase inhibitor. Neurodiab Meeting, Bratislava, Czechoslovakia, September 13-14, 1992.

5. Kamijo, M., Hohman, T. and Sima, A.A.F.: Chronic galactosemia produces a diabetes-like neuropathy and is partially prevented by aldose-reductase inhibition. *J. Neuropathol. Exp. Neurol.* 1993;52:276.
6. D'Amato C., Tworek, J. and Sima, A.A.F.: Primary limbic lobe gliosis mimicking Alzheimer's disease. *J. Neuropathol. Exp. Neurol.* 1993;52:279.
7. Sima, A.A.F., Douglas, V. and D'Amato, C.: Diffuse Lewy Body Disease (DLBD) - A retrograde degeneration of the mesocortical dopa-minergic system? *J. Neuropathol. Exp. Neurol.* 1993;52:282.
8. Stevens, M., Dananberg, J., Lattimer, S., Sima, A.A.F. and Greene, D.: Sorbitol pathway mediated slowing of nerve conductin involves a nitric oxide mechanism in the streptozotocin diabetic rat. *Diabetes* 1993;42:149A.
9. Cherian, P.V. and Sima, A.A.F.: Redistribution of nodal sodium channels in diabetic neuropathy of the BB/W-rat. *Diabetes* 1993;42:194A.
10. 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, April 17, 1993.*
11. 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, April 17, 1993.*

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

**ANNUAL DEPARTMENT REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "*In vitro* Models of Neutrophil Membrane Fusion", Office of the Vice President for Research Briding Support, Allocated Support to Pediatrics/J. Smolen, \$15,000, 12/1/92-5/31/93.
- B. Principal Investigator. "The Initiation of Granulocyte Responses", National Institutes of Health, Allocated Support to Pediatrics/J. Smolen, \$1,080,037, July 1980-December 1992.

PROJECTS UNDER STUDY:

- A. Degranulations and Fusion in Neutrophils.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. University of Michigan, Department of Pediatrics, Departmental Appointments, Promotions, Titles and Affirmative Action Committee.

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 Pathologist.
- E. Member, American Society of Hematologists.
- F. Member, American Association for the Advancement of Science.
- G. NIH, Special Study Sections for Individual Proposals.

- H. NIH, Special Study Sections for Program Projects.
- I. NIH, *ad hoc* Review Committee for AIDS.
- J. Veterans Administration - Infectious Diseases Merit Review Board.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Biochemical Pharmacology, Reviewer.
- B. Biochimica et Biophysica Acta, Reviewer.
- C. Blood, Reviewer.
- D. Cancer Research, Reviewer.
- E. European Journal of Hematology, Reviewer.
- F. Infection and Immunity, Reviewer.
- G. Journal of Biological Chemistry, Reviewer.
- H. Journal of Cellular Physiology, Reviewer.
- I. Journal of Immunology, Reviewer.
- J. Journal of Leukocyte Biology, Reviewer.
- K. Life Sciences, Reviewer.
- L. Molecular Pharmacology, Reviewer.
- M. Nature, Reviewer.
- N. Pharmacology and Toxicology, Reviewer.
- O. The Journal of Clinical Investigation, Reviewer.

INVITED LECTURES/SEMINARS:

- 1. Co-Chairman at FASEB session.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REVIEWED JOURNALS:

- 1. Smolen, J.E., Kuczynski, B., Koh, E.K., Balazovich, K.J. and Woronoff, A.: "Depletion" of ATP by 2-deoxyglucose: Secretion by electroporated human neutrophils is not restored by re-addition of ATP. *Biol. Signals* 1992;1:22-33.
- 2. Francis, J.W., Balazovich, K.J., Smolen, J.E. and Boxer, L.A.: Human neutrophil annexin I promotes granule aggregation and modulates Ca²⁺-dependent membrane fusion. *J. Clin. Invest.* 1992;90:537-544.
- 2. Smolen, J.E.: Neutrophil signal transduction: Calcium, kinases, and fusion. *J. Lab. Clin. Med.* 1992;120:527-532.

BOOKS/CHAPTERS IN BOOKS:

- 1. 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, pp.1-46, 1992.

**LLOYD M. STOOLMAN, M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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 and postdoctoral investigators:
 - 1. Eric Kaldjian, M.D., Pathology Research Fellow (July, 1991 - present)- 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 in preparation. He has been accepted into 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 presented her work on leukocyte-endothelial cell adhesion under shear stress at a FASEB 1993 minisymposium. The study demonstrated, for the first time, that the $\beta 1$ -integrin VLA-4 can initiate attachment at physiologically relevant levels of linear-shear stress without assistance from other adhesion receptors. This finding challenges the prevailing view that members of the selectin family must initiate contact before the integrins can act.
 - 3. Jennifer Ballew, undergraduate student (July, 1990 - present) - projects focus on development of basic and advanced laboratory skills including tissue culture, immunostaining and operation of flow cytometer. Ms. Ballew currently conducts flow cytometric analysis for several research laboratories and provides hand-on instruction to research personnel.
 - 4. 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. Vennay is the most recent addition to the undergraduate staff in the laboratory. My laboratory provides instruction to 1-2 undergraduates/year willing to commit summers and 5-10 hours per week during the school year. Six 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.

- B. Laboratory Instructor, Organ Systems Pathology (Pathology 600) - joined group of ten instructors as permanent faculty in the course. Instructors selected for interest and skill in teaching.
- C. Section leader, Hematopathology Section of Pathology 600 Course.
- D. Co-director, Hematology Sequence in Component II (new 2nd year curriculum for Medical School).
- 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, Hematology/Oncology and Cancer Center Research Seminars.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- 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 Sept 1992- 31 Aug 1996.
- C. Co-Principal Investigator, (J. Curtis, PI), 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, "Endothelial Binding Lectins of Lymphoid Malignancies", NIH, RO1, CA49256, 0% effort (no cost extension), \$425,000; 30 September 1989 - 31 August 1993.

PENDING:

- A. 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.
- B. Co-Principal Investigator, (Y. Shimizu, PI), "Structure/Function Analysis of Human T Cell β 1-Integrins", 5% effort.
- C. Co-Principal Investigator, (BJ Richardson, PI), project 1- "T-cell effector mechanisms in Lupus", NIH, SCOR in Systemic Lupus Erythematosus, 3% effort.

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. "P-selectin-dependent Attachment to Synovial Venules in Rheumatoid Arthritis", Upjohn Pharmaceutical Co., Kalamazoo, Michigan, February 1993.
2. "Leukocyte Adhesion and the Metastatic Process", International Association of Pathologists, Hematopathology Society, annual meeting, New Orleans, Louisiana, March 1993.
3. Chair, Minisymposium on Leukocyte Adhesion, American Society of Investigative Pathology, FASEB annual meeting, New Orleans, Louisiana, March 1993.
4. "The Function and Regulation of the Selectins", Mosbach Symposium on Glyco- and Cell-biology, Mosbach, Germany, May 1993.
5. "a4-containing Integrins Mediate Lymphoblast Adhesion to Cytokine-treated Endothelium Under Shear", Department of Physiology, Free University of Berlin, Berlin, Germany, May 1993.
6. "Leukocyte Adhesion to Endothelium in the Pathogenesis of Rheumatoid Arthritis", New Advances in the Pathogenesis and Treatment of Rheumatoid Arthritis, Ann Arbor, Michigan, June 1993.
7. Co-chair Brooks Lodge Symposium on Leukocyte-Endothelial Adhesion- invited by Upjohn Pharmaceutical Co. to organize (together with Nancy Hogg, Ph.D., MRC, London) 3-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 PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ley, K., Linnemann, G., Meinen, M., Stoolman, L.M. and Gaetgens, P.: Fucoidin, but not yeast polyphosphomannan PPME inhibits leukocyte rolling in venules of the rat mesentery. *Blood*. 1993;81:177.
2. Stoolman, L.M., Wang, T.-L., Situ, R. and Varani, J.: Regulation of fibronectin and laminin binding activity in cultured human lymphoblastic Cell Lines. *J. Cell. Physiol.* 1993;154: 593-600.
3. Stoolman, L.M.: Adhesion molecules involved in leukocyte recruitment and lymphocyte recirculation. *Chest*. 1993;103:79S-86S.
4. Grober, J.S., Bowen, B.L., Ebling, H., Athey, B., Thompson, C., Fox, D.A. and Stoolman, L.M.: Monocyte-endothelial adhesion in chronic rheumatoid arthritis: *In situ* detection of selectin and integrin-dependent interactions. *J. Clin. Invest.* 1993;91:2609-2619.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Kaldjian, E., Reddy, B.P. and Stoolman, L.M.: Transcriptional regulation of L-selectin expression- protein kinase C and calcium-dependent signalling pathways mediate divergent effects on expression of specific mRNA.
2. Craig, R., Yednock, T., Bowen, B., Singer, M., Rosen, S.D. and Stoolman, L.M.: Synthesis of fluorescent probes for assaying the carbohydrate-binding activity of L-selectin.
3. Wolber, F., Craig, R., Abassi, O., Ballew, J., Lobb, R. and Stoolman, L.M.: VLA-4 mediates lymphocyte binding to endothelium under shear.

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*, 1993.

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

1. Regulation of L-selectin expression in Jurkat cells: Divergent transcriptional responses to activation stimuli, presented by Eric Kaldjian at Keystone Symposium on Leukocyte-Endothelial Adhesion, Keystone, Colorado, January 1993.
2. Wolber, F., Craig, R., Abassi, O., Ballew, J., Lobb, R. and Stoolman, L.M.: VLA-4 mediates lymphocyte binding to endothelium under shear. *FASEB J.* 1993;7:A639.
3. Craig, R., Yednock, T., Bowen, B., Singer, M., Rosen, S.D. and Stoolman, L.M.: Synthesis of fluorescent probes for assaying the functional activity of L-selectin. *FASEB J.* 1993;7:A829.
4. Stoolman, L.M.: Adhesion molecules involved in the trafficking of normal and malignant leukocytes. *Am. J. Surg. Pathol.* 1993;17:207-208.

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

**ANNUAL DEPARTMENTAL REPORT
1 APRIL 1992-30 JUNE 1993**

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.

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 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. None

II. TEACHING ACTIVITIES:

- A. General Pathology for Dental and Graduate Students (Courses 630/631).
Lectures on inflammation and wound healing.
- B. Andreas Seekamp, M.D. - Postdoctoral Fellow.
- C. You-Yin Fu - Graduate Student.
- D. James Lai - Medical Student/Research.
- E. Kambiz Monem - Undergraduate/Research.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Principal Investigator with Dr. P. A. Ward, Lung Injury Produced by Oxygen Metabolites (NIH GM-29507).

PENDING SUPPORT:

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

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

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

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

- A. Reviewer for the following scientific journals:
 - 1. American Journal of Pathology.
 - 2. Biochemical Pharmacology.
 - 3. Blood.
 - 4. Clinical Immunology and Immunopathology.

5. International Archives of Allergy and Applied Immunology.
6. Journal of Critical Care.
7. Journal of Leukocyte Biology.

V. OTHER RELEVANT ACTIVITIES:

- A. Member Editorial Advisory Board Immunology.

VI. INVITED LECTURES/SEMINARS:

1. Invited Workshop Chairperson, "Polymorphonuclear Leukocytes in the Immune Response" at the 8th International Congress of Immunology, Budapest, Hungary, August 23-28, 1992.
2. Invited Symposium Chairperson, "Adhesion Molecules" at the 16th Annual Conference on Shock, Santa Fe, New Mexico, June 13-16, 1993.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Mulligan, M.S., Varani, J., Warren, J.S., Till, G.O., Smith, C.W., Anderson, D.C., Todd, R.F., III and Ward, P.A.: Roles of $\beta 2$ integrins of rat neutrophils in complement- and oxygen radical-mediated acute inflammatory injury. *J. Immunol.* 1992;148:1847-1857.
2. Murphy, H.S., Shayman, J.A., Till, G.O., Mahrougui, Owens, C.B., Ryan, U.S. and Ward, P.A.: Superoxide responses of endothelial cells to C5a and TNF- α : Divergent signal transduction pathways. *Am. J. Physiol. Lung Cell. Mol. Physiol.* 1992;263:L51-L59.
3. Punch, J., Rees, R., Cashmer, B., Wilkins, E., Smith, D.J. and Till, G.O.: Xanthine oxidase: Its role in the no-reflow phenomenon. *Surgery* 1992;111:169-176.
4. Till, G.O., Lee, S., Mulligan, M.S., Wolter, J.R., Smith, C.W., Ward, P.A. and Marak, G.E., Jr.: Adhesion molecules in experimental phacoanaphylactic endophthalmitis. *Invest. Ophthalmol. Vis. Sci.* 1992;33:3417-3423.
5. Seekamp, A., Mulligan, M.S., Till, G.O. and Ward, P.A.: Requirements for neutrophil products and L-arginine in ischemia-reperfusion injury. *Am. J. Pathol.* 1993;142:1217-1226.
6. Hultquist, D.E., Xu, F., Quandt, D.S., Schlafer, M., Mack, C.P., Till, G.O., Seekamp, A., Betz, A.L. and Ennis, S.R.: Evidence that NADPH-dependent methemoglobin reductase and administered riboflavin protect tissues from oxidative injury. *Am. J. Hematol.* 1993;42:13-18.
7. 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.* 1993;34:684-694.
8. Seekamp, A., Mulligan, M.S., Till, G.O., Smith, C.W., Miyasala, 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.*, In Press.
9. Seekamp, A., Warren, J.S., Remick, D.G., Till, G.O. and Ward, P.A.: Requirements for tumor necrosis factor- α and interleukin-1 in limb ischemia/reperfusion injury and associated lung injury. *Am. J. Pathol.*, In Press.
10. Rodriguez, J.L., Kelly, 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.

11. 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.
12. Wilkins, E.G., Rees, R.S., Smith, D., Cashmer, B., Punch, J., Till, G.O. and Smith, D.J.: Identification of xanthine oxidase activity following reperfusion in human tissue. *Surgery*, In Press.
13. 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.
14. Winn, W.C., Davis, G.S., Durda, J.P. and Till, G.O.: The effect of neutropenia on experimental *Legionella pneumonia*. *Infect. Immun.*, In Press.
15. 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.

BOOKS/CHAPTERS IN BOOKS:

1. Till, G.O. and Ward, P.A.: Oxygen radical-mediated endothelial cell injury, in, Faist, Meakins and Schildberg (eds.), *Host Defense Dysfunction in Trauma, Shock, and Sepsis. Mechanisms and Therapeutic Approaches. Section 3.1 Shock and Ischemia*, Springer-Verlag, Heidelberg, Berlin, pp. 85-93, 1993.
2. Friedl, H.P., Trentz, O., Till, G.O. and Ward, P.A.: Role of oxygen radicals in multiple organ failure, in, Faist, Meakins, Schildberg (eds.), *Host Defense Dysfunction in Trauma, Shock and Sepsis: Mechanisms and Therapeutic Approaches. Section 3.3 Sepsis*, Springer-Verlag, Heidelberg, Berlin, pp. 287-295, 1993.
3. Marak, G.E., Till, G.O. and Ward, P.A.: Endothelial cell regulation of acute uveitis, in, Dermouchamps, J.P., Verougstraete, C., Caspers-Velu, L., Tassignon, M.J. (eds.), *Recent Advances in Uveitis, Proceedings of the Third International Symposium on Uveitis*, Brussels, Belgium, May 24-27, 1992, Kugler Publications, Amsterdam, Netherlands, pp. 91-94, 1993.
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 (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 (ed.), *Proceedings of Free Radicals, Diseased States and Anti-Radical Interventions*, the Richelieu Press, London, In Press.

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

1. Seekamp, A., Till, G.O. and Ward, P.A.: Role of selectins in ischemia/reperfusion injury. *FASEB J.* 1993;7:A493.
2. Marak, G.E., Lee, S., Ward, P.A. and Till, G.O.: Xanthine oxidase in experimental phacoanaphylactic endophthalmitis. *Invest. Ophthalmol. Vis. Sci.* 1993;34:1476.
3. Seekamp, A., Till, G.O., Warren, J.S., Remick, D.G. and Ward, P.A.: Requirement for TNF α and IL-1 in ischemia/reperfusion injury. *Circ. Shock* 1993;1:10.

4. Seekamp, A., Till, G.O. and Ward, P.A.: Effect of antioxidants and neutrophil adhesion molecule antagonists in ischemia-reperfusion injury. AAOS 60th Annual Meeting, 1993.
5. Rodriguez, F.L., Garner, W.L., Till, G.O., Remick, D.G. and Smith, D.J.: Interleukin-8: neutrophil dysfunction and nosocomial pneumonia. AAST, In Press.
6. 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.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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 Soong (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 two post-doctoral fellows, four undergraduate students, and 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, "Biochemical Control of Microcarrier Culture", NIH CA33052, 9/1/90-8/30/92.
D. Co-Investigator, "Protease-Oxidant Interactions in Lung Inflammation", NIH HL42607, 7/1/89-6/30/94.
E. Principal Investigator on Project 10, "Retinoic Acid and Cells of the Skin", Johnson and Johnson Corporation, 7/1/91-6/30/2001.

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 a-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.
- D. NIH Study Section Member: Comprehensive Cancer Center Site Visit, Jefferson Cancer Center, Philadelphia, Pennsylvania, September 12-14, 1992.

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

1. Invited Speaker, Surfaces in Biomaterials Symposium, Minneapolis, Minnesota, October 14-16, 1992.
2. Invited Speaker, 1st International Conference on Advanced Pharmaceutical Substance Screening, Vienna, Austria, November 29- December 1, 1992.
3. Co-Chairman, Minisymposium on Growth Factors and Tissue Organizations, FASEB, March 29-April 3, 1993.
4. Invited Speaker, Johnson and Johnson Symposium on Retinoids and Skin, Princeton, New Jersey, May 27-28, 1993.
5. Invited Speaker, Department of Medicinal Chemistry, University of Tennessee, June 2, 1993.

PATENTS PENDING:

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., Taylor, C.G., Riser, B., Schumaker, D.K., Yeh, K.-Y., Dame, M., Todd, R.F., Dumler, F. and Killen, P.D.: Mesangial cell killing by leukocytes: Role of leukocyte oxidants and proteolytic enzymes. *Kidney Inter.* 1992;42:1169-1177.
2. Ginsburg, I., Misgav, R., Pinson, A., Varani, J., Ward, P.A. and Kohen, R.: Synergism among oxidants, proteinases, phospholipases, microbial hemolysins, cationic proteins and cytokines: A possible major cause of cell and tissue injury in inflammation. *Inflammation* 1992;16:519-538.
3. Ginsburg, I., Misgav, R., Samuni, A., Gibbs, D.F., Varani, J. and Kohen, R.: Human neutrophils stimulated by cetyltrimethyl ammonium bromide generate luminol amplified and non-amplified chemiluminescence but no superoxide production: A paradox. *Immunopharmacol.* 1992;1:337-351.
4. Ginsburg, I., Misgav, R., Gibbs, D.F., Varani, J. and Kohen, R.: Chemiluminescence in activated human neutrophils: Role of buffers and scavengers. *Inflammation*, In Press.
5. Ginsburg, I. and Varani, J.: Interaction of viable group A streptococci and hydrogen peroxide in killing of vascular endothelial cells. *Free Rad. Biol. Med.* 1993;14:495-500.
6. Situ, R., Inman, D.R., Fligiel, S.E.G. and Varani, J.: Effects of all-trans retinoic acid on melanocyte adhesion and motility. *Dermatology* 1993;186:38-44.
7. 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.*, In Press.
8. Varani, J., Fligiel, S.E.G., Schuger, L., Perone, P., Inman, D.R., Griffiths, C.E.M. and Voorhees, J.J.: Effects of all trans retinoic acid and Ca²⁺ on human skin in organ culture. *Am. J. Path.* 1993;142:189-198.

9. Huber, A.R., Ellis, S., Johnson, K.J., Dixit, V.M. and Varani, J.: Monocyte diapedesis through an *in vitro* vessel wall construct: Inhibition with monoclonal antibodies to thrombospondin. *J. Leuko. Biol.* 1992;52:524-528.
10. Varani, J., Sitrin, R.G. and Hillegas, W.: Expression of heterogeneous profiles of plasminogen activator and plasminogen activator inhibitor mRNA in human fibroblasts grown on different substrates. *Cytotechnology* 1992;9:157-162.
11. Schuger, L., Killen, P.D., Skubitz, A.P.N., Chang, J. and Varani, J.: Expression of laminin-A and B chains and their mRNA in the epithelium and mesenchyme during murine lung development. *Develop. Dynamics* 1992;195:43-54.
12. Varani, J., Larson, B.K., Perone, P., Inman, D.R., Fligel, S.E.G. and Voorhees, J.J.: All-trans retinoic acid and extracellular Ca^{2+} differently influence extracellular matrix production by human skin in organ culture. *Am. J. Pathol.*, In Press.
13. Varani, J., Fligel, 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*, In Press.
14. Schuger, L., Mitra, R., Varani, J. and Gilbride, K.: Effect of retinoic acid on mouse lung branching activity. *Develop. Biol.*, In Press.
15. Varani, J. and Taylor, C.: Further studies on the mechanism of mesangial cell killing by activated neutrophils. *Euro. J. Biochem.*, In Press.
16. Varani, J., Fligel, S.E.G., Inman, D.R., Beals, T.F. and Hillegas, W.J.: Modulation of adhesive properties of DEAE-dextran with laminin. *J. Biomed. Materials Res.*, In Press.
17. Varani, J., Inman, D.R., Fligel, S.E.G. and Hillegas, W.J.: Use of recombinant and synthetic peptides as attachment factors for cells on microcarriers. *Cytotechnology*, In Press.
18. Ginsburg, I., Mitra, R., Gibbs, D.F., Varani, J. and Kohen, R.: Killing of endothelial cells and release of arachidonic acid: synergistic effects among hydrogen peroxide, membrane-damaging agents, cationic substances and proteinases. *Inflammation*, In Press.
19. Varani, J., Perone, P., Fligel, S.E.G., Inman, D.R. and Voorhees, J.J.: All-trans retinoic acid stimulates outgrowth of keratinocytes and fibroblasts from full-thickness human skin and fibroblasts from isolated dermis in organ culture. *J. Invest. Dermatol.*, In Press.
20. Fligel, S.E.G. and Varani, J.: In situ epithelial cell invasion in organ culture. *Invasion and Metastasis*, In Press.

BOOKS AND CHAPTERS IN BOOKS:

1. Varani, J. and Johnson, K.J.: Modulation of endothelial cell injury by all trans retinoic acid (RA): Role in anti-inflammatory effects of RA, in, Jesaitis, A. (ed.), *Molecular Basis of Oxidative Damage by Leukocytes*, CRC Press, pp. 297-302, 1992.
2. Johnson, K.J., Varani, J. and Smolen, J.E.: Neutrophil activation and function in health and disease, in, Coffey, R.D. (ed.), *Granulocyte Response to Cytokines: Basic and Clinical Research*, Marcell Dekker, Inc., New York, 1993.
3. Varnai, J. and Ward, P.A.: Neutrophil-endothelial interactions, in, Maini, R.N. and Zvaifler, N.J. (eds.), *Rheumatology*, Mosby, London, 1993.
4. 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.

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

1. Varani, J., Lowe, J. and Petryniak, J.: Differential expression of glycoproteins containing a-D-galactosyl groups on cells of high and low-malignant potential. *J. Cell. Biochem.* 1993;17A:375.
2. Takagaki, M., Varani, J. and Goldstein, I.J.: Monoclonal antibodies that recognize the trisaccharide epitope (Gal a 1,3 Gal b 1,4 GlcNAc) present on Ehrlich tumor cell membrane glycoproteins. *J. Cell. Biochem.* 1993;17A:374.
3. Schuger, L., Mitra, R., Varani, J. and Gilbride, K.: Effect of retinoic acid on mouse lung branching activity. *Mol. Biol. Cell* 1992;3:105a.
4. Varani, J., Inman, D.R., Perone, P., Fligel, S.E.G. and Voorhees, J.J.: Repair of sun-damaged skin by all-trans retinoic acid in organ culture depends on stimulation of extracellular matrix synthesis. *J. Invest. Dermatol.* 1993;100:551.
5. Taylor, C.G., Dame, M.K. and Varani, J.: Potential role of apoptosis in the spontaneous injury of late passage human umbilical vein endothelial cells. *FASEB J.* 1993;7:A137.
6. Varani, J., Inman, D., Perone, P., Fligel, S.E.G. and Elder, J.T.: Regulation of skin structure and function in organ culture. *FASEB J.* 1993;7:A492.
7. Dame, M. and Varani, J.: Respiratory epithelial cell injury by neutrophils: Interaction of oxidants and other effector mechanisms. *FASEB J.* 1993;7:A569.
8. Gibbs, D.F., Varani, J. and Johnson, K.J.: The cooperative interaction of proteases and oxidants in endothelial cell injury by rat neutrophils. *FASEB J.* 1993;7:A714.
9. Taylor, C.G. and Varani, J.: Inhibition of apoptosis reduces spontaneous injury to late passage human umbilical vein endothelial cells. *CFBS Proc.* 1993;36:131.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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. Amy Gilardi, D.V.M., Postdoctoral Fellow.
 - b. Ara Vaporciyan, M.D., Postdoctoral Fellow.
 - c. Kimberly McElroy, M.D., Postdoctoral Fellow.
 - d. Jami Foreback, Pathology Graduate Program Student (mentor).
 - e. Undergraduate Honors Students:
 - Hiliary Cohen, Freshman.
 - Amy Totochaud, Sophomore.
 - Nicole Dooskin, Freshman.
 - 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, February 17, 1993, one hour.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Lung Immunopathology" (Training Grant), NHLBI-NIH-HL-07517 (5%), \$288,584/year, 6/1/92-5/30-1/93.
- B. Principal Investigator, "Lung Injury by Oxygen Metabolites", NIGMS-NIH-GM-29507 (20%), \$221,266/year (\$1,271,378/five years), 7/1/92-6/30/97.
- C. Principal Investigator, "Inflammatory Cells and Lung Injury", NHLBI-HL-31963 (5%), Section I - \$93,321, Sectin V-\$58,941/year (\$1,010,734/five years), 3/1/89-2/28/94.
- D. Co-Investigator, "Mechanisms of Glomerular and Tubular Injury", NIADDK-NIH-DK-39255 (5%), \$45,000/year, 8/1/93-7/31/93.
- 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. Ambulatory Care Strategic Planning Steering Committee, The University Hospitals, 1991--
- B. Advisory Committee for the Howard Hughes Medical Institute, 1984--
- C. Board of Directors, M-Care, 1986--
- D. Center Advisory Committee for The University of Michigan Multipurpose Arthritis Center, 1987--
- E. Clinical Quality Improvement Lead Team, 1991--
- F. Dean's Advisory Council, 1985--
- G. Executive Advisory Committee for Gene Expression and Gene Transfer in the Cardiovascular System, August, 1991--
- H. Executive Director's Advisory Council, 1988--
- I. Geriatric Center Steering Committee, 1990--
- J. Internal Medicine Advisory Committee for the University of Michigan George M. O'Brien Renal and Urologic Center, 1991--
- K. Medical Service Plan Advisory Committee, 1987--
- L. Michigan Diabetes Research and Training Center Policy Committee, 1981--
- M. Michigan Eye Bank Research Review Committee, 1980--
- N. National Task Force on Organ Transplantation, 1985--
- O. Presidential Initiatives Fund, The University of Michigan, March, 1987--
- P. University of Michigan Medical School Executive Committee, September 1, 1990-1993

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, 1993-0.
- 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. Cytogen, 1983--.
- O. A. James French Society of Pathologists, 1988--.
- P. Health Policy Agenda for the American People, Advisory Committee.
- Q. Institute of Medicine, July 1, 1990.
- R. 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-.
- S. Michigan Society of Pathologists.
- T. Michigan Thoracic Society, 1988--.
- U. National Research Council
Institute of Laboratory Animal Resources.
1. Committee on Human Rights, Correspondent.
- V. The Oxygen Society, 1988--.
- W. Phi Rho Sigma, President, The University of Michigan Chapter,
September, 1988.
- X. Society of Medical Consultants to the Armed Forces:
1. President, 1988.
- Y. 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, "Leukocyte Adhesion Molecules: Biology and Therapeutic Strategies", 2nd International Conference on New Drugs in Allergy and Asthma, sponsored by the Swiss Institute of Allergy and Asthma Research, Davos, Switzerland, July 8-10, 1992.
2. Mentor, Undergraduate Research Opportunity Program (UROP), The University of Michigan, Ann Arbor, Michigan, August 9, 1992.
3. Invited Lecturer, "Anti-inflammatory Effects of L-Arginine Analogues", Conference on Nitric Oxide: Brain and Immune System sponsored by the Universities of Rome "Tor Vergata" and Reggio Calabria, Calabria, Italy, September 14-20, 1992.
4. Invited Lecturer and Co-Chair Session, "Ischemia/Reperfusion Events in Acute Thermal Injury", in the session on Ischemia/Reperfusion Injury, 6th Inflammation Conference, White Haven, Pennsylvania, September 23-24, 1992.
5. Invited Lecturer, "The Biology of Free Radicals and Their Roles in Pathology", Symposium on Free Radicals, Group of Research and Study on Mediators of Inflammation (GREMI), Pasteur Institute, Paris, France, October 10-13, 1992.
6. Invited Lecturer, "Lung Injury and Adhesion Molecules", the Upjohn Company, Kalamazoo, Michigan, October 16, 1992.
7. Invited Lecturer, "Lung Inflammation and Adhesion Molecules", in the Symposium on Cellular Adhesion: Molecular Definition to Therapeutic Potential, King of Prussia, Pennsylvania, October 20, 1992.
8. Invited Lecturer, "Lung Inflammation and Adhesion Molecules", T Cell Sciences, Cambridge, Massachusetts, October 30, 1992.
9. Invited Lecturer, "Mechanisms of Lung Inflammatory Injury", Institute for Environmental Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, November 13, 1992.
10. Invited Dickinson W. Richards Memorial Lecturer, "Determinants of Inflammatory Injury in Lung", 65th Scientific Session of the Council on Cardiopulmonary and Critical Care, the American Heart Association, New Orleans, Louisiana, November 16-18, 1992.
11. Invited Lecturer, "Adhesion Molecules and Lung Injury", Ciba-Geigy Strategic Planning Workshop, Short Hills, New Jersey, November 22-24, 1992.
12. Invited Lecturer, "Cytokines, Adhesion Molecules and Lung Injury", National Heart, Lung and Blood Disease Symposium on Cytokines and Cytokine Receptors in Health and Disease, National Institutes of Health, Bethesda, Maryland, December 1-3, 1992.

13. Guest Speaker, "Mechanisms of Lung Inflammatory Injury", Cardiovascular Research Center Symposium sponsored by Merck Pharmaceuticals Company, Medical College of Wisconsin, Milwaukee, Wisconsin, December 16, 1992.
14. Invited Lecturer, "Role of Selectins in Lung Inflammation", Cardiology Conference, Henry Ford Hospital, Detroit, Michigan, January 6, 1993.
15. Invited Lecturer, "Inflammation and System Reaction of Soft Tissue Injury", in Symposium on Future Applications of Cellular Biology, Kona, Hawaii, January 9-11, 1993.
16. Invited Lecturer, "Role of Selectins in Lung Inflammation", Genentech, Inc., South San Francisco, California, January 13-15, 1993.
17. Invited Lecturer, "Role of L-Arginine Products in Lung Inflammatory Injury", US-Japan Meeting on Nitric Oxide Synthase and Carcinogenesis, National Cancer Institute Workshop, Williamsburg, Virginia, January 18-20, 1993.
18. Invited Participant, "The Role of Selectins in Lung Injury", in Cell Adhesion Mechanisms in Leukocyte Traffic, Keystone Symposium, Keystone, Colorado, January 29-30, 1993.
19. Invited Participant, "Critical Care/Reperfusion Injury", for the Upjohn Company Critical Care Advisory Panel Meeting, Chicago, Illinois, February 10-11, 1993.
20. Invited Participant, "Role of the Basic Scientist in Surgical Research Education", Society of University Surgeons Committee on Education's Forum on Research Training in Academic Surgery, Seattle, Washington, February 11-12, 1993.
21. Invited Lecturer, "Ischemia, Reperfusion and Organ Dysfunction", National Heart, Lung and Blood Institute, Bethesda, Maryland, February 18, 1993.
22. Co-Chair Symposium, "Leukocyte Chemotaxis/Activation", Experimental Biology 93 FASEB Meeting, New Orleans, Louisiana, March 29, 1993.
23. Invited Lecturer, "Adhesion Molecules and Lung Inflammatory Injury", IBC USA Conference on Cell Adhesion Molecules: Targets for the Development of Therapeutics and Diagnostics, Sheraton at Fisherman's Wharf, San Francisco, California, May 14, 1993.
24. Invited Speaker, "Pulmonary Function and Gas Exchange", 2nd Clintec International Horizons Conference: Organ Metabolism and Nutrition: Ideas for Future Critical Care, Amsterdam, the Netherlands, May 16-20, 1993.
25. Co-Chair and Invited Lecturer, "Role of Selectins in Lung Inflammation", Joint Meeting of the American Association of Immunologists and Clinical Immunology Society, Denver, Colorado, May 23-24, 1993.
26. Invited Lecturer, "Role of Selectins in Lung Injury", Chiron Corporation, Emeryville, California, June 8-9, 1993.
27. Invited Lecturer, "Role of Selectins in Acute Lung Injury", in Seminar, Adhesion Molecules and Lung Disease, Boehringer Ingelheim Pharmaceuticals, Inc., Somerset, New Jersey, June 17, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Jones, M.L., Mulligan, M.S., Flory, C.M., Ward, P.A. and Warren, J.S.: Potential role of monocyte chemoattractant protein 1/JE in monocyte/macrophage-dependent IgA immune complex alveolitis in the rat. *J. Immunol.* 1992;149:2147-2154.
2. Jones, M.L. and Ward, P.A.: Monocyte chemoattractant protein 1 in a rat model of pulmonary granulomatosis. *Lab. Invest.* 1992;66:498-503.

3. Mulligan, M.S., Moncada, S. and Ward, P.A.: Protective effects of inhibitors of nitric oxide synthase in immune complex-induced vasculitis. *Br. J. Pharmacol.* 1992;107:1159-1162.
4. Mulligan, M.S., Swiderski, D.L., Wrad, P.A., Deeb, G.M. and Lupinetti, F.M.: Expression of adhesion molecules by lung allografts. *Surg. Forum* 1992;43:431-433.
5. Mulligan, M.S., Polley, M.J. Bayer, R.J., Nunn, M.F., Paulson, J.C. and Ward, P.A.: Neutrophil-dependent acute lung injury: Requirement for P-selectin (GMP-140). *J. Clin. Invest.* 1992;90:1600-1607.
6. Mulligan, M.S., Warren, J.S., Smith, C.W., Anderson, D.C., Yeh, C.G., Rudolph, A.R. and Ward, P.A.: Lung injury after deposition of IgA immune complexes: Requirements for CD18 and L-arginine. *J. Immunol.* 1992;148:3086-3092.
7. Murphy, H.S., Shayman, J.A., Till, G.O., Mahrougui, M., Owens, C.B., Ryan, U.S. and Ward, P.A.: Superoxide responses of endothelial cells to C5a and TNF α : Divergent signal transduction pathways. *Am. J. Physiol.* 1992;263:L51-L59
8. Phan, S.H. Gannon, D.E., Ward, P.A. and Karmioli, S.: Mechanism of neutrophil-induced xanthine dehydrogenase to xanthine oxidase conversion in endothelial cells: Evidence of a role for elastase. *Amer. J. Resp. Cell Molec. Biol.* 1992;6:270-278.
9. Stubbs, E.B., Jr., Walker, B.A.M., Owens, C.A., Ward, P.A. and Agranoff, B.W.: Formyl peptide stimulates and ATP γ S potentiates [3 H]cytidine 5'-diphosphate diglyceride accumulation in human neutrophils. *J. Immunol.* 1992;148:2242-2247.
10. Till, G.O., Lee, S., Mulligan, M.S., Wolter, J.R., Smith, C.W., Ward, P.A. and Marak, G.E., Jr.: Adhesion molecules in experimental phacoanaphylactic endophthalmitis. *Invest. Ophthalmol. Vis. Sci.* 1992;33:3417-3423.
11. Varani, J., Dame, M.K., Gibbs, D.F., Taylor, C.G., Weinberg, J.M., Shaywitz, J. and Ward, P.A.: Human umbilical vein endothelial cell killing by activated neutrophils: Loss of sensitivity to injury is accompanied by decreased iron content during *in vitro* culture and is restored with exogenous iron. *Lab. Invest.* 1992;66:708-714.
12. Mulligan, M.S., Johnson, K.J., Todd, R.F., III, Issekutz, T.B., Miyasaka, M., Tamatani, T., Smith, C.W., Anderson, D.C. and Ward, P.A.: Requirements for leukocyte adhesion molecules in nephrotoxic nephritis. *J. Clin. Invest.* 1993;91:577-587.
13. Mulligan, M.S., Jones, M.J., 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.* 1993;150:5585-5595.
14. Mulligan, M.S., Paulson, J.C., De Frees, S., Zheng, Z-L., Lowe, J.B. and Ward, P.A.: Protective effects of oligosaccharides in P-selectin-dependent lung injury. *Nature* 1993;364:149-151.
15. Mulligan, M.S., Smith, C.W., Anderson, D.C., Todd, R.F., III, Miyasaka, M., Tamatani, T., Issekutz, T.B. and Ward, P.A.: Role of leukocyte adhesion molecules in complement-induced lung injury. *J. Immunol.* 1993;150:2401-2406.
16. Mulligan, M.S., Vaporciyan, A.A., Miyasaka, M., Tamatani, T. and Ward, P.A.: Tumor necrosis factor α regulates *in vivo* intrapulmonary expression of ICAM-1. *Amer. J. Pathol.* 1993;142:1739-1749.
17. Mulligan, M.S., Wilson, G.P., Todd, R.F., Smith, C.W., Anderson, D.C., Varani, J., Issekutz, T., Miyasaka, M., Tamatani, T., Rusche, J.R., Vaporciyan, A.A. and Ward, P.A.: Role of β 1, β 2 integrins and ICAM-1 in lung injury following deposition of IgG and IgA immune complexes. *J. Immunol.* 1993;150:2407-2417.

18. 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 β 2-integrins and ICAM-1 in lung injury following ischemia-reperfusion of rat hind limbs. *Amer. J. Pathol.* 1993;143:4:64-472.
19. Seekamp, A., Mulligan, M.S., Till, G.O. and Ward, P.A.: Requirements for neutrophil products and L-arginine in ischemia-reperfusion injury. *Amer. J. Pathol.* 1993;142:1217-1226.
20. Seekamp, A., Warren, J.S., Remick, D.G., Till, G.O. and Ward, P.A.: Requirements for tumor necrosis factor- α and interleukin-1 in limb ischemia/reperfusion injury and associated lung injury. *Amer. J. Pathol.* 1993;143:453-463.
21. Vaporciyan, A.A., Jones, M.L. and Ward, P.A.: Rapid analysis of leukocyte-endothelial adhesion. *J. Immunol. Methods.* 1993;159:93-100.
22. Ward, P.A. and Mulligan, M.S.: Molecular mechanisms in acute lung injury. *Adv. Pharmacol.* 1993;24:275-292.
23. Morganroth, M.L., Schoeneich, S.O., Till, G.O., Pickett, W. and Ward, P.A.: Complement and neutrophil-mediated injury of perfused rat lungs. *Lab. Invest.*, In Press.
24. 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 β 2 integrins, VLA-4 and ICAM-1 in nephrotoxic nephritis. *J. Clin. Invest.*, In Press.
25. 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.*, In Press.
26. 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.*, In Press, August, 1993.
27. Mulligan, M.S., Paulson, J.C., DeFrees, S., Zheng, Z-L., Lowe, J.B., and Ward, P.A.: Protective effects of oligosaccharides in P-selection-dependent lung injury. *Nature*, In Press.
28. 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.
29. Mulligan, M.S., Smith, C.W., Anderson, D.C. and Ward, P.A.: *In vivo* recruitment of neutrophils: Consistent requirements for L-arginine and variable requirements for adhesion molecules. *J. Immunol.*, In Press.
30. Mulligan, M.S., Sulavik, C., Bavorik, P.A., Ward, P.A. and Johnson, K.J.: The delayed phase of anti-GBM nephritis in deferroxamine: Sensitive but catalase-insensitive. *Inflammation*, In Press.
31. 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.*, In Press.
32. Mulligan, M.S., Watson, S.R., Fennie, C. and Ward, P.A.: Protective effects of selectin chimeras in neutrophil-mediated lung injury. *J. Immunol.*, In Press.
33. 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.
34. Seekamp, A. and Ward, P.A.: Ischemia - reperfusion injury. *Agents in Actions (Supplement)*, In Press.
35. Till, G.O., Friedl, H.P. and Ward, P.A.: Role for histamine and xanthine oxidase in complement- and oxiant-mediated acute lung injury. *Free Rad. Biol. Med.*, In Press.

36. 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.
37. Till, G.O. and Ward, P.A.: Immunologic and phagocytic cell defects in thermally injured patients. *J. Crit. Care Med.*, In Press.
38. Vaporciyan, A.A. and Ward, P.A.: Enhanced generation of O_2^- by human neutrophils via a complement iC3b/Mac-1 interaction. *J. Leukocyte Biol.*, In Press.
39. Vaporciyan, A.A. and Ward, P.A.: Induction by C5a of P-selectin dependent endothelial adhesiveness for neutrophils. *J. Immunol.*, In Press.
40. 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.
41. Ward, P.A.: The wound environment - Local and systemic perturbations: Inflammation and the burn wound. *J. Burn Care & Rehab.*, In Press.
42. 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.
43. Ward, P.A. and Johnson, K.J.: Lung inflammatory mechanisms. *J. Human Pathol.*, In Press.
44. Ward, P.A., Johnson, K.J. and Till, G.O.: Mechanisms of lung injury. *Prax. Klin. Pneumonol.*, In Press.

BOOKS/CHAPTERS IN BOOKS:

1. Mulligan, M.S., Johnson, K.J. and Ward, P.A.: Mechanisms of inflammatory oxidant damage in tissues, Chapter 7, in, Cochrane, C.G. and Gimbrone, M.A., Jr. (eds.), *Cellular and Molecular Mechanisms of Inflammation; Volume 4. Biological Oxidants: Generation and Injurious Consequences*, Academic Press, New York, New York, pp. 157-174, 1992.
2. Simon, R.H. and Ward, P.A.: Adult respiratory distress syndrome, in, Gallin, J.I., Goldstein, I.M. and Snyderman, R. (eds.), *Inflammation: Basic Principles and Clinical Correlates*, 2nd edition, Raven Press, New York, 999-1016, 1992.
3. 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*, Raven Press, New York, New York, pp.69-78, 1992.
4. 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.
5. Till, G.O. and Ward, P.A.: 3.1 - Shock and ischemia: Oxygen radical-mediated endothelial cell injury, in, Faist, Meakins and Schildberg (eds.), *Host Defense Dysfunction in Trauma, Shock and Sepsis*, Springer-Verlag, Berlin Heidelberg, pp. 85-94, 1993.
6. Fantone, J.C. and Ward, P.A.: Mechanisms of inflammation, in, Cohen, A.S. (ed.), *Rheumatology and Immunology*, Grune and Stratton, In Press.
7. Friedl, H.P., Trentz, O., Gill, G.O. and Ward, P.A.: Role of oxygen radicals in multiple organ failure, in, *The Immune Consequences of Trauma, Shock and Sepsis*, Springer-Verlag, Heidelberg, In Press.
9. 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.

12. 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.
13. Mulligan, M.S. and Ward, P.A.: Lung inflammation and adhesion molecules, in, Christoffersen, R.E., Hook, J.B. and Poste, G. (eds.), *Cellular Adhesion: Molecular Definition to Therapeutic Potential*, Plenum Publishing Corporation, New York, In Press.
14. Strieter, R.B., Phan, S.H. and Ward, P.A.: Inflammation, injury and repair, in, Murray, J.F. and Nadel, J.A. (eds.), *Textbook of Respiratory Medicine*, Second Edition, W.B. Saunders, Co., Orlando, In Press.
15. 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.
16. Ward, P.A. and Mulligan, M.S.: The role of cytokines and adhesion molecules in lung inflammation, in, Schlag, G. (ed.), *Third wiggers Bernard Conference on Shock, Sepsis, and Organ Failure*, Hotel Schloff Obermayerhofen, Vienna, Austria, May 16-21, 1992., In Press.
17. Ward, P.A., Mulligan, M.S. and Vaporciyan, A.A.: Endothelial-leukocyte adhesion molecules in the pathogenesis of acute pulmonary disease, in, Zucker, M.B. (ed.), *XIVth Congress State-of-the Art Book, Thrombosis and Haemostasis*, 1993, New York, New York, In Press.
18. Ward, P.A. and Till, G.O.: The autodestructive consequences of thermal injury, in, Ninnemann, J. (ed.), *The Immune Consequences of Thermal and Traumatic Injuries*, In Press.

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

1. Gilardy, A.K., Jones, M.J., Johnson, K.J. and Ward, P.A.: *In vivo* methods of monoclonal antibody production are used extensively. *FASEB J.* 1993;7:A41.
2. Vaporciyan, A.A. and Ward, P.A.: Enhanced generation by human neutrophil of O₂⁻ via a complement iC3b/Mac-1 interaction. *FASEB J.* 1993;7:A195.
3. Jones, M.L., Vaporciyan, A.A. and Ward, P.A.: A rapid fluorescent multi-well method for measuring neutrophil and monocyte chemotaxis. *FASEB J.* 1993;7:A365.
4. Seekamp, A., Till, G.O. and Ward, P.A.: Role of selectins in ischemia/reperfusion injury. *FASEB J.* 1993;7:A493.
5. Mulligan, M.S. and Ward, P.A.: Role of selectins in acute inflammatory lung injury in rats. *FASEB J.* 1993;7:A640.
6. Murphy, H.S. and Ward, P.A.: Phorbol-ester stimulated influx of extracellular calcium in endothelial cells. *FASEB J.* 1993;7:A786.
7. Gilardy, A.K., Baker, J.R., Jr., Ward, P.A. and Johnson, K.J.: An *in vivo* model of pulmonary delayed-phase allergic inflammation. *J. Immunol.* 1993;150:63A.
8. Mulligan, M.S., Ward, P.A. and Johnson, K.J.: Role of serine and metalloproteinases in the dermal arthus vasculitis model. *J. Immunol.* 1993;150:137A.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

- A. Director, Division of Clinical Pathology/Clinical Laboratories, May 1993-present.
- B. Director, Clinical Immunopathology Laboratory; September 1989-present.
- C. Autopsy pathology, staff coverage (1 week plus one weekend).

II. TEACHING ACTIVITIES:

- A. Pathology 630/631 (60 contact hours)
- B. ICS 600 lectures"
 - 1. "Autoimmunity" (10/20/92)
 - 2. "Multiple myeloma" (1/25/93)
- C. Clinical Pathology Grand Rounds:
 - 1. "Anti-LKM-1 chronic active hepatitis"
 - 2. "Myasthenia gravis and Lambert-Eaton myasthenic syndrome" (1/29/93)
- D. Immunopathology journal club (1 hour; biweekly)
- E. Immunopathology signout: Pathology residents, M-4 medical students, EMU medical technology students (daily; every other week)
- F. M-4 Laboratory Medicine Elective; 4th year medical students, 4 week block; (8 contact hours)
- G. M-1 Histopathology sequence; 1st year medical students; (7 contact hours).
- H. Supervision of Research activities for:
 - 1. Craig Flory, Ph.D. (postdoctoral fellow); (6/15/90-present).
 - 2. Peter A. Barton (M-2 medical student); (5/1/92-present) (sponsored by Howard Hughes Medical Institute post-sophomore fellowship).
 - 3. Sanjiv Ghogale (undergraduate; University of Michigan): (1/15/92-3/1/93).
 - 4. Barbara Markey, M.D. (Pathology resident); (3/12/92-10/15/92).
 - 5. Joseph Shen (interflex student); (5/10/93-7/30/93) (sponsored by American Heart Association of Michigan summer fellowship).
 - 6. Athear Alrawi (interflex student); (5/10/93-7/30/93) (sponsored by American Heart Association of Michigan summer fellowship).

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.
- C. Consultant, "CRP Peptides Activating Anti-Cancer Networks in the Lung", NIH-RO1, Barbara Barna, Ph.D., Principal Investigator, Cleveland Clinic Foundation.
- D. Principal Investigator, Project III; "Monocyte trafficking in lung inflammation", NIH (PO1-HL31963), (40% effort), \$653,235; direct costs, (Submitted 2/1/93; to supercede A.) 3/1/94-2/28/99.

PROJECTS UNDER STUDY:

- A. Role of cytokines (tumor necrosis factor, interleukin 1) in immune complex lung injury.
- B. Platelet-activating factor in immune complex alveolitis.
- C. Pathogenesis of endotoxic shock in mice with homozygous C5 deficiency.
- D. Cloning and expression of rat monocyte chemoattractant protein 1 (MCP1) in a baculovirus system.
- E. Role of MCP 1 in lung inflammation models.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

- A. Interviewer, Medical Scientist Training Program.

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.
- F. Preclinical Advisory Program, 1992-present.
- G. Laboratories communications Committee, 1993-present.
- H. Chairman's Advisory Committee, 1993-present.
- I. Eastern Michigan University Medical Technology Advisory Committee, 1993-present.
- J. Chairman, Search Committee for Hematopathology faculty position, 1993-present.
- K. Chairman, Search Committee for Clinical Pathology/Chemistry faculty position, 1993.

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.
- B. Preparation of Immunopathology Subspecialty Board Exam Questions, 1990-present.
- C. Ad hoc reviewer, Research Training Review Committee (Institutional Training Grants (T32s) and Clinical Investigator Development Awards (CIDA/KO8s); National Institutes of Health (NHLBI): Bethesda, MD: June 27-29, 1993.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Antinuclear antibody testing: a contemporary approach", ASCP Workshops, Las Vegas, Nevada, October 13, 1992.
2. "Immunopathology rounds: Anti-LKM-1 chronic active hepatitis", ASCP Workshops, Chicago, Illinois, March 28, 1993.
3. "Role of monocyte chemoattractant protein-1 in the pathogenesis of inflammatory lung disease", University of Michigan, Ann Arbor, Michigan, May 12, 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Warren, J.S., and Barton, P.A.: *In vitro* analysis of pulmonary inflammation using rat lung organ cultures. *Exp. Lung Res.* 1992;18:55-67.
2. Mulligan, M.S., Varani, J., Warren, J.S., Till, G.O., Smith, C.W., Anderson, D.C., Todd, R.F. and Ward, P.A.: Roles of β 2 integrins of rat neutrophils in complement-and oxygen radical-mediated acute inflammatory reactions. *J. Immunol.* 1992;148:1847-1857.
3. DeForge, L.E., Kenney, J.S., Jones, M.L., Warren, J.S. and Remick, D.G.: Biphasic production of IL-8 in LPS-stimulated human whole blood. Separation of LPS-cytokine-stimulated components using anti-TNF and anti-IL-1 antibodies. *J. Immunol.* 1992; 148:2133-2141.
4. Jones, M.L. and Warren, J.S.: Monocyte chemoattractant protein 1 in a rat model of pulmonary granulomatosis. *Lab. Invest.* 1992;66:498-503.
5. Mulligan, M.D., Warren, J.S., Smith, C.W., Anderson, D.C., Yeh, G., Rudolph, A. and Ward P.A.: Lung injury following deposition of IgA immune complexes: Requirements for CD18 and L-arginine. *J. Immunol.* 1992;148:3086-3902.
6. Brieland, J., Jones, M., Clarke, S., Warren, J., and Fantone, J.: Effect of acute inflammatory lung injury on the expression of monocyte chemoattractant protein

- 1 (MCP1) in rat alveolar macrophages. *Am. J. Respir. Cell. Molec. Biol.* 1992;7:134-139.
7. Warren, J.S.: Relationship between for interleukin 1b and platelet-activating factor in the pathogenesis of acute immune complex alveolitis in the rat. *Am. J. Pathol.* 1992;141:551-560.
8. Jones, M.L., Mulligan, M.S., Flory, C.M., Ward, P.A., and Warren, J.S.: Potential role of monocyte chemoattractant protein 1/JE in monocyte/macrophage-dependent IgA immune complex alveolitis in the rat. *J. Immunol.* 1992;149:2147-2154.
9. Barton, P.A., and Warren, J.S.: Complement components modulate the systemic tumor necrosis factor response in murine endotoxic shock. *Infect. and Immun.* 1993;61:1474-1481.
10. McCurry, K.A., Campbell, D.A., Jr, Warren, J.S., Scales, W.E., and Remick, D.S.: Tumor necrosis factor, interleukin-6 and the acute phase response following hepatic ischemia reperfusion. *J. Surgical Research*, In Press.
11. 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.*, In Press.
12. 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.*, In Press.
13. 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.*, In Press.
14. 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.*, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Jacobs, J.C., McNeeley, S.G., Elkins, T.E., Warren, J.S., and Hoeft-Loyer, C.M.: Rabbit model for polymicrobial upper genital infections. Submitted to *Int. J. Fertil.*
2. Grande, J.P., Jones, M.L., Swenson, C.L., Killen, P.D., Warren, J.S.: Regulation of monocyte chemoattractant protein-1 mRNA expression in rat mesangial cells. Submitted to *Clin. Immunol. and Immunopathol.*
3. 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-1b. Submitted to *J. Immunol.*
4. Markey, B.M. and Warren, J.S.: Use of antineutrophil cytoplasmic antibody to distinguish between vasculitic disease activity and complications of immunosuppressive therapy. Submitted to *Am. J. Clin. Pathol.*
5. Flory, C.M., Jones, M.L., and Warren, J.S.: Regulatory role of tumor necrosis factor- α in monocyte chemoattractant protein-1-mediated pulmonary granuloma formation in the rat. Submitted to *J. Immunol.*
6. Vaporciyan, A.A., Mulligan, M.S., Warren, J.S., Barton, P.A., Miasaka, M., and Ward, P.A.: Complement dependency for upregulation of lung vascular ICAM-1 in rats. Submitted to *J. Immunol.*

BOOKS/CHAPTERS IN BOOKS:

1. Keren, D.F. and Warren, J.S.: Diagnostic Immunology: Laboratory Diagnosis of Immunologic Diseases, Williams and Wilkins, Baltimore, Maryland, 1992.
2. Warren, J.S.: Role of cytokines in experimental lung injury, in, Remick, D.G. and Kunkel, S.L. (eds.), Cytokines in Health and Disease, Marcel Dekker, Inc, New York, New York, 1992;257-269.
3. Warren, J.S., Johnson, K.J., and Ward, P.A.: Consequences of oxidant injury, in, Crystal, R.G. and West, J.B. (eds.), Lung Injury, Raven Press, New York, New York, 1992;69-78.
4. Ward, P.A., Warren, J.S., Varani, J., and Johnson, K.J.: PAF, cytokines, toxic oxygen products and cell injury Molecular Aspects of Medicine, Proceedings of the VIIth Annual Inflammation Meeting, Birmingham, UK Pergamon Press, In Press.
5. Ward, P.A., Mulligan, M.S., and Warren, J.S.: Neutrophils, cytokines, oxygen radicals and lung injury. The Immune Consequences of Trauma, Shock and Sepsis - Mechanisms and Therapeutic Approaches, Proceedings of the Symposium, Munich, Germany, Springer-Verlag, Berlin Heidelberg, 1993:177-180.
6. Warren, J.S., and Ward, P.A.: Role of cytokines in pulmonary diseases, in, Gearing, A., Rossio, J. and Oppenheim, J.J. (eds.), Clinical Applications of Cytokines: Role in Pathogenesis, Diagnosis, and Therapy, Oxford University Press, Oxford, United Kingdom, In Press.
7. Warren, J.S.: Immunodeficiency disease, in, McClatchey, K.D. (ed.), Clinical Laboratory Medicine, Williams and Wilkins, Baltimore, Maryland, In Press.
8. Warren, J.S.: Inflammation, in, Spilker, B. (ed.), Drug News and Perspectives, Raven Press, New York, New York, In Press.

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

1. Markey, B.M. and Warren, J.S.: Use of anti-neutrophil cytoplasmic antibody to distinguish between vasculitic disease activity and complications of cytotoxic therapy. Abstract. Amer. Soc. Clin. Pathol., Las Vegas, Nevada, 1992.
2. Flory, C.M., Jones, M.L., and Warren, J.S.: Monocyte chemoattractant protein 1 mediates glucan-induced granulomatous vasculitis in the rat. Abstract. Cardiovascular Research Forum, American Heart Association of Michigan, Detroit, Michigan, September 24, 1992.
3. 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 alveolar macrophages. Abstract. Soc. Leukocyte Biol. Charleston, South Carolina, December 2-5, 1992.
4. Warren, J.S., Jones, M.L., and Flory, C.M.: Analysis of MCP 1-mediated lung injury using rat lung organ cultures. Abstract. Soc. Leukocyte Biol. Charleston, South Carolina, December 2-5, 1992.
5. Flory, C.M., Jones, M.L., and Warren, J.S.: In situ hybridization analysis of monocyte chemoattractant protein 1 (MCP 1) expression during evolving pulmonary granulomatous vasculitis in the rat. Abstract. Soc. Leukocyte Biol. Charleston, South Carolina, December 2-5, 1992.
6. Ghogale, S.J., Jones, M.L., Miller, B.F., Flory, C.M., and Warren, J.S.: Pathogenesis of monocyte chemoattractant protein 1 (MCP 1)-mediated granulomatous vasculitis; *in vitro* studies. Abstract. University of Michigan Student Biomedical Research Forum, Ann Arbor, Michigan, October 14, 1992.

7. Pearson, J.P. and Warren, J.S.: Antineutrophil cytoplasmic antibody - stimulated neutrophils and monocytes exhibit disparate endothelial cell killing capacities. Abstract. United States and Canadian Academy of Pathology, New Orleans, Louisiana, March 13-19, 1993.
8. 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 inflammatory lung injury. Abstract. FASEB, New Orleans, Louisiana, March 28-April 2, 1993.
9. Flory, C.M., Jones, M.L., and Warren, J.S.: Glucan induced pulmonary vasculitis in the rat. Regulatory role of TNF-alpha in MCP 1 induced granuloma formation. Abstract. FASEB, New Orleans, Louisiana, March 28-April 2, 1993.
10. Warren, J.S., Jones, M.L., and Flory, C.M.: Monocyte chemoattractant protein 1 (MCP-1)-mediated lung injury: In vitro analysis using rat lung organ cultures. Abstract. FASEB, New Orleans, Louisiana, March 28-April 2, 1993.
11. Miller, B.F., Ghogale, S.J., Jones, M.L., Flory, C.M., and Warren, J.S.: Monocyte chemoattractant protein 1 (MCP-1)-mediated granulomatous vasculitis: In vitro studies. Abstract. FASEB, New Orleans, Louisiana, March 28-April 2, 1993.
12. Barton, P.A. and Warren, J.S.: Complement component C5 modulates the TNF-mediated systemic response to endotoxin infusion in mice. Abstract. FASEB, New Orleans, Louisiana, March 28-April 2, 1993.
13. Pearson, J.P. and Warren, J.S.: Antineutrophil cytoplasmic antibody-stimulated neutrophils and monocytes exhibit disparate endothelial cell killing capacities. Abstract. FASEB, New Orleans, Louisiana, March 28-Apr 2, 1993.
14. Kunkel, R.G., Flory, C.M., Jones, M.L., and Warren, J.S.: Digital video morphometric quantitation of granuloma size and frequency: Analysis of MCP 1-mediated granulomatous vasculitis in the rat. Abstract. FASEB, New Orleans, Louisiana, March 28-April 2, 1993.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992**

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.

III. RESEARCH ACTIVITIES:

COOPERATIVE STUDIES:

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:

LOCAL:

- 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:

- 1. Wan, J., Ohl, D.L., Weatherbee, L.: Primary mucinous adeno carcinoma of renal pelvis in solitary pelvic kidney. Urology 1993;41(3):292-294.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Organizer and discussion leader of seminar on Ethics in Science -Cellular and Molecular Biology Training Program.
- B. Supervision of three postdoctoral fellows.
- C. Advisor for one graduate student, Cellular and Molecular Biology Training Program.
- D. Member, Program Committee - Cellular and Molecular Biology Training Program.
- E. Program Committees, Graduate Program in Pathology.
- F. Chairman, Examination Committee, Graduate Program in Pathology.
- G. Member, dissertation committees for two graduate students.
- H. Seminar, Pathology Department.
- I. Organizer, Pathology Department research discussion series.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Mutants for DNA Enzymes", American Cancer Society, NP77C 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. The consequences of replacing thymine with uracil in DNA.
- 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:
 - 1. National Science Foundation.
 - 2. Medical Research Council of Canada.
- B. Referee for the following journals:
 - 1. Journal of Bacteriology.
 - 2. Biochemistry.
 - 3. Molecular Microbiology.

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. El-Hajj, H.H., Wang, L. and Weiss, B.: Multiple mutant of *Escherichia coli* synthesizing virtually thymineless DNA during limited growth. *J. Bacteriol.* 1992;174:4450-4456.
- 2. Wang, L., and Weiss, B.: dcd (dCTP deaminase) gene of *Escherichia coli*: Mapping, cloning, sequencing, and identification as a locus of suppressors of lethal dut (dUTPase) mutations. *J. Bacteriol.* 1992;174:5647-5653.
- 3. Wu, J. and Weiss, B.: Two-stage induction of the soxRS (superoxide response) regulon of *Escherichia coli*. *J. Bacteriol.* 1992;174:3915-3920.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES

- A. Sophomore Medical Class:
 - 1. Pathology 600 - lecture - two contact hours.
 - 2. M-4 Clerkship Rotation - twelve 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. Peter Kind, University of Munich, December, 1992, Dr. Fred Stoner, Shadyside Hospital (Pittsburgh), September 26-October 3, 1992, and Dr. Young Chu, Korea, January-December, 1993.

III. RESEARCH ACTIVITIES

SPONSORED SUPPORT:

- A. Southwest Oncology Group, SWOG study 9055, \$3,197.
- B. Director, Tissue Procurement Core, University of Michigan Cancer Center, 5% effort.

PROJECTS UNDER STUDY:

- A. Correlation of grade and flow cytometric analysis in soft tissue tumors.
- B. Carpal tunnel syndrome.
- C. CD-34 expression in selected soft tissue tumors.
- D. Epithelioid smooth muscle tumors of soft tissue.
- E. Borderline vascular tumors.
- F. Typical and atypical giant cell tumors.
- G. Frozen section utilization.
- H. p53 expression as a marker of tumor progression in soft tissue tumors.

- I. 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 and Director of Tissue Procurement Core.
- C. Member, Tissue and Invasive Procedures Committee.
- D. Member, Musculoskeletal Core, Year II Curriculum.
- E. Member, Operating Room Committee.
- F. Member, Curriculum Policy Committee

REGIONAL AND NATIONAL

- A. Chairman, WHO Committee for Classification of Soft Tissue Tumors.
- B. US-Canadian Academy of Pathology:
 - 1. Benjamin Castleman Award Committee.
 - 2. International Vice President - North American Division.
- C. Association of Directors of Anatomic Pathology:
 - 1. Program Chairman.
 - 2. Executive Council.
- 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. Ad hoc reviewer, 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 Diagnostic Pathology.
- D. Editorial Board, Journal of the National Cancer Institute.
- E. Editorial Board, AFIP Fascicles (3rd Series).

INVITED LECTURES:

1. Faculty, "Soft Tissue Sarcomas: An Overview", US-CAP Diagnostic Pathology 1992, Seattle, Washington, August, 1992.
2. Speaker, "Aggressive Osteoblastoma and Aneurysmal Bone Cyst", Closed Meeting, International Skeletal Society, Stockholm, Sweden, September, 1992.
3. Speaker, "Vascular Tumors of Bone", Plenary Session, International Skeletal Society, Stockholm, Sweden, September, 1992.
4. Speaker, "WHO Classification of Soft Tissue Tumors: The Revision", International Academy of Pathology, Madrid, Spain, October, 1992.
5. Slide Seminar, International Academy of Pathology, Madrid, Spain, October, 1992.
6. Speaker, "Fibrohistiocytic Tumors of the Skin", International Academy of Pathology, Madrid, Spain, October, 1992.
7. Program Chairman, Association of Directors of Anatomic Pathology Annual Meeting, Chicago, Illinois, October, 1992.
8. Speaker, "Fibrohistiocytic Neoplasia", American Academy of Dermatology, San Francisco, California, December, 1992.
9. Faculty, "Intraoperative (Frozen Section) Consultation", Surgical Grand Rounds, University of Michigan, February, 1993.
10. Moderator, Bone and Soft Tissue Specialty Conference, US-CAP Annual Meeting, New Orleans, Louisiana, March, 1993.
11. Visiting Professor, Ohio State University, May, 1993.
12. Speaker, "Soft Tissue Sarcomas: An Overview", Twelfth Annual Nobuhisa Baba Memorial Lecture, Ohio State University, May, 1993.
13. Keynote speaker, "Malignant Fibrous Histiocytoma: A Historical Perspective", Third Annual Course in Soft Tissue Pathology, University of Padua, Abano, Italy, June, 1993.
14. Slide Seminar, Third Annual Course in Soft Tissue Pathology, University of Padua, Abano, Italy, June, 1993.
15. Speaker, "Soft Tissue Tumors: An Overview", XIX Annual Meeting of the Brazilian Society of Pathology, Santos, Brazil, June, 1993.
16. Slide Seminar, XIX Annual Meeting of the Academy of Pathology, Sao Paulo, Brazil, June, 1993.
17. Speaker, "Borderline Vascular Tumors", XIX Annual Meeting of the Brazilian Academy of Pathology, Sao Paulo, Brazil, June, 1993.

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

1. Goldblum, J.R. and Weiss, S.W.: Elastofibromatous change of the rectum; A lesion simulating amyloidosis. *Am. J. Surg. Pathol.* 1992;16:793-795.
2. Weiss, S.W. and Rao, V.K.: Well-differentiated liposarcoma (atypical lipoma) of deep soft tissue of the extremities, retroperitoneum, and miscellaneous sites: A follow up study of 92 cases with analysis of the incidence of "dedifferentiation". *Am. J. Surg. Pathol.* 1992;16:1051-1058.
3. Jones, M.W., Norris, H.J., Wargotz, E.S. and Weiss, S.W.: Fibrosarcoma-malignant fibrous histiocytoma of the breast. A clinicopathological study of 32 cases. *Am. J. Surg. Pathol.* 1992;16:667-674.

4. Rao, V.K. and Weiss, S.W.: Angiomatosis of soft tissue: An analysis of the histologic features and clinical outcome in 51 cases. *Am. J. Surg. Pathol.* 1992;16:764-771.
5. Perosio, P.M. and Weiss, S.W.: Ischemic fasciitis: A juxta-skeletal fibroblastic proliferation with a predilection for elderly patients. *Mod. Pathol.* 1993;6:69-72.
6. 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 lymphangiomatosis. *Am. J. Surg. Pathol.* 1993;17:321-328.
7. Smith, S.H., Weiss, S.W., Jankowski, S.A., Coccia, M.A. and Meltzer, P.S.: SAS amplification in soft tissue sarcomas. *Cancer Res.* 1992;52:3746-3749.
8. Weiss, S.W. and Nickoloff, B.J.: CD-34 is expressed by a distinctive cell population in peripheral nerve, nerve sheath tumors, and related lesions. *Am. J. Surg. Pathol.*, In Press.
9. Weiss, S.W.: Tumoral amyloidosis of soft tissue ("amyloidoma"): New approaches to an old problem (Editorial). *Am. J. Clin. Pathol.*, In Press.

SUBMITTED FOR PUBLICATION

1. Sondak, V.K., Lawrence, T.S., Robertson, J.M., Saran, P.A., Walker-Andrews, S.C., Dwarzanin, L.M., Weiss, S.W. and Chang, A.E.: Preoperative iododeoxyuridine and radiation in locally advanced sarcomas. *Arch. Surg.*
2. Goldblum, J.R., Beals, T.F. and Weiss, S.W.: Neuroblastoma-like neurilemoma. *Am. J. Surg. Pathol.*

BOOKS AND CHAPTERS IN BOOKS

1. Laskin, W.B. and Weiss, S.W.: Benign fibrous lesions of upper limb, in, Bogumull, G.P. and Fleegerl, E.S. (eds.), *Tumors of the Hand and Upper Limb*, Churchill Livingstone, London, 1993.
2. Weiss, S.W. and Sobin, L.: *WHO Classification of Soft Tissue Tumors*. Springer Verlag, Berlin, In Press.

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

1. Weiss, S.W.: The WHO classification of Soft tissue tumors: An overview. *Proceedings of the IAP Meeting, Madrid, 1992.*
2. Weiss, S.W.: Benign fibrohistiocytic tumors of skin, *Proceedings of the IAP Meeting, Madrid, 1992.*
3. Willis, J., Jansen, J., Goldblum, J. and Weiss, S.W.: Frozen section consultation: A correlation between utilization patterns and knowledge base of surgical faculty. *Mod. Pathol.* 1993;88:141A.
4. Robertson, J.M., Sondak, V.K., Weiss, S.W., Sussman, J.J., Chang, A.E. and Lawrence, T.S.: Preoperative radiation therapy and iododeoxyuridine for large retroperitoneal sarcomas. *American Society of Therapeutic Radiology and Oncology.*

SECTION REPORTS

DIVISION OF ANATOMIC PATHOLOGY**DEPARTMENT OF PATHOLOGY****ANNUAL REPORT****1 JULY 1992 - 30 JUNE 1993**

The close of the academic year regrettably marked the departures of two valued faculty, Dr. Ricardo Lloyd, the Warthin/Weller Professor of Pathology and renowned endocrine pathologist, and Dr. Lisa Del Buono, a promising young gastrointestinal pathologist. Although their departures will be felt for some time, the Division renewed its recruitment efforts and was fortunate to attract Dr. Joel Greenson from Ohio State to replace Dr. Del Buono. Dr. Greenson is an accomplished surgical pathologist who completed his fellowship training in gastrointestinal pathology at the Johns Hopkins Hospital. This year represents a significant milestone in anatomic pathology with the recruitment of Dr. Michael Caplan to head the new forensic pathology program within the Department. Dr. Caplan, returning from a fellowship in forensic pathology at the New York City Medical Examiner's Office, will supervise all forensic cases within Washtenaw County and assume an important presence on the autopsy service.

Our educational activities were many and diverse. Fellowship programs in surgical and cytopathology are now in their fourth and sixth years respectively. Dr. Phil Perkins, completing his cytopathology fellowship, will be followed by Drs. Patricia Perosio and Priscilla Lindley. Drs. John Goldblum, Joe Willis, and Jack Jansen leave their surgical pathology fellowships for positions at the Cleveland Clinic, Case Western Reserve, and St. John's Hospital respectively. Our incoming fellows, Drs. Kyle Carr, Suzanne Cook, and Phil Perkins, will be joined by Dr. Kenneth Lidonnici from State University of New York at Stonybrook. As an extension of the philosophy of the fellowship, our residents presented 13 papers at the recent US-CAP meeting under the tutelage of the faculty in our Division, one of which earned the Binford-Dammin Award in infectious disease (Drs. Suzanne Cook and Tom Frank). Our faculty, in addition, commanded an impressive presence at this annual meeting. Four faculty are currently involved in Short Course offerings and one member of our faculty will be directing the 1995 Long Course. This year's Fourth Annual Visiting Professor of Anatomic Pathology was Dr. Jonathan Epstein from Johns Hopkins, who presented a lecture on "Prostatic Intraepithelial Neoplasia" and a slide seminar on "Problematic Prostatic Lesions".

Significant administrative change has occurred within Anatomic Pathology. An Anatomic Pathology Molecular Diagnostic Laboratory, headed by Dr. Thomas Frank, has been created. This laboratory, working closely with its clinical pathology counterpart, will develop a small volume of billable tests based on tissue specimens, serve as an integral part of the Cell and Molecular Biology Core facility, and as an extended Pathology Core for the Cancer Center. Dr. Andrew Flint has developed an Image Analysis Laboratory with the capacity to perform semi-quantitation of receptor proteins and ploidy. Finally, the Tissue Procurement Core of the Cancer Center, supervised by the Surgical Pathology service, was officially reinstated after a two-year hiatus providing investigators institute-wide with fresh human tissues for research purposes.

Over the coming year, our division looks forward to the development of a five-year plan to address future recruitment needs, sources of income and space, laboratory utilization, and academic goals of the faculty. We see this as a vital step to defining our academic direction and integrating them with those of the Department as a whole.

Sharon W. Weiss, M.D.
Director, Anatomic Pathology

AUTOPSY SERVICE**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992**

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 the Washtenaw County Medical Examiner's Office.

MEDICAL EXAMINER'S CASES:

The Autopsy Service continues to perform forensic autopsies on medical examiner's cases on patients who die at the University of Michigan, bodies that are found, and bodies of individuals who die at suspected crime scenes. The bill which was introduced in the State Legislature which would allow us to return bodies to the county of injury failed to be reported out of the Senate Subcommittee. Since all bills die with a newly elected House, the bill has been re-written, and re-introduced by Representative Kirk Profit as House Bill 4439 to the House Committee on Judiciary. Its progress is being closely monitored, and we will again testify before the Subcommittee.

CONTRACT FOR FORENSIC SERVICES:

The Department of Pathology has successfully negotiated a contract with the Washtenaw County Medical Examiner's Office for performing forensic autopsies on medical examiner's cases in Washtenaw County. Under the terms of the contract, all medical examiner cases which require autopsy as part of the investigation will be brought to the University of Michigan (even if patients die in other hospitals). The University, however, has the right to refuse to perform autopsies requested by deputy medical examiners. Currently, we are in a process of arranging a mutually satisfactory transfer of medical records from other hospitals.

As a result of this new contract, the University of Michigan has recruited a full-time forensic pathologist. Michael Caplan, M.D. Dr. Caplan will begin on August 15, 1993 and we are pleased to have him join our staff.

TIMELY COMPLETION OF AUTOPSY REPORTS:

Autopsies protocols are still not being completed in a timely manner and this has resulted in a probable 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 78 days, with over 45% of cases requiring more than 90 days to completion. This is unacceptably slow. We are planning a combined approach towards relieving this problem: 1) There will be a restructuring of how autopsy brains are processed, with a substantial reduction

in the number of cases which are evaluated by neuropathologists. Essentially normal brains will come under the purview of the general pathologists, who will consult with a neuropathologist as needed. 2) We will look at each step of the autopsy paperwork to determine where the problems lie, and specific, targeted action will be taken.

STATISTICS:

	1991/92	1992/93
Total U of M Cases	322	420
M-Labs cases	8	5
Medical Examiners' Cases	58	101
In-Hospital Cases	24	47
Outside Cases	34	54
Autopsy Rate (includes tetralogy cases)	35%	39%

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

CYTOPATHOLOGY LABORATORY

**DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1992 - 30 JUNE 1993**

During the past year, the Cytopathology Service has undergone operational changes to comply with the new federal government regulations. In conjunction with Pathology Data Systems, a new computer software package was developed and implemented for the reporting of cervicovaginal cytology utilizing the Bethesda Nomenclature System. Automatic SNOMED coding for gynecologic and non-gynecologic cytology reports was deployed.

In the seventh year of our cytopathology fellowship, Dr. Philip Perkins completed his training with distinction. The indispensability of the Fellows is well recognized by the cytopathology staff persons. The Fellowship in cytopathology has been accredited in by the Accreditation Council for Graduate Medical Education. Persons who complete the fellowship after having become eligible to take the primary examination in anatomic pathology of The American Board of Pathology and who become so certified will then be eligible to take the examination for the Special Qualification in Cytopathology of the Board.

The number of fine needle aspirations continues to rise for a total of 1,716 cases. Gynecologic specimens numbered 28,000 and non-gynecologic specimens numbered 7,000, for a total of all cytologic specimens of 35,000.

Bernard Naylor, M.D.
Director, Cytopathology Laboratory

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

**DERMATOPATHOLOGY SERVICE
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

The Dermatopathology Service receives diagnostic case material from five different sources: (1.) UMMC (ID) cases; (2.) outside contractual (MD) cases; (3.) personal consultations (HE) cases; and (4.) outside slides reviewed for referred patients (TD) cases; and informal consultations (intramural, VAH, and MU) cases:

Work load volume is as follows:

	1991-1992	1992-1993
HE	731	981
ID	5651	4255
MD	NA	1347
TD	NA	550
Informal	300	225
Flow	95	NA
EM	2	2

There was a slight decrease in overall workload with a 10% increase in revenue from HE consultation cases.

Correlative activities included participation in Melanoma Clinics (biweekly), Cutaneous Lymphoma Conference (monthly) and Dermatology Grand Rounds (weekly).

Teaching included scheduled presentations to medical and dental students.

1991-1992 found increases in personal referred cases and in MD cases.

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

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

ELECTRON MICROSCOPY SERVICE

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1992 - 30 JUNE 1993

The Electron Microscopy facility continues to provide an important service to the Department of Pathology from the standpoint of analyzing clinical biopsies as well as for research purposes. The demand for EM has increased for clinical as well as research biopsies as described below.

The clinical EM facility processed a total of 503 biopsies this year, an increase of 19 cases over the previous year. The primary uses of diagnostic EM continue to be in the area of renal biopsies as well as nerve and muscle biopsies. In the analysis of kidney biopsies, EM continues to be essential for the diagnosis of many types of glomerulonephritis and during this past year, 240 renal biopsy cases were processed by the facility. Around 50% of these cases were from outside hospitals, with 14 hospitals submitting EM specimens. This continues to be an area with increasing demand since most of the renal biopsies in this state are interpreted either by us or by the Mayo Clinic.

The other major usage of the Clinical EM facility is that of the diagnosis of neuropathological specimens; particularly those of nerve and muscle biopsies for peripheral neuropathies and various types of muscular dystrophies. EM is critical to the diagnosis of many of these conditions and the Department of Neurology, in conjunction with Dr. Mila Blaivas, a neuropathologist in the Department of Pathology, has established a special clinic for the diagnosis and treatment of these patients. Dr. Blaivas utilizes EM extensively as manifested by the fact that over 200 biopsies submitted to EM this past year were nerve and/or muscle biopsies. Finally, the clinical EM service continues to process a number of tumor cases for ultrastructural analysis as well as for miscellaneous disease processes such as amyloidosis, various storage diseases and viral infections.

The volume of cases submitted to the research EM facility continues to increase dramatically from year to year. Faculty from every department in the Medical School utilize this facility for studies done in collaboration with the Department of Pathology facility with the largest number of cases coming from investigators studying lung and kidney disease. The scope of the research EM volume is reflected in the fact that over 300 cases were processed during this past year. In addition to routine ultrastructural analysis, many of these samples were also utilized for morphometric and steriologic studies to more precisely quantify pathologic alterations. This facility also routinely processed over 500 additional samples which were embedded for light microscopy only. Analysis of these 1 mm "thick" toluidine blue stained sections is used routinely, instead of paraffin sections by many investigators for light microscopy analysis as well as morphometric interpretation. The research service also offers immunoelectronmicroscopy and transmission electron microscopy in conjunction with Dr. Theodore Beals.

In summary, the EM service continues to provide an important service and research function for the Department of Pathology as well as the Medical School and outside hospitals. With the increasing demands for quantitative morphometry, plans are underway to provide the capability for digital analysis of ultrastructure alterations directly from the microscopy without having to have photographic prints made. These digitized images should allow for more rapid analysis of specimens as well as allowing this

information to be electronically transmitted to investigators and other pathologists. Finally, plans are underway to develop a core facility for researchers using molecular probes in tissues such as *in situ* hybridization and PCR

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

ANATOMIC PATHOLOGY MOLECULAR DIAGNOSTICS**DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1992- JUNE 30 1993**

The development of diagnostic applications of molecular biology to anatomic pathology has continued with much of the investigational work being performed by residents and medical students engaged in research projects. The results of several such studies have been accepted this year by journals including Diagnostic Molecular Pathology, the American Journal of Surgical Pathology, Modern Pathology, and the American Journal of Clinical Pathology. In addition, one resident's work on an assay for rapid characterization of mycobacteria by PCR was the winner of the Binford-Dammin Award in infectious disease research as well as a Stowell-Orbison Certificate of Merit at the 1993 meeting of the United States-Canadian Academy of Pathology. With the departmental commitment of additional resources for the development of a Preserved Tissue Analysis (PTA) laboratory it is anticipated that resident training in this area will continue to grow. The PTA laboratory has been established to provide diagnostic service and teaching for the department of pathology, and will make available molecular biology techniques for selected faculty projects. The PTA laboratory will provide ancillary nucleic acid-based diagnostic analyses on paraffin-embedded tissue, with testing for DNA viruses (such as CMV, EBV, and hepatitis B) and mycobacteria scheduled to begin by 1994.

Tom S. Frank, M.D.
Director,
AP Molecular Diagnostics
Laboratory
(Preserved Tissue Analysis)

**NEUROPATHOLOGY SERVICE
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

The Laboratory of Neuropathology continues to have three interrelated functions: Laboratory diagnostic service, teaching and research. Dr. Samuel P. Hicks was on Active Emeritus status, and made significant contributions to the Autopsy Neuropathology Service. Dr. Mila Blaivas, Ms. Constance J. D'Amato, Dr. Paul E. McKeever, and Dr. Anders A.F. Sima also contributed to the Neuropathology Service.

CLINICAL ACTIVITIES:

The following examinations were completed with the support of our neurohistology, electron microscopy, general histology, immunohistology, and secretarial staff.

1. There were 846 neurosurgical cases including CNS, pituitary, muscle and nerve examined this year. 82 of these cases were from outside hospitals in consultation. A portion of these were part of an interdepartmental study of PET/BUDR and neuropathology funded by NIH. 317 surgical specimens required special neurohistologic procedures.
2. There were 327 brains histologically processed out of 420 autopsies which is 78% of all University Hospital autopsies. An additional 63 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 207 muscle biopsies, nearly all with histochemistry, 44 with electron microscopy. There were 50 peripheral nerve biopsies. There were 25 teased fiber preparations, 25 thick plastic sections and 18 had electron microscopy performed. There were 214 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 244 cases in semithin or thin section from electron microscopy. The majority of these cases were nerve, pediatric muscle, and neurosurgical biopsy cases.
5. The ceroid service, buffy coat division, reported 14 cases. There were 7 skin biopsies done for storage disease, and there were 3 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. 15 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 faculty taught the regular Neuropathology sequence to our medical students (13 hours) in the Neural and Behavioral Sciences (NBS) 600 curriculum. NBS Neuropathology consists of lectures, handouts, and posters for all second year medical students. In addition to being

Director of the NBS Program for 40% of her time and lecturing, Ms. D'Amato conducted 10 hours of brain cutting sessions for small groups of the second year students.

2. House Officers, Graduate Students, Postgraduate and other students and faculty: These include 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: Three pathology residents, two neurosurgery residents, and two neurology residents chose elective rotations on the Neuropathology Service.
4. Two Neuromuscular fellows were instructed at conferences held twice a week.

RESEARCH ACTIVITIES:

1. Dr. Hicks and Ms. D'Amato provided neuropathologic diagnostic support for MADRC.
2. Dr. Blaivas and associates investigate ocular muscle (aging and botulinum effect). She is also investigating musculature related to cleft palates in children and mice. She is investigating muscles and spinal cord in mnd mice.
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 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
ANNUAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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. Anatomic pathology staff on the autopsy service provided coverage for Dr. Heidelberger's sabbatical (1/1/93 - 6/30/93).

Necropsy figures are as follows:

M/W/H Unit Deaths (20 weeks gestation or any live born, to 18 years)	=192
Necropsies on Above	=124
Necropsy Percentage	=65%

Of the 124 posts, 45 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. Seventy-nine patients were posted by the residents and senior staff in Pathology, primarily Dr. Heidelberger. Necropsies categorized in the adult general hospital statistics as "Medical Legal" posts included 12 posts on pediatric patients including SIDS cases, child abuse cases and trauma cases, only 6 of which were also classified as inpatient deaths, because of treatment here.

A total of 465 necropsies for UMMC Hospitals patients was performed (including the 12 pediatric "Medical Legals"), 45 by Dr. Barr in the Teratology Unit and 420 by the Pathology Department Staff. Thus, 30% of the total posts at the UMMC were pediatric posts.

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 194 - including both all referred fetuses and infants and inborn newborn fetal losses at less than 20 weeks' gestational age.

The total number of pediatric surgical specimens (including placentas) examined is 2,350. 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 steady level over the last three years.

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

SURGICAL PATHOLOGY SERVICE**DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1992 - 30 JUNE 1993**

Over the past year we experienced several staffing changes. Drs. Ricardo Lloyd and Lisa Del Buono departed for new positions at the Mayo Clinic and Toledo Hospital respectively. We, however, were fortunate to attract Dr. Joel Greenson from Ohio State to replace Dr. Del Buono. In addition, we expect the arrival of Dr. Kirk Wojno, a genitourinary pathologist from Johns Hopkins Hospital, in July 1994. Our fellowship continues to grow in popularity, both within our own residency as well as on a national level. Drs. John Goldblum, Jack Jansen, and Joe Willis served with distinction this year as our fellows and have now accepted positions at the Cleveland Clinic, St. John's Hospital, and Case Western Reserve respectively. Surgical pathology fellows for the upcoming academic year are Drs. Kyle Carr, Philip Perkins, Suzanne Cook, and Kenneth Lidonnici from State University of New York at Stonybrook.

Several new professional activities were initiated within surgical pathology. A staff consensus conference, held daily for review of all difficult and interesting cases, serves as the cornerstone for our surgical pathology QA/QC program. Dr. Andrew Flint has developed an image analysis laboratory which offers a limited number of tests including semi-quantitation of estrogen and progesterone receptor proteins on tissue sections. In conjunction with the surgical pathology fellows, we completed a study of the patterns of frozen section utilization, the results of which were presented at Surgical Grand Rounds.

Several administrative changes were made in the histopathology laboratory to better address the complex and diverse tasks of the laboratory. Ms. Anne Lemieux was appointed as Assistant Laboratory Supervisor with immediate responsibilities of supervising the Accessioning Area and Room I, and a dedicated Room I Assistant has been appointed to facilitate the daily operational tasks in this area. Ms. Ellen Poy was appointed as the new Tissue Procurement Technician. Supervised by the surgical pathology service, she harvests human tissues for the Cancer Center and distributes them to investigators throughout the Medical Center.

Over the next year, the surgical pathology service plans several new initiatives. We will explore methods to monitor and automate the check-out and return of slides and will launch two utilization studies, one dealing with immunohistochemistry and the other with electron microscopy. The results of these studies will hopefully help standardize the application of these techniques by the faculty.

Sharon W. Weiss, M.D.
Chief,
Surgical Pathology

DIVISION OF CLINICAL PATHOLOGY**DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1992 - 30 JUNE 1993**

The Clinical Pathology Laboratories have completed another challenging yet rewarding year. The laboratory directors, chief technologists, supervisors, laboratory personnel, and departmental administration are to be commended for the professional manner in which they have responded to the Hospital's ongoing Cost Effectiveness Program (CEP). Despite a net loss of laboratory personnel and hospital imposed budget reductions the clinical laboratories have continued to provide excellent service and to operate efficiently. The nearly flat cost per unit of activity (test) 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 1992-93 the clinical labs performed 3.24 million billable tests. 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.

In preparation for its future move into the current Ligand Laboratory space the Cytogenetics Laboratory completed the first phase of consolidation. The Chemistry Section (Ligand, General Chemistry, Drug Analysis/Toxicology, and Immunopathology Laboratories) consolidation has progressed administratively and awaits laboratory renovations (scheduled to commence in September 1993). The overall benefits of these consolidations will be to streamline the operations of the Cytogenetics Laboratory, to better integrate the Chemistry Section, and to provide more departmental space in Medical Science Building I.

The clinical laboratories successfully completed the biannual on-site, College of American Pathologists (CAP) inspection in June, 1993. Due in no small part to the superlative organizational skills of the Administrative Coordinator, Deborah Day-Jansen, the CAP inspection team was highly laudatory of the clinical laboratory operation. Again, all administrative and laboratory personnel are to be commended for their efforts. 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. Ms. Suzanne Butch, Chairperson, Quality Assurance Committee, is to be commended for her outstanding efforts.

Faculty and laboratory staff participated in a wide variety of educational programs during 1992-93. Laboratory personnel played a major and invaluable role in the education of medical technology students from Eastern Michigan University, medical students, residents, and fellows. Numerous faculty and laboratory staff participated in educational activities within the medical school, and at the regional and national levels (see individual reports). The first M4 course in laboratory medicine was completed in April, 1993. Evaluations from enrolled senior medical students were highly laudatory. A revised clinical pathology residency training format that organizes pathology residents into two to four person teams that rotate through three blocks of clinical laboratories which are grouped according to relatedness of discipline will increase longitudinal exposure of residents to the various clinical pathology disciplines, foster acceptance of to

graded responsibility, and formalize the content of clinical pathology teaching at the University of Michigan. The revised CP training format will be implemented on July 1, 1993. The Department continues to support the Hematopathology Fellowship Program. The high quality of trainees in this position has enhanced both the service and academic missions of the Hematopathology group.

The academic achievements of faculty members within the Clinical Pathology Division have seen outstanding (see individual faculty reports). As a group, the CP faculty had over 100 articles published in peer reviewed journals. Most faculty members participated in meetings, courses, symposia, or research review study sections; an illustration of their high levels of recognition throughout the United States. Numerous faculty members received extramural funding that supported a variety of scholarly activities.

The Clinical Pathology Division will be faced with numerous challenges in the future. In addition to ongoing initiatives that include educational issues, development of rapid, flexible, point of care testing, analysis and control of blood product utilization, continued leadership and development in quality assurance, and general 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 MLabs program, to optimize its position in the regional clinical laboratory market. Achievement of these objectives will require the continued commitment, professionalism, and hard work of the faculty, laboratory staff, administration, and house officers.

Jeffrey S. Warren, M.D.
Director, Clinical Pathology Division

UNIVERSITY HOSPITALS BLOOD BANK AND TRANSFUSION SERVICE**DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1992 - 30 JUNE 1993****PATIENT CARE:**

In a trend first evident last year, blood utilization remained relatively level during this fiscal year. This may be related to a national tendency for clinicians to be more conservative in transfusing blood components, and possibly to the requirement of the JCAHO that the appropriateness of transfusions be audited.

In line with the latter requirement, the Blood Bank implemented an auditing program under the direction of Dr. Robertson Davenport. During this year this focused on transfusions given to patients on Internal Medicine services. With the assistance of clinicians in that Department, monitoring of transfusions revealed a high level of appropriateness of transfusions. However, the indications for the transfusions were not evident in the medical record in a large number of cases. During the coming year this review will be extended to the Departments of Surgery and Pediatrics, and subsequently to the blood transfusion activities of the Department of Anesthesiology.

In reviewing blood utilization statistics, it is evident that the number of transfused units of red blood cells and platelet concentrates did not differ significantly from the number transfused during the previous year. However, there was a marked reduction in transfusion of plasma. Surprisingly, autologous blood utilization did not increase, but remained relatively constant. This differs from increased use of this technique throughout the country. 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.

The Transfusion and Apheresis area experienced a modest decline in activity during the past year. This can be attributed to outpatient blood transfusion occurring at other sites in the Hospital and also to the increased use of intravenous immune globulin for treatment of some neurologic diseases formerly treated by therapeutic plasmapheresis. However, the modest decline in therapeutic plasmapheresis was countered by increased collections of peripheral blood stem cells for autologous bone marrow transplantation. The latter activity can be expected to increase as this program expands.

EDUCATIONAL ACTIVITIES:

As in the past, the medical, technical and nursing staff of the Blood Bank/Transfusion Service were active in education at the departmental, institutional, regional and national levels. The customary two-week Blood Bank orientation course was provided for all first-year Clinical Pathology House Officers. In addition, daily patient care "rounds" were conducted by the medical staff of the Blood Bank, and attended by House Officers and senior technologists. Drs. Oberman and Davenport, and Mr. Judd, presented Grand Rounds for the Clinical Pathology program during the past year, and also participated in the weekly Case Presentation Conference. 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 20th Annual Postgraduate Course, "Current Topics in Blood Banking" was held on June 2, 3 and 4, 1993. The Course, under the direction of Mr. Judd, attracted over 200 technologists and physicians from throughout the United States. This continues to be one of the largest postgraduate courses in the country devoted to blood bank topics, and also is one of the largest postgraduate courses held in the Medical Center. Members of the Blood Bank and Transfusion Service staff presented workshops on a variety of topics, and Ms. Steiner, Ms. Butch, Mr. Judd and Dr. Oberman participated in the lecture program of the Symposium.

Members of the Blood Bank and Transfusion Service faculty and staff participated in the Annual Meeting of the American Association of Blood Banks. Dr. Davenport's talk on the role of cytokines in intravascular hemolysis was selected for special presentation at the Meeting. In addition, members of the laboratory, including Mr. Judd, Ms. Butch, Mrs. Stoe and Ms. Steiner presented invited lectures to a variety of regional and national blood banking organizations and State societies.

PROFESSIONAL ACTIVITIES:

Blood Bank and Transfusion Service staff were active at the regional and national level in numerous settings. Dr. Oberman served as Associate Editor of TRANSFUSION and also chaired the Awards Committee of the American Association of Blood Banks. Mr. Judd was the North Central District representative to the Board of Directors of the American Association of Blood Banks, served on the Editorial Board of TRANSFUSION, and authored a section in the 11th edition of the Technical Manual of the American Association of Blood Banks. Other instances of his participation are indicated in his individual faculty report. Similarly, Dr. Oberman's and Dr. Davenport's activities are noted in their individual faculty reports.

Ms. Butch served as a member of the Standards Committee, Information Systems Committee, and Administrative Section Coordinating Committee of the American Association of Blood Banks. She chaired the PathNet Users' Group relating to the blood donor module for Cerner and also co-chaired the Annual Meeting of the Michigan Society of Medical Technology. She was Editor-in-Chief of Clinical Laboratory Science and, most significantly, received the Founders' Award of the Michigan Association of Blood Banks. Ms. Butch co-chaired the Department of Pathology's Clinical Pathology Quality Assurance Committee. Ms. Steiner served as President of the Michigan Association of Blood Banks and assisted in selection of the American Association of Blood Banks' medical technology scholarship awardees. Several of the laboratory's technologists served as Inspectors for the American Association of Blood Banks' Inspection and Accreditation program.

RESEARCH ACTIVITIES:

The individual reports of Drs. Davenport and Oberman, and of Mr. Judd, record publications and investigative efforts relating to Blood Banking and Transfusion Medicine. In addition, Ms. Butch played a leadership role in defining a method for ensuring the compatibility of transfused blood through use of the computer, the so-called

"Computer Crossmatch". This procedure has been accepted by the Standards Committee of the American Association of Blood Banks, and should be adopted throughout the country in the near future. During the coming year the laboratory will examine blood utilization in adult extracorporeal membrane oxygenation (ECMO).

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

CLINICAL CYTOGENETICS LABORATORY**DEPARTMENT OF PATHOLOGY****ANNUAL REPORT****1 JULY 1992 - 30 JUNE 1993**

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, 827 amniotic fluid specimens, 66 tissues and 36 chorionic villus biopsy specimens were analyzed; this is a slight decrease 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, the volume is again increasing. The number of bone marrow specimens increased by almost 30% to 405; 308 routine blood specimens, 32 high resolution studies and 77 fragile X analyses were done as well. The laboratory has decreased the number of neonatal emergent marrows for diagnosis of genetic disease by instituting new culture procedures which reliably decrease the turnaround time blood specimens in newborns to 50-55 hours (from 4-5 days); the demand for this service, however, has gone from one case per month to one every few days.

After almost 4 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. 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.

Cytogenetics 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.

Thomas W. Glover, Ph.D.
Co-Director, Clinical Cytogenetics
Laboratory

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

CLINICAL FLOW CYTOMETRY LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1992 - 30 JUNE 1993

Over the past year, the Clinical Flow Cytometry Laboratory processed approximately 2400 immunophenotyping specimens. This included nearly 600 specimens submitted for leukemia/lymphoma immunophenotyping, nearly 1000 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 3100 specimens of peripheral blood for flow cytometric reticulocyte analysis. The Flow Cytometry Laboratory also supports the hematopathology section of the Molecular Diagnostics Laboratory; in the past year, immunoglobulin and T-cell receptor gene rearrangement analysis by Southern blot was performed on 230 clinical specimens.

The laboratory has fully implemented two-color flow cytometric analysis for all leukemia profiles. Although reagents for two-color assays are more expensive than those for single-color analysis, the significant reduction in preparation and analysis time has afforded compensatory savings. Laboratory efficiency has also been enhanced by acquisition of a second Becton-Dickinson FACScan cytometer; this replaces the outmoded Coulter Profile instrument. In addition, the laboratory has completed development of automated analysis software in conjunction with Verify Software Systems. This package permits semi-automated analysis of 2-color flow cytometry data further reducing turn-around times.

Ongoing development projects for future clinical applications include: the implementation of three-color phenotypic analysis for leukemias and lymphomas; the assessment of a two-color approach for anti-platelet antibody testing; the assessment of flow cytometric methods for nuclear TdT analysis; and implementation of limited immunocytochemical testing as a supplement to flow analysis for selected markers. In addition, plans are underway to institute direct transfer of patient report data from the instruments to Pathology Data Systems; this will dramatically reduce manual data entry and enhance report accuracy. Finally, the laboratory has provided collaborative support to several investigators in other departments. These clinical research activities include: phenotyping of lymphocytes in lymphoma patients receiving experimental anti-CD20 therapy (Division of Hematology/Oncology); bone marrow stem cell enrichment study (adult bone marrow transplant program).

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 165 specimens last year) are cancelled. Quality assurance conferences are held twice a month to enable medical and technical staff to review all 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. Finally, quality assurance programs are also in place to monitor speed of turn-around for transplant monitoring (OKT3 therapy) and clinical indications for anti-platelet antibody tests.

Teaching activities in the laboratory include daily case sign-out with the residents, hematopathology fellow and technologists. Continuing medical education for the technologists and house staff is also offered at the biweekly leukemia conference. A resident rotation through molecular diagnostics includes detailed instruction in Southern blot and polymerase chain reaction techniques, as well as clinical sign-out of gene rearrangement analyses.

Charles W. Ross, M.D.
Director

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

CLINICAL MOLECULAR DIAGNOSTICS

DEPARTMENT OF PATHOLOGY ANNUAL REPORT 1 JULY 1992 - 30 JUNE 1993

During the past year, the Molecular Diagnostics Laboratory has been supported by a full-time research assistant, Donald Zhou, and has performed the following activities:

I. DIAGNOSTIC MICROBIOLOGY

The establishment of a PCR-based clinical test for the detection of mycobacterium tuberculosis has been the main effort of the laboratory during the past year. The aim of the work is to establish a diagnostic test to assess Mycobacteria in clinical specimens. The project has been undertaken in collaboration with the Clinical Microbiology Laboratory. Two DNA sequences of the Mycobacterium genome have been selected for PCR amplification: the IS6110 repetitive sequence which is specific for the M. tuberculosis complex and the gene encoding the 65 kDa antigen GRoEL which is shared by all Mycobacterium species.

A. PCR AMPLIFICATION OF IS6110 REPETITIVE SEQUENCES

This project is being performed in several phases. First, methodology has been developed for the isolation of DNA suitable for PCR amplification from sputum specimens. Second, we have assessed the sensitivity of the test and found that our detection level is 3-5 organisms. Third, we have performed experiments to study the specificity of the test. DNA from 13 different species of Mycobacteria were tested and found that only M. tuberculosis is amplified under our experimental conditions. Recent experiments using 80 sputum samples have revealed a 100% specificity of the test. Some of the DNA preparations from sputum exhibited inhibition of the PCR. We are currently constructing a control plasmid to monitor adequate PCR amplification using the same PCR primers. Detection of the amplified PCR product is being performed with biotinylated oligonucleotide probes. Our plan is to implement the IS6110 PCR-based method as a routine clinical test in the Fall of 1993.

B. DETECTION OF PCR PRODUCTS BY ELOHA

Detection of PCR products by gel electrophoresis is time-consuming and cumbersome in clinical laboratories. We have developed a method termed enzyme-linked oligonucleotide hybridization assay (ELOHA) for the detection of PCR products in 96-well trays. The assay is non-radioactive and is based on the amplification and capture of biotinylated PCR products on avidin-coated wells. After a washing step, the PCR product is detected by hybridization with an oligonucleotide complementary to the amplified sequence. ELOHA has been used for the detection of the gene encoding the 65 kDa mycobacterial antigen GRoEL. During the next months, we will assess the feasibility of the ELOHA to detect Mycobacteria in clinical samples.

C. USE OF URACIL N-GLYCOSYLASE TO PREVENT PCR CARRY-OVER

Contamination by carry-over of PCR product is a major problem in clinical laboratories dealing with a large number of samples. We have performed experiments to assess the use of an enzymatic method to degrade specifically PCR products from previous PCR amplifications. Our initial experiments have shown the Uracil N-glycosylase system is as good as the conventional PCR for the amplification of IS6110 sequences. It is expected that such methodology will reduce significantly false-positive reactions in clinical laboratories.

II. GENOTYPING CORE FOR CF MUTATIONS

The Core performed genotyping for 84 cystic fibrosis patients using a reversed dot-blot assay. The analysis included seven mutations of the CFTR gene. The Core has been funded by a grant from the Cystic Fibrosis Foundation. The funding ended 1 April 1993 due to the departure of Dr. Francis Collins from The University of Michigan. No further activities are planned for the Core.

Gabriel Nuñez, M.D.
Director
Clinical Molecular
Diagnostics

CLINICAL HEMATOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL REPORT 1 JULY 1992 - 30 JUNE 1993

LABORATORY ACTIVITIES:

- A. Implemented autoverification for CBC's and platelets (50% autoverifying on weekdays and 65% on weekends) thus decreasing turn-around time and decreasing number of incoming telephone calls for results.
- B. Reduced the number of F.T.E.'s by one in accordance with budget reduction program.
- C. 4% increase in billable tests while actual work performed did not increase but stayed stable.
- D. Hematology Laboratory is a beta site for testing of Coulter MAXM with autoloader.
- E. 9.5% decrease in the number of fluid and manual differential counts performed but an increase of 6% in the number of specimens reviewed by pathologist due to a revision of criteria emphasizing more review of abnormal peripheral blood smears. Also instituted pre-review of specimens by senior technologists to reduce number of specimens for pathologist review.
- F. 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.
- G. Daily signout of in-house and UM clients' cases of abnormal smears and body and joint fluids takes place 7 days per week.
- H. A quality assurance program has continued in the area of bone marrow cytochemical stains for leukemia and other labor intensive "specialty" tests within the laboratory. This program has led to a substantial decrease in the number of special tests and cytochemical stains performed, resulting in improved utilization of resources.
- I. Quality assurance indicators comparing positive fluids in Hematology with Cytology results and monitoring turn-around times for PHO patient results in the Taubman Lab.

TEACHING ACTIVITIES:

- A. Pathology House Officers, Hematopathology Fellows, Fellows from Pediatric and Adult Hematology/Oncology and visitors from other institutions participated in the following activities:
 - 1. Daily review of abnormal blood smears, body fluids, joint fluids for crystals, bone marrow aspirates and bone marrow biopsies.
 - 2. Daily review of in-house and transfer consultation cases in hematopathology (lymph node biopsies, bone marrow biopsies, aspirates, splenectomy specimens, etc.).
 - 3. Daily review of outside consultation cases of Drs. Schnitzer and Hanson.
 - 4. Correlation of morphology with special studies (cytochemistry, flow cytometry, immunoperoxidase and occasionally electron microscopy).
 - 5. Daily review of abnormal blood smears from M-Labs clients.
 - 6. A formal teaching conference for House Officers has been continued.

7. Review of SWOG cases.
 8. Weekly Interdepartmental Lymphoma Conference.
 9. Biweekly Interdepartmental Leukemia Conference.
 10. Pediatric 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 1993/1994 GOALS:

- A. Implementation of cost-containment programs.
- B. Review and development of laboratory utilization.
- C. Continue to 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. Transfer of hemoglobin electrophoresis from the Chemistry Laboratory to the Hematology Laboratory.

Bertram Schnitzer, M.D.

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

CLINICAL IMMUNOPATHOLOGY LABORATORY**DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1992 - 30 JUNE 1993****OVERVIEW:**

With the ongoing chemistry "mega-lab" consolidation and a hospital-administration imposed budget restructuring, fiscal year 1992-93 has been challenging. The immunopathology laboratory experienced a modest increase in test volume and several new assays/programs were instituted. John Lowe, M.D. has again provided an invaluable service commitment to the laboratory. Kent Johnson, M.D., and Kevin Cooper, M.D. (Dermatology) continue to signout tissue immunofluorescence studies under the auspices of Anatomical Pathology Division. Paul Killen, M.D., Ph.D., also under the auspices of Anatomical Pathology, joined the renal biopsy service. Dr. Killen provided invaluable technical oversight of tissue immunofluorescence studies.

CLINICAL SERVICES:

As the fiscal year approached its conclusion, the laboratory had experienced a modest increase in total volume (approximately 4%). Particularly gratifying has been the growth in several relatively new assays; these include the neutrophil cytoplasmic antibody (ANCA) test and immunoglobulin G subclass determinations. Neutrophil cytoplasmic antibody determinations have increased from approximately 50/month to more than 70/month and immunoglobulin G subclass determinations increased approximately 30%. We have recently evaluated and initiated a variety of utilization control measures in the laboratory. Most notable in this area is sendout assays of circulating immune complexes, as a cost of \$180/test. By instituting necessary approval by IP laboratory professional staff the number of these requests declined 5-fold resulting in a \$10,000 savings.

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 has been 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 a clinical study of atypical antinuclear antibodies in conjunction with Dr. Joseph McCune (Department of Medicine, University of Michigan). After conducting a method comparison study of IgG subclasses quantitated by microELISA versus radial immunodiffusion, we have recently switched to the later method. The RID method should prove to be more reliable and the laboratory should realize a significant annual cost savings. 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.

QUALITY ASSURANCE:

The laboratory completed two QA projects. These relate to proper specimen procurement for CSF oligoclonal bands and proper screening requests for Bence Jones proteins. Ongoing efforts have been directed towards analyzing 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. Two clinical pathology grand rounds were presented by Dr. Warren. Dr. John Carey (Henry Ford Hospital, Detroit) presented a CP grand rounds entitled "Organ-specific autoantibodies" and Paul Killen, M.D., Ph.D. presented "Renal immunopathology cases" as part of the immunopathology series. Other professional activities of faculty and staff in the laboratory are summarized under individual faculty reports.

Jeffrey S. Warren, M.D.
Director
Clinical Immunopathology Laboratory

DRUG ANALYSIS AND TOXICOLOGY LABORATORY**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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 major changes were implemented during the last year. First, performance of the therapeutic drugs digoxin, methotrexate, amikacin, gentamicin, tobramycin, and vancomycin was formally transferred into this laboratory. The implementation of these tests was a major step in the formal consolidation process of the Biochemistry Section.

Second, the laboratory modified its personnel and staffing structure to be able to expand to a 24 hour schedule. This expansion of hours should be very beneficial to both the patients at this medical center as well as those outside locations who send specimens to this institution.

The laboratory continues to be certified by the College of American Pathologists for the forensic drug testing program. The laboratory successfully passed the 1993 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 clinical laboratory inspection by the College of American Pathologists and performed very well during the accreditation review.

The laboratory has been involved in several ongoing quality assurance projects. These projects involve review of corrected reports, turn-around times, and accuracy of data entry. The laboratory is also involved 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 investigate the clinical applications of some novel chromatographic resins, and is also investigating approaches for monitoring testosterone and epitestosterone in urine. 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.

As is happening with many areas of health care, cost efficiency goals have continued to be a primary factor in the long term planning process for the laboratory. The

changes outlined above - expansion of service, consolidation of functions, and ability to obtain external funding - are positive ways in which the laboratory contributes to these goals.

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

HISTOCOMPATIBILITY AND IMMUNOGENETICS LABORATORY**DEPARTMENT OF PATHOLOGY****1 JULY 1991 - 30 JUNE 1992**

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. This resulted in increased revenues for the Department. In addition, two new staff members were incorporated in the laboratory that helped increase the quality of our service.

CLINICAL ACTIVITIES:

Clinical Activities in the Histocompatibility Laboratory showed a consistent increase from last year with approximately a 17% overall increase in the number of test performed and a 21% increase in overall revenue. This was despite a decrease of approximately 22% in consumable cost. A new laboratory test, the lymphocyte proliferation assay, was added and has progressively increased its activity to approximately 2 to 3 per week.

Two personnel were added to the laboratory this year. These two individuals Debra Marantis and Mary-Lee Sharp markedly improved the efficiency of the laboratory and helped in the cost savings.

Technical improvements in the laboratory included the full implementation of Class II HLA typing by magnetic beads, which as 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 Data Supervisor of the Laboratory in conjunction with Tomas 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 alternate for the University for its UNOS membership. 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 "Women 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

PATHOLOGY DATA SYSTEMS
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993

The activities of Pathology Data Systems for the past year can be divided into five separate categories: (1) instrument and foreign system interfaces; (2) PathNet/VMS enhancements and modifications; (3) joint projects with INS; (4) PC and Novel network projects; and (5) education and communication.

INSTRUMENT AND FOREIGN SYSTEM INTERFACES:

1. Implemented the Nova/Eagle interface to the Mott operating room. This interface was designed to allow the input of blood gas results performed by anesthesiology personnel in the Mott operating room into the PathNet database.
2. Implemented the Ligand/Eagle Statlia interface. This interface was part of the conversion of the Ligand Laboratory from the deinstalled PDP-1144 to Mac-based software to support the laboratory activities. The interface writes Ligand test results to the PathNet database.
3. Implemented the Foot Hospital/Eagle order entry interface. This was an M-LABS project which allows a client hospital, Foote Hospital, to order tests directly into PathNet.
4. Implemented the Flow Cytometry/Novell instrument interface using the Novel NFS (Network Filing System).
5. Installed multiple new instrument interfaces on PathNet (BactiAlert, Array 360, IL-BGE, and ACS 180)
6. Completed the installation of WPLink software on PCs for support of outside faculty consultation cases in surgical pathology.
6. Brought up an EDA/SQL interface which will ultimately allow data transfer between heterogeneous host computers in the hospital.
7. Continued to refine PDSRDB, a RDB-based relational database management server which is used to download laboratory information to hospital clients like the Organ Transplantation Information System (OTIS).

PATHNET/VMS/VAX ENHANCEMENT AND MODIFICATIONS:

1. Introduced numerous enhancements to POC, a result reporting program for PathNet which was developed in PDS, such as the option for physicians of accessing both Radiology and Nuclear Medicine reports. Also in the final stages of development is a program which logs the identity of PathNet users who access "protected" results such as those associated with HIV testing.
2. Upgraded gynecology Cytology software on PathNet for compliance with CLIA '88 standards.
3. Implemented the Patient Care Letter program in several clinics, including the OB/Gyn clinic and the Briarwood Medical Group. The software extracts cytology and cholesterol test results from the PathNet database and inserts them into a form letter which is then mailed to a patient.
4. Added several new DISCERN rules in various laboratories such as the one which automatically adds coded comments to Ligand test results.

5. Added a PathNet instrument interface which permits autoverification of batch-oriented tests in Hematology. Approximately 60% of tests passing through Hematology are now autoverified.
6. Installed the "container tracking" application on PathNet which allows tracking of specimens from the time they are drawn in a remote clinic, such as an M-Care Clinic, until the tests are performed and the results are uploaded to the database.
7. Installed numerous PathNet program fixes and enhancements.
8. Installed new VAX processor (4600) and new DSSI drives as well as an upgraded VMS operating system.
9. Installed PathNet 306 in a certification environment.
10. Advanced planning to automate autopsy reports using WPLink and PCs, with integration of the final reports into the PathNet database.
11. Began project in collaboration with the Admitting Department to print bar-coded information on patents' identification wrist bands.

JOINT PROJECTS WITH INS:

1. Installed a new communications protocol for enhancement of PDS/INS connectivity.
2. Installed a new ADT interface software to support the HealthQuest Patient Management and Financial software.
3. Reorganized PDS billing procedures to support the new HealthQuest financial package.
4. Assessed order communication software running on IBM mainframe computers to assist INS in the selection of such a system.

PC AND NOVELL NETWORK PROJECTS:

1. Implemented a new email system (P-Mail; Pegasus Mail) which allows departmental personnel to read their email from the All-in-1 system directly on their PCs.
2. Developed a strategic plan for ongoing management and upgrades of the Novell network.
3. Developed a plan to curtail use of unauthorized software on PCs and Macs in the department.

EDUCATION AND COMMUNICATION:

1. PDS sponsored the 11th annual laboratory information symposium held at the Towsley and Power Centers on 9-11 June 1993. This was the most successful symposium to date, attracting some 210 registrants and 36 vendors. The conference is considered to be the best of its kind in the country. Several interested vendors had to be turned away, so that a decision has been made to open up the Rehearsal Room at the Power Center for additional vendor displays. This will allow the symposium to accommodate 45 or more vendors in 1994.
2. Nine house officers rotated through PDS for a two-week rotation in pathology informatics.

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

PHLEBOTOMY SERVICES AND CENTRAL DISTRIBUTION**DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1992 - 30 JUNE 1993**

1. As part of the continuing cost efficiency (CEP) program, FTEs were reduced by 1.5 in Central Distribution and by 3.0 in Phlebotomy. These personnel reductions necessitated the closing of the first floor blood drawing station in the Taubman Health Center.
2. Strategic planning for a pilot program involving a new way to deliver phlebotomy services in the hospital was undertaken. Under this program, a unit phlebotomist will be assigned to high-volume patient care units (6 A, B, and C; Mott general care for the pilot). This phlebotomist will be permanently assigned to the unit during the day shift and will be dispatched to draw blood from patients in that unit on an as-needed basis. This individual will be assisted at times of peak demand for phlebotomy services by sweep team personnel.
3. Strategic planning was also undertaken with regard to the possibility of transferring FTEs and specimen transport responsibility from the Messenger Service to Phlebotomy. The feasibility of such a transfer is still under consideration.
4. As a joint project with Pathology Data Systems, Central Distribution personnel are now entering point-of-care test results generated by nursing personnel and recorded on manual log sheets into the PathNet database. As the result of this project, the hospital is now generating revenue from POC testing as well as enjoying the benefits of a more complete laboratory database.
5. At the suggestion of Phlebotomy personnel, the tourniquet used by Phlebotomy personnel was changed from a Penrose drain to a simple rubber tubing, saving the hospital approximately \$8200/year.
6. Pediatric indwelling catheter blood drawing services were expanded to evenings, Monday through Friday.
7. The problems associated with carpal tunnel/tendonitis, particularly in Central Distribution, were studied and a number of changes were introduced to help ameliorate the problem. These changes included the installation of ergonomic chairs, computer screens raised to eye level, redesign of centrifuge lid levers, myomassage for personnel, and production of a training video on how to draw blood samples most efficiently.
8. The operations of the Pneumatic Tube System continue to be analyzed by Central Distribution personnel in order to optimize the system.
9. Continuing emphasis is being placed on Total Quality Management in both Phlebotomy and Central Distribution. Six personnel participate in a total of eight QITs.

10. The handling of M-LABS specimens has been extensively studied, with redesign of the flow of specimens. A medical technologist is currently being hired to manage M-LABS specimens in Central Distribution.
11. Additional efforts have been undertaken to optimize data collection for sendout specimens in Central Distribution.
12. Personnel in Central Distribution and Phlebotomy have been nominated for more than twenty "Supergrams" by patients and other hospital personnel in recognition of their outstanding performance and particular attention to client relations.
13. The Phlebotomy Team has been very active in community outreach activities, including sponsorship of a phlebotomy training session for visiting nurses.

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

EDUCATIONAL ACTIVITIES
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993

The Department of Pathology continues to offer a number of diverse programs within the Medical School, Dental School, School of Public Health, College of Literature, Science and the Arts, and the Rackham School of Graduate Studies. These include: courses requiring formal lecture and laboratory exercises, senior medical and undergraduate student Pathology clerkships, and research training for undergraduate, graduate, and medical students, as well as postdoctoral fellows. Within the Medical Center, Departmental teaching activities extend not only to medical students, but also house officers and the staff of many clinical departments in the form of regularly scheduled clinical conferences. Departmental teaching also extends to practitioners in the region and nation through courses given through Continuing Medical Education Programs of The University of Michigan and the United States and Canada Association of Pathologists (USCAP).

MEDICAL AND DENTAL STUDENT PROGRAMS:

In the Fall of 1992, the Medical School initiated the first phase of a revised medical curriculum. Departmental faculty have played major leadership roles in both the development and implementation of this program. Drs. Joseph Fantone and Gerald Abrams serve as Directors of the first and second year curriculum and faculty within the Department have teaching responsibilities in; Molecular and Cell Biology, Histology, Host Defense and Introduction to Pathology sequences during the first year and in each of the organ system sequences in the second year. In addition, a new one month Laboratory Medicine clerkship was offered to 15 fourth year medical students. This rotation complements our current fourth year Pathology clerkship and medical student research rotations. Formal student evaluations noted it to be excellent. These new educational initiatives occurred in addition to the established educational responsibilities of Department faculty in the second year medical student Pathology 600, Neural and Behavioral Sciences, and ICS 600 and 601 Courses

This was the third year the Department of Pathology offered a summer clinical program for underrepresented minority medical students. The goal of this program is to provide medical students, who have completed their first year, the opportunity to participate in Departmental clinical activities and promote the integration of Basic Science studies with patient-oriented clinical problems. In addition, it is hoped that the early exposure to the multiple opportunities available in Pathology will encourage students to consider careers in the specialty. Thirteen students participated in the program and formal evaluations indicate that the program is viewed very positively by the students.

The Department of Pathology continues to have primary responsibilities for the teaching of general and systemic pathology to dental students. This includes the presentation of formal lectures (Pathology 630) and preceptors of laboratory sessions (Pathology 631). Formal student evaluation indicates that the course functions smoothly and is well received by the students.

DOCTORAL PROGRAM:

The graduate program in Pathology, which was initiated four years ago currently has seven students enrolled. The primary goal of the Doctoral in Pathology Program is to train individuals for careers as independent scientific investigators with a focus on the study of the cellular and molecular basis of disease processes. Five graduate level courses are offered by the Department. Three students are enrolled in combined M.D./Ph.D. programs and three students have achieved candidacy status. Susan Moore, Ph.D. graduated from the program during the past year and is currently completing a postdoctoral fellowship at University of Texas, San Antonio. An Immunopathology Training grant (Dr. R. Miller, P.I.) was recently awarded that supports both graduate student and postdoctoral fellow training.

Graduate Medical Education:

The Department of Pathology provides formal advanced training to M.D.'s and Ph.D.'s through the Residency Training Program, clinical fellowships and postdoctoral research fellowships. These programs are integrated to provide trainees the greatest opportunity for clinical and research training in their chosen discipline and to foster academic excellence.

Clinical Fellowships:

The Department provides advanced training in surgical pathology, cytopathology, hematology, and transfusion medicine through formal fellowship programs. Six positions are currently supported with the clinical fellowships closely integrated with the Residency Training Programs (see Anatomic and Clinical Pathology Sections).

Postdoctoral Research Training:

The Department of Pathology provides advanced research training for approximately 40 postdoctoral fellows which includes Pathology residents seeking training in experimental pathology. Fellows are located within the faculty research laboratories of the Department. Support is provided by an NIH-funded Lung Immunopathology Training grant (HL-07517, P.A. Ward, Principal Investigator), an Immunopathology Training grant (NIH AI-07413, R. Miller, Principal Investigator), and externally-funded faculty research grants. This past year six fellows completed their training and have assumed the positions at the following institutes:

- 1.) Marco Frincher, employment information not available at this time.
- 2.) Carol Laherty, Fred Hutchinson Cancer Research Center, Washington.
- 3.) Serhan Alkan, Lee Mofit Cancer Center, Florida.
- 4.) Ara Vaporciyan, University of Houston, Texas.
- 5.) Craig Flory, Parke Davis Pharmaceutical Research, Michigan.
- 6.) Soverin Karmiol, Research and Development Clonetics Co., California.

RESIDENCY TRAINING:

The Department of Pathology offers resident training in both anatomic and clinical pathology with opportunities to pursue basic research training in experimental pathology. The program continues to be exceedingly competitive with over 110 completed applications received, and 32 candidates invited to interview in the Department this past year. Five outstanding residents were recruited to the Department:

Jill A. Cohen, M.D., Jonathan W. Homeister, M.D., Ph.D., Caroline Henderson, M.D., Carol D. Poston, M.D., and Caroline R. Reilly, M.D.

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. Seven residents graduated from the program this past year. Two assumed positions as staff pathologists at The Cleveland Clinic and Botsford Hospital, Michigan. Five residents are continuing training, one in a Hematopathology Fellowship at the National Institutes of Health, two in Anatomic Pathology (University of Virginia and Washington University), one in a Surgical Pathology Fellowship at the University of Michigan, and one in a Hematopathology Fellowship at the University of Michigan.

A significant number of residents continue to be involved in both clinical and experimental research projects which have resulted in the presentation of their work at national meetings, as well as publications in peer-reviewed journals. Two residents were recipients of Stowell Orbison Awards at the 1993 USCAP Meeting (Dr. Eric Hsi, Winner, Dr. Suzanne Cook, Honorable Mention). The residents again completed the American Society of Clinical Pathologists' in-service examination and performed well above the national average.

Publications/Presentations:

- 1.) JR Goldblum, T Beals, SW Weiss: Elastofibromatous Change of the Rectum: A Lesion Mimicking Amyloidosis. *Am J Surg Pathol* 16:793-795, 1992.
- 2.) PM Perosio, SW Weiss: Ischemic Fasciitis: A Juxta-skeletal Fibroblastic Proliferation with a Predilection for Elderly Patients. *Mod Pathol* 6:69-72, 1993.
- 3.) LR Zukerberg, BJ Nickoloff, SW Weiss: Kaposiform Hemangioendothelioma of Infancy and Childhood: An Aggressive Neoplasm Associated with Kasabach-Merritt Syndrome and Lymphangiomatosis. *Am J Surg Pathol* 17:321-328, 1993.
- 4.) J Willis, J Jansen, JR Goldblum, SW Weiss: Frozen Section Consultation: A Correlation Between Utilization Patterns and Knowledge Base of Surgical Faculty. (Abstract) *Mod Pathol* 88:141A, 1993.
- 5.) JR Goldblum, TF Beals, SW Weiss: Neuroblastoma-Like Neurilemoma. Submitted, May 1993.
- 6.) S.M. Cook and T.S. Frank, Detection and Characterization of Atypical Mycobacteria by the Polymerase Chain Reaction. Abstract presented US and Canadian Academy of Pathology Annual Meeting, March, 1993, New Orleans, LA.
- 7.) J.R. Goldblum, K.A. Carr, and T.S. Frank, Overexpression and Loss of Heterozygosity of p53 Tumor Suppressor Gene in Hepatocellular Carcinoma. Abstract presented US and Canadian Academy of Pathology Annual Meeting, March, 1993, New Orleans, LA.
- 8.) B.A. Markey, J.T. Headington, Hypertrophic Dermal Dendrocytes Phagocytose Neutrophils in Sweet's Syndrome, Abstract presented US and Canadian Academy of Pathology Annual Meeting, March, 1993, New Orleans, LA.
- 9.) J.P. Pearson and J.S. Warren, Antineutrophil Cytoplasmic Antibody-Stimulated Neutrophils and Monocytes Exhibit Disparate Endothelial Cell Killing Capacities Abstract presented U.S. and Canadian Academy of Pathology, March, 1993, New Orleans, LA.
- 10.) E.D. Hsi, L.R. Zukerberg, B. Schnitzer, N.L Harris, Development of Extrasalivary Lymphoma in Myoepithelial Sialadenitis (Benign Lymphoepithelial Lesion. Abstract presented U.S. Canadian Academy of Pathology, March, 1993, New Orleans, LA.

- 11.) E.D. Hsi, D.G. Remick, Monocytes are the Major Producers of Interleukin-1 Beta in an Ex-vivo Model of Local Cytokine Production. Abstract presented U.S. and Canadian Academy of Pathology, March, 1993, New Orleans, LA.
- 12.) P.J. Boyer, L. Rutkowski, G. Tuite, R. Dauser, K Muraszko and G.O Tennekoon, Isolation of Human Schwann Cells from Pediatric Dorsal Nerve Roots From Dorsal Rhizotomy and Adult Sciatic Nerve From Autopsy. Abstract Presented Society for Neuroscience Annual Meeting, October 25-30, 1992, Anaheim CA.

Formal courses in which the Department of Pathology faculty have a major role:

I. COURSES IN THE MEDICAL CURRICULUM:

- A. First year Medical Curriculum:
 1. Molecular and Cellular Biology:
 2. Introduction to Histology/Histopathology Pathology:
 3. Host Defense
4. Multidisciplinary Conferences
- B. Second Year Medical Curriculum
 1. ICS 600
 2. ICS 601
 3. NBS 600
 4. Pathology 600
- C. Clinical Clerkships
 1. Pathology
 2. Laboratory Medicine
- D. Summer Clinical Program in Pathology for Underrepresented Minority Students

II. COURSES IN THE DENTAL CURRICULUM:

- A. Pathology 630: General Pathology Lectures (45 contact hours).
- B. Pathology 631: Pathology Laboratory

III. GRADUATE COURSES IN PATHOLOGy:

- A. Pathology 580: General Pathology for Biologic Scientists
- B. Pathology 581: Cellular and Molecular Basis of Disease
- C. Pathology 620: Genetics and Cell Biology of Aging
- D. Pathology 850: Research Colloquium
- E. Pathology 599: Non-Dissertation Research
- F. Pathology 990: Pre-Candidate Dissertation Research
- G. Pathology 995: Candidate Dissertation Research

IV. POSTGRADUATE MEDICINE/CONTINUING MEDICAL EDUCATION:

- A. Current Topics in Blood Banking Symposium, June 2 - June 4, 1993.
- B. Clinical Laboratory Computers Symposium, June 9 - June 11, 1993.
- C. Pathology 858: Neuropathology (18 contact hours).

V. CLINICAL CONFERENCES:

The Department of Pathology provides an important educational service to many other clinical departments through regular participation in interdepartmental working/teaching conference. The Department is involved in many such conferences on a weekly, bi-weekly, and monthly basis. The units served include:

Internal Medicine

- Gastroenterology
- Nephrology
- Hematology/Oncology
- Nuclear Medicine
- Pulmonary Medicine
- Arthritis
- Cardiology
- General (Necropsy Review, CPC)

DermatologyThoracic SurgeryUrologyPediatrics

- Cardiology
- Oncology
- Gastroenterology
- General (Death Conference, CPC)

Obstetrics and Gynecology

- Oncology

Oral SurgeryGeneral Surgery (Breast, GI)Otorhinolaryngology

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

UM Department of Pathology House Officers and Fellows 1993-1994



Philip L. Perkins, M.D.
Cytopathology Fellow



Cheryl A. Utiger, M.D.
Hematology Fellow



Patricia M. Perosio, M.D.
Cytopathology Fellow



Suzanne M. Cook, M.D.
Surgical Pathology Fellow



Kenneth R. Lidonnici, M.D.
Surgical Pathology Fellow



Kyle A. Carr, M.D.
Surgical Pathology Fellow



Priscilla R. Lindley, M.D.
Chief Resident
Cytopathology Fellow



Eric P. Kaldjian, M.D.
House Officer V
(5th Year)



David A. Start, M.D.
Assistant Chief Resident
House Officer IV
(4th Year)



Hedwig S. Murphy, Ph.D., M.D.
House Officer IV
(4th Year)



Sonya K. Brown, M.D.
House Officer IV
(4th Year)



Jeffrey P. Pearson, M.D.
House Officer IV
(4th Year)



Eric D. Hsi, M.D.
House Officer IV
(4th Year)



Philip J. Boyer, Ph.D., M.D.
House Officer III
(3rd Year)



Robert A. Stern, M.D.
House Officer III
(3rd Year)



Walter H. Henricks, M.D.
House Officer III
(3rd Year)



Margaret M. Moll, M.D.
House Officer V
(3rd Year)



Scott C. Silveira, M.D.
House Officer III
(3rd Year)



Lyndon D. Su, M.D.
House Officer II
(2nd Year)



Joseph A. Tworek, M.D.
House Officer II
(2nd Year)



Vonda K. Douglas, M.D.
House Officer II
(2nd Year)



Lois J. Arend, Ph.D., M.D.
House Officer II
(2nd Year)



Jill A. Cohen, M.D.
House Officer II
(1st Year)



Jonathan W. Homesteier, Ph.D., M.D.
House Officer I
(1st Year)



Carol D. Poston, M.D.
House Officer II
(1st Year)



M. Caroline Henderson, M.D.
House Officer I
(1st Year)



Caroline R. Reilly, M.D.
House Officer I
(1st Year)

M-LABS**DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1992 - 30 JUNE 1993**

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
LABORATORY SERVICE**

**DEPARTMENT OF PATHOLOGY - UNIVERSITY OF MICHIGAN
ANNUAL DEPARTMENTAL REPORT
1 JULY 1992 - 30 JUNE 1993**

INTRODUCTION:

The Department of Veterans Affairs Medical Center (VAMC) is a Dean's Committee institution affiliated with the University of Michigan. The VAMC Pathology and Laboratory Medicine Service maintains a close relationship with the University Department of Pathology at every level. The pathologists in the Laboratory Service have academic appointments and participate in University departmental activities in a manner similar to other sections. Recruitment efforts for pathologists are combined and candidates are selected on the basis of academic performance and potential as well as professional competence similar to any departmental candidate. There are four full-time pathology staff positions and although one vacancy existed for some time a candidate for the position, Dr. Peter Brawn, was identified and has been on the staff since October 1992. Three resident training positions have been maintained at the VAMC for university pathology residents who serve monthly rotations in Surgical Pathology, Autopsy Pathology, and a number of arranged electives including Electron Microscopy and special study programs in Surgical Pathology. The Chief, Pathology and Laboratory Medicine Service is a voting Member of the Dean's Committee.

ANATOMIC PATHOLOGY:

- A. Surgical Pathology: 5,201 surgical cases have been accessioned and reported during this period of time. This is an increase of approximately 200 cases over the past year. The resident assigned to surgical pathology, usually a first year resident, acts as coordinator of the section and in that capacity has the opportunity to examine all of the specimens grossly and microscopically under close one-to-one supervision by the staff pathologist. The resident interacts with the clinical staff, the medical students and the other laboratory sections appropriate to obtain a broad educational experience and to aid in providing high quality medical care. There is an extensive quality improvement program within Surgical Pathology including regular consultations with the Armed Forces Institute of Pathology, University of Michigan, and other outside consultants. There is extensive review and analysis of frozen sections, amended diagnoses and surgical appropriateness within the medical center.
- B. Autopsy Pathology: 63 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 or 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.

- C. Cytology: 2,498 cases were examined and diagnosed during this period. Although there is not a mandated rotation in cytology within the VAMC the cytologic material is readily available and is used as correlative information for surgical and autopsy pathology.
- D. Electron Microscopy: 377 electron microscopy cases were reported. An elective rotation is available for pathology residents in electron microscopy. In other rotations the electron microscope findings are used to complement surgical or cytopathology diagnoses. During the academic year Dr. Beals presents biweekly electron microscopy seminars at the University of Michigan. This VAMC is a "Center of Excellence" in electron microscopy and serves as consultant to other VA Medical Centers, to the University of Michigan Hospital, and to other hospitals by contract.

CLINICAL PATHOLOGY:

During the last fiscal year (Fiscal Year 1992) 1,489,712 clinical pathology procedures were done in the laboratory. In chemistry there were 823,688; in hematology 143,473; in microbiology 208,299; and in blood bank 135,107 tests were done. This represents raw data rather than weighted test numbers. There is not a formal clinical pathology rotation available for pathology residents at this time although the residents may participate or observe clinical pathology procedures when this activity is appropriate in relation to their other rotations. Dr. Chensue is director of clinical pathology and makes available interesting and pertinent clinical laboratory information to the residents as desired. Clinical Pathology data is available to residents via computer for their information in surgical pathology, autopsy pathology and elective rotations.

EDUCATION AND TEACHING:

In surgical pathology the staff pathologists provide one-to-one teaching during the surgical sign out time. In addition, there is a surgical pathology conference approximately every other week and an autopsy conference with the entire staff following each autopsy. Because of the closeness of various sections of the laboratory there is frequent consultation among the pathologists and the residents are involved throughout. Since the VAMC is relatively close to the University the residents are permitted and expected to attend the appropriate teaching conferences at the university as well. The entire staff participates in the laboratory and lecture portions of the second year medical students at the University of Michigan. Lectures in bone pathology are also given to the dental students. The VA staff also participate in other ad hoc lectures and in a moderate number of seminars for the resident staff, most often given at the University of Michigan.

RESEARCH:

The specific efforts of the pathology staff are included on individual reports. Dr. 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 serve 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 VA Medical Center the pathology staff members serve on all major committees involved with institutional policies and procedures. Dr. Beals has been designated as the National Veterans Administration Office Representative to oversee anatomic pathology within Veterans Medical Centers. He 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 an 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. During the time covered by this report, renovation has been completed of the autopsy suite and an expansion of laboratory administrative space including three additional offices, a conference room and enlargement of the residents' room.

Lee Weatherbee, M.D.
Chief, Laboratory Service
Ann Arbor VA Medical Center

